Clinical Practice Guideline on the Comprehensive Care of People with Alzheimer's Disease and other Dementias

NOTE:

More than 5 years have passed since the publication of this Clinical Practice Guideline, and **its validity has not been reviewed**.

Therefore, **it is unclear whether its recommendations remain valid**; they should therefore be treated with caution and applied in accordance with **clinical judgement and the individual circumstances of each patient**.

CLINICAL PRACTICE GUIDELINTES IN THE NHS
MINISTRY OF HEALTH, SOCIAL SERVICES AND EQUALITY

MINISTERIO DE CIENCIA E INNOVACIÓN
MINISTERIO DE SANIDAD, POLÍTICA SOCIAL E IGUALDAD
Plan de Calidad para el Sistema Nacional de Salud
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This CPG is a healthcare decision aid. It is not mandatory and it is not a substitute for the clinical judgement of healthcare personnel.

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Presentation

Scientific information is more accessible than ever today, but however, the enormous volume of information requires the use of tools aimed at helping to take the correct, effective and safe clinical decisions, as well as practitioners with updated skills and knowledge. Clinical Practice Guidelines (CPG) provide answers to the most relevant questions that may be asked about patients with a specific pathology, and they present scientific evidence in the form of graded recommendations according to the quality of the studies that support them.

The Quality Agency supports the drawing-up, dissemination and use of CPGs as it is aware that they provide daily support to clinical decision-making and that they are also a tool to improve health outcome. It also ensures that the CPGs drawn up in Spain reach a certain quality level.

In 2003, the Spanish National Health Service (SNS) International Council created the GuiaSalud Project whose ultimate aim is to improve clinical decision-making based on scientific evidence, through training activities and the configuration of a library of CPGs in the SNS. Since then, the GuiaSalud project has assessed dozens of CPGs in agreement with explicit criteria generated by its scientific committee, and it has registered them and disseminated them online.

At the beginning of 2006, the Directorate General of the Quality Agency of the Spanish National Health Service (SNS) drew up the Quality Plan for the SNS, which was divided into 12 strategies. The purpose of this plan is to increase the cohesion of the SNS and help guarantee maximum quality healthcare for all citizens regardless of their place of residence.

The purpose of the tenth strategy of the plan is the improvement of Clinical Practice and one of its objectives is to reduce the variability of clinical practice and foster the drawing up and use of CPGs. With the creation of a library, training and advice, the CPG development programme and the creation of new guidelines, GuiaSalud is providing an answer to the objectives set out in the Quality Plan.

Since 2006, with the participation of the scientific associations involved, CPGs, such as this one have addressed the comprehensive care of people with Alzheimer's disease and other dementias, which is presented today.

Dementia as a clinical syndrome is characterised by an acquired impairment affecting more than one cognitive domain, which represents a decline from a previous level that is serious enough so as to affect personal and social functioning.

Given the increase in life expectancy and progressive population ageing in western countries, dementia represents an enormous challenge for the public health systems of those societies.

The impact of dementia is felt directly by the patient, but it also has a considerable impact on relevant aspects of the social environment, such as affection, emotion, organisation, role change, as well as on economic aspects. In this sense, dementia is a problem that affects everyone and that must be addressed as a real family disease, and in short, as a disease of society.

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Care of people with dementia and of their relatives requires a multidisciplinary approach, and each professional must purport the specific aspects, typical of their disciplines.

Recommendations are given in this guideline on the care of patients with Alzheimer's disease and other dementias, such as, for example, vascular dementia, Parkinson's disease dementia, dementia with Lewy bodies and frontotemporal lobar degeneration.

Important research studies are being carried out all over the world to study the different aspects that make up the clinical syndrome of dementia, as well as its multiple affectations and effects, so we must be attentive to potential advances in clinical care, genetics, diagnosis techniques, as well as new drugs or other non-pharmacological interventions.

This CPG has been reviewed by Spanish experts in the care of patients with Alzheimer's disease and other dementias, by association of patients and relatives, scientific societies and other entities involved in the care of these people.

CARMEN MOYA GARCÍA
General Director of the Quality Agency of the SNS

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Questions to be answered

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DEFINITIONS AND CLASSIFICATION OF DEMENTIAS

1. What is dementia?
2. What is the incidence and prevalence of dementia?
3. How is dementia classified?
4. What are the clinical manifestations of dementia?
5. How does the natural course of dementia evolve?
6. What is understood by degenerative dementia?
7. What is Alzheimer's disease?
8. What is dementia with Lewy bodies?
9. What is Parkinson's disease dementia?
10. What is frontotemporal lobar degeneration?
11. What other neurodegenerative diseases are accompanied by dementia?
12. What are vascular dementias?
13. What is and how is secondary dementia classified?
14. What is understood by mild cognitive impairment (MCI)?
15. What types of MCI exist?
16. What is the incidence and prevalence of MCI?
17. What are the risk markers for conversion from MCI to dementia?
18. Is there any treatment that modifies the progression of MCI?

PATHOPHYSIOLOGY AND RISKS FACTORS OF DEMENTIAS

19. What are the pathophysiological mechanisms of degenerative dementia?
20. What are the pathophysiological mechanisms of vascular dementia?
21. What are the risk factors of dementias?

TREATMENT

22. Is primary prevention of dementia possible?

GENETIC STUDY OF DEMENTIAS

23. When are genetic analyses indicated to identify pathogenic mutations in patients with dementia?
24. When is a predictive genetic analysis indicated in asymptomatic individuals?

DEMENTIA DIAGNOSIS

25. How is dementia diagnosed?
26. What is the differential diagnosis of dementia?
27. What are the advantages of neuropsychological testing assessment in cognitive impairment and dementia?
28. What neuropsychological tests, questionnaires or functional evaluation scales must be performed on patients with dementia?
29. Which laboratory tests are essential in diagnosing dementia?
30. Must the determination of apolipoprotein E (apoE) be requested?

31. What are the advantages of analysing cerebrospinal fluid (CSF) in the diagnosis of dementia?
32. Which is the structural neuroimaging technique of choice in the diagnostic process of dementia and its different types?
33. Which is the functional neuroimaging technique of choice in the diagnostic process of dementia and its different types?
34. What are the advantages of EEG/mapping in the diagnosis of dementia?
35. What are the indications for performing a cerebral biopsy in the etiologic diagnosis of dementia?

DIFFERENT CARE LEVEL ACTIONS

36. What are the care levels and how are they classified?
37. What role does primary care play in the all-round care of dementia? Must dementia screening be carried out in the general population? What are the criteria for referring to Specialist Dementia Care Team (SDCT)? What monitoring must be carried out by primary care on patients with dementia?
38. Which specialised care teams are required to address dementia (SDCT) and what role do they play?
39. What role does the social-health network play in a comprehensive approach to dementia?
40. What role do the mental health services play in the care of dementia?
41. Which social services are involved and what role do they play in the care of people with dementia?
42. How must the care continuity between the different dementia healthcare levels be coordinated and guaranteed?

TREATMENT OF DEMENTIA

General measures:

43. When and how must patients and their families be informed of the dementia diagnosis?
44. What basic content must the information given to patients and family have?

Specific pharmacological treatment of dementia:

45. Is there a specific pharmacological treatment for dementia?
46. Is the specific pharmacological treatment equally effective in all people?

Alzheimer's Disease

47. Which pharmacological treatment is effective in the treatment of mild, moderate and severe Alzheimer's disease?
48. Which specific pharmacological treatment is effective in cognitive, behavioural, functional manifestations and/or quality of life in Alzheimer's disease?
49. What adverse effects and contraindications exist for the specific pharmacological treatment in Alzheimer's disease?
50. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe Alzheimer's disease?
51. When must specific treatment in Alzheimer's disease end?

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Parkinson's Disease Dementia

52. Which specific pharmacological treatment is effective in Parkinson's disease dementia?
53. What adverse effects and contraindications exist in the pharmacological treatment of Parkinson's disease dementia?
54. How effective and safe is the combination of two or more specific drugs in Parkinson's disease dementia?

Dementia with Lewy Bodies

55. Which specific pharmacological treatment is effective in dementia with Lewy bodies?
56. What adverse effects and contraindications exist in the specific pharmacological treatment of dementia with Lewy bodies?
57. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe dementia with Lewy bodies?
58. How useful are drugs with dopaminergic action in dementia with Lewy bodies?

Frontotemporal lobar degeneration

59. Which pharmacological treatment is effective in cognitive and behavioural manifestations of frontotemporal lobar degeneration?

Vascular Dementia

60. Which pharmacological treatment is effective in mild, moderate and severe vascular dementia?
61. What influence does pharmacological treatment have on vascular dementia with respect to cognitive, behavioural, functional manifestations and/or quality of life?
62. What adverse effects and contraindications exist in the specific pharmacological treatment of vascular dementia?

Other pharmacological treatments

63. Are any other types of drugs effective in cognitive and functional manifestations in people affected by any type of dementia?

Non-pharmacological treatment of dementias:
Cognitive intervention or stimulation

64. What is cognitive intervention or stimulation?
65. What types of cognitive intervention exist?
66. Are cognitive intervention programmes effective in dementia?
67. Are computer-based cognitive intervention programmes effective in patients with Alzheimer's disease?
68. Are cognitive intervention programmes indicated in illiterate individuals or in patients with severe sensory limitations?
69. Are individual cognitive interventions recommendable?

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Intervention programmes on activities of daily living

70. What do intervention programmes on activities of daily living consist of in patients with dementia?
71. Do intervention programmes on activities of daily living improve the functionality of people with dementia?

Physical activity programmes

72. Are physical activity programmes effective in improving or stabilising the functional capacity and cognitive functions of patients affected by dementia?

Other non-pharmacological treatments

73. Are there any other non-pharmacological treatments that are effective in cognitive, functional, motor and/or quality of life manifestations in dementias?

Safety of non-pharmacological treatments:

74. Could non-pharmacological treatments used in dementia have harmful effects?

Treatment of behavioural and psychological symptoms of dementia

75. What do we understand by behavioural and psychological symptoms of dementia (BPSD)?
76. Why are behavioural and psychological symptoms of dementia important?
77. How can the intensity and frequency of behavioural and psychological symptoms of dementia be quantified?
78. At what moment in time do BPSD appear in the evolution of dementia?
79. Are there some BPSD that are characteristic of some types of dementia?
80. Which non-pharmacological measures are indicated in each behavioural and psychological symptom in dementia?
81. What are the general recommendations for the pharmacological treatment of BPSD?
82. Which is the optimal pharmacological treatment for each behavioural and psychological symptom in dementia?
83. What adverse effects and contraindications do drugs used to control BPSD have?
84. How effective is it to combine pharmacological and non-pharmacological treatment to treat behavioural and psychological symptoms in mild, moderate and severe dementia?
85. Which are the most effective recommendations to avoid BPSD in patients with dementia?
86. How must BPSD, which are difficult to monitor in outpatients, be treated?
87. What attitudes must the caregiver satisfy to deal with patients with behavioural and psychological symptoms?

Alternative treatments of dementias

88. Are there any plant-based medications or food supplements that have proved to be useful in the treatment of dementia?

Assessment of the treatment of dementias

89. How must the response to the treatment of dementia be assessed in clinical practice?

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CAREGIVERS OF PATIENTS WITH DEMENTIA

90. What is understood by primary caregiver of a patient with dementia?
91. Are the characteristics of caregivers the same for people with different types of dementia?
92. What repercussions does caring for a person with dementia have on the caregiver?
93. What scales are useful to assess caregiver burden?
94. Are there effective interventions to prevent caregiver burden?
95. Are there effective interventions to deal with caregiver burden?
96. What are mutual aid groups (MAG)?
97. What benefits are obtained from participating in MAG?
98. In what cases is psychological treatment of the caregiver necessary?
99. What are associations of families of people affected by dementia and what role do they play in a comprehensive approach to dementia?
100. What must the relationship between the associations and the public social and health network be like?

EARLY ONSET OR PRE-SENILE DEMENTIA

101. What is understood by early onset or pre-senile dementia?
102. What are the most frequent causes of early onset or pre-senile dementia?
103. Do patients with early onset dementia have different clinical manifestations to patients with later onset?
104. Must the diagnostic process in people with early onset dementia be different to the process of a patient who is more than 65 years old when the disease starts?
105. Is the pharmacological treatment of a person with early onset dementia different to that of a person with late onset dementia?
106. Is the non-pharmacological treatment prescribed to a person with early onset dementia different to that of a person with late onset dementia?
107. Are there differences in impact and psychological, social, family, occupational and economic repercussion between a group of people diagnosed with early onset dementia and a group of people with late onset dementia?
108. What health and social-health resources do people with early onset dementia require?

ETHICS AND LEGAL ASPECTS OF DEMENTIAS

Abuse of people with dementia

109. What is understood by abuse of people with dementia?
110. How frequent is abuse in dementia and what are the risk factors?
111. What intervention strategies exist to detect a case of abuse?
112. What must professionals do when a case of abuse is detected?
113. What social resources exist to address abuse?

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Advance directives

114. When must the possibility of drafting advance directive documents, living wills and/or granting powers of attorney be suggested to people with dementia?

Evaluation of competences

115. Are there instruments that have been strictly designed to assess the competence of patients with dementia?
116. How are the specific competences assessed: driving licence, firearms licence and participation in clinical trials?
117. Which are the indications to start the legal incapacitation process of a patient with dementia?

Aspects relating to the patient's legal protection

118. What does legal incapacitation consist of?
119. What type of legal protection exists for a patient with dementia?
120. What is guardianship?

Restraint of the patient

121. What are the indications for pharmacological and/or psychological restraint of a patient with dementia?
122. What are the indications for physical restraint of a patient with dementia?
123. What are the ethical and legal aspects of restraint?
124. What are the indications for involuntary admission and what process must be followed?

CARE OF PEOPLE WITH ADVANCED DEMENTIA AND AT END-OF-LIFE STAGE

125. Which criteria define an advanced and terminal situation with prognosis of limited life in patients with dementia?
126. Is it possible to determine, in people with advanced dementia at end-of-life stage, if their survival is going to be less than 6 months?
127. When must palliative care be started on people with dementia?
128. Which are the most suitable health resources to care for people with dementia at end-of-life stage?
129. How are the clinical manifestations and the needs of people with dementia and their caregivers identified and managed in the advanced and terminal phase of the disease?
130. How can worsening due to the natural evolution of the illness be differentiated from worsening caused by a potentially reversible concomitant process?
131. What are the objectives of caring for people with dementia in terminal phase?
132. What extraordinary or greater measures should be questioned in the care of people with advanced dementia?
133. What therapeutic intermediate measures should be questioned in the care of people with advanced dementia?

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134. What information and aid must be provided to the families of people with terminal dementia?
135. What legal regulations and ethical principles exist relating to communication with people with advanced dementia or with their families at the end-of-life stage?
136. In what cases is a post-mortem pathoneurological study recommended?

DIFFUSION, TRAINING AND RESEARCH INTO CARE OF PEOPLE WITH DEMENTIA

Diffusion

137. How must the topic of dementias be dealt with in the media in order to suitably inform the public, and which are the most appropriate media?

Training

138. What undergraduate dementia training must be given to health sciences and social services professionals?
139. What dementia training must be given in health branches of vocational training?
140. What post-graduate dementia training must health professionals in general receive?
141. What post-graduate dementia training must health professionals engaged in the specific care of people with dementia receive?

Research

142. How important is research in the field of dementia?
143. What role must the different healthcare levels play in research on dementia?

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SIGN levels of evidence and grades of recommendation

Level of evidence	
1++	High quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with a very low risk of bias.
1+	Well-conducted meta-analyses, systematic reviews of clinical trials or well-conducted clinical trials with a very low risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with a high risk of bias.
2++	High-quality systematic reviews of case control or cohort of studies. Well-conducted studies of case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.
3	Non-analytic studies, such as case reports and case series.
4	Expert opinion.
Grades of recommendation	
A	At least one meta-analysis, systematic review or clinical trial rated as 1++ and directly applicable to the target population of the guidelines; or a body of scientific evidence consisting principally of studies rated as 1+ and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population of the guideline and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable to the target population of the guideline and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2 ++
D	Evidence level of 3 or 4; or extrapolated evidence from studies rated as 2+.

The studies rated as 1 and 2 must not be used in the recommendations preparation process due to their high possibility of bias.

Good clinical practice

√[1]	Recommended practice based on the clinical experience and the guideline development group.

[1] At times, the development group realised that there were some important practical aspects that they wished to stress but for which there was probably no scientific evidence to support them. In general these cases have to do with some aspects of the treatment considered as good clinical practice and that nobody would normally question. These aspects are evaluated as good practice points. These messages are not an alternative to the scientific evidence-based recommendations, but rather, they must only be considered when there is no other way to highlight this aspect.

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Recommendations of the CPG

Grade of recommendation: A, B, C or D, depending on whether the quality of the evidence is very good, good, moderate or low.

√ Good clinical practice: Recommendation by consensus of the development group.

DEFINITIONS AND CLASSIFICATION OF DEMENTIAS	
Mild cognitive impairment (MCI) and conversion to dementia	
C	Different biological and neuroimaging markers can be used to help predict the progression of MCI to dementia in a research context, but they cannot be recommended for use yet in normal clinical practice.
A	The use of ACE inhibitors to avoid or delay the progression of MCI to dementia is not currently recommended.
A	The use of NSAID, replacement therapy with oestrogens, ginkgo biloba or vitamin E to avoid or delay the progression of MCI to dementia is not currently recommended.
C	There is not enough evidence to recommend cognitive stimulation or physical exercise to avoid or delay the progression of MCI to dementia.
PREVENTION OF DEMENTIAS	
C	The control of vascular risk factors (HBP, DM, hypercholesterolemia) and healthy lifestyle habits (consumption of omega-3 fatty acids, physical and mental exercise) is recommended due to the clear evidence that exists about their benefit on other aspects of health, although their possible benefit on the reduction of the risk of dementia is not supported by appropriately designed studies.
C	Although moderate alcohol consumption or chronic consumption of NSAIDs has been associated with a lower risk of AD, it also has other risks for health and there is not enough evidence to recommend it in the prevention of dementia.
C	Neither the intake of vitamin C nor vitamin E nor hormonal replacement therapy is recommended to prevent dementia.
GENETIC STUDY OF DEMENTIAS	
D	Patients with a likelihood of suffering dementia due to genetic causes should be referred to specialist genetic counselling units.
C	Performing genetic analyses to detect causal mutations is indicated in patients with AD and an autosomal, dominant family history of pre-senile onset.

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C	In patients with FTLD, genetic analyses would be indicated in cases with a family history of a similar disease.
B	In patients with prion diseases, genetic studies would be indicated in all cases, regardless of family history or age.
B	Genetic studies are recommended if Huntington's disease is suspected, to confirm the diagnosis.
According to applicable legislation	The execution of genetic analyses in clinical practice must be authorised in writing by the actual individual or his/her legal representative after receiving genetic counselling.
C	Predictive genetic studies can be performed on people of legal age who are at risk of being carriers of a pathogenic mutation known to cause dementia and who wish to have them conducted, following informed written consent and multidisciplinary genetic counselling prior to the genetic analysis and subsequent monitoring.
D	The study of genetic risk factors of dementia, such as the APOE genotype, is not indicated for genetic counselling purposes in asymptomatic individuals.
DEMENTIA DIAGNOSIS	
✔	The assessment of the impact of cognitive impairment on the activities of daily living is recommended, given their affectation, which forms a dementia diagnostic criterion and determines the subsequent management of these patients.
✔	Obtaining data from an independent and reliable informant is recommended, whenever possible.
✔	An assessment of the psychological and behavioural symptoms is recommended, due to their importance for the diagnosis.
✔	The execution of a general physical and neurological examination of patients with dementia is recommended to detect comorbidity and associated neurological signs that may help towards the differential diagnosis of some subtypes of dementia.
D	The use of DSM-IV-TR and ICD-10 clinical criteria is recommended to diagnose dementia.
B	The use of DSM-IV-TR or NINCDS/ADRDA criteria is recommended to diagnose EA.
B	The use of NINDS/AIREN criteria or the Hachinski scale is recommended to facilitate the diagnosis of VD.
D	The use of Emre et al. (Movement Disorder Society) criteria to diagnose Parkinson's disease dementia is recommended.
B	The use of McKeith criteria is recommended to diagnose DLB.

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B	The use of Lund-Manchester or Neary criteria to help diagnose FTLD is recommended.
B	Patients with cognitive complaints must be assessed by means of global cognition screen tests, neuropsychological test batteries, short cognitive instruments focused on specific aspects of cognition and/or standardised structured questionnaires to quantify the degree of cognitive impairment.
A	The dementia diagnosis must include a formal objective cognitive assessment with validated instruments.
A	The use of the Spanish standardised version of the MMSE or the MEC is recommended to screen dementia in individuals with cognitive complaints or advanced age in our medium.
B	Other short screening tests, such as the Pfeiffer test, the MIS, the 7-minute test, the clock test, the Eurotest or the T@M can also be recommended to screen dementia in individuals who are suspected of having cognitive impairment.
B	The neuropsychological examination using general brief-intermediate type evaluation tests is recommended when the aim is to make an evaluation of the most important neuropsychological areas in a reasonable time.
D	The performance of a detailed neuropsychological assessment via specific tests is recommendable when there are differences between the clinical impression and the screening tests, diagnostic doubts or else when the complaints are limited to just one cognitive domain or evolve over a short period of time.
C	The use of specific scales is recommendable to quantify the degree of global functional impairment in individuals who are suspected of having cognitive impairment.
✔	The choice of a specific instrument must be made depending on the time available, on the clinical experience and on the availability of regulatory data in the language and in the environment where they will be applied.
D	The performance of the following laboratory tests is recommended in all patients assessed for possible dementia: Haemogram, TSH, electrolytes, calcium and glucose, to rule out potentially reversible causes of dementia and to screen comorbidities.
D	The determination of folate levels can also be added, especially in patients with limited cereal intake and c levels, above all in older adults.
D	Serologies are also recommended for syphilis or HIV only in patients in whom these infections are clinically suspected as a potential cause of dementia or as comorbidity.
D	The determination of homocystein as a risk factor associated with cognitive impairment or AD is not recommended.

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A	The determination of the apoE genotype is not recommended in healthcare practice to diagnose AD.
B	The determination of T-tau, Aß-42 and P-tau in CSF can be used an additional test in cases of doubtful differential diagnosis between AD and other dementias. Its routine use is not recommended to diagnose dementia.
B	The determination of T-tau, Aß-42 and P-tau in CSF can be used as an additional test in cases of mild cognitive impairment when the clinical, neuropsychological and evolutionary features lead to AD being suspected as an aetiology of such impairment.
A	The 14-3-3 protein test in CSF is recommended when CJD is suspected.
✔	The CSF analysis must always be performed whenever dementia secondary to an infection or encephalitic process is suspected.
B	Structural neuroimaging (CT and MRI) is recommended as a supplementary tool in the initial diagnosis of dementia, above all to identify lesions that can be treated by surgery, and vascular diseases.
✔	The MRI is recommended to detect vascular changes with greater sensitivity than the CT.
B	The execution of an MRI with diffusion sequences is recommended if CJD is suspected.
B	SPECT and PET can be used as a complement to structural neuroimaging to support the diagnosis or to help differentiate between different types of dementia when the diagnosis is uncertain. Its routine use or its use as a sole diagnosis tool is not recommended.
B	The ^{123}I-FP-CIT SPECT is recommended to support the diagnosis of DLB (as a suggestive diagnostic feature) and for the differential diagnosis between DLB/PDD and AD.
B	The execution of an EEG is recommended if the presence of delirium, complex partial epileptic crises or non-convulsive status epilepticus is suspected.
A	The use of EEG to diagnose CJD is recommended.
D	The execution of a cerebral biopsy for diagnostic purposes must only be considered in highly selected patients when a reversible cause is suspected that cannot be diagnosed in any other way.
DIFFERENT CARE LEVEL ACTIONS	
D	The PCT professionals must suspect the existence of cognitive impairment and/or dementia if they observe memory complaints, behavioural changes and difficulties to carry out advanced and instrumental ADL, carrying out screening tests and starting complementary examinations to be able to formulate a diagnosis and refer to the SDC depending on the results.

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C	There is not enough scientific evidence to permit the recommendation of population-based dementia screening in people over the age of 65.
C	The PCT must refer people to the SDCT who have: a) early, family or genetic onset dementia, b) doubts in the diagnosis of cognitive impairment, c) potentially severe secondary dementia, d) suspicion of neurodegenerative disease, e) unpredictable or difficult to manage complications in the course of already diagnosed dementia.
D	The referral of patients with MCI or secondary dementia that can be solved by the PCT, or pluripathological patients with bad functional basic status, is not recommended.
D	The PCT must assume responsibility for the management, care and monitoring of people with dementia and of their caregivers.
D	People with a predictable evolution must be periodically controlled by the PCT. If there is unexpected worsening, alarm signals, behavioural crises, etc. they must be quickly attended by PCT, and if it is difficult to control them, they must be referred to the SDCT.
D	Coordination and communication between PCT, SDCT, SHC and AFA must be established to guarantee seamless healthcare throughout the entire process.
D	It is recommendable for the multi-disciplinary team of the SDCT to include an expert specialist physician in dementias (neurologist, geriatrician or psychiatrist), a psychologist/neuropsychologist, a nursing professional, a social worker and administrative staff. The SDCT must have access to diagnosis means to be able to design treatment, monitor strategies and satisfy their healthcare, teaching, research and management objectives.
D	Patients and/or their families must be informed about the diagnosis, the prognosis and the strategy to be followed.
D	Patients and/or their families must receive a written report listing all the examinations carried out, the diagnostic guideline and treatment, and monitoring plan. This information must be given to the PCT and/or to the referring practitioner.
D	The existence of specific resources is recommendable to care for people with dementia, and the SHC network must have specific resources that adapt to each phase of the disease.
✔	To optimise the comprehensive treatment of dementia, it is recommendable for there to be referral, admission and discharge criteria for each healthcare resource.
D	Treatment in specific day hospitals for dementia is recommended in the mild and moderate phases of dementia.

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✔	It must be taken into account that the mental health services carry out an essential role in the care of people with dementia, as they contribute to the aetiological diagnosis, the treatment and hospitalised care if severe BPSD appear. They provide coordinated, comprehensive and multidisciplinary care.
D	It is recommendable for health and social services professionals to know about the problems that affect their dementia patients to be able to provide an answer to their demands and know what tasks caregivers must carry out, the time they spend, the environment where they live, and the cost it represents for the family.
D	The Administration, through its social services network, must adapt to the increase in demand for care and services for people with dementia.
D	Favouring access to social services is recommendable as well as providing the services to give adequate support to the task of caring of families that care for people with dementia.
D	It is recommendable to step up the support measures to make it easier for people with dementia to remain at home.
C	Psychological support and psychoeducational interventions geared towards families with people with dementia are recommendable, in order to favour their task of caring, reduce the care burden and improve the quality of life.
D	In each case and depending on the moment of evolution of the dementia, it is recommendable to dynamically select the best social service resource that must be provided to a family caring for a person with dementia.
D	To ensure seamless social and health care in the care of people with dementia and their families, it is recommendable, throughout the entire process, for there to be coordination between the different care levels, social services and community resources.
D	To favour the comprehensive care of the person/family with dementia, it is recommendable for the communication and coordination between the different levels (health, social and community) to be fast, efficient, effective and multidirectional.
D	It is recommendable for all the care levels to collaborate in obtaining a fail-safe diagnosis, favouring the obtaining of biological and neurological tissue samples.
D	Coordination of the different healthcare levels is recommendable in order to favour respect for the rights and freedoms of patients in decision-making (advance directives).

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D	Coordination between the healthcare levels, the SDCT, universities, pharmaceutical industry, teaching and research institutions and the AFA is recommendable to favour an increase in knowledge (training and research) of dementias (health, social, community aspects).
D	It is recommendable for the different professionals who intervene in the care of dementia to collaborate in drawing up a record of dementias to have a better knowledge of reality and rationally plan new intervention strategies.
TREATMENT OF DEMENTIA	
General measures	
D	Informing patients and their families of the dementia diagnosis is recommended when there is reasonable suspicion of dementia. The SDCT physician and/or PCT is the person who must inform the patient and family.
C	Informing patients who request this and the family of the diagnosis is recommended, as it has been proven that the information received does not predispose or generate a disorder in the person affected.
D	The patients' right to be informed or not must be respected, as well as their right, if they are capacitated to do so, to choose those people around them who must be informed of the process.
C	Offering information via understandable, sensible, respectful, empathetic, verbal communication, and an adequate environment and conditions is recommended, to facilitate two-way dialogue. To make it easier to understand the diagnosis and its consequences, further information can be provided via information leaflets, booklets, videos, Internet and other audiovisual means, and associations of relatives of dementia patients. If there are language barriers, communication must be facilitated through an independent cultural mediator.
D	The individual evaluation of the possible impact that communicating the diagnosis may generate is recommended, as well as doing so in instalments if necessary, providing further information during successive visits and in information sessions (SDCT, PCT, AFA).
C	Giving information to patients and families about dementia is recommended, as well as about its evolution, clinical manifestations, comprehensive treatment and support to the caregiver, which will enable them to plan their future.
D	It is advisable for the group information sessions aimed at families to contemplate basic aspects of dementia; function of the different professionals and healthcare levels; comprehensive treatment and available resources; management of emerging problems; detection of burdens derived from the task of caring, and support to the caregiver.

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D	The execution of specific training programmes for families who live with people affected by DLB, FTLD or VD and in advanced or terminal dementia stages is recommended.
D	Training health practitioners, social services professionals and volunteers/ professionals is recommended so that they can manage a group of patients and/ or families affected by dementia.
D	It is recommendable to train caregivers (families or professionals) to empower them to manage non-pharmacological interventions of dementia.
Specific pharmacological treatment of dementia	
A	ACE inhibitors are recommended for the specific and symptomatic treatment of mild to moderate AD.
A	Treatment with ACE inhibitors is recommended to manage mild to moderate VD.
B	ACE inhibitors have proved to be beneficial in DLB and PDD.
B	No differences have been shown regarding ACE inhibitors (donepezil, rivastigmine and galantamine) in respect of efficacy and safety profiles.
A	Memantine is recommended as specific treatment for moderate to severe AD in mono-therapy or combined with ACE inhibitors.
-	We have little evidence about whether specific pharmacological treatment is equally effective in all people due to the lack of studies that assess the individual response to different drugs.
Alzheimer's Disease	
A	Treatment is recommended with ACE inhibitors (donepezil 5-10 mg/day, galantamine 16-24 mg/day or rivastigmine 6-12 mg/day oral/4.6-9.5 mg/day transdermal) in patients with mild or moderate AD.
B	An ACE inhibitor can be used (donepezil or galantamine) in severe AD, although there is less evidence of its benefit.
A	Treatment with memantine is recommended, at a dose of 20 mg/day in patients with moderate to severe AD.
A	Treatment with ACE inhibitors is recommended in patients with mild to moderate AD, to manage the cognitive and functional symptoms.
A	Treatment with ACE inhibitors is recommended in patients with mild to moderate AD, to manage behavioural alterations (apathy, anxiety and depression), despite the benefit being modest.
A	Treatment with memantine is recommended in patients with moderate to severe AD, to manage the cognitive and functional symptoms.

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B	There is no evidence to recommend treatment with ACE inhibitors to improve the quality of life of patients with AD.
✔	Following the indications of the technical data sheet of the drug is recommended to avoid adverse effects and contraindications of the ACE inhibitors and memantine.
D	The administration of a progressive dose of the drug is recommended to avoid or reduce the adverse effects of the ACE inhibitors, starting the treatment at low doses, to reach the optimal tolerated therapeutic dose.
D	ACE inhibitors must be used with caution in patients with a background of epilepsy, asthma or obstructive lung disease, arrhythmias, syncopes, low blood pressure, presence of bradycardia or long QT, active peptic ulcer, urinary retention, renal or hepatic insufficiency. Memantine must be used with caution in patients with a background of epilepsy, renal insufficiency and urinary retention.
D	Domperidone can be used to treat mild gastrointestinal effects secondary to ACE inhibitors.
B	The addition of memantine is recommended in patients with moderate to severe AD, treated with donepezil at stable doses in combined therapy.
B	The addition of memantine to donepezil is not recommended to treat patients with mild to moderate AD.
√	The addition of memantine to donepezil is not recommended to treat patients with mild to moderate AD.
Parkinson's disease dementia	
B	The use of rivastigmine or donepezil is recommended in PDD.
B	The use of donepezil may be considered to treat cognitive and functional symptoms in PDD.
C	There is not enough evidence to recommend the use of memantine in PDD.
B	In patients affected by PDD, treatment with donepezil and memantine is associated with a rate of adverse effects similar to the placebo group, unlike with rivastigmine, which showed a higher rate of secondary effects, an increase in tremors and a lower rate of mortality than the placebo group.
Dementia with Lewy bodies	
B	The use of rivastigmine is recommended to treat BPSD in DLB.
C	The use of donepezil or galantamine may be considered to treat cognitive symptoms and BPSD in DLB.

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C	There is no evidence to recommend the use of memantine in DLB.
✔	The most frequent adverse effects observed in treated patients with DLB are: nausea, vomiting, weight loss and drowsiness. These were more frequent in patients treated with rivastigmine than with placebo, and also in those treated with memantine than with placebo. The potential adverse effects of rivastigmine must be detected and monitored during treatment.
C	Levodopa can be used in monotherapy to treat the motor symptoms of DLB.
D	It is advisable to avoid the use of dopaminergic and anticholinergic agonists in DLB due to their potential effect of worsening the cognitive and psychotic symptoms and producing sleep alterations and orthostatic hypotension.
Frontotemporal lobar degeneration	
B	The use of ACE inhibitors or memantine to treat cognitive-behavioural symptoms of patients with FTLD is not recommended.
B	The use of selective serotonin reuptake inhibitors, trazodone or atypical neuroleptics is recommended to treat agitation, inappropriate behaviour, compulsions or stereotypes in patients with FTLD.
Vascular Dementia	
A	The use of ACE inhibitors is recommended in mild to moderate VD.
A	ACE inhibitors are recommended to improve the cognitive symptoms of mild to moderate VD.
A	Donepezil is recommended to improve the global clinical impression and functional deficiencies (ADL) in VD.
A	The use of galantamine is recommended to treat cognitive symptoms, functional deficiency and BPSD in patients with mild to moderate VD, mixed dementia and/or AD with cerebrovascular disease.
C	Rivastigmine may be used to improve cognition in VD.
A	Memantine may be used to treat cognitive symptoms of moderate and severe VD.
B	ACE inhibitors may be used to treat cognitive symptoms of VD.
B	ACE inhibitors and/or memantine are not recommended to manage behavioural symptoms in VD.
√	Bearing in mind that patients with VD usually suffer a high cardiovascular risk, treatment with ACE inhibitors should be assessed individually, paying special attention to how the treatment is managed.

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✔	It is advisable to follow the indications given in the product technical data sheet.
Other pharmacological treatments	
A	Hormonal therapies (ACTH, prednisone, oestrogens, dehydroepiandrosterone) are not recommended as treatment of AD.
A	Neither ibuprofen, indometacine nor low doses of naproxen are recommended to treat AD.
A	Piracetam is not recommended to treat AD.
A	Propentofylline is not recommended to treat AD or VD.
B	Nimodipine is not recommended to treat VD.
A	Selegiline is not recommended to treat AD.
A	Ibedenone is not recommended to treat AD.
B	Dihydroergotoxine mesylate is not recommended to treat AD or VD.
B	Neither citicoline nor oral CDP-choline are recommended to treat VD.
D	Neither citicoline nor CDP-choline via parenteral administration are recommended to treat vascular cognitive impairment.
NON-PHARMACOLOGICAL TREATMENT OF DEMENTIAS	
Cognitive intervention or stimulation	
B	The participation in cognitive intervention programmes is recommendable for patients with mild or moderate AD, to maintain their cognitive function, their functionality and quality of life, although the magnitude of the effect attributable to the actual cognitive intervention is not well established.
C	There is currently no evidence of the efficacy of cognitive stimulation in individuals with VD to recommend its use in this dementia subtype.
-	A type of specific cognitive intervention cannot be recommended at the present time, based on the degree of efficacy in patients with mild or moderate AD, although interventions that require a general type of processing seem to have a greater overall benefit than those where cognitive training of specific functions is carried out.
C	The use of computer-based cognitive intervention programmes in initial AD or mild cognitive impairment cannot be recommended at the present time.
B	Individual cognitive interventions are recommendable to stabilise the cognitive function and functionality of individuals with AD.

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-	The use of individual interventions rather than group interventions or vice versa cannot be recommended.
Intervention programmes on activities of daily living	
B	Intervention programmes on activities of daily living are recommended to improve the functionality of patients with dementia and decrease the strain of the caregiver in the medium term, both in institutionalised people and those who live in their family homes.
Physical activity programmes	
B	Long-term physical activity programmes are recommended to maintain the functionality of institutionalised patients with dementia.
Other non-pharmacological treatments	
C	The use of therapeutic massages or touches, transcutaneous electrical nervous stimulation, music therapy or multisensory therapy cannot be recommended at the present time to treat cognitive or functional manifestations in patients with dementia or specifically with AD.
B	Behavioural changes, programmed hygiene and induced urination are recommendable to reduce urinary incontinence in individuals with dementia.
Safety of non-pharmacological treatments	
✔	Cognitive intervention programmes, especially those based on reality counselling therapies and cognitive training, must be adapted to the cognitive skills and to the emotional tolerance of each patient, in order to avoid adverse emotional consequences.
Treatment of behavioural and psychological symptoms of dementia	
✔	The systematic assessment of the presence of BPSD is recommended as it is a fundamental component of the clinical picture, it appears very frequently, it is difficult to manage, it has an impact on the quality of life and is a frequent reason for urgent care, family claudication and institutionalisation.
✔	The use of specifically designed instruments is recommended to evaluate BPSD in dementia, independently from cognitive and functional alterations.
✔	NPI (Neuropsychiatric Inventory) is recommended as an instrument to assess the intensity and frequency of BPSD, the CSDD scale (Cornell Scale for Depression in Dementia) to assess depressive symptomatology and DMAI (Cohen Mansfield Agitation Inventory) to assess agitation.
B	It is advisable to bear in mind that BPSD may appear at any time during the evolution of dementia, whatever its aetiology, and it is not unusual for it to be the first manifestation.

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B	If delusions and hallucinations appear in a person with early stage dementia, FTLD or DLB must be suspected. If there are REM sleep behaviour disorders, the first suspicion will be DLB.
B	BPSD must be detected as soon as possible, in mild dementia stages, or throughout its subsequent evolution; they must be quantified and grouped into syndromes that facilitate differential diagnosis between the different dementias.
B	It is advisable to know and recognise the BPSDs that appear in AD, VD, FTLD, DLB and PDD.
B	When a BPSD appears, health practitioners should perform a systematic evaluation of this and of the other symptoms in order to be able to perform a differential diagnosis with idiopathic psychiatric diseases.
B	Health practitioners must bear in mind the importance of BPSD from the semiological, repercussion, prognosis and resource viewpoint. BPSD must be detected as soon as possible, in mild dementia stages, or throughout its subsequent evolution, quantifying them and grouping them into syndromes that will enable us to provide a differential diagnosis between the different neurodegenerative entities and treat them appropriately.
B	It is advisable to know and recognise the groups of BPSDs that appear in AD, VD, FTLD, DLB, PDD, PSP, DCB and HD.
✔	Starting treatment with non-pharmacological strategic measures to manage BPSD is recommended.
C	It is especially important for caregivers to receive information and training that capacitates them to prevent the appearance of BPSD and act as co-therapists when they are already present.
C	Stimulation-orientated treatment with recreational activities and pleasurable activities has proved to be effective to cope with depression.
✔	Non-pharmacological sleep management mainly consists of establishing guidelines and good sleep hygiene.
C	There is limited evidence that therapeutic massages may be effective to treat agitation.
D	The use of electronic identification techniques on dementia patients who present erratic wandering is recommended.
D	It is advisable to start with the non-pharmacological management of BPSD and use drugs in severe or rebellious symptoms.

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D	The symptom that is going to be treated as well as its possible causes or triggers must be identified.
D	The general recommendation regarding pharmacological treatment of BPSD is to start basic treatment (ACE inhibitors and/or memantine) and, if the response is not sufficient, add a specific psychotropic drug.
✔	Bear in mind the special sensitivity of these patients to adverse effects, especially the risk of anticholinergic effects, orthostatic hypotension, falls, extrapyramidal effects, worsening of cognitive function, confusion and delirium. Review the dose and the actual treatment need at regular intervals, generally every 3 months.
✔	Start with low doses and slowly reach the minimum effective doses. Preferential use of oral route. If necessary, intramuscular is preferable to intravenous route.
B	The use of ACE inhibitors and/or memantine is recommended as treatment of dementia, not only for cognitive symptoms but also for non-cognitive ones.
B	The use of rivastigmine is recommended to treat BPSD in patients with DLB or PDD.
D	The use of psychotropic drugs is recommended to treat BPSD, although evidence about their efficacy in patients with dementia is generally low and the risk of adverse effects is high.
B	The use of these drugs in patients, on whom the use of ACE inhibitors or memantine is indicated, is recommended to treat BPSD, too.
✔	If they do not improve, non-pharmacological measures or specific psychotropic drugs will be used for the symptom, considering their adverse effects.
A	Risperidone may be used in patients with AD and psychotic symptoms.
B	Donepezil may be used in patients with AD and psychotic symptoms. Rivastigmine may be used to treat psychosis in DLB.
D	Atypical anti-psychotics may be used in patients with AD or VD and psychotic symptoms.
B	Antidepressants, preferably sertraline and citalopram may be used in patients with dementia and depression. Tricyclic antidepressants are not recommended due to their adverse effects, despite their similar efficacy.
D	Psychostimulants, amantadine, bromocriptine or bupropion may be used in patients with dementia and severe apathy.
-	There is not enough evidence to make recommendations about the treatment of anxiety in dementia.
D	Risperidone may be effective in erratic wandering in AD.

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D	Benzodiazepines, trazodone or hypnotics may be used to treat sleep disorders in dementia. Melatonine is not recommended.
B	The use of neuroleptics is recommended to treat agitation and aggressiveness. The evidence is greater for risperidone than for other drugs.
D	In the case of intolerance to antipsychotics, donepezil (if indicated), SSRI or carbamazepine may be used to treat agitation and aggressiveness.
D	Antidepressants, antipsychotics, mood stabilisers, hormonal agents, cimetidine or pindolol may be used to treat inappropriate sexual behaviours.
A	Antipsychotics must be used with caution in patients with dementia, due to the risk of adverse reactions, always considering the risks of treating compared with the risks of not treating.
B	Antipsychotics are contraindicated in DLB due to the high risk of adverse effects.
C	Treatments with benzodiazepines must be short-term due to the adverse effects.
✔	The association of non-pharmacological and pharmacological measures is recommended to manage behavioural and psychological symptoms of dementia.
✔	A meticulous assessment is recommended if BPSD appear, to rule out concomitant pathology and achieve optimal environmental surroundings.
✔	Sensory stimulation, behavioural therapy, structured activities and social contact may be used to reduce the incidence of BPSD, although there is no scientific evidence to support this.
A	The use of atypical or typical antipsychotics is recommendable in agitation.
B	To control delirium in a person with dementia, atypical antipsychotics (risperidone, olanzapine, quetiapine) may be used.
D	If the behaviour crises do not respond to the normal pharmacological measures in the home/nursing home, admission into hospital or into specific units is advised to diagnose the symptoms and aetiology, treat comorbidities, optimise the treatment of BPSD and guarantee the safety of patients and of their environment.
✔	It is advisable to inform and train caregivers of dementia patients in strategies to address and manage the BPSD so that it is possible to adopt and promote an appropriate attitude towards patients and prevent the strain and claudication of caregivers.
Alternative treatments of dementias	
B	Vitamin E supplements are not recommended to treat AD.

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A	The use of B1, B6, B_{12} vitamin or folic acid supplements is not recommended in patients with cognitive impairment that do not present a clear deficiency of these elements.
B	The use of copper supplements is not recommended to treat patients with AD.
B	There is not enough evidence in literature about the efficacy of ginkgo biloba to recommend its use in the treatment of AD or VD.
C	Existing evidence does not permit recommending the use of lecithin, alpha-lipoic acid, omega-3 fatty acids, ginseng or yokukansan (TJ-54) in the treatment of cognitive symptoms of AD.
Assessment of the treatment of dementias	
D	The periodic assessment of cognitive, functional, motor and behavioural aspects is recommended, as well as of the degree of strain on the caregiver when monitoring patients with dementia.
D	The use of tests, scales or questionnaires is recommended to quantify the therapeutic response and the appearance of complications in patients with dementia.
✔	The choice of a test, scale or questionnaire will be based on the physician's experience and on its applicability in the context.
C	The use of the MMSE is recommended to assess the response to dementia treatment in clinical practice.
CAREGIVERS OF PATIENTS AFFECTED BY DEMENTIA	
C	During the care of every person with dementia, their individual characteristics and the actual characteristics of the disease must be evaluated to be able to assess the needs and prevent the burden of the caregiver, and act consequently to optimise their support network.
D	Dementia is a dynamic process, which, as it progresses, increases the commitment and obligations of the caregiver. It is recommendable to meticulously evaluate the burden supported by primary caregivers and the support they receive in their task of caring. If the burden is too much, it is advisable to establish the appropriate measures to prevent this from affecting their physical and psychological health, thus giving rise to the risk of claudication.
C	The use of the Zarit scale (long and short versions) is recommended to quantify the caregiver burden.
✔	The use of specific adapted and validated instruments is recommended to assess other aspects that may be affected by the caregiver burden.
D	A basal evaluation of caregivers of people with dementia is recommendable in order to identify the factors that affect the burden of caring, the difficulties that might arise in the course of the disease and the degree of burden that caregivers already have at the time of the diagnosis.

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D	Caregivers should be informed well and progressively about the disease and its possible complications, offering them the available social resources, as well as the formal or informal support systems to prevent strain.
B	To improve the care of caregivers of people with dementia and reduce their burden in the task of caring, as well as anxiety and depression, a programme that combines educational support, emotional support and the provision of resources may be beneficial.
B	Interventions carried out in the caregiver's own home and in a personalised manner are recommendable.
D	Comprehensive care of caregivers must contemplate many different actions: Welcome programme, information sessions, theoretical and practical training, advisory services, emotional support, adaptation of resources, pharmacological treatment if required and accompaniment throughout the entire process.
D	There should be a professional in the MAGs to favour and foster the skills of the group members.
D	It is advisable and desirable for caregivers of people with dementia to participate in MAGs, as they provide many different benefits, which will enable them to cope better with the task of caring and improve their personal situation.
D	Participation in TAGs or EESG to improve the strategies to cope with dementia is recommendable, relieving the burden and improving the level of anxiety and depression that might affect the caregiver.
D	Professionals that run the TAG or EESG must personalise their interventions to be more effective.
✔	It is recommended for those caregivers who express a significant degree of stress and/or depression to be referred to their primary care physician and/or mental health specialists for their assessment and treatment.
C	Psychotherapy, especially cognitive-behavioural therapy, would be recommended to treat stress or depression due to excess caregiver burden when they present clinically relevant symptomatology.
D	Health practitioners and social services professionals who care for people with dementia and their families should comment on the existence of the AFAs and the benefits that they can obtain from them, and insist on their experience in living with people with dementia.
D	To achieve optimisation in the approach and management of dementia throughout the entire process, from diagnosis until after death, the existence of good coordination between the different healthcare levels and the AFAs is recommendable.

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D	The Public Administration and the AFAs should continue to maintain and improve their collaboration, in order to improve the quality of life of people affected by dementia.
D	There must be a close relationship between the tertiary sector and the Public Administration with permanent dialogue, thus favouring the exchange of knowledge both on the needs and collaboration proposals (programmes, subsidies, agreements, etc.).
D	It is recommendable to continue improving the relationship between the Public Administration and the AFAs, drafting referral protocols, recognising the role of the AFAs in the training of caregivers and professionals; fostering the creation of TAG and/or EESG and therapeutic programmes (DH, DC, rehabilitation workshops) and aid to develop complementary activities.
EARLY ONSET OR PRE-SENILE DEMENTIA	
D	The use of neuropsychological test batteries validated for this age group is recommended in the assessment and characterisation of cognitive impairment in people with pre-senile dementia.
D	The aetiological study of a patient with early onset dementia should include the study of low incident causes in later age groups and atypical presentations of frequent dementias.
✔	It is recommendable for patients with early onset dementia to be assessed by professionals with experience in this age group and at centres that have the appropriate complementary tests to carry out this study.
✔	Lacking specific evidence in this age group, the therapeutic guidelines recommended for other age groups should be followed, depending on the type of dementia suffered by the patient.
✔	It is advisable for people with presenile dementia to carry out the same non-pharmacological therapies that have proved to be effective in people over the age of 65.
✔	If we wish to favour their adherence to individual or group non-pharmacological therapeutic programmes, they must be adapted to the specific needs of the person with early onset dementia.
✔	It is recommendable for people with early onset dementia to have access to social-health and health resources that focus specifically on their care.

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ETHICS AND LEGAL ASPECTS OF DEMENTIAS	
Abuse of people with dementia	
D	It is necessary for health practitioners, the social services and society in general to be concerned and become aware of the abuse that many elderly people suffer, whether they are affected or not by dementia. It is a personal, family, intergenerational, health problem, as well as one of justice and human rights. Its detection permits the establishing of prevention strategies, changes in attitude and the promotion of solutions.
D	Health and social services professionals must be trained and made aware how to detect, declare, prevent and treat problems derived from the abuse of people with dementia.
D	It is important to identify the type of abuse (action or omission), and determine its characteristics (psychological, physical, sexual, economic).
D	If abuse is suspected, the person must be questioned in private and with delicacy, given their fragility, bearing in mind the state of mind and the fear of the consequences that discovery of abuse may entail, in their environment.
D	For a complete diagnosis of abuse, it is advisable to evaluate the risk factors, those that depend on the patient, on the abusing caregiver and the circumstances that surround it.
D	The possibility of the existence of abuse must be suspected, if the person with dementia is hostile, aggressive, provocative, dependent for ADL and there is a lack of an appropriate support network.
D	Caregivers must be suspected as abusers if we observe symptoms of anxiety, depression, strain in the task of caring, low cultural level and when the person they are looking after is very dependent for ADL and/or presents BPSD.
D	If the person has mild to moderate dementia, we must get them to give us information about their physical and psychic state of health through fluent and true communication. In initial stages, this can be relatively easy to obtain; in fluctuating dementia, the most appropriate and reliable moment must be sought; in advanced stages, it will be possible to obtain information at moments of lucidity.
D	A meticulous and thorough clinical examination is recommendable to detect signs that lead us to suspect the possibility of abuse, evaluating physical, psychological and behavioural aspects.
D	It is advisable to be mindful of the possibility of abuse, as this facilitates its detection and permits protection, prevention and correction measures.

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B	We must systematically question aspects related to the abuse of any elderly person, with or without dementia, and use standardised scales to detect it.
B	We must assess caregivers of people with dementia to detect a possible person responsible for abuse. Scales can be used to detect it.
D	Health and social services professionals must be trained to prevent, detect, care for, protect, declare and recuperate a person with dementia suffering from abuse.
✔	The fundamental rights of the person to dignity, participation, autonomy and self-determination must be preserved.
✔	People suffering abuse must be informed, respecting their right to confidentiality, in order to cover their basic needs, and to preserve their social relationships.
✔	The victim's demands must be defined and identified individually, without prejudices or value judgements, determining an action strategy and seeking the best possible solution for all involved in a situation of abuse.
✔	If there is probable suspicion of abuse, the health personnel must activate the judicial resources that permit the defence of the victim of abuse. If there are physical injuries, a judicial report of injuries will be drafted. If there are injuries or other acute contingencies, the Public Prosecutor will be informed.
D	When abuse is detected and diagnosed, it is recommendable to launch strategies that permit improving the situation of the victim and of the aggressor. The actions of the different professionals must be coordinated, recording all the data of the abuse in the clinical record.
D	To prevent and treat abuse, avoiding social isolation, optimising patient care, adapting their home and institutionalising them if the family cannot guarantee their care, is recommended.
D	It is advisable to attend to the abuser, who is often a stressed or sick relative, or with an excessive burden. The burden can be reduced by sharing the task of caring, removing the patient from the family environment, participating in support groups, guaranteeing rest and offering medical treatment if required.
Advance directives	
D	Health and social services professionals, and relatives must try to discover the AD of sick people to be able to comply with their wishes and respect their medical, legal and financial preferences.

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D	It is important to continue informing and raising the awareness of the population at large as well as of the health and social services professionals, about the need for able and free adult people to exercise their rights to draw up an AD document containing their wishes regarding the care and treatment they accept to receive, as well as the appointment of a valid representative that can decide on their behalf in each health circumstance, and after death, about the destination of their organs.
D	It is advisable to draw up the AD document in adult age and being of sound mind. In respect of people with dementia, this must be attempted as soon as possible to guarantee their cognitive integrity to the utmost.
D	Health professionals must recommend the AD document to their patients, and insist upon it especially if they detect emerging cognitive impairment.
D	It is recommendable for the AD document to include everything that is important for the person, bearing in mind that another person, to whom they delegate, will have to take decisions in their name, following their own indications.
D	To make it easier for a person to have access to the AD, the AD document must be registered in the autonomous community and at the National Registry Office for advance directives or AD of the Ministry of Health and Consumer Affairs, and it must be attached to the clinical record and to the health card.
Evaluation of competences	
D	The utmost efforts should be made to maintain the autonomy of people affected by dementia, respecting their decision-making capacity, whenever possible, even at the end of their days.
D	It is recommendable for health and social services professionals, as well as the legal institutions that attend to them, to use a common language and share knowledge.
D	The decision capacity of any person affected by dementia should be assessed, using the assessment instrument of the Sitges 2009 document.
D	It is advisable to involve the patient in decisions made about the treatment. The patient's desire must prevail; however, differences in opinion between patient and caregiver must be evaluated.
D	Total or partial incapacitation must be used as a legal resource to protect people with dementia.
D	When carrying out a comprehensive and multidisciplinary assessment of people with dementia, the evaluation of their decision-making capacity must be included, as well, if there is appropriate legal protection or not.

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D	The ability of people with dementia to drive a vehicle should be assessed, even during the initial stages, as an increase in the risk of suffering accidents has been proven.
D	A full psychological evaluation should always be carried out at drivers' examination centres to detect people with cognitive impairment in mild dementia.
D	Health professionals must inform patients with dementia and their families about the risk that continuing to drive may entail.
D	If a person with mild dementia continues to hold a licence, their ability to drive must be reviewed every 6 to 12 months, or earlier if necessary, to evaluate their risk.
D	A driving limitation must be proposed when alterations, although mild, are detected in attention, orientation, executive functioning or in visuospatial perception.
D	It is advisable to keep firearms or elements that might be dangerous to them or to third parties, away from people with dementia, above all if there are behavioural disorders.
D	People with dementia and their relatives must be informed of the possibility of participating in clinical trials.
D	People participating in research studies must receive extensive, detailed and understandable information, and they must sign an informed consent.
D	Good Clinical Practice Guidelines must be implemented in research studies.
D	The RCTs should satisfy a series of conditions: a) correct methodology and competent research team; b) acceptable risk-benefit ratio; c) independent supervision; d) fair load distribution, random distribution, with equal probability of efficacy and safety in all groups; e) informed consent and confidentiality; f) safety guarantees, and g) appropriate payment.
D	Professionals taking part in research studies must know about the agreements relating to human rights and biomedicine as well as the standards established by international ethical guidelines.
D	It is very important to respect the autonomy and freedom of the people at the time of the diagnosis and throughout the entire evolution process, bearing in mind that, despite the existence of advance directives, people, with age, due to circumstances and/or due to the actual disease process, may change their way of seeing things, and thus change their decisions.

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D	Beginning the incapacitation process must be recommended when the dementia progresses and the cognitive and/or behavioural impairment determines the taking of inadequate decisions that might harm the person affected by dementia and their environment.
D	The incapacitation process must be the result of a multidisciplinary evaluation, and must contemplate multiple aspects such as diagnosis, clinical manifestations, degree of dependence, social aspects, use of services and evolution of the process.
Aspects relating to the patient's legal protection	
According to applicable legislation	To request the incapacitation or modification of the capacity to act, the procedure laid down by the Spanish Procedural and Civil Registration Law must be followed, whereby, based on a demand, the case is studied, challenged and the judge gives judgement.
✔	People with mild cognitive impairment and mild dementia should be advised to protect themselves through decision-making powers, or giving special power or writing the advance directive document.
✔	Any person with dementia, who still has sufficient capacity to act, should appoint a guardian, foreseeing the possibility of being declared incapable. What is more provision referring to their personal care or the administration of their assets, identifying any person who should not be appointed, under any circumstances should be adopted.
✔	People with dementia who have lost their self-management skills, should have a legal representative or guardian to protect them, and substitute them.
✔	People with dementia with a reduced decision capacity should name a representative who shall care for their conservatorship, accompanying them, advising them and helping them take decisions.
✔	People with dementia with a reduced decision capacity should name an administrator for their estate to administer their assets if these are considerable.
✔	A judicial defender of the person with dementia must be named, to cope with urgent situations if a tutor has not been named or when important differences arise between guardian and the ward.
Restraint of the patient	
B	It is recommendable to prevent and detect psychomotor agitation and aggressiveness of people with dementia at an early stage and treat it. The measures to be followed may be pharmacological or non-pharmacological, using mechanical restraint if required.

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A	The use of atypical antipsychotic drugs is recommendable as a primary pharmacological treatment of psychomotor agitation and aggressiveness of people affected by dementia.
D	When it has not been possible to control a person with dementia with pronounced psychomotor agitation using verbal and/or pharmacological measures, and they continue to be dangerous or at risk of causing harm to themselves or to others, mechanical restraint (MR) must be proposed.
D	Approved fastening elements must be used in the MR, in agreement with the legislation in force, and they must be in perfect conditions to be effective and safe.
D	To achieve adequate and safe MR, a coordinated team is required, comprised of four or five well-trained people, who secure patients properly, taking care not to harm them, and acting calmly and with serenity, but firmly and surely. Throughout the entire MR procedure, all those measures aimed at preventing direct or indirect complications must be maximised, guaranteeing the patient's comfort, privacy and respect. The MR measure will be stopped as soon as possible, and progressively, when the symptoms are under control.
D	MR is a therapeutic physical restriction measure that must only be applied under medical prescription. It must only be used if other restraint methods are not applicable or have failed. Its objective is to protect the actual patient and other people, objects or surrounding environment. It cannot cause greater harm than the harm aimed to be avoided.
D	Excessive use of MR should be avoided in people with dementia, only using it when it is really justified, either due to the intensity of the symptoms and the possibility of them harming themselves or others. It must be as brief as possible to preserve the dignity and freedom of the person and reduce the risk of complications.
D	It is advisable for the MR to be a shared decision, agreed upon by the other members of the interdisciplinary team. The parentage details, the type and date of application of the measure, the reason for the restriction, the care guideline to follow, the periodicity of the controls, as well as the information given to the patient and to the family, and the informed consent, must be described in the clinical record, and signed by the physician.
C	The MR must be used in the following cases: To prevent injuries to the actual patients and to other people around them. To avoid interferences in the treatment (routes, probes, etc.), and material damage to the patient's surroundings. To avoid escapes and prevent falls, and maintain the correct position of the body. To achieve the centre's organisational objectives. To maintain a comfortable social environment.

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C	The contraindications of MR must be respected and it must not be carried out if not explicitly indicated by the health professional responsible, or if there are medical orders not to apply it. It must not be used, either, if there are equally effective alternative measures or procedures that have not been tried. It must never be used as punishment or as a show of force, or as a substitute for surveillance, or for the exclusive convenience or comfort of the professionals caring for them.
C	It is advisable for the MR to be maintained for a short period of time (hours, days), monitoring the patient to guarantee adequate observation to avoid risks and complications. When appropriate control has been achieved, it must gradually be brought to an end.
D	As restraint measures affect people's freedom of movement, and their freedom of decision, and they are not free from complications, before starting to apply them, the legal regulations that govern them must be carefully and strictly observed and enforced. The action must contemplate the principles of beneficence, non-maleficence and justice, and respecting the right to personal autonomy.
C	People with dementia with severe behavioural disorders that entail a risk for the actual patient and/or for the people around them, and which are not adequately controlled in outpatients (primary and specialised care), should be admitted into specialised units to control the crisis and enable the family to rest. Admission into these centres should satisfy the dual objective of diagnosis and treatment.
D	Admissions in order to control crisis situations must be as short as possible, guaranteeing, at the time of discharge, that the symptoms have been controlled, that the environment and the receiving family are adequate, the caregiver's burden has been reduced and support measures for them to continue with their task of caring have been established.
According to applicable legislation	The legal regulation that protects people who are involuntarily submitted to admission into hospital must be respected. The opinion and consent of the family will be required as well as the judicial authorisation before carrying out the admission. The reasons must be suitably justified, ensuring their beneficence and respect for the dignity and freedom of the person affected.
D	If involuntary internment is urgently required, for a person with dementia and severe behavioural disorders, it will be the physician attending to that person who shall take the decision. In this case, the person responsible at the centre must inform the competent court as soon as possible.

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CARE OF PEOPLE WITH ADVANCED DEMENTIA AND AT END-OF-LIFE STAGE	
D	The term SEAT can be used in advanced degenerative dementia in terminal phase which corresponds to stage GDS 7.
B	Evaluate the stage of SEAT using the Gold Standards Framework (GSF) instrument. The GSF is recommendable to find out the expectations of the caregivers regarding the death of the patient, the need to establish palliative measures, the limitation of the therapeutic effort, and about the consumption of resources, complications and crisis situations.
C	Advanced dementia must be considered as terminal dementia if cognitive impairment is severe and there is severe dependence for the BADL, there is no possibility of therapeutic benefit with the specific treatment, there is multiple comorbidity and a suitable nutritional status cannot be maintained.
B	To establish a life prognosis of less than 6 months in a person with advanced dementia, parameters with predictive power must be identified, such as degree of cognitive impairment, degree of functional disability, presence of malnutrition and presence of systemic complications and comorbidity.
D	Palliative care must be implemented in the management of people with dementia, and this must be introduced early on after carrying out the diagnosis and it must be prolonged and increased as the disease progresses.
D	The aim of palliative care is to relieve physical and psychological suffering, provide quality of life and consider death as a natural process. Psychosocial and spiritual aspects must be integrated, giving support to relatives.
D	Health and social service professionals must be prepared to offer palliative care to people affected by dementia.
D	All people with advanced dementia must be provided with PC, whatever the healthcare level that is being applied.
D	Healthcare continuity must be maintained in PC when there is a change in the healthcare level of the person with advanced dementia.
D	Health organisations should foster training of all professionals to provide basic PC.
D	Health organisations must guarantee accessibility to specialised PC when necessary.
D	Coordination between the different services and healthcare areas must be guaranteed, as well as continuity of palliative care.

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D	Initial management of delirium must include the identification and treatment of the triggering causes, as well as appropriate information for relatives and caregivers, and an evaluation of the need to use pharmacological treatment.
B	Haloperidol is the drug of choice for treating delirium in patients in terminal phase.
C	Benzodiazepines are effective in the management of delirium with marked agitation.
D	The use of haloperidol and atypical antipsychotics must be avoided in patients with PDD and DLB, due to the risk of extrapyramidal reactions.
D	In people with advanced dementia at end-of-life stage due to a concomitant process, the diagnosis of depression must be based on the clinical observation, the information provided by relatives and, if possible, the use of specific scales.
B	If necessary, antidepressant drugs, such as SSRI and tricyclics may be used, bearing in mind the possibility of central anticholinergic effects.
D	Psychostimulants such as methylphenidate, dextroamphetamine, modafilin and pemoline may have a fast response and are well-tolerated.
D	Treatment of dysphagia requires individualised assessment of each case in order to identify and if possible, treat the cause.
D	The diet must be adapted to the clinical characteristics of the dysphagia. In the case of liquid dysphagia, thickeners may be effective. A soft diet that adapts as much as possible to the patient's tastes is recommended. If the patient collaborates, the adoption of postures that facilitate swallowing with the supervision of the speech therapist is effective.
D	Whenever possible, liquids must be administered orally.
D	The parenteral administration of liquids during the end-of-life stage must be carried out weighing up the advantages and disadvantages, and always after discussing it with relatives.
B	The use of a nasogastric probe or permanent percutaneous gastrostomy must be assessed individually and with caution in patients with advanced dementia, as there is evidence of a bad relationship between benefit and risk.
C	The presence of pain must always be suspected in advanced dementia. This must be assessed through the patient's behaviour, observation of relatives and appropriate scales such as PACSLAC and DOLOPLUS.
D	The use of the WHO analgesic ladder guideline is recommended for the pharmacological treatment of pain in advanced dementia, and, if necessary, adding adjuvants.

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B	It is recommendable not to treat pneumonia with antibiotics in a person with advanced dementia as it does not entail a benefit.
B	Hospital admission is not recommendable to treat pneumonia in a person with advanced dementia.
B	Treatment with antibiotics is recommendable in people with advanced dementia who have breathing difficulties due to over-infection of bronchial secretions.
C	To prevent the appearance of pressure ulcers, there must be frequent changes in posture, using mechanical protections and maintaining a good state of nutrition, hydration and hygiene of the skin.
D	The psychosocial well-being of patients with life-threatening chronic diseases must be evaluated on a regular basis.
D	The psychosocial assessment of patients in PC should include the following fields: Aspects related to the moment in life, the meaning and impact of the disease, coping style, impact on the perception of oneself, relationships, sources of stress, spiritual resources, economic circumstances, doctor-patient relationship and social resources network.
D	Health and social services professionals attending them should offer basic emotional support.
D	People with significant levels of psychological suffering should receive specialised psychological help.
D	The team attending people with dementia must bear in mind their beliefs and spiritual needs.
D	In the absence of appropriate evidence about what is the best way to provide spiritual support, offering this support as an integral part of the care is recommended, whatever the care context, and with an approach based on the principles of effective communication.
D	It is important to consider cultural differences with respect to spirituality, but this does not justify a lack of attention to these aspects in people who belong to different cultural or religious groups to our own.
C	Caregivers must be offered the possibility to express their needs for support and information.
D	Identifying the most vulnerable or depressed caregivers is recommended in order to offer them intensive psychosocial support or specialised services.

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CARE OF PEOPLE WITH DEMENTIA AND THEIR FAMILIES DURING THE FINAL DAYS OF THEIR LIVES	
D	Appropriate care during the final days of their lives should include: • Informing the family and caregivers of the situation of approaching death and, in general, provide the necessary information that adapts to their needs. • Explaining and agreeing to the care plan with the patient, and whenever possible, with their families. • Evaluating the medication the patient takes, suspending non-essential drugs, after explaining the reasons for this. • Treating symptoms that produce suffering. The necessary drugs must be available if the patient is at home. • Interrupting unnecessary or futile interventions or tests, according to the patient's desires. • Evaluating psychological, religious and spiritual needs of the patient, family and caregivers. • Providing care in a quiet atmosphere, respecting privacy and facilitating proximity with family and friends. • Providing the channels and resources necessary both for hospitalisation and for home care.
B	Referral of patients with complicated grief to specialised services (psychology, psychiatry, etc.) is recommended for them to receive specific and structured care.
B	Regular monitoring is recommended in risk grief, with emotional support, individually evaluating the need for specific and structured psychotherapies.
B	Formal or structured interventions are not recommended in normal grief.
D	In normal grief, providing information about the grief and about the available resources is recommended, as well as basic emotional support.
D	Professionals caring for patients at the end-of-life stage as well as their relatives, should have access to elementary training in grief, which will enable them to provide basic care to the grievers, understand and explore their needs, evaluate the risk factors, detect people with complicated grief and refer them to specialised service.
D	In a person with advanced dementia, the existence of a concomitant process must be suspected if the progression suddenly speeds up and above all if there are unpredictable changes.
D	When considerable worsening appears, regardless of the cause, a series of factors must be evaluated that may affect the therapeutic decision, always bearing in mind the values of the person and of the family.

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D	It is recommendable to evaluate the possibility of therapeutic limitation if the dementia has reached a very advanced stage: FAST of over 7c in AD; when the Barthel index is 0; if the progression is very fast from the onset; if the infections are serious, repeated and with no relevant benefit with the treatment; if the dysphagia is problematic, with malnutrition and/or dehydration, and if there are refractory pressure ulcers.
D	Whatever their location, it is recommendable for patients with advanced or terminal dementia to receive palliative measures to improve their comfort, suffering and quality of life, insofar as this is possible.
B	Cardiopulmonary resuscitation is not indicated in people with advanced dementia, as it is an extraordinary therapeutic measure that does not provide any significant benefit.
B	Neither artificial respiration nor dialysis are recommendable, either, in advanced dementia, because they provide no benefit.
B	At the end-of-life stage of patients with advanced dementia, the use of intermediate range therapeutic measures (intravenous infusions, administration of antibiotics, artificial feeding, hospitalisation and execution of unnecessary diagnostic tests) is not recommended.
C	The use of intermediate range therapeutic measures should only be considered on those occasions when they can reduce suffering or they are the only available resource.
D	It is recommendable to give information and support to caregivers of people with advanced dementia for them to continue assuming their work as caregivers, take decisions, adapt and engage more.
D	Informing and communicating bad news to the caregivers of people with dementia at the end-of-life stage requires adequate preparation of the professionals.
D	The participation of patients and caregivers in decision-making at the end-of-life stage must be fostered.
D	If patients are not able to decide at this end-of-life stage, the advance directives expressed by them or their wishes included in the clinical record, or else the opinion of their legal representative and/or closest family, must be contemplated.
D	Informing the team of the decisions adopted at this end-of-life stage is recommended, recording the process in the clinical record.
D	If there are doubts during the decision-making process, consulting other expert professionals or the healthcare ethics committee is indicated.

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D	It is recommended for the medical team attending to the patient at this end-of-life phase to request the post-mortem neuropathological study to confirm the diagnosis (above all in those cases where there is not an accurate diagnosis, or if a prion disease is suspected or any other disease of compulsory declaration) and foster the investigation.
DIFFUSION, TRAINING AND RESEARCH INTO THE CARE OF PEOPLE WITH DEMENTIA	
Diffusion	
✔	Information about dementia through the media must be based on ethical principles and good practice.
✔	The existence of specialised journalism in health issues is recommendable. The media, competent professional associations and family associations must collaborate in fostering good information about dementia.
Training	
✔	It is recommendable for health sciences university students to receive general training in dementia, in aspects such as epidemiology, pathophysiology, clinical manifestations, diagnosis techniques, pharmacological and non-pharmacological treatment, on the needs of the patients and relatives, and resources available, as well as on associated ethical and legal aspects.
✔	Health vocational training must guarantee the acquisition of theoretical and practical knowledge, as well as positive attitudes of respect and tolerance, to appropriately manage dementia.
✔	VT health personnel must be prepared to carry out continuous ecological stimulation aimed at maintaining the capacities of the individual affected by dementia at a maximum level, delaying the decline of the person affected and giving information about the management and resources in dementia.
✔	All health and social services professionals must update their knowledge to be competent in the comprehensive management of dementia. Dementia must be addressed in an interdisciplinary fashion, providing care seamlessly from the moment it is detected until the end of life.
✔	All health and social services professionals integrated into the specialised care of people with dementia must receive specific training that will cover aspects related to the diagnosis and treatment, needs and resources available, ethical and legal aspects, and the need for it to be managed in an interdisciplinary manner.

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Research	
✔	The collaboration of everyone involved (health and social services professionals, patients and relatives) is important to make a joint effort in the study and research of dementia.
✔	Research in dementia must be promoted and fostered from the public administrations, the governing bodies of the State and of the autonomous communities; it must be coordinated with other countries and it must favour the exchange of knowledge between the different teams that work in the same research line in dementia.
✔	The three healthcare levels, PCT, SDCT and the social-health network should participate in research in dementia; to this end, training in research methodology is required.

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1. Introduction

Dementia as a clinical syndrome is characterised by an acquired impairment affecting more than one cognitive domain, which represents a decline from a previous level that is serious enough so as to affect personal and social functioning. In the majority of the cases, behavioural and psychological symptoms are added.

All the epidemiological studies have confirmed that age is the main risk factor for the development of dementia; in such a way that both the prevalence and the incidence practically double every 5 years as from the age of 65.1 Given the increase in life expectancy and the progressive ageing of the population in developed and developing countries, dementia is understood to represent an enormous challenge for the public health systems of these societies.

Different systematic reviews (SR) on epidemiological studies performed in Europe have concluded that the prevalence of dementia (percentage of sick people within the population at a given time) varies between 5-10% among the population of over 65 [2,3,4], and that there are about 5 million sick people.5 There is also coincidence in the fact that Alzheimer's Disease is the most frequent dementia (60-70% of the cases, followed by vascular dementia, 12.5-25%).[3]

In Spain, epidemiological studies on the population over the age of 65 have shown prevalence figures that vary between 5 and 14.9% and in the group of over 70s, between 9 and 17.2%. [6,7] A recent SR coordinated by the National Epidemiology Centre concludes that the prevalence in the Spanish population over the age of 70 is 10%, a similar figure to that of other countries of our environment.[8]

These are relevant data for the Spanish society, as it is one of the societies in the world that has aged the most due to the increase in life expectancy that has caused the spectacular social, economic and health advance experienced over the last 50 years. The proportion of people aged 65 and over in Spain was 16.5% in 2008[9] and it has doubled over the last 30 years; the Spanish population is the seventh most aged among European countries. Furthermore, the population segment of over 80, the most susceptible to dementia, is the segment that has most increased.[10]

If an average prevalence of 7% is calculated, it can be concluded that there are approximately 500,000 to 750,000 people with dementia in Spain.[6,7] The case of pre-senile onset dementia would have to be added to these figures, but we have no epidemiological studies in Spain and they are very scarce in Europe. A study conducted in London found a prevalence of 52/100,000 and that the main causes of presenile dementia are Alzheimer's disease, frontotemporal degeneration, post-trauma dementia, alcohol-related dementia and dementia associated with infection due to human immunodeficiency virus (HIV).[11]

Dementia has a direct impact on patients but it also has an enormous repercussion on their social environment, causing considerable moral, physical and economic harm to the family unit. In this sense, dementia must be addressed as a true family disease, and as a disease of society. Caring for people with dementia and their relatives requires a multidisciplinary approach, with active participation of the professionals involved; it must be comprehensive and it must guarantee *healthcare continuum* so that the participation of each professional and resource adapts to the changing needs of the patient and of the caregivers at each stage in the evolution of the disease. The standard must be a coordinated, flexible and effective exchange of knowledge and resources among professionals from the social-health area, placed at the disposal of sick people and of their caregivers.

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Having common consultation elements may help enormously towards this coordinated work. The main aim of this clinical practice guideline (CPG) on Alzheimer's disease and other dementia is for it to be a consultation tool that will provide every one of the professionals involved in the care process of people with dementia and their caregivers with effective answers, in each situation and at every moment of the disease, from the mild cognitive impairment (MCI) stage to the terminal stages of the disease. It also aims to be a learning, training and dissemination tool.

Recommendations are given in this CPG on care of patients with Alzheimer's disease and other dementias, such as, for example, vascular dementia, Parkinson's disease dementia, dementia with Lewy bodies and frontotemporal lobar degeneration. References to other dementias, such as Huntington's disease, other degenerative dementias, post-trauma dementia, HIV-associated dementia or metabolic-deficiency dementias are not so broad, but the majority of the recommendations are also valid for them.

The ambition of this guideline is to cover a national field and it has some characteristics that make it special: it has been demanded by the Spanish Federation of Associations of Families of Alzheimer's and other Dementias (CEAFA), supported and financed by the Ministry of Health and Social Affairs, and drafted by representatives of all the professionals that work on a day-to-day basis in the field of care of people with dementia, both on the health side and on the social side.

Recommendations are given in this guideline and the most frequent questions asked in regular clinical practice are answered: how must a fast and early diagnosis of MCI and of dementia be carried out, how to select the neuropsychological tests and the laboratory examinations that adapt best to each case, how must patients and their relatives be informed about the diagnosis, prognosis and resources, what pharmacological and non-pharmacological treatment options exist; how to prevent and treat behavioural and psychological symptoms of dementias (BPSD), how must the monitoring of the disease be carried out, how must the strain on the caregiver be prevented, what is the role of cognitive stimulation, what options are correct in the terminal stage of the disease. It also aims to give adequate information about the best coordination between the different healthcare levels and about the role of the social-health resources, especially in advanced stages. Finally, it responds to questions on genetic counselling and on multiple legal and ethical type aspects that usually arise throughout the disease.

The recommendations of this guideline have been drawn up based on the best available evidence in medical literature and on the recommendations of experts when no conclusive evidence existed. Finally, the complete document has been reviewed by experts of acknowledged national prestige in the field of dementias. The methodology of the guideline has been supervised by the Agencia d'Informacio, Avaluacio i Qualitat en Salut (AIAQS) of the Department of Health of the Generalitat of Catalonia.

As in any CPG, however good the methodology used in its preparation, its use must not prevail over the responsibility of the professionals when taking the decisions that adapt best to patients' circumstances,

always respecting their opinions, values and beliefs, and always or, whenever possible, consulting their legal representatives.

Important advances have been made over the last few years in clinical genetics and diagnosis techniques, through studies in the cerebrospinal fluid (CSF) and neuroimaging tests; publications on the efficacy of new drugs are also being awaited. This tendency is undoubtedly going to continue in coming years, so this guideline will have to be revised and re-published within 5 years at the latest, if any significant advance is made, although an earlier update of its online version is not ruled out.

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2. Scope and objectives

Target population

This CPG focuses on the comprehensive care of people affected by dementia, whatever the age of onset of the process, of their relatives and caregivers. People under the age of 65 are included as they have different clinical manifestations and considerable social repercussion.

The clinical entities that are addressed with greater detail are: Alzheimer's disease (AD), vascular dementia (VD), Parkinson's Disease Dementia (PDD), dementia with Lewy bodies (DLB) and frontotemporal lobar degeneration (FTLD).

Field of action

Spanish National Health System (SNHS).

Healthcare Levels

Primary care team (PCT), specialised dementia care team (SDCT) and health and social care (HSC).

Aspects included

Clinical areas: prevention, detection, diagnosis, genetic counselling, pharmacological and non-pharmacological treatment, prognosis, health and social resources and aid, monitoring and care at end-of-life stage.

Family and professional caregivers: Information and training for caregivers. The co-therapist caregiver. Needs and burdens of the caregiver. Caring for the caregiver. Free time. Associationism.

Other areas: Legal and ethical aspects, and considerations related to teaching and research.

Interventions

This CPG includes the following treatments:

- Specific and symptomatic pharmacological treatment
- Non-pharmacological treatment
- Concomitant pathology treatment
- Palliative cures in dementia and accompaniment during the end-of-life stage.
- General measures
- Training of caregivers and self-help strategies.

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Aspects excluded from the CPG

The CPG does NOT include:

- Dementias secondary to vitamin B_{12} deficiency and normotensive hydrocephalia
- Dementia associated with infectious diseases: HIV, viral or bacterial infections
- Dementias due to human spongiform encephalopathies (prionopathies)

Objective

To prepare an evidence-based CPG on the comprehensive care of people with Alzheimer's disease and other dementias, with national scope that offers "systematically developed recommendations to help professionals and patients take decisions about the most appropriate healthcare, and select the most adequate diagnostic or therapeutic options to address a specific clinical condition or health problem", integrating and coordinating the different SNHS health devices involved.

Secondary objectives

- Guarantee equity in health and social care of people affected by dementia and their families, regardless of their age, sex, social status, education or culture.
- Reduce the variability of clinical practice in comprehensive care of dementias, both regarding its diagnostic aspects and its therapeutic management.
- Offer comprehensive and integral care to the people, relatives and their environment, with a multi-interdisciplinary vision, evaluating biological, psychological and social aspects (bio-psychosocial approach),
- Improve the clinical skills of the health and social professionals involved in the care of people with dementia and their relatives.
- Use the most up-to-date diagnosis and treatment options based on the best scientific evidence and on the consensus of experts.
- Assess the effectiveness, safety and efficacy of the different diagnosis techniques and of the pharmacological (specific and symptomatic) and non-pharmacological therapeutic proposals.
- Provide useful information to the population, people affected by mild cognitive impairment or dementia, relatives of the people affected, caregivers, health and social services professionals, and other professionals related to any of the aspects involved in the care of dementia, to facilitate decision-making.
- Develop quality healthcare indicators that permit assessing the implementation of the recommendations established in the CPG.
- Establish recommendations to increase the knowledge of all the professionals involved at undergraduate, post-graduate and lifelong training level.
- Prepare general and specific information material for people affected by dementia and above all for their relatives and caregivers, which will give them a better idea of the dementia process as a whole and each one of the elements that affects the course of the disease.

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- Establish recommendations for the participation and development of research in dementias, from the different healthcare levels, in collaboration with the University, and the institutes and organisations dedicated to research.

Main users

This CPG is aimed at:

- Health professionals who have direct contact and have to take decisions about the care of people affected by dementia (general practitioners, neurologists, geriatricians, psychiatrists, neuropsychologists, psychologists, nurses, pharmacists, internists, physiotherapists, occupational therapists, social workers, etc.).
- Professionals from other areas that have direct contact with people affected by dementia (social services, media, justice).
- People affected by dementia.
- Caregivers (relatives or not) of people affected by dementia.

The CPG provides information for patients with dementia (**Appendix 2**) that may also be used by their relatives and friends as well as by the general population.

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3. Methodology

The methodology used in this guideline is contained in detail in the Methodology Manual for the preparation of CPG in the SNS[12].

The steps below have been followed:

- Formation of the guideline development group, comprised of health professionals, specialists in neurology, geriatrics, psychiatry, family medicine, neuropsychology, psychology, nursing, pharmacy, psychogeriatrics, preventive medicine and public health, forensic medicine and social work, and non-health professionals (lawyers and economists) involved in the study and treatment of dementia. Some of them have experience in the legal and bioethics area, are linked to the Social and Health Steering Plan of the Catalan Departament de Salut (DS) or are specialised in methodology from the AIAQS. The development group has been guided by a coordination team. To incorporate the perspective of relatives, representatives from associations of relatives and patients have participated in the development group and in the external view of the guideline.

- Formulation of clinical questions following the format: patient / intervention / comparison / result.

- Bibliographic search in: Pubmed/Medline, The Cochrane Library, Psycinfo, Scopus, Tripdatabase, CMA Infobase (Canada), CPG GuíaSalud Library of the SNS, International Guidelines Library (GIN), National Electronic Library for Health and U.S. National Guidelines Clearinghouse. Timeline: From January 2006 to February 2009. Languages: Spanish, Catalan, French, English and Italian. The first phase involved a preliminary search for CPGs and systematic reviews in the aforementioned databases. CPGs were identified and evaluated using the AGREE instrument[13], after which it was decided whether to include them as a secondary source of evidence, apart from serving as an inspiration and example for some of the sections of this guideline, due to their rigour and clarity. This was carried out in agreement with the preparation-adaptation-updating methodology used in the CPG on asthma of the Basque Country.[14] part from these CPGs, consensus documents and position papers (recommendations) of scientific societies have been considered, **(Appendix 6).** A second phase entailed an extended search for original studies (randomised control trial, RCT; cohort studies, case and control studies, etc.) until July 2009. Later, search alerts were created in Pubmed to identify relevant studies in high impact biomedical journals, and the entire development group was consulted until May 2010, when the first draft of the guideline was closed.

- Assessment of the quality of the studies and summary of evidence for each question, following SIGN (Scottish Intercollegiate Guidelines Network) recommendations.

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– Formulation of recommendations based on the "formal assessment" or "reasoned judgement" of SIGN. - The classification of the evidence and grading of the recommendations have been carried out using the SIGN system. The Oxford Centre for Evidence-Based Medicine system has been used for the diagnosis questions (grade A: Level of evidence Ia or Ib [in the guideline it appears as 2++]; grade B: level of evidence II [in the guideline it appears as 2+]; grade C: level of evidence III [in the guideline it appears as 2-]; grade D: level of evidence IV [in the guideline it appears as 3 or 4]) as suggested by the CPG preparation manual of the SNS for diagnostic test studies.12 Controversial recommendations or those where there was a lack of evidence have been solved by simple consensus of the development group.

– External reviewers have participated in the review of the second draft. The different scientific societies involved have been contacted (Sociedad Española de Neurología, Societat Catalana de Neuropsicologia, Societat Catalana de Medicina Familiar i Comunitària, Societat Catalana de Infermeria en Salut Mental, Sociedad Española de Psicogeriatría, Sociedad Española de Medicina Familiar y Comunitaria and Sociedad Española de Geriatría y Gerontología).

– The material, with detailed information about the methodological process of the CPG, is available at www.guiasalud.es.

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4. Definition and Classification of dementias

Questions to be answered

4.1. What is dementia?
4.2. What is the incidence and prevalence of dementia?
4.3. How is dementia classified?
4.4. What are the clinical manifestations of dementia?
4.5. How does the natural course of dementia evolve?
4.6. What is understood by degenerative dementia?
4.7. What is Alzheimer's disease?
4.8. What is dementia with Lewy bodies?
4.9. What is Parkinson's disease dementia?
4.10. What is frontotemporal lobar degeneration?
4.11. What other neurodegenerative diseases are accompanied by dementia?
4.12. What are vascular dementias?
4.13. What is and how is secondary dementia classified?

Mild cognitive impairment and conversion to dementia

4.14. What is understood by mild cognitive impairment (MCI)?
4.15. What types of MCI exist?
4.16. What is the incidence and prevalence of MCI?
4.17. What are the risk markers for conversion from MCI to dementia?
4.18. Is there any treatment that modifies the progression of MCI?

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4.1. What is dementia?

Dementia as a clinical syndrome is characterised by an acquired impairment affecting more than one cognitive domain, which represents a decline from a previous level and which significantly reduces functional autonomy. Dementia frequently appears with behavioural and psychological symptoms (BPSD), also called behavioural and emotional symptoms or neuropsychiatric symptoms.[6,15]

The dementia diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR)[16,17] and of the International Classification of Diseases (ICD) 10th edition (ICD-10) of the World Health Organisation (WHO)[18] **(Appendices 1.1 and 1.2)** state that the presence of mnesic impairment is compulsory. However, certain forms of dementia, such as frontotemporal lobar degeneration (FTLD), dementia with Lewy bodies (DLB), Parkinson's disease dementia (PDD) or vascular dementia (VC) may not entail severe memory impairment until advanced stages. This has led to amnesia being excluded as a compulsory element to establish the diagnosis of dementia syndromes. Thus, this symptom does not appear as compulsory in the criteria of the Spanish Society of Neurology (SEN)[19] **(Appendix 1.3)**.

Cognitive impairment must be prolonged; for example, the ICD-10 criteria arbitrarily establish a minimum duration of 6 months. Although this timeline is useful for the differential diagnosis of dementia with acute confusion syndrome, in regular clinical practice, it is excessive, as it prevents classifying as dementia, sub-acute evolution cases that reach intense impairment in a few weeks or months, as in the Creutzfeldt-Jacob disease (CJD).

4.2. What is the incidence and prevalence of dementia?

The dementia incidence and prevalence figures show very variable results due to the lack of a diagnostic biological marker in the great majority of the diseases that cause dementia, and to methodological differences of the studies.

Incidence of dementia

The global incidence of dementia in the world is estimated at around 7.5/1,000 people/year.[20] The appearance of new cases remains more or less stable until 65-70 years of age (< 5/1,000 people/year) and from then on the growth is exponential (around 15, 30, 50 and 70-75/1,000 people/year towards 75, 80, 85 and 90 years of age, respectively).[21] The annual incidence of dementia in a study performed in Spain was estimated at between 10-15 cases per 1,000 people/year in the over-65 population.[22]

Prevalence of dementia

A prevalence of dementia in the European population is estimated at around 5.9 and 9.4% in over-65s, according to data of the Eurodem consortium and from subsequent studies.[6,7]The prevalence doubles approximately every 5 years; for example, in Eurodem it was 1% between people aged 60 to 65, 13% in people aged 80 to 85, and 32% in the 90 to 95 age group. [23]A systematic review of the EuroCoDe group, published in 2009, showed that the prevalence of dementia in Europe has not changed significantly with respect to the data of Eurodem, except for a greater prevalence in very elderly women (http:// ec.europa.eu/health/archive/ph_information/dissemination/diseases/docs/eurocode.pdf).

Prevalence Studies in Spain have shown figures that vary between 5 and 14.9% for over 65s,[6,7]and between 6.6 and 17.2% for over 70s, according to a recent review of the National Centre of Epidemiology of population-based surveys conducted in Spain. [8]In the under-65 population, there are few studies; the prevalence of dementia in people aged between 30 and 64 years living in an area of London was estimated at around 54/100,000. [11]In general, the prevalence is higher in women and it increases with age. [8,24]

Incidence and prevalence according to type of

Dementia Alzheimer's Disease (AD)

The incidence of AD increases with age, from 1-3/1,000 people/year between 65 and 70 years of age, up to 14-30/1,000 between 80-85,[25] and it appears to be greater in women. In very elderly people it is even greater, up to 38.6/1,000 between 85 and 89 years of age and more than 65/1,000 people per year in people over 95 years of age, according to date from the Framingham study.[26]

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The prevalence of AD is around 0.6-0.7% in Europe at the age of 65-69 years according to the Eurodem study, and it also increases with age (1.8% in men and 4.3% in women in the 75-79 age group; 6.3 and 8.4% respectively in the 80 to 84 age group; 8.8 and 14.2% in the 85 to 89 age group, and 17.6 and 23.6%% in the over 89 age group).[1] The prevalence of AD in our country is around 6% in the over 70s age group and it represents 70% of the dementias.[27]

Vascular Dementia (VD)

VD represents 12.5-27% of the dementias. [6,7,27]Whilst it is estimated that in AD the prevalence doubles every 5.3 years, in VD, it does so every 4.5 years. The prevalence of VD is less in women than in men in the population under the age of 80, and after that the proportion is inverted (0.1% in women and 0.5% in men in the age range between 65 and 69 years; 0.9 and 1.2% respectively between 75 and 79; 3.5 and 3.6% between 85 and 89; and 5.8 and 3.6% in the over 90s).[25]

Dementia with Lewy bodies (DLB)

DLB represents 10-15% of the cases of dementia in the clinical-pathological series originating from specialised units. [28]The prevalence of DLB in epidemiological studies varies from 0.1% in a Japanese study of people over the age of 65[29] to 5% in a Finnish study of people over the age of 75. [30]Two independent studies in Spain showed a prevalence of 1% [27,31]that is, around 8.9% of the dementias. [27]There are not enough studies to estimate the incidence of DLB.

Frontotemporal lobar degeneration (FTLD)

The prevalence of FTLD varies between 0% in a Japanese study[29] and 3% in a Swedish study on patients aged 85 years. [32]A study performed in El Prat de Llobregat (Barcelona)[27] on people over 70 showed a prevalence of 0.3%, the same as the study in Islington (London)[33]. There are not enough data to estimate the incidence of FTLD.

4.3. How is dementia classified?

Currently, we do not have a specific methodology that enables us to address the classification of dementia according to "evidence-based medicine".[34] The most wide-spread classification criterion is the aetiological one. Three main aetiological categories can be considered: primary degenerative dementias (AD, FTLD, DLB, PDD and others), secondary dementias and combined or mixed dementias (with multiple aetiology). [6,35]

Other forms of classifying dementia are based on the presence of other neurological symptoms, onset age or topographic distribution. It can also be classified according to non-clinical criteria: neuropathological, molecular, genetic.36 A possible classification would be that shown in **Appendix 1.4** adapted from the SEN CPG (2009). [6,35]

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4.4. What are the clinical manifestations of dementia?

Cognitive alterations

The clinical manifestations of dementia are heterogeneous due to the existence of multiple aetiologies, different lesion patterns and variability in the course of evolution.[25,37]

Initially, in the typical presentation form of AD, an episodic memory disorder appears, because the limbic circuits of the memory are altered at a very early stage. When the lesions extend to posterior temporal parietal associative areas, apraxic, aphasic and agnostic disorders become evident.

In FTLD and at the onset of the disease, an alteration of the personality and of the social behaviour may prevail, due to the impairment of prefrontal regions, or progressive non-fluent aphasia may stand out, due to affectation of the perisylvian frontal portion of the dominant hemisphere, or an outstanding language impairment in the form of progressive fluent aphasia (semantic dementia) due to greater initial affectation of the temporal lobe of the dominant hemisphere.

The impairment of the so-called executive function or series of cognitive skills is frequent in the different types of dementia. These permit anticipating and establishing goals, designing plans and programmes, the start of activities and of mental operations, self-regulation and monitoring of tasks, the exact choice of behaviours, cognitive flexibility and their organisation in time and space.

Mnesic impairment may appear in any type of dementia at any time of its evolution. Generally speaking, when the cortical regions are more affected, it is normal to find, in different combinations, aphasia, apraxia, agnosia, amnesia and affectation of executive functioning. This occurs in degenerative cortical dementias such as AD and DLB, in lobar atrophies that occur with progressive aphasia or progressive apraxia, in corticobasal degeneration (CBD) or posterior cortical atrophy and in any other dementia whose lesions are preferably located on the surface of the brain (many cases of multi-infarct dementia and other processes due to non-degenerative cortical focal brain lesions). When the alteration prevails in subcortical structures, such as, for example, in subcortical VD or in progressive supranuclear palsy (PSP), the mental processing slows down more (bradypsychia), there is a gradual reduction of sustained attention and verbal fluency, mnesic evocation difficulties, impairment of executive functioning and, because of the affectation of projection fibres originating from motor and premotor cortex areas, hypokinesia and pseudobulbar symptoms appear.

Behavioural and psychological symptoms of dementia (BPSD)

Approximately 80% of patients with dementia present BPSD at some moment of its evolution. [38]In some cases, their presence makes diagnosis difficult, but in others they help differentiate the type of dementia (**question 10.4.1**). For example, disinhibited social behaviour, eating or sexual behaviour disorders, compulsions, stereotyped behaviour and apathy are more common in FTLD. [39]Psychotic symptoms are frequent in DLB, especially visual hallucinations. In DLB and PDD,

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behavioural disorder associated with the REM sleep phase is typical. In subcortical predominant dementias (PSP, CBD, some forms of VD), apathy or pseudobulbar symptoms such as spasmodic crying or laughter are frequent.

People with dementia are vulnerable to changes in their environment, which may cause a worsening of both the cognitive deficiencies and the BPSD.[42]

Other symptoms

Some diseases that occur with dementia present other accompanying symptoms that help diagnose the type of dementia, such as parkinsonism (DLB, PDD, PSP, CBD), motor neuron signs (in some cases of FTLD), involuntary movements (such as in HD), cerebellar syndrome (spinocerebellar ataxias), autonomic disorders (DLB, PDD) or release of primitive reflexes (AD). In the case of AD, motor manifestations are scarce.[6,35]

4.5. How does the natural course of dementia evolve?

Neurodegenerative origin dementias have in common a normally insidious start and progressive evolution.

In initial stages and in the majority of the cases, AD is characterised by an affectation of the memory for recent events, and later on deficiencies in other cognitive functions appear, as well as a progressive impairment in advanced, instrumental and, finally, basic activities of daily living. This is followed by an impairment of motor functions, with the appearance of gait disorders, tremors, myoclonia, sphincter incontinence, dysphagia and, finally, immobilisation of the patient and death due to an intercurrent complication such as thromboembolism or infections. The spontaneous evolution of the disease varies between some patients and others, although it does not usually last for more than 15 years. The presence of plateaux has been described through the course of evolution and mood fluctuations, although these are more frequent and marked in DLB, so they have even been incorporated into the diagnostic criteria for this disease.[40]

FTLD, DLB and Parkinson dementias (PDD, DCB, PSP) also naturally evolve towards progressive worsening, often aggravated by the presence of the extrapyramidal syndrome, of other motor alterations (dysphagia, dysarthria) and of autonomic dysfunction. The evolution of FTLD is often accelerated by the co-existence of a motor neuron disease.[43]

BPSD complicate the evolution and are the frequent cause of early institutionalisation and the need for pharmacological treatment which sometimes worsens the cognitive deficiency. BPSD may already occur in initial stages, above all in FTLD, although they are also frequent in AD (apathy, irritability, affective disorders), when they tend to become more frequent and severe as the disease progresses.[6,44,45]

The evolution of VD is less predictable. Certain stability is often observed for longer or shorter periods of time, although a new vascular event may cause a sudden decline of the cognitive function, like a step. These stability periods have been objectified in some clinical trials, probably due to the better management of the cardiovascular risk factors. On other occasions, the evolution pattern of VD, especially subcortical type, is a progressive impairment similar to that ofdegenerative dementia. [6,46]Strategic infarct dementia usually has acute onset. Some symptoms may improve over the first few months and the residual picture tends to remain stable.

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The natural cognitive evolution of the three main types of dementia (AD, VD and DLB), measured with a simple screen test such as MMSE, shows a similar impairment rate of close to 3-4 points a year. [25]

The evolution of secondary dementias will depend on the cause and how quickly the treatment, if any, is established.

There are different scales to measure the evolution of dementias and that are used for the clinical monitoring and assessment of the therapeutic response in clinical trials **(question 8.4)**.

4.6. What is understood by degenerative dementia?

Degenerative dementias are diseases characterised by neuronal and synaptic loss and by the accumulation on the brain of intra and/or extracellular insoluble protein aggregates **(question 5.1)**. Each type of protein deposit tends to follow a topographic pattern that is correlated to the clinical characteristics that define each type of dementia. Dementia may be the predominant clinical manifestation, as in AD, or form part of the clinical picture without being the predominant manifestation, as in Parkinson's disease. The majority of degenerative dementias are diseases that appear at older ages, from 65 years onwards, and sporadically, although there are hereditary and early onset forms in almost all of them. They start insidiously, and continue to evolve progressively and irreversibly.[6,35]

4.7. What is Alzheimer's disease?

AD is a degenerative type clinical-pathological entity that evolves progressively, which is clinically characterised by cognitive impairment and dementia, and neuropathologically by the presence of neurofibrillary tangles and neuritic plaques. It is the most frequent type of dementia, representing up to 70% of the dementia cases. In the majority of cases, the presentation is sporadic, but there are familial cases, some of which are associated with known autosomal dominant transmission mutations.[6,44]

The main symptom of AD is the loss of episodic memory, which is initially expressed by greater difficulty to register new information. Later on, aspects of speech, visuospatial skills, constructive capacities, motor praxis and executive functioning are affected. Although AD typically occurs as a loss of memory, there are infrequent atypical onset forms that occur with a frontal syndrome, a picture of progressive aphasia, progressive apraxia or a visual agnostic syndrome due to posterior cortex atrophy. As the disease evolves, there is a progressive loss of autonomy in the normal activities of daily living. The majority of patients also present behavioural and psychological symptoms. These may already appear in mild stages although they are usually more obvious in moderate and advanced stages. These symptoms are important due to their frequency and their impact on the patients' quality of life of the patients and on the burden of caregivers. The clinical criteria for the diagnosis of AD are described in **Appendices 1.5-1.7.**

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4.8. What is dementia with Lewy bodies?

DLB is clinically characterised by the association of fluctuating dementia-cognitive impairment, parkinsonism and psychotic symptoms, and pathologically by the presence of Lewy bodies and neurites in the brain cortex, and normally, too, in subcortical nuclei. [6,47]Dementia usually occurs with fluctuations of cognitive deficiency and level of awareness. Parkinsonism is typically predominantly akinetic and usually symmetric with early alteration of gait although this may be absent in up to 25% of patients with pathologically confirmed diagnosis, thus making diagnosis difficult. Typical psychotic symptoms are detailed visual hallucinations and structured delusions. Signs of autonomic dysfunction, behavioural disorder of REM sleep, hypersomnia, falls and hypersensitivity to neuroleptics are also frequent.

Typical pathological lesions are Lewy bodies and neuritis, which consist of pathological alpha-synuclein aggregates which extend over the limbic area, the cortex and brain stem. Similar plaques to the typical AD plaques are also observed.

The diagnostic criteria of DLB were formulated in 1996 by McKeith et al and they showed low sensitivity but specificity of around 85-90%. These criteria were revised in 2005 **(Appendix 1.l8)**[40] and their sensitivity and specificity still have not been determined.

4.9. What is Parkinson's disease dementia?

Parkinson's disease dementia (PDD) is dementia that appears in the context of a typical established Parkinson's disease, and which affects more than one cognitive domain, mainly attention a well a executive and visuospatial functioning.[16,48] By convention it is different to DLB in that in this disease the dementia appears prior to or at the same time as the Parkinson symptoms. For the operational diagnosis of PDD, it is considered that at least one year must have elapsed from the onset of parkinsonism and the appearance of dementia. [40]The neuropathology is similar to DLB **(question 4.8).**

A longitudinal study observed that around 60-80% of patients with Parkinson's disease (PD) ended up developing dementia in the 8-year control period, depending on the patient's age.[49]

Much like VD, the anatomopathological lesions of PD and of DLB are often found, too, in autopsies on patients with AD, and vice versa, so there are controversies about the independence of both entities. Cases of disease with pure Lewy pathology without Alzheimer type pathology are rare.

Some diagnostic criteria were established in 2007 to diagnose PDD as probable or possible[41] **(Appendix 1.9).**

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4.10. What is frontotemporal lobar degeneration?

FTLD are a group of neurodegenerative diseases that are clinically characterised by prominent behaviour and/or language alterations, and pathologically by focal brain atrophy, normally of the frontal and/or temporal lobes, which may be symmetric or asymmetric. Although it is not very frequent, it is the second cause of dementia in people under the age of 65, after AD. It does not usually have a predominant effect on the memory or spatial skill.[6,45]

Three major symptoms are distinguished in clinical practice: The frontal variant (FTLD) when frontal type behavioural disorder prevails, and semantic dementia (SD) and progressive non-fluent aphasia (PNFA) when language disorder prevails. There are some less frequent forms where a progressive apraxia syndrome prevails. The most frequent presentation form is FTLD (50-60% of the cases), followed by PNFA and SD.[50]

The main characteristics of FTLD are:

- Changes in early onset behaviour such as a behavioural alteration that affects the social sphere, lack of judgement, inflexibility, disinhibition, perseverance, gluttony, hyperphagia, hyperorality, emotional incontinence, loss of empathy and anosognosia, which prevail over memory alteration.

- Progressive prominent alteration of expressive language with hypofluent speech, logopenia, anomia, agrammatism and repetition disorder (progressive non-fluent aphasia). Language alteration usually occurs at early stages too, although frontal behavioural symptoms or apraxia may be associated later on.

- Progressive alteration of the understanding of words, with hyperfluent speech, anomia and progressive loss of the semantic contents of words, objects and concepts (semantic dementia). Associated prosopagnosia may appear if the affectation is right-hand. Semantic alteration initially prevails, although frontal behavioural symptoms or apraxia may be associated later on.

Initially, there is not usually memory affectation or apraxia (except in the forms of progressive apraxia). In any of the three major symptoms, parkinsonism and motor neuron affectation may also be associated.[51]

The predominant and early symptoms of behaviour and of speech, and less affectation of the memory until advanced stages, together with progressive impairment that is usually faster, differentiate FTLD from AD, although the clinical evolution of both may be very heterogeneous.

In this type of dementia around 20-40% of the patients have a family history, although only 10-15% of the cases have an autosomal, dominant inheritance pattern **(Section 7).**

Different diagnostic criteria have been published. The most commonly used are the criteria of Neary[51] **(Appendix 1.10).**

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Atrophy of the frontal and/or temporal lobes is observed in the anatomopathological examination, which is usually asymmetric, and sometimes degeneration of black matter and atrophy of the basal ganglia. Different diseases with histological features have been defined, depending on the presence of certain protein inclusions (tau, progranulin, TDP-43). [6,52]

Atrophy of the frontal and/or temporal lobes is observed in the macroscopic anatomopathological examination, which is usually asymmetric. The majority of the cases of FTLD are characterised by the presence of certain intracellular inclusions and current nosology classifies the cases of FTLD into neuropathological subtypes, based on the most characteristic molecular and histochemical findings.[6,53,52] 85-90% of the cases present tau protein or TDP-43 protein deposits. The rest normally present FUS (*fused in sarcoma*) protein deposits, although there is a small percentage of cases where the identification of typical protein deposits is not possible according to current knowledge. Any of the different neuropathological entities may be expressed with any of the clinical syndromes described and vice-versa. The only exception that can be made is that when motor neuron disease is associated, it can be anticipated that the neuropathological correlate will not be a taupathy.

4.11. What other neurodegenerative diseases are accompanied by dementia?

Other neurodegenerative diseases that may be accompanied by dementia are:

Huntington's Disease: a hereditary neurodegenerative autosomal dominant transmission disease **(Section 7)**. The mutation is found in the Huntingtin gene (HTT) in chromosome 4, a protein with an unknown function, and it gives rise to a variable expansion of CAG triplets. The most affected cells are the spinal neurons of the striate. It occurs with motor (korea, dystonia, tremors, stiffness), cognitive (memory, executive functioning and visual-motor skills) and psychiatric (irritability, mania, depression, psychosis or obsessive-compulsive disorder) alterations. Cognitive disorders usually appear in advanced stages, although they may also appear in initial stages, especially in juvenile forms (Westphal variant). The most important deficiencies are disexecutive and visual-perceptive.[6,54]

Prion diseases or transmissible spongiform encephalopathies: Neurodegenerative processes characterised by the accumulation of pathological isoforms of prion protein, neuronal loss, gliosis and spongiosis. The most frequent is Creutzfeldt-Jakob disease (CJD). They are not very prevalent, and are accompanied by a variable combination of dementia, ataxia, myoclonus, pyramidal and extrapyramidal signs and behaviour alterations. It has a rapidly progressive picture and death usually occurs in less than 1 year. Prion diseases may occur sporadically, genetically or they may have been acquired iatrogenically.[6,55]

Progressive supranuclear palsy: a neurogenerative disease that is characterised by gait disorder, falls, postural alterations, akinetic rigid parkinsonism with axial prevalence, eye-motor alterations, pseudobulbar palsy and frontosubcortical cognitive alterations such as apathy and executive dysfunction. The pathology is characterised by tau protein deposits (4R isoforms) on neurons and glial cells in certain areas of the basal ganglia and brain stem. Due to its neuropathological characteristics, progressive supranuclear palsy is included within the frontotemporal lobar degenerations.[56]

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Corticobasal degeneration: neurodegenerative disease characterised by an asymmetric apraxia syndrome and frontal parietal dysfunction, feeling of foreign limb, loss of cortical sensitivity, myoclonus, focal dystonia, and signs of progressive supranuclear palsy. It is frequently associated with progressive aphasia or speech apraxia. It is an infrequent disease. The typical pathology consists of neuronal loss in frontal parietal cortex and black matter with astrocytic plaques, achromatic convex cells, and tau protein inclusions (4R isoforms) in neurons and glial cells. Due to its neuropathological characteristics, corticobasal degeneration is included within the frontotemporal lobar degenerations. Lacking histological confirmation it is called "corticobasal syndrome", as the same clinical syndrome can be produced by another pathological substrate; in addition, the pathology of CBD may give rise to other clinical syndromes. The term "corticobasal degeneration" is reserved for cases with histological confirmation.[52]

Other infrequent degenerative diseases: dementia with argyrophilic granules, spinocerebellar degenerations, leukodystrophies, Hallervorden-Spatz disease, familial encephalopathy with neuroserpin bodies, familial British and Danish familial amyloidosis, dementia with intranuclear inclusion bodies, etc.

Mixed dementias: overlapping of different neuropathological processes, although one type usually prevails over the rest. One of the most frequent is the combination of VD and AD. It is normal for both types of lesion to co-exist, with interaction between them. In each case, the clinical data and the neuroimaging findings must dictate which of the two pathologies is the most important in the patient's clinical picture. In this sense, it would be desirable to use terms such as "Alzheimer's disease with cerebrovascular pathology" or "vascular dementia with possible AD" instead of the mixed dementia diagnosis. The finding of mixed pathology is normal in neuropathological studies (Alzheimer's, vascular pathology, argyrophilic granules, synucleinopathy), which represented 53% of the cases in a review by the BrainNet consortium of 3304 brains of patients with dementia originating from European centres.[57]

4.12. What are vascular dementias?

VDs are dementias secondary to one or several vascular brain lesions, of whatever aetiology. They include the following entities:[6,46]

- Multi-infarct dementia: dementia secondary to the repetition of cortical infarcts in the medium or large calibre artery territory. It is the form of VD that most adapts to the classical pattern of acute onset dementia and stepwise evolution with worsening related to new vascular events. The cognitive and focal deficiencies depend on the location of the infarcts.

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- Strategic infarct dementia: dementia due to an infarct in a location that affects several cognitive functions. They include dementias due to infarcts in paramedian thalamus, angular gyrus, knee of the internal capsule, bilateral caudate or deep territory of the anterior brain artery.
- Subcortical vascular dementia: Accumulation of lacunar infarct or vascular lesions of the periventricular deep white matter due to disease of the small vessels, normally hypertensive (arteriolosclerosis); it may also be diabetic, due to amyloid angiopathy, hereditary angiopathies such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), hypercoagulability states or hypoxia. The course is usually progressive with frontosubcortical type mental impairment, focal signs, slowness, gait alteration and incontinence. The term "subcortical vascular dementia" eliminates the use of the former diagnosis of Binswanger's disease.
- Post-stroke dementia: any type of dementia that develops after a stroke.
- Mixed dementia: The most frequent anatomopathological findings in population-based studies of dementia is the combination of different alterations (amyloidopathy, synucleinopathy, tauopathy and vascular disease). The term, mixed dementia, is normally applied to the combination of AD and vascular disease.
- Dementia due to haemorrhagic lesions.

There are different diagnostic criteria that are based on the presence of dementia, focal signs and evidence of cerebrovascular disease. All of them have high specificity but very low sensitivity. The most commonly used criteria, NINDS/AIREN[58] **(Appendix 1.11)** permit the diagnosis of possible VD when there are focal signs, in the absence of neuroimaging, or when there is relevant cerebrovascular disease with no clear temporal relationship between dementia and stroke. The Hachinski ischaemia scale helps distinguish between VD and AD[59] **(Appendix 1.12)**. It is used to identify and grade vascular disease in general and it has high sensitivity and low specificity. Both patients with AD with cerebrovascular disease and those with multi-infarct dementia may have a high score.

There is not enough evidence to specify a vascular load threshold or to specify a necessary location of the lesions that define VD in neuroimage, and the diagnosis of VD must be based on the correlationship between the degree of vascular load and the clinical and neuropsychological data.[6,46]

The term **"Alzheimer's disease with cerebrovascular disease"** corresponds to patients who satisfy criteria of possible AD and who in turn have evidence of relevant cerebrovascular disease.

4.13. What is and how is secondary dementia classified?

Secondary dementias are those caused by a non-degenerative neurological disorder or that do not originate in the nervous system. The cause may be vascular, infectious, deficient, endocrine-metabolic, toxicological or due to other medical pathologies which, during the clinical evolution, may end up developing dementia.

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The processes that might cause dementia include structural lesions of the CNS (tumours, subdural haematomas, normotensive hydrocephalia), traumatic brain injuries, endocrinological alterations (hypothyroidism, hypercalcaemia, hypoglycaemia), nutritional alterations (deficiency of vitamin B_{12}, thiamin or niacin), infections (HIV, neurolues, Cryptococcus), hepatic and/or renal insufficiency, neurological diseases (multiple sclerosis), adverse pharmacological effects (benzodiazepines, beta blockers, anticholinergics), systemic autoimmune diseases (systemic lupus erythematosus, Hashimoto encephalopathy, neurosarcoidoisis), environmental toxins (heavy metals, organic hydrocarbides), as well as the effects of long exposures to toxics such as the case of alcohol.[42,6,60,35]

As a general rule, they are not very frequent, but as they usually accompany isolated dementia they are diagnosed by clinical context. The clinical record and execution of certain additional tests (neuroimage, analytics) help us distinguish primary degenerative dementias from secondary dementias, whose aetiology, in some cases, could be potentially treatable. However, it must be taken into account that potentially reversible causes are infrequent and that there is no clinical test-based evidence vis-à-vis its treatment being able to reverse dementia. [25]Furthermore, the presence of a process that is able to cause dementia does not mean that it is responsible for it. According to the NINCDS-ADRDA criteria of AD possible AD can be diagnosed when there is another brain disorder or another systemic process that is sufficient to cause a dementia, but which is not considered to be the real cause of it **(Appendix 1.6).**

4.14. What is understood by mild cognitive impairment?

Different cognitive impairment syndromes with respect to a previous state are included within the concept of mild cognitive impairment, also called light cognitive impairment, but which is not sufficiently intense to be considered dementia.[42]

MCI is an attempt to identify AD in its earliest stage. [61,62]To this end, special consideration was given to memory deficit. Its criteria to define MCI included the fact that the patient expressed memory problems, had low performance in memory tests (the point of a standard and average deviation below expected with respect to a population of the same age and education level was generalised as reference), whose global cognitive function was normal, had an autonomous life without the memory deficit having an influence on activities of daily living and did not satisfy dementia criteria.

The development and clinical use of the MCI concept demanded its classification to include the non-amnestic subtype, where there would be no memory alteration but other cognitive functions would be affected.[63]

For the European Alzheimer's Disease Consortium,64 the MCI diagnostic criteria would be:

- Subjective complaint of loss of memory by patient or by a valid informant (family or person living with them).
- Objective evidence of cognitive disorders: impairment of memory or of another domain.
- There must be a change respect to previous levels and for change must last for at least 6 months.
- No major repercussions on activities of daily living.
- Pathologies that might explain memory impairment, such as acute confusion syndrome, depression or mental retardation are excluded.

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- The dementia diagnostic criteria are not satisfied. This latter part is the most complicated to determine. It is necessary to define well what is understood by significant reduction of functional autonomy to talk about dementia, and there is no objective criterion to define it.

These criteria could be modified, especially in respect of the former, due to the fact that a non-amnestic MCI can be defined, that is, with no memory alteration.[63]

The SEN Behavioural Neurology and Dementia study group defends a broad concept of MCI that includes alteration in any cognitive area, of whatever aetiology, but, in turn it defines MCI as being attributable to AD when there is a combination of certain clinical features and diagnostic markers. The criteria proposed by the SEN are described in **Appendix 1.1.**[36,65]

Diagnosing MCI as early as possible is a key factor, due to the high probability of it being the first manifestation of a degenerative disease and entailing, therefore, a high risk of progression to dementia.

The diagnostic criteria of MCI are largely clinical, and perhaps they are not sufficiently operationalised, but they are useful to draw the clinician' attention to identifying a clinical situation that might get worse.

Some anatomopathological studies have shown that more than half the patients with MCI have senile plaques and neurofibrillary tangles in their brains, which are typical of AD. In vivo studies with amyloid marker radiopharmaceuticals (PIB-PET) or with amyloid determination and TAU in cerebrospinal fluid (CSF) have shown similar findings in the sense that approximately 60% of patients with amnestic MCI have PIB-PET and CSF patterns that are very similar to those of AD.

4.15. What types of MCI exist?

MCI is classified as amnestic or non-amnestic depending on whether it affects the memory or not. Depending on the number of cognitive functions affected, it is classified into MCI- single domain or MCI-multiple domains. [25]Petersen et al. [66]defend a classification into four groups: Amnestic with one single cognitive alteration, amnestic with multiple cognitive alterations, non-amnestic with one single cognitive alteration, and non-amnestic with multiple cognitive alterations.

4.16. What is the incidence and prevalence of MCI?

Given the absence of a unanimous definition, MCI does not have an exact epidemiology. Its incidence and prevalence depend, to a great extent, on the diagnostic criteria used in the studies performed and on their interpretation. The prevalence varies, according to data of a large-scale cross-cutting population based study in the United Kingdom, between 2.5 and 41%.[66]

In the LEILA75+ study, the prevalence varied between 3 and 20% depending on the criteria used. [67]The incidences of amnestic MCI varies between 9.9 and 40.6 per 1000 people-year according to a recent SR of studies on incidence of MCI, [68]and that of non-amnestic MCI between 28 and 3.63 per 1000 people-year. These findings indicate the need for there to be commonly-agreed and operational criteria.

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4.17. What are the risk markers of conversion of MCI to dementia?

The main use of the diagnosis of MCI is to identify population with a greater risk of suffering Alzheimer's disease in pre-dementia stage (prodromic AD). This population group will be converted into dementia in 10 to 15 % of the cases every year.[37]

In the Canadian consensus conference of 2006[69] they offer a list of possible markers that are currently under study, which have shown differences at group level between patients with MCI who have progressed to dementia and those that have not. Some variables that suggest a greater risk are: Age, number of neuropsychological areas altered, deficit in memory encoding and storage, incipient alteration of activities of daily living, hippocampus atrophy in magnetic resonance, cortical hypometabolism in PET or focal hypoperfusion in SPECT, accumulation of amyloid markers in SPECT, decrease of protein Aβ-42 and/or increase of tau protein in cerebrospinal fluid or the presence of APOE allele ε4. [6,70]

Observational study, 2+/2– Expert opinion, 4

The PIB PET has proved to be very reliable as a marker of the accumulation of amyloid in pathological anatomy. It happens that patients with MCI and positive PIB progress to probable Alzheimer's disease whilst the negative PIB do not do so.[71,72,73,74]

PET with glucose (FDG) has shown sensitivity and specificity figures of over 80% to predict progression and diagnose probable AD in a recent meta-analysis. [75,76]

The CSF data begin to be convincing, too. Patients (up to 100% according to the ADNI study) with MCI who develop probable Alzheimer's disease have biochemical patterns of AD in their CSF.[75,77,78,79,80]

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Summary of evidence

2+/2–	There is evidence based on case and control, and cohort studies, the majority of which are not masked and with no neuropathological confirmation, that some biological markers (age, encoding and storage deficiency, incipient alteration of the ADL, hippocampus atrophy, hypometabolism or focal hypoperfusion in PET/SPECT, accumulation of amyloid markers, decrease of Aβ-42 or increase of tau in CSF, presence of APOE allele ε4) are associated with a higher risk of progression to dementia in patients with MCI at group level, not being validated for use in clinical practice.[69,37,6]

Recommendations

C	Different biological and neuroimaging markers can be used to help predict the progression of MCI to dementia in a research context, but they cannot be recommended for use yet in normal clinical practice.

4.18. Is there any treatment that modifies the progression of MCI?

RCT have been performed with acetylcholinesterase inhibitors (ACE inhibitors) [donepezil, rivastigmine and galantamine, NSAID (rofecoxib), replacement therapy with oestrogens, ginkgo biloba and vitamin E, which have not shown any symptomatic benefit or reduction of the risk of progression to dementia in patients with MCI.[69,81]

RCT, 1++/1+/1– Observational study, 2+/2–

At times, MCI is a clinical manifestation of a potentially reversible process. The results of RCT and cohort, variable quality, studies on the effect of cognitive stimulation activities or physical training programmes have not provided enough evidenced to prevent the progression of MCI.[69]

Summary of evidence

1++/ 1+	The treatment with ACE indicators and with other drugs such as NSAID, oestrogens, ginkgo biloba or vitamin E have not shown any symptomatic benefit or modification of risk of progression to dementia in patients with MCI in quality RCT.[69]
1+/1–/ 2+/2–	The cognitive stimulation or physical exercise programmes have not provided consistent evidence that they can prevent progression to dementia in variable quality studies and with methodological limitations.[69]

Recommendations

A	The use of ACE inhibitors to avoid or delay the progression of MCI to dementia is not currently recommended.
A	The use of NSAID, replacement therapy with oestrogens, ginkgo biloba or vitamin E to avoid or delay the progression of MCI to dementia is not currently recommended.
C	There is not enough evidence to recommend cognitive stimulation or physical exercise to avoid or delay the progression of MCI to dementia.

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5. Pathophysiology and risk factors of dementias

Questions to be answered

5.1. What are the pathophysiological mechanisms of degenerative dementia?
5.2. What are the pathophysiological mechanisms of vascular dementia?
5.3. What are the risks factors of dementias?

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5.1. What are the pathophysiological mechanisms of degenerative dementias?

The term, neurodegeneration, is applied to name a progressive and inexorable phenomenon of loss of activity, of tropism and of nervous tissue functions, whose cause is not due to a known external agent or to a severe accident with brain injury. Thus, the term neurodegeneration excludes brain injury caused by vascular accidents, trauma, infectious diseases, inflammatory diseases, neo-formative processes and congenital malformation diseases. Some ailments known previously as neurodegenerative diseases are currently considered to be included in other areas. For example: Mitochondrial cytopathies, peroxisomal diseases, amino acid metabolism diseases or lysosomal lipid and carbohydrate metabolic diseases.

A common fact of neurodegenerative diseases is the selective loss of certain populations of neurons, and this selective neuronal loss is the morphological substrate of the main clinical manifestations of each disease. Thus, the affectation of the entorhinal cortex, hippocampus and deep regions of the temporal lobe is the neuropathological substrate of the loss of recent memory in AD and in argyrophilic granule dementia, whilst the greater vulnerability of the frontal and temporal lobes explains the syndrome of frontotemporal dementia in different diseases, regardless of the molecular defect of each one of them. Other typical examples are the affectation of the black matter in PD and other parkinsonisms, the degeneration of the cerebellum in dominant spinocerebellar ataxias, the degeneration of striate nuclei and of the brain cortex in HD and the selective affectation of the upper and lower motor neurons in amyotrophic lateral sclerosis. This relationship between the clinical symptoms and the neuropathological lesions, together with the name of the author who discovered the disease, has been used for many years to classify the different neurodegenerative diseases.

Environmental factors and genetic factors of risk that intervene in the sporadic forms are known in practically all degenerative diseases. The percentage of family cases due to mutations of individual genes amounts to 5-10% in the majority of the neurodegenerative diseases. Curiously, mutations of different genes may give rise to what is known today as one same disease. Thus, familial early onset AD is associated with mutations of APP, PS1 and PS2, whilst familial PD with dominant or recessive autosomal inheritance has been proved to be linked to mutations of such different genes as those that encode α-synuclein, parkina, PINK1, DJ1 ad LRRK2, among others. Other diseases only appear in the context of dominant or recessive autosomal inheritance, and the appearance of new cases is due to the appearance of a new mutation. That is the case in HD, in spinocerebellar ataxias with dominant autosomal inheritance and in dentatorubropallidoluysian

atrophy or in Friedreich's ataxia, respectively. The prion diseases, where there are sporadic, familial and transmissible forms, are an exception. A curious fact also occurs in the case of prion diseases: the disease seems different depending on the mutation in PRNP. Thus, pictures of familial CJD or of lethal familial insomnia associated with the D178N mutation in PRNP are known, the former with methionine at codon 129 of the mutated allele and the latter with valine at the same codon. Different diseases emerge from the PRNP mutation in other locations that give rise to the Gerstmann-Straüssler-Scheinker disease and to other hereditary prion diseases with clinical pictures of multisystemic degeneration.

Genetic studies have led to the discovery of the causal agents of the different diseases, but they have produced certain categorisation confusions, as the apparently same disease is caused by mutations in different genes. In this sense, there is no doubt that Huntington's disease is a huntingtinopathy as the cause of the disease is an increase in the number of CAG triplets in the Huntingtin gene in chromosome 4p16.3, or that Friedreich's disease is a frataxinopathy resulting from a mutation in the gene of the frataxin mitochondrial protein in chromosome 9q13-21.1 and that it entails a very reduced protein expression. However, PD, from a genetic viewpoint, may be an α-synucleinopathy, a parkinopathy, a PINK1pathy or a DJ1pathy, among others, depending on the mutated gene causing the familial PD.

The majority of the neurodegenerative diseases are associated with the accumulation of abnormal protein aggregates. This fact has given rise to a classification of the neurodegenerative diseases that depends on the predominant abnormal protein accumulated in the brain. Taupathies are known where there is an accumulation of hyperphosphorylated tau in the neurons, and at times, in the glial cells; the α-synucleinopathies where there are deposits of phosphorylated, nitrated, oxidised α-synuclein and with aggregability and solubility modifications; prionopathies, where the normal prion protein has been transformed into a protein with aberrant folding in beta laminae, or the amyloidopathies (amyloidosis) where there is an accumulation of amyloid and between which there are β-amyloidopathies, gelsolinopathies, cystatinopathies or amyloidosis linked to mutations in the ITM2B gene (BRI2) caused by the ABri and ADan amyloidogenic peptides.

Taupathies include Pick's disease, corticobasal degeneration, progressive supranuclear palsy, dementia with argyrophil granules, and frontotemproal dementias linked with mutations of the tau gene *(MAPT)* among others. PD, DLB and multisystemic atrophy are included in β-synucleinopathies, among others. AD and Down syndrome are expressed as a taupathy and a β-amyloidosis, and as a predominantly amigdalar α-synucleinopathy in many cases.

In a small proportion of cases, the molecular data coincide with specific genetic defects and the genetic and protein alteration nomenclatures coincide. For example, frontotemporal degenerations linked to MAPT mutations are taupathies from a genetic and molecular viewpoint, but not all taupathies are the result of mutations of the tau gene.

Although the pathogeny is not totally known, there are different alterations that are common to the majority of the neurodegenerative diseases. One of them is the presence and accumulation of abnormal proteins. This aggregation is due to the production of abnormal protein, either due to genetic causes (mutations) or to post-translational changes of the protein, such as phosphorylation, oxidative lesion or structure modifications; but also to the loss of cellular capacity to destroy the abnormal proteins through the autophagic pathways or the ubiquitin proteasome system. The altered proteins accumulate on the inside of the neurons and glial cells, and give rise to typical inclusions: Neurofibrillar degeneration in AD and taupathies, Lewy bodies in PD and DLB, intranuclear and cytoplasmic inclusions in expanded CAG triplet diseases, immunoreactive inclusions for TDP-43 in amyotrophic lateral sclerosis and in the majority of non-tau frontotemporal degenerations. Such inclusions are currently interpreted as residual structures of the disease, not as causal agents of the degeneration. There is also a deposit of proteins in the extracellular space, as occurs with the amyloid deposits in AD and other cerebral amyloidoses, and with deposits of

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protease resistant PrP in prion diseases.

Other common changes in the majority of neurodegenerative diseases are mitochondrial alterations, oxidative damage to DNA, RNA, to lipids and to proteins, secondary alteration of energy pathways and the modification of the lipid composition of the cellular membranes. All of this entails a reduction of energy production and an excess demand which leads to neuronal energy fatigue.

The energy defect, the difficulty in the exchange of cellular components, the reduction of trophic signals by neighbouring cells and the "primary" defect of each disease lead to neuron death caused by different mechanisms, including apoptosis, necrosis, autophagy or intermediate or complex forms.

The classification of neurodegenerative diseases is currently a convention with instrumental implications. It is a classification that is useful to understand and classify the different diseases, but it is not a dogma. New diseases or new mechanisms of better known diseases appear frequently. A progressive change in the classification and categorisation of the current neurodegenerative diseases is likely to occur in the next few years.

5.2. What are the pathophysiological mechanisms of vascular dementias?

VD is a very heterogeneous entity and dementia may occur due to multiple mechanisms (**question 4.13**). Mixed dementia is also frequent. This term is normally applied to the combination of AD and vascular disease and for which there are no clinical or neuropathological criteria.[6]

VD occurs due to the accumulation of ischaemic or haemorrhagic origin brain lesions. In multi-infarct dementia, infarcts may have atherothrombotic, cardioembolic origin in the territory of medium or large calibre arteries and they affect more or less extensive cortical or cortico-subcortical areas.

Subcortical vascular dementia occurs in the majority of the cases because of a disease of a small vessel that gives rise to the accumulation of lacunar infarcts and/or changes in white matter (leukoaraiosis). The most frequent aetiology is hypertensive arteriolosclerosis. It may also be due to diabetic angiopathy, hereditary angiopathies (CADASIL), amyloid angiopathy and, in rarer cases, it may be related to states of hypercoagulability. The etiopathogeny of changes in white matter is not altogether clear. Not all the changes in white matter have a clinical effect in the form of cognitive impairment. Punctiform lesions or non-confluent patch lesions with limited extension are often asymptomatic. Lesions that are associated with cognitive impairment, subcortical dementia and motor disorder are periventricular lesions that spread to the deep white matter, extensive confluent patch lesions and diffuse lesions. In these cases there is a clear association with arteriolosclerotic changes in the vessels of the white matter and the ischaemic mechanism has been demonstrated. Punctiform lesions are the reflection of the dilation of the Virchow-Robin perivascular spaces and they may be associated with global atrophy. An anatomopathological correlation of patch lesions may be perivascular spongiosis and the extravasation of plasma proteins into brain parenchyma. In any case, these mechanisms would also have a relationship with pathology of the wall of small deep vessels. The role of venous stasis due to venous colagenosis in the etiopathogeny of leukoaraiosis has also been postulated. The pathology of the small brain vessels may also give rise to cortical micro-infarcts. This pathological finding, which is not detectable with normal neuroimaging techniques, is frequent in patients with VD and also in patients with AD and associated amyloid angiopathy.

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The etiopathogenic mechanisms of VD due to strategic infarct correspond to the mechanisms that produce capricious location infarcts.

The existence of a form of VD related to hypoperfusion or hypoxia mechanisms has been defended rather than classical atherothrombotic, cardioembolic or lacunar infarct mechanisms. There would be an acute form related to episodes of intense global cerebral anoxia (due to cardiorespiratory arrest, for example) and another more "chronic" form secondary to the repetition of less important hypoperfusion-hypoxia episodes (bradyarrhythmias, syncopes, sleep apnoea, repeated pneumonias, epileptic crises, anaemia, etc.). The existence of situations of symptomatic misery perfusion from the cognitive viewpoint, which are reversible beyond the confusion states that are related to hypotension, hypoxhaemia or hypercapnia, has not been demonstrated. The proven efficacy of carotideal surgery as treatment of VD has not been demonstrated. In any case, this form of VD due to hypoperfusion-hypoxia, would be the result of the presence of structural brain damage: border zone infarcts, changes in white matter or selective hippocampus or cortical vulnerability phenomena. Hippocampus sclerosis could be due to hypoxic mechanisms in some cases, but whether its origin is vascular or degenerative has still not been definitely clarified.

The accumulation of brain haemorrhages may give rise to dementia (haemorrhagic VD). The origin may be hypertensive angiopathy, but amyloid angiopathy must be suspected in the case of lobar haemorrhages. The importance of the role of microhaemorrhages detected via magnetic resonance is becoming more and more consolidated, if gradient echo sequences are applied. Secondary microhaemorrhages to amyloid angiopathy are usually located in the posterior (parieto-occipital) region and are juxtacortical whilst those related to hypertensive angiopathy tend to be located in deep regions.

Some rare forms of VD may respond to inflammatory (vasculitis), infectious or metabolopathy (Fabry's disease) mechanisms.

The etiopathogeny of many cases of dementia related to vascular cerebral pathology depends on the concomitant presence of AD. The presence of a brain infarct in the modification and precipitation of the expression of a latent AD has been extensively proven. The interaction between vascular disease and AD relating to the occurrence of cognitive impairment and dementia may vary considerably. It could be a simple accumulation of brain damage due to the coincidence of both pathologies but a specific etiopathogenic interaction cannot be ruled out. AD may be the cause of ischaemic and haemorrhagic vascular pathology due to the accumulation of β-amyloid on the vascular wall and vice-versa, the pathology of the vascular wall could be a factor that favours the accumulation of β-amyloid if its elimination mechanisms were altered through the blood-brain barrier. [82]

5.3. What are the risks factors of dementia?

The risk factors of dementia may be divided into non-modifiable and potentially modifiable. There are also protective factors. However, it must be taken into account that there are no prospective RCTs with prolonged follow-up period that prove that the modification of certain risk factors may reduce the incidence of dementia. It is also important to remember that the finding of an epidemiological association between a clinical or social-demographic variable and a greater or lesser risk of dementia does not entail a causal relationship and that lacking well-designed RCT, we cannot state that an action on this variable would modify the risk of dementia.

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1. Non-modifiable risk factors

Age

Age may be a risk factor per se or it may reflect the effect of the time when other factors have an influence. Age is the greatest risk factor for AD, VD and DLB, but other less frequent dementias (FTLD, CJD, HD) are more common in midlife. [25]In general, the prevalence of AD and of VD doubles every 5 years, approximately.

Population-based case and control study, 2++

The incidence of dementia remains more or less stable up to 65-70 years of age (around five cases per 1000 people-year) and from the age of 70 onwards, the growth is exponential (up to 65-75 cases per 100 people-year at the age of 90).[21,24]

Females

Several studies associate the female sex with a greater risk of suffering dementia, especially AD, although others do not observe this association until very advanced ages. [83]With reference to VD, the risk is greater in men in all age groups, and there are also less differences in older age groups. [84]However, these differences could be due to other risk factors classified as modifiable.

Population-based case and control study, 2++

Family history of dementia

First-degree relatives of patients with AD have between 10 and 30% more probabilities of developing the disease. [85]It is possible that if the onset of dementia in relatives takes place after the age of 75-80, this family history may not entail a greater risk.

Population-based case and control study, 2++

Genetic factors related to AD

Genetic origin Alzheimer's disease represents just 0.5-1% of the cases **(Section 7)**. Only 10% of the cases of presenile onset AD (< 60 years) are due to rare high-penetrance mutations (dominant autosomal). [86]The most frequent are those of PSEN1 (30-70%), followed by APP (10-15%) and PSEN2 (< 5%) (www.genetests.org). No mutation has been identified for the others, to date.

Population-based case and control study, 2++

No simple causal mutation has been identified until now for late onset AD. It is believed that the majority of the cases are complex and influenced by a mixture of genetic and acquired risk factors. [87]Many genes have been involved but only the APOE α4 allele has been confirmed as a risk factor in large population-based studies.

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The association between APOE ε4 and AD is greater in women than in men, and between the ages of 55 and 65, and it is weaker in older ages. [87]The risk of late onset AD is greater in homozygote's APOE ε4 (8x) than in single copy carriers (3x), whilst having an ε2 allele has been associated with a lower risk of AD and a somewhat higher onset age[89] Apo ε4 is also probably a risk factor for VD and DLB. [25]An MA on the possible relationship between APOE ε4 and PDD did not show conclusive results due to the heterogeneity of the studies.[90]	Population-based case and control study, 2++
Multiple polymorphisms have been studied and some have been associated with AD, but their real impact on the disease as well as their interaction with other factors and genes is unknown, so they currently have no clinical utility.[91,87]	Population-based case and control study, 2++

2. Potentially modifiable factors

The majority of the studies that associate non-genetic risk factors with AD or dementia are usually cohort studies, but there are no RCT that permit establishing solid recommendations.

Vascular risk factors

Having suffered a cerebral vascular accident (CVA) prior to dementia is a diagnostic criterion for VD. However, a CVA also increases the risk of suffering AD (RR ~1.8) and dementia in general. Likewise, the presence of silent infarcts in imaging tests has been associated with a greater risk of VD and of dementia of any cause.[92]	SR of observational study, 2+/2–
In a SR that included longitudinal population based studies that evaluated the incidence of dementia in connection with diabetes mellitus (DM) (n = 14), high blood pressure (HBP) (n = 13), dyslipemia (n = 8) and obesity (n = 9), the four factors were associated with a greater risk of dementia; the most consistent are DM and obesity. The magnitude of the effect was similar (OR of around 1.5 for "any dementia"). The risk of dementia was greater in studies that evaluated HBP, obesity and dyslipemia in midlife than in the elderly, whilst DM confers a greater risk of dementia in the elderly.[93]	SR of observational study, 2+/2–

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HBP

The relationship between HBP and dementia is complex. Data from the Kungsholmen project, a Swedish population-based cohort study, showed that both a high systolic BP (> 180 mmHg) and a systolic BP < 140 mmHg are associated with a greater risk of AD and dementia, in general, in the same population. [92]This association could vary depending on the age. Longitudinal studies have shown a more marked consistent relationship between HBP in midlife (40-64 years) and cognitive impairment in the elderly (>65 years), in untreated patients. Some of these studies also indicate an association between HBP in midlife and the incidence of AD and dementia in general in the elderly, and in one of these studies, this association was only present in untreated patients. With respect to HBP in the elderly, the data are inconsistent, as some studies have found an association with cognitive impairment or dementia whilst others have not. On the other hand, a consistent association has been found between low blood pressure in the elderly and a greater risk of cognitive impairment or dementia. [94,95]

Observational study, 2+/2–

Hypercholesterolemia

Longitudinal studies have shown that the increase of total cholesterol in midlife is associated with a greater risk of dementia and AD. However, a SR of 18 prospective studies with a control period of between 3 and 29 years did not find any association between total cholesterol and AD or dementia in general during the end stage of life. [96]

A MA of two studies did not find any significant association between total cholesterol (in middle age or in the elderly) and VD. [96]

SR and MA of observational study, 2+/2–

These results suggest that high cholesterol is a risk factor in midlife but not in the elderly, and that the cardiovascular risk factors may be different for AD and VD.

Diabetes Mellitus

In several SR, the incidence of dementia, AD and VD was higher in individuals with DM than without DM in the majority, but not all the studies.[93,97,98,99]

SR of observational study, 2–

A prospective study on nurses found that the duration of DM was associated with a lower basal cognitive performance and with an increase in the risk of cognitive impairment after 2 years, and that the treatment of DM reduced this risk. Furthermore, hyperinsulinaemia seems to increase the risk of AD.[99] However, the possible effect of the control of glycaemia and of the comorbidity with cerebrovascular disease and HBP is not analysed.

Observational study, 2-

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In the Cardiovascular Health Study,[100] patients with DM type 2 and APOE ε4 had a greater risk of AD (RR 4.99) than those who did not have either of the two risk factors, and greater than those that only had DM (RR 1.623) or only APOE ε4 (RR 2.50) separately. The joint risk is greater than expected due to a simple additive effect. No increase in risk of VD was found for either of the two risk factors. This study suggests that the presence of APOE ε4 allele modifies the risk of AD in diabetics.

Observational study, 2-

Hyperhomocysteinaemia

A prospective study has associated hyperhomocysteinaemia with an increase in the incidence of dementia due to any cause and AD. [92,84]However, no cognitive improvement has been observed when the homocystein levels were normalised by taking vitamin B complex.[84]

Observational study, 2+

Nicotine addiction. Lifestyles.

Obesity. Body weight in lifestyles.

Anaemia

A MA of two longitudinal studies that associated low haemoglobin and dementia showed significant results (HR 1.94). A retrospective study of cases and controls presented similar results but only significant in women, and a study on women did not obtain significant data. There is little literature in this regard, and the methodology is variable, so no conclusions can be drawn.[101]

MA of observational study, 2–

Other biological factors:

Hyperthyroidism

One study associated low levels of TSH with a greater risk of suffering AD. [92]

Observational study, 2+

Levels of sex hormones in blood

There are few studies. Data from the Rotterdam study, a population-based study monitoring chronic diseases, including dementia, associate high levels of total estradiol with a 43% increase of suffering dementia in women, whilst another longitudinal study on a male population associated the index of free testosterone with a lower risk of suffering AD.[92]

Observational study, 2-/2+

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Depression

A MA of case and control, and cohort studies, carried out in 2006, concluded that depression is not only a prodromic symptom but also a risk factor of suffering AD, and the interval between the diagnosis of depression and the diagnosis of AD is correlated with a greater risk of AD (OR 2.03; 1.53 if it is adjusted by years elapsed between the onset of depression and the development of dementia).[102]	MA of observational study, 2++

Lifestyles:

Nicotine addiction

Although the initial case and control studies suggested that smoking reduced the risk of dementia, more recent longitudinal cohort studies have identified a greater risk of AD (RR 1.99) in smokers.[92]	Case and control study, cohort study, 2++/2+
An analysis of four European population-based studies concluded that current smokers, but not ex-smokers, had a greater risk of AD.[87]	Population study, 2++/2+
In a MA of 19 prospective studies, smokers had a greater risk of dementia than non-smokers (RR 1.79 of AD, 1.78 of VD, 1.27 of dementia) than ex-smokers (RR 1.7 of AD, but no difference for VD and dementia in general).[103]	MA of observational study, 2++/2+
Another more recent MA found a greater risk of AD in current smokers (OR 1.59), a non-significant risk of VD or non-specific dementia and that there was a clear relationship in ex-smokers. [104]This MA concludes that being a smoker increases the risk of AD, and perhaps of other dementias, although it must be taken into account that very different studies have been combined in the MAs.	MA of observational study, 2++/2+

Diet rich in fat and poor in omega-3

Biological and epidemiological studies suggest that a reduced intake of omega-3 polyunsaturated fatty acids is associated with a higher risk of dementia due to any cause (RR 2.4). Likewise, another longitudinal study puts forward that the Mediterranean diet and the consumption of fish are associated with a decrease in the risk of AD (RR 0.3) and of dementia in general (RR 0.4-0.8). The consumption of crustaceans has also been associated with a lower risk of VD (RR 0.45).[87,92]	Observational study, 2+/2–

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A cohort study found no effect of the consumption of fish and omega-3 fatty acids on the cognitive function in normal ageing, whilst in some studies, its consumption showed a tendency to reduce the risk of dementia and improve cognitive functioning.[105]	Cohort study, 2+/2–
According to a SR of 2005, which included four cohort studies and a low quality RCT, the available data are not enough to obtain conclusions.[105]	SR of observational study and RCT, 2+/2–/1-

Physical activity

It has been associated with a decline in the incidence of dementia. In a Canadian study, the answer "yes" to a question on regular exercise was associated with an RR of 0.69 of developing AD in those who did more exercise than walking three or more times a week. This association was also observed in the Cardiovascular Health Study when it compared the quartile of people who consumed most energy every day doing exercise, with the quartile of those that consumed the least, both for dementia due to any cause and due to AD (RR 0.5-0.6). [92]	Observational study, 2+/2–
A relationship between physical activity and less risk of developing dementia was also observed in one SR.[21]	SR observational study, 2+/2–

Intellectual activity

Carrying out regular intellectual activity has also been associated with a decrease in the risk of suffering dementia in longitudinal studies, especially in individuals who carry out new tasks or tasks they are not familiar with. There also seems to be a relationship with the type of work: The most challenging and complex work would have a protective effect.[21]	Observational study, 2+/2–

Consumption of alcohol

The moderate consumption of wine (250-500 mL/d) has been associated with a lower risk of dementia (RR 0.6) and of AD (RR 0.53) compared with a higher or lower consumption. [92]A study on nuns also showed that the consumption of < 15g/d reduced the risk of dementia but the consumption of 15-30 g/d did not produce any benefit. Another study [99]showed that the consumption of 1-6 drinks/week was associated with a lower risk of dementia and of AD (OR 0.46) and that the benefit was lost at a higher consumption (7-13/week OR 0.69, > 14 OR 1.22). The type of drink is not important.[92]	Observational study, 2+

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A recent MA on 23 longitudinal studies suggested that the moderate consumption of alcohol may protect from dementia (RR 0.63) and from AD (RR 0.57), but not from VD (RR 0.82) or cognitive impairment (RR 0.89), but the studies are very heterogeneous vis-à-vis the duration of the control period, measurement of the alcohol intake, inclusion of real teetotallers, and confusion factors.[106]	MA observational study, 2+
Consumption of coffee	
In a SR that included two case and control studies, and two cohort studies, the consumption of coffee was associated with a significant reduction of the risk of suffering AD (weighted RR 0.7), although the authors warn that the great heterogeneity between the studies may affect the results.[107]	SR of observational study, 2+
Body weight	
It was observed in a longitudinal population-based study on women that a greater body mass index (BMI) was associated with greater atrophy of the temporal lobe.[84]	Observational study, 2–
A SR and a MA of prospective cohort studies showed a U-shaped association between BMI and dementia, with an increase in risk for obesity and also for underweight. In the case of obesity, the overall OR was 1.8 for AD and 1.73 (non-significant) for VD,[108] and it was greater in studies with a longer control period and lower basal age.	SR of observational study, 2++
In another SR that focuses on the risk of dementia due to any cause and BMI, eight studies were selected, four of which found significant differences and the other four none, above all analysing overweight and obesity. The articles that published statistically significant differences had a large sample size, so the authors suggest that the non-significance could be due to a lack of statistical power, or that the association is complex, due to different cardiovascular risk factors that could act as a confusion factor in the relationship between BMI and dementia. Thus, they conclude that more studies are necessary to determine this relationship. [109]	SR of observational study, 2+/2–
Craniocerebral trauma	
In studies performed on soldiers, who were hospitalised due to trauma with loss of consciousness, a RR was observed of between 2.3 and 4.5 of AD or dementia in general, depending on the severity of the trauma. However, this association has not been found in other studies.[92]	Observational study, 2–

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Social-demographic factors:

Schooling level

A low or intermediate schooling level is associated with a higher risk of dementia and AD compared with a high level. [110,111,21] A lower risk of AD has also been observed in people who participate in cognitive activities and a lower risk of AD and VD in people who participate in cognitively demanding leisure activities. [25,87] These findings have given rise to the brain reserve theory.	Observational study, 2+
In a MA of cohort studies, and case and control studies, a significantly higher risk of AD is estimated (OR of around 1.8) in people with low schooling level, compared with those with a high level, which is not significant in other dementias. [110]	MA of observational study, 2+
A SR of cohort studies concluded that a high schooling level delays the onset of dementia in AD, but does not shorten survival after diagnosis.[112]	RS of cohort studies, 2+

Social media, civil status

There are few studies. Divorced people or people who have never married could have a greater risk of suffering dementia. In the Kungsholmen project, an index was drawn up with different social components (marital status, friendships, having been a mother or a father, living with others), and a decreasing curve of the risk of suffering dementia was observed the greater the index. [21]	Observational study, 2-

Socioeconomic level

Community epidemiological studies, with variable methodology, suggest an association between low socioeconomic level and a greater incidence of dementia, but the data are not consistent in all the studies; the association may depend on other variables such as age, sex or education level, and the results are difficult to interpret. The existing evidence is not enough to support the association between socioeconomic level and development of dementia. [21]	Observational study, 2-

Exposure to toxins

Environmental exposure to pesticides and fertilisers has been associated with a greater risk of suffering VD (RR 2.05) and the exposure to fumigants and exfoliates to a greater risk of AD (RR 4.35) in prospective cohort studies in Canada.[92]	Observational study, 2+

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In one SR that included 24 studies (21 case and control studies, and 3 cohort studies) on the association between occupational exposure to toxics and AD, a relationship between exposure to pesticides and AD was observed, consistent among the different studies, whilst, due to the inconsistency of the results and to the low quality of the studies, no relationship was found between AD and exposure to solvents, lead or aluminium.[113]

SR of observational study, 2++

Exposure to low frequency electromagnetic fields

One MA suggested an increased risk of AD in men who were occupationally exposed (RR 2.05). The studies are very heterogeneous. No dose-response relationship was found.[114]

MA of observational study, 2–

In another review, the authors consider that the relationship between the electromagnetic fields and the risk of AD is not consistent and that the studies are biased.[113]

SR of observational study, 2–

Use of drugs

Statins. Hypercholestolaemia.

Non-Steroid Anti-Inflammatory drugs (NSAID)

Although one SR did not find statistically significant differences between the chronic consumption of NSAIDs and a lower risk of suffering AD or dementia in general, a more extensive and recent SR estimates that exposure to NSAIDs is associated with a decrease in the risk of dementia due to any cause in prospective (RR 0.74) and non-prospective (OR 0.51) studies. The risk is similar in ibuprofen, which reduces peptide Aβ-42, and naproxen, which does not reduce it.[92]

SR of observational study, 2++

Benzodiazepines

The results of the studies are inconsistent. Some prospective studies estimate an increase in the risk of dementia, whilst in others there is a reduction.[92]

Observational study, 2-

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Vaccines

Data from the Canadian Study of Health and Ageing showed that individuals who had been vaccinated in the past for diphtheria, tetanus, poliomyelitis or flue had a lower risk of developing AD than those who had not been vaccinated.[92]	Observational study, 2-

Vitamins for hyperhomocysteinaemia. Hyperhomocysteinaemia.

Hormone replacement therapy (HRT)

A Cochrane SR and a MA of observational studies and of RCT[116] did not observe a consistent benefit of HRT on cognition and the risk of dementia in cognitively intact post-menopause women over 65.	SR and MA of observational study and RCT, 1++
Furthermore, the largest RCT performed (WHIMS: *Women's Health Initiative Memory Study*) showed that HRT almost doubled the risk of dementia of any cause and of cognitive impairment.[84]	RCT, 1+

Some authors suggest that the discrepancy between the protective effect found in some observational studies and the higher risk of dementia shown in this RCT could be due to a bias, due to the greater tendency of women with a healthier lifestyle to use HRT, or to the fact that the results of the WHIMS are not applicable to the population of under 65s, which was excluded from the study, whilst in observational studies, HRT began during menopause and ended before the age of 65. There could be a perimenopause window where oestrogens would be protective, whilst from the age of 65 onwards, they would increase the risk.[117,118]

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Summary of evidence

Age, sex, first-degree family background and APOE ε4 allele	
2++	The main risks factors of non-modifiable dementia are: age (main risk factor for AD, VD and DLB),[25,21,24] sex (AD is somewhat more frequent in women and VD in men),[83,84] family background (10-30% more risk of AD in first degree relatives affected)[85] and APOE ε4 allele (greater risk of AD)[87,91,90,88,86] according to population-based studies, and case and control studies.
Vascular risk factors	
2+/2–	Vascular risk factors influence the risk of dementia according to cohort studies. This relationship is complex and the results are difficult to interpret due to their variability and the many different confusion factors.[92,93]
HBP	
2+/2–	HBP in midlife, especially if not treated, has been associated with a greater risk of developing AD or dementia in general, in longitudinal cohort studies. In the elderly, on the contrary, an association has been observed between low blood pressure and dementia.[92,94,95]
Hypercholesterolaemia	
2+/2–	High total cholesterol in midlife has been associated with a greater risk of developing AD or dementia in general, but not VD in cohort studies.[96]
Diabetes Mellitus (DM)	
2-	Diabetes mellitus has been associated with a higher risk of dementia in the majority of the studies but not all of them. The presence of APOE ε4 allele increases the risk of AD in patients with DM type 2.[100,99,93,97,98]
Hyperhomocysteinaemia	
2+	Hyperhomocysteinaemia was associated with a higher risk of AD and dementia in general in one prospective study.[92,84]

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Anaemia, TSH or sex hormone levels.	
2-	Anaemia[101] and alterations of the TSH[92] or sex hormone[92] levels have been associated with a higher risk of dementia in some studies.
Depression	
2++	Depression increases the risk of AD (OR of around 2) and the interval between the depression diagnosis and the AD diagnosis correlates with the risk of AD, according to a MA of cohort studies, and case and control studies.
Nicotine addiction	
2++/ 2+	Being an active smoker (not being an ex-smoker) is associated with almost twice the risk of suffering AD according to at least two MA of prospective studies.[103,104]
Diet rich in fat and poor in omega-3	
2+/ 2–/1–	The consumption of omega-3 fatty acids (fish, Mediterranean diet) could reduce the risk of dementia according to data from observational and biological studies.87,92 However, one SR that included four cohort studies and one low quality RCT did not find enough evidence to draw conclusions.[105]
Physical and intellectual activity	
2+/2–	The execution of physical and intellectual activity is associated with a lower risk of AD or dementia in the majority of longitudinal studies,[92,87,21] but it has not been possible to determine what type and how much activity is necessary or the mechanisms whereby this association occurs.
Consumption of alcohol	
2+	The moderate consumption of alcohol, but not excessive consumption or abstinence, is associated with a lower risk of AD and dementia, according to a MA of 23 longitudinal studies.[106]
Consumption of coffee	
2+	The moderate consumption of alcohol, but not excessive consumption or abstinence, is associated with a lower risk of AD and dementia, according to a MA of 23 longitudinal studies.[106]
Body weight	
2++/ 2+/2–	Obesity and underweight have been associated with a higher risk of dementia according to a meta-analysis of prospective cohort studies (for obesity, OR of 1.8 for AD). Some studies did not find significant differences, probably due to the small sample size and because the association is complex due to different, possibly confusing, cardiovascular risk factors of the association between BMI and dementia.[108,109]

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Traumatic brain injury	
2–	A past history of severe traumatic brain injury was associated with a greater risk of AD in some studies but not in others.[92]
Schooling level	
2+	A low schooling level is consistently associated with a greater risk of AD in different studies.[110,111,21,25,87,112]
Social media, civil status	
2–	Married people or people with more social relations showed a lower incidence of dementia in one longitudinal study of a Swedish population.[21]
Socioeconomic level	
2–	A greater incidence of dementia has been observed in patients with a low socioeconomic level in some cohort studies. The association may depend on other variables and there is not enough evidence to establish a relationship. [21]
Exposure to toxins	
2++	One SR consistently found a greater risk of AD in patients with a history of occupational exposure to pesticides.[113]
Exposure to low frequency electromagnetic fields	
2-	No consistent association has been observed between exposure to electromagnetic fields and the risk of AD.[114,113]
NSAID	
2++	In a recent study a lower risk of dementia was observed in individuals exposed to chronic consumption of NSAID.[92]
Benzodiazepines	
2–	The relationship between exposure to benzodiazepines and risk of dementia is inconsistent among studies.[92]
Vaccines	
2–	Individuals vaccinated for diphtheria, tetanus, poliomyelitis or flu had a lower risk of dementia than those not vaccinated according to the Canadian Study of Health and Ageing. [92]
Hormone replacement therapy (HRT)	
1+/ 1++	HRT has not demonstrated a consistent benefit on the risk of dementia in post-menopause women over the age of 65 in a Cochrane SR[115] and a MA. [116]Observational study data suggest that there could be a peri-menopause window where HRT would have a protective role.[84,117,118]

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6. Dementia prevention

Questions to be answered

6.1. Is primary prevention of dementia possible?

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6.1. Is primary prevention of dementia possible?

To perform primary prevention, it is necessary to know the risk factors of dementia, the degree to which these are modifiable and there must be evidence that modifying these factors gives rise to a reduction in the incidence. [25]Following the same outline as in the previous section, in this chapter we analyse evidence from studies that assess whether certain preventive actions on the possible risk factor can modify the risk of dementia.

HBP

There are no prospective RCT designed to evaluate if blood pressure treatment in midlife reduces the risk of dementia in the elderly.

The few prospective studies that exist only evaluated the cognitive function as a secondary variable, and they had a much shorter control period, less patients and more elderly than in the observational studies.	Cohort study, 2+/2–
A Cochrane SR (2009)[94] did not find convincing evidence based on a RCT that a decrease in blood pressure prevents the development of cognitive disorders and dementia in patients with no previous and manifest cerebrovascular disease. The combined analysis of SHEP 1991, Syst-Eur 1997, SCOPE 2003 and HYVET 2008 studies did not show significant differences between anti-hypotensive treatment and placebo in the incidence of dementia (secondary variable) after an average control period of about 3 years on a total of 15,936 hypertensive patients aged between 60 and 89 years (OR 0.89. CI 0.74-1.07). Only the Syst-Eur 1997 study showed a reduction of the incidence of dementia with the use of nitrendipine, but, lacking individual data, it is not possible to evaluate if the effect of the treatment depends on other basal risk variables such as sex, age or blood pressure level.	SR and MA of RCT, 1–

Unfortunately, due to the considerable heterogeneity between the RCT, to the presence of adverse events that caused the drop-out of many patients, and to the fact that some control individuals received antihypertensive drugs to recover the pre-established values, it was not possible to use the available data to assess the efficacy of antihypertensive treatment in the prevention of cognitive disorders and dementia.

Hypercholesterolaemia

There is no large-scale RCT aimed at studying the effect of hypolipemiant treatment on the cognitive function or the risk of dementia.[94,99]

A MA of cohort studies, and case and control studies (2005) designed to assess the effect of statins on the development of dementia and AD did not show any benefit of these drugs.[119]

MA of cohort case and control study, 2+/2+

In two large RCTs that evaluated the effect of statins on the risk of vascular disease, no reduction of the incidence of dementia was observed after 3-5 years in the group treated with pravastatin or simvastatin,[87] and observational and case and control studies have shown variable results. Some statins seem to have a preventive effect due to mechanisms not related to the reduction of cholesterol.[120]

RCT, 1+
Observational study, 2+/2–

Diabetes Mellitus (DM)

In the Nurses' Health Study, on diabetic women over the age of 70 and a 2-year control period, the sub-group treated with oral antidiabetic medication had an OR of 1.06 of bad basal cognitive performance with respect to the non-diabetes, whilst the untreated subgroup had an OR of 1.71.[99] On the contrary, hyperinsulinaemia or treatment with insulin could increase the risk of dementia. Non-diabetic women with peptide C levels (insulin secretion marker) in the upper quartile, had a greater risk of dementia after 10 years than women with levels in the lower quartile (OR 3.2); likewise, in the WHICAP study, patients with insulin levels in the upper quartile had a greater risk of AD than patients in the lower quartile (HR 1.7); the greater association was in non-diabetes, and they calculated that hyperinsulinaemia would explain the 40% of the cases of AD in their population.[99]

Observational study, 2+

Hyperhomocysteinaemia

The normalisation of homocystein levels by the intake of complex B vitamins in healthy elderly people with high levels did not show any cognitive improvement, in one single and not very appropriately design study.[121]

Observational study, 2-

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Diet rich in fat and poor in omega-3

A Cochrane SR (2005) found that available epidemiological clinical studies that compare the presence of AD among elderly people with different dietetic intake levels of omega-3 polyunsaturated fatty acids suggest a significant reduction of the risk of this disease among those with higher consumption levels of fish and omega-3 polyunsaturated fatty acids. There are no RCT that permit confirming or refuting the usefulness of omega-3 to prevent cognitive impairment or dementia in elderly people without pre-existing dementia.[122]

SR of observational study, 2+/2–

Physical activity

One SR concludes that the RR of cognitive impairment could decrease with age in physically active people. The majority of the studies have found an association between physical exercise and a lower risk of dementia, although others have not. The cause-effect ratio is not clear; in other words, if participating in physical activities improves cognition or if those that have a better cognitive function participate more. Furthermore, there could be other variables such as possible endogenous substance levels that stimulate both physical activity and the cognitive function. We do not know what type of exercise is more beneficial (the study results vary depending on the type of exercise) nor the recommended duration or intensity. There is no RCT that investigates if exercise by previously sedentary people would reduce the risk of dementia.[123]

SR of observational study, 2+/2–

Intellectual activity

One SR that included seven RCT that have evaluated the effect of mental exercise on cognitive performance for at least 3 months in healthy elderly people, showed a favourable effect compared with non-training (weighted average difference = 1.07, CI: 0.32-1.83, z = 2.78, N = 7, p = 0.06, N = 3.94). Studies of more than 2 years did not produce a greater effect. The quality of the studies is low, and the incidence of dementia is not specifically evaluated. We still do not have any appropriately designed trials that demonstrate that cognitive exercise prevents the incidence of dementia.[124]

SR of RCT, 1-

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Consumption of alcohol

In the Nurses' Health Study it was observed that women over 70 years of age that consumed less than 15 g/d of alcohol had a lower risk (RR 0.81) of cognitive impairment after 2 years than non-consumers. The benefit was not observed in higher consumptions. Likewise, in the Cardiovascular Health Study, individuals over the age of 65 who consumed 1-6 drinks per week had a lower risk of dementia (OR 0.46) than teetotallers, whilst the benefit was lost in consumptions of 7-13 drinks, and the risk increased in more than 14 drinks (OR 1.22); the results were similar for AD, and with no differences regarding the type of drink.[99]	Observational study, 2++/2+
There is no RCT on the consumption of alcohol, and observational studies support the moderate consumption of alcohol (< = 1 drink per day in women and < = 2 in men) to reduce the risk of cardiovascular disease and cognitive impairment with no significant risk of adverse effects.[99]	Observational study, 2++/2+

Use of statins (hypercholesterolaemia)

Use of NSAID

MA of observational and prospective studies have shown a lower risk of dementia in users of NSAIDs (ibuprofen or naproxen), but not when cognitive impairment was used as a major clinical variable. No effect was observed in studies with aspirin. There are no prospective RCT that confirm this benefit.[25] One trial with naproxen was negative.[125]	MA of observational study, 2++/2+

Vitamins

Observational studies with vitamin C or E have shown variable results, and there are no RCT or consistent data of efficacy that support their use to reduce the risk of dementia.[25]	Observational study, 2-

Hormone replacement therapy (HRT)

Some studies suggest that HRT may delay the onset of AD if started in a peri-menopause "opportunity window" where oestrogens would be protective, whilst from the age of 65 onwards, they would increase the risk **(question 5.3)**. [117,118]Current data are not sufficient to make recommendations in this regard.	Observational study, 2++

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Other risk factors

There are no prospective RCT aimed at assessing if the modification of other possible risk factors (hyperthyroidism, sex hormone levels in blood, depression, nicotine addiction, consumption of coffee, obesity and low weight, social-demographic factors, exposure to toxins and electromagnetic fields, use of benzodiazepines, use of vaccines) may reduce the risk of dementia.

Despite the absence of RCT, the available data of observational studies suggest that action on these risk factors could be associated with a lower risk of developing dementia **(question 5.3).**

Observational study, 2++/2+

Overall, there is still no clear evidence of the risk factors to develop dementia and how to prevent it. The majority of the recommendations of documents are based on scientific evidence, but they are not specifically focused on the prevention of dementia but on the prevention of the risk factors that may be accompanied by dementia.

Summary of evidence

Vascular risk factors (HBP, DM and hypercholesterolaemia)	
1–/2+/2–	The available data of cohort studies or RCT designed to assess other variables do not permit demonstrating that the treatment of vascular risk factors (HBP,[94] DM,[99] hypercholesterolaemia[99,119,87,120]) reduces the risk of developing dementia. No RCT have been appropriately designed to assess it.
Hyperhomocysteinaemia	
2–	The correction of hyperhomocysteinaemia via vitamin B in healthy elderly individuals did not show a cognitive improvement in an inappropriate design study.[121]
Diet rich in fat and poor in omega-3	
2++	A higher consumption of omega-3 fatty acids was associated with a lower risk of AD in one Cochrane SR of case and control studies, but there is no RCT that permits confirming or refuting its usefulnesss.[122]
Physical or mental activity	
2+/2–	There are no RCTs that assess if the execution of physical[123] or mental[124] exercise reduces the risk of developing dementia.
Consumption of alcohol or chronic consumption of NSAID	
2++/2+	The moderate consumption of alcohol[99] or the chronic consumption of NSAID[25] has been associated with a lower risk of AD in cohort studies, and case and control studies, but there are no RCT that confirm this benefit.

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Vitamins	
2–	There are no RCT or consistent data from observational studies that support a benefit of taking vitamins C or E over the risk of dementia. [25]
Hormone replacement therapy (HRT)	
2++	Observational studies suggest that HRT could reduce the risk of dementia in a peri-menopause window and increase it from 65 years onwards,[117,118] but there are no RCT that confirm this.
Other risk factors	
2+/2–	There are no RCT that assess the effect of the intervention on other possible risk factors (hyperthyroidism, sex hormone levels in blood, depression, nicotine addiction, consumption of coffee, obesity and low weight, social-demographic factors, exposure to toxins and electromagnetic fields, use of benzodiazepines, use of vaccines) on the risk of developing dementia **(question 5.3)**.

Recommendations

C	The control of vascular risk factors (HBP, DM, hypercholesterolemia) and healthy lifestyle habits (consumption of omega-3 fatty acids, physical and mental exercise) is recommended due to the clear evidence that exists about its benefit on other aspects of health, although its possible benefit on the reduction of the risk of dementia is not supported by appropriately designed studies.
C	Although moderate alcohol consumption or chronic consumption of NSAIDs ha been associated with a lower risk of AD, they also have other risks for health and there is not enough evidence to recommend them in the prevention of dementia.
C	Neither the intake of vitamin C nor vitamin E nor hormonal replacement therapy are recommended to prevent dementia.

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7. Genetic study in dementias

Questions to be answered

7.1. When are genetic analyses indicated to identify pathogenic mutations in patients with dementia?
7.2. When is a predictive genetic analysis indicated in asymptomatic individuals?

Less than 1% of the cases of neurodegenerative dementias are genetically determined, that is, a specific genetic alteration is the cause of the disease.[6,126] These cases often present a phenotype that is difficult to distinguish from the non-genetic forms, with the exception of the onset age, which is normally earlier in genetic cases.

The genetic alterations causing primary neurodegenerative dementia that have been identified to date are transmitted with an autosomal dominant inheritance pattern with high penetrance, although the age range for the onset of the disease varies depending on the gene involved.[6,126]

In genetic origin AD, which represents between 0.5 and 1% of the cases according to the series,[25,6,126] causal mutations have been identified in three different genes: the amyloid precursor protein (APP), presenilin 1 (PSEN1) and presenilin 2 (PSEN2).

Causal mutations in five genes have been identified to date in FTLD, representing between 10 and 15% of the cases, but they do not explain all the familial cases. These genes are the gene of the microtubule-associated protein tau (MAPT), progranulin (PGRN), the gene of the Chromatin modifying protein 2B (CHMP2B), the valosin-containing protein gene (VCP) and the gene of the TAR DNA binding protein (TARDBP); mutations in MAPT and PGRN are the most frequent.

Genetic prion diseases (between 10 and 15% of the cases) are produced by mutations in the prion protein gene (PRNP).[6,126]

Genetic origin DLB is currently considered to be an exception, as is its familial presentation.

Huntington's disease is produced by the alteration of exon 1 of gene IT15, a gene that encodes the huntingtin protein. The genetic alteration of HD consists in an expansion of cytosine-adenine-guanine (CAG) triplets, which normally presents around 16 repetitions, but its expansion over 35 repetitions may cause symptomatology. Huntington's disease is the paradigm of genetic dementias and, unlike the other types of dementias, mentioned above, it has an exclusively genetic origin.

The detection of a genetic change in one of the genes involved in the pathogeny of the disease in a patient with dementia does not mean that this is the cause of the disease (existence of polymorphisms or non-pathogenic mutations). For a change in the genome to be considered as causal, the segregation of this change with the disease in the family must be demonstrated, as well as its absence in normal population, and this change must cause an alteration at biological functioning level that justifies its involvement in the pathogeny of the disease. However, in the majority of the cases, pathogenic mutations are recurrent in different families, so the existing bibliography is enough to support the pathogenic role of a mutation, without it having to be demonstrated in each case.

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The majority of the cases of dementia, therefore, are not determined by a specific genetic defect, although the genetic component may exercise a predisposing factor in the development of a dementia. Thus, in AD, the presence of allele ε4 of the APOE gene has proved to be a risk factor for the development of the disease in many association studies; in sporadic Creutzfeldt-Jakob's disease there is an overrepresentation of the methionine-methionine homozygosis at codon 129 of the PRNP gene and in some of the frontotemporal lobar degeneration forms, an overrepresentation of haplotypes H1 of gene MAPT6 is objectified. None of these genetic risk factors is, however, necessary or sufficient, for the development of these diseases, so their usefulness in clinical practice is controversial **(Section 5.2).**

The detection of a genetic alteration as the cause of dementia not only has implications for the patient, but it also places direct relatives at a risk of having inherited that same alteration and therefore of suffering the same disease in the future. To date there are no preventive or curative therapies. In this sense, the genetic analyses have a legal and practical consideration in daily clinical practice that differs from other diagnostic tests.

7.1. When are genetic analyses indicated to identify pathogenic mutations in patients with dementia?

The NICE guideline[25] recommends that patients with a likelihood of suffering dementia due to genetic causes should be referred to genetic counselling.	Expert opinion, 4
The CPG of the EFNS,[5] as a point of good clinical practice, recommends genetic analysis in patients with certain phenotypes or autosomal dominant familial history. This study should only be carried out at specialised centres following genetic counselling and prior informed consent.	Expert opinion, 4
The great majority of the cases of genetic caused AD appear as presenile onset AD and autosomal dominant history. The cases of genetic FTLD normally appear with a family history. Genetic cases of prion diseases may appear without family history. The CPG of the SEN,[6,126] based on case and control studies, recommends performing genetic analyses on patients with AD and an autosomal, dominant family history of pre-senile onset. In patients with FTLD, the execution of genetic studies would be indicated in patients with autosomal dominant family history. In patients with prion diseases, the prion protein genetic study would be indicated in all cases, regardless of family history or age.	Case and control study, 2++/2+

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The majority of patients with Huntington's disease have a high number of CAG repetitions in the Huntingtin gene, so the diagnostic reliability of genetic studies in cases where Huntington's disease is suspected is high.[6] Given that Huntington's disease is a purely genetic disease, in the event of clinical suspicion, different experts recommend performing the genetic study.	Diagnostic test study, 2++/2+ Expert opinion, 4
The Spanish Law on Biomedical Research (Law 14/2007)[127] explains that prior written consent from the person affected or from their legal representative is necessary to perform genetic analyses. On the other hand, "when a genetic analysis is performed for health purposes, appropriate genetic counselling will have to be guaranteed for the interested party. The professional giving or coordinating the genetic counselling must offer adequate information and advice, related both to the importance of the resulting genetic diagnosis and to possible alternatives that the individual may choose in view of the diagnosis".	According to applicable legislation

Summary of evidence

4	Patients with likelihood of suffering genetic origin dementia and their relatives require genetic counselling.
2+	The great majority of the cases of genetic cause AD appear as presenile onset AD and autosomal dominant history.[6,126]
2+	The great majority of the cases of FTLD appear as familial FTLD.[6,]
2++/ 2+	The genetic cases of prion diseases may appear with or without family history. The genetic study of all patients with prion diseases has been proved necessary to detect genetic cases, even in the absence of family history.[6,126]
2++/ 2+	Huntington's disease is a purely genetic disease and the diagnostic reliability of the genetic study for its diagnosis is high.[6,126]
According to applicable legislation	The prior written consent from the affected person or from his or her legal representative must be obtained to perform genetic studies, and appropriate genetic counselling must also be guaranteed for the interested party.[127]

Recommendations

D	Patients with a likelihood of suffering dementia due to genetic causes should be referred to specialist genetic counselling units.

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C	Performing genetic analyses to detect causal mutations is indicated in patients with AD and an autosomal, dominant family history of pre-senile onset.
C	In patients with FTLD, genetic analyses would be indicated in cases with a family history of a similar disease.
B	In patients with prion diseases, the genetic study would be indicated in all cases, regardless of family history or age.
B	The genetic study is recommended if Huntington's disease is suspected, to confirm the diagnosis.
According to applicable	The execution of genetic analyses in clinical practice must be authorised in writing by the actual individual or his/her legal representative after receiving genetic counselling

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7.2. When is a predictive genetic analysis indicated in asymptomatic individuals?

The NICE guideline[25] recommends that non-affected relatives at risk of developing genetic dementia in the future should be offered and referred to genetic counselling.	Expert opinion, 4
Predictive genetic analysis on asymptomatic individuals at risk of developing genetic origin dementia has proved to be safe in the short to medium term when carried out in specialised genetic counselling units.	Cohort, and case and control studies, 2+
Based on case and control studies, the CPG of the SEN[6,126] proposes that presymptomatic or predictive genetic studies could be conducted on individuals of full legal age with a clear family history of dementia and known pathogenic mutation in patients of their family, following multidisciplinary assessment and genetic counselling before and after the genetic analysis, following the predictive study model for Huntington's disease, given that this context has proved to be safe.	Case and control study, 2+
One RCT[128] showed that relevant psychological alterations were not objectified in the short term in a group of individuals on whom it was carried out and who were informed about their APOE genotype.	RCT, 1-

However, the guidelines of the EFNS[5] and of the SEN[6] consider that studying non-determining genetic risk factors, such as the APOE genotype in AD or others, would not be indicated with genetic counselling purposes given that its validity as a predictive test has not been demonstrated.	Diagnostic test study, 2++

Summary of evidence

2+	Presymptomatic predictive genetic studies have has proved safe in a multidisciplinary genetic counselling context.[6,126]
1–	The APOE genetic study has proved safe in asymptomatic individuals in a multidisciplinary genetic counselling context.[128]
2++	The study of the APOE genotype has not proved to be valid as a predictive test of AD in non-selected individuals.[5,6,126]

Recommendations

C	The predictive genetic study can be performed on people of full legal age who are at a risk of being carriers of a pathogenic mutation known to cause dementia and who wish to have it conducted, following informed written consent and multidisciplinary genetic counselling prior to the genetic analysis and subsequent monitoring.
D	The study of genetic risk factors of dementia, such as the APOE genotype, is not indicated for genetic counselling purposes in asymptomatic individuals.

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8. Dementia diagnosis

Questions to be answered

8.1. How is dementia diagnosed?
8.2. What is the differential diagnosis of dementia?
8.3. What are the advantages of neuropsychological testing assessment in cognitive impairment and dementia?
8.4. What neuropsychological tests, questionnaires or functional evaluation scales must be performed on patients with dementia?
8.5. Which laboratory tests are essential in diagnosing dementia?
8.6. Must the determination of apolipoprotein E (apoE) be requested?
8.7. What are the advantages of analysing cerebrospinal fluid (CSF) in the diagnosis of dementia?
8.8. Which is the structural neuroimaging technique of choice in the diagnostic process of dementia and its different types?
8.9. Which is the functional neuroimaging technique of choice in the diagnostic process of dementia and its different types?
8.10. What are the advantages of EEG/mapping in the diagnosis of dementia?
8.11. What are the indications for performing a cerebral biopsy in the etiologic diagnosis of dementia?

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8.1. How is dementia diagnosed?

Diagnostic assessment of dementia

The diagnosis of dementia is largely clinical and is based on DSM-IV-TR or ICD-10 criteria **(Appendices 1.1 and 1.2).**

Expert opinion, 4

The diagnostic process is usually based on a suspicion of cognitive impairment, either by the actual person affected, by a relative or the primary care team. Other possible causes of cognitive impairment must be ruled out before making a diagnosis of dementia **(question 8.2.).** All the information required to know if the patient satisfies the clinical criteria of dementia and of its subtypes must be collected in the case history and examination.[129]

A possible family background of dementia, previous diseases, vascular risk factors, the patient's schooling level and social-family context must be studied in depth. The symptoms of cognitive dysfunction, its form of onset and evolution must then be evaluated. A functional assessment must be carried out on the patient, as the loss of capacity to undertake basic and instrumental activities is one of the main criteria for diagnosing dementia and which distinguishes it from mild cognitive impairment (MCI). [130]

Expert opinion, 4

It is important to have a source of information that is close to the patient, for the case history, given the frequent presence of anosognosia. Several questionnaires have thus been designed for informants, such as the Blessed scale or the IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly) **(question 8.3)**. The BPSD as well as functional and social problems must be assessed, as these are the main causes of strain and stress in the caregiver **(question 11.4).**

Neurological examinations in early phases of dementia are usually normal, although alterations may be evident that guide towards a specific aetiology (extrapyramidal signs, oculomotor alterations, gait apraxia, etc.).[5]

Expert opinion, 4

Formal neuropsychological examinations permit the detection of mild cases and help make a differential diagnosis, and determine subtypes of dementia **(question 8.2).**

The data obtained via the case history, clinical and neuropsychological examinations will enable us to make a syndrome-based diagnosis (cortical vs. subcortical impairment, parietotemporal, frontal syndrome, etc.) and based on this, we will continue the study with the relevant complementary tests.

The aetiological diagnosis of certainty of degenerative dementias is based on neuropathological examinations, so, in the majority of the cases, we will only reach an aetiological diagnosis of probability, with the exception of cases of known pathogenic mutation.

Diagnostic criteria

The definition of dementia is based on diagnostic criteria. There are also different clinical criteria of consensus for the diagnosis of the different types of dementia **(Appendices 1.3-1.11).**

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The most commonly used for AD are the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and of the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA),[131] which stratify the diagnostic precision with the degree of possible, probable or definite, or those of the DSM-IV-TR.[17] The DSM-IIR criteria for Alzheimer's type dementia and those of the NINCDS/ADRDA for probable AD have been validated in clinical-pathological studies and have shown high average sensitivity (around 80%) and lower specificity (around 70%).[132]

Diagnostic test study, 2++/2+

The NINCDS-ADRDA[131] criteria have been recently reviewed by Dubois et al.[133] for a research context and they have still not been validated for clinical application.

Each new version of criteria shows greater specificity than the previous ones, above all because they incorporate new diagnosis markers (neuropsychological, neuroimaging, biochemical, genetic). The new criteria proposed by Dubois et al. in 2007 are of interest, as they permit the establishment of the clinical diagnosis of "probable AD" in patients who only present a prolonged disorder of episodic memory (more than 6 months), providing that an AD marker (support criteria) appears in the complementary test, and there are no data that identify any other cause of dementia (exclusion criteria). This diagnosis, in a patient who does not satisfy the dementia syndrome-based criterion (which requires an alteration of multiple cognitive domains), represents an advance in the early aetiological diagnosis of patients with cognitive function impairment, and a change in the concept shared by all criteria valid until 2007, which demanded the presence of dementia to be able to diagnose AD.

Currently, the final determination of the existence of AD requires the person to have satisfied the clinical criteria of AD, also, the anatomopathological criteria of AD must have been confirmed in brain studies or the presence of any of the mutations that cause familial AD must have been detected.

The most commonly used criteria for VD are those of the National Institute of Neurological Disorders and Stroke/Association Internationale pour la Recherche et l'Enseingement en Neurosciences (NINDS/AIREN), of great specificity (around 95%) but very low sensitivity (less than 43%).[6,46]

Diagnostic test study, 2+

The Hachinski ischaemia scale has high sensitivity to distinguish AD (score < 4) and VD (score < 7), but it is not reliable for mixed cases. [59]The Hachinski scale was not designed as a diagnostic criterion for VD but to detect vascular brain lesions in patients with dementia. A meta-analysis of the Hachinski scale on patients with dementia and neuropathological confirmation, showed that it was effective to differentiate Alzheimer's type dementia from multi-infact vascular dementia but not to differentiate it from mixed dementia.[134]

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There are no clinical or neuropathological criteria for the diagnosis of mixed dementia (if there are signs of both VD and AD, the NINDS / AIREN classifies it as AD dementia associated with cerebrovascular disease).[58]	
The diagnostic criteria for DLB were formulated by McKeith[28] and reviewed in 2005 by the DLB International Workshop. [40]The 1996 criteria have shown high specificity (95-100%) and variable sensitivity according to the studies (31-83%).[6,47]	Diagnostic test study, 2+
The diagnostic criteria for probable or possible dementia associated with Parkinson's disease was defined by consensus by the group of experts from the Movement Disorder Society in 2007.[41]	Expert opinion, 4
The Lund-Manchester criteria can be applied (The Lund and Manchester Groups, 1994) for FTLD, as well as the criteria of the NINDS Work Group on Frontotemporal Dementia[135] or those of Neary,[51] that are more operative and have shown 85% sensitivity and 99% specificity when applied together with neuropsychological and neuroimaging tests.	Diagnostic test study, 2+

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Summary of evidence

4	The diagnosis of dementia is largely clinical. The information required to know if the clinical criteria of dementia and of its subtypes are satisfied, must be compiled in the case history and examination. The case history includes: Family background of dementia, previous diseases, vascular risk factors, patient's schooling level, social-familial context, cognitive dysfunction symptoms, form of onset and evolution, assessment of the capacity of activities of daily living, BPSD and social problems. The neurological examination is usually normal with the exception of advanced stages or in diseases with associated neurological signs.[5] The neuropsychological examination helps to detect mild cases and the differential diagnosis. The aetiological diagnosis of certainty of degenerative dementias is based on neuropathological examinations with the exception of case with known pathogenic mutation.
2++/ 2+	To diagnose AD, the NINCDS / ADRDA criteria for probable AD and the DSM-IIR criteria for Alzheimer type dementia have shown an average sensitivity of 81% and average specificity of 70% in clinical-pathological studies.[132]

2+	To diagnose VD, the NINDS/AIREN criteria have shown 43% sensitivity and 95% specificity in a clinico-pathological study. [6,46]The Hachinski scale helps to detect brain infarcts in patients with dementia and may distinguish between EA (< 4) and VD (> 7), but it is not useful in mixed dementia.
2+	To diagnose DLB, the McKeith criteria have shown variable sensitivity (31-83%) and 95-100% specificity in prospective clinico-pathological studies. [6,47]
4	To diagnose probable or possible dementia associated with Parkinson's disease, a group of experts from the Movement Disorder Society (Emre et al.) established some consensus criteria in 2007.[41]
2+	To diagnose FTLD, the Lund-Manchester or Neary criteria have shown 85% sensitivity and 99% specificity in small retrospective clinico-pathological studies.[51]

Recommendations

✓	The assessment of the impact of cognitive impairment on the activities of daily living is recommended, given their affectation, which forms a dementia diagnostic criterion and determines the subsequent management of these patients.
✓	Obtaining data from an independent and reliable informant is recommended, whenever possible.
✓	An assessment of the psychological and behavioural symptoms is recommended, due to their importance for the diagnosis.
✓	The execution of a general physical and neurological examination of patients with dementia is recommended to detect comorbidity and associated neurological signs that may help towards the differential diagnosis of some subtypes of dementia.
D	The use of DSM-IV-TR and ICD-10 clinical criteria is recommended to diagnose dementia.
B	The use of DSM-IV-TR or NINCDS/ADRDA criteria is recommended to diagnose AD.
B	The use of INDS/AIREN criteria or the Hachinski scale is recommended to facilitate the diagnosis of VD.
D	The use of Emre et al. (Movement Disorder Society) criteria is recommended to diagnosis Parkinson's disease dementia.
B	The use of McKeith criteria is recommended to diagnose DLB.
B	The use of Lund-Manchester or Neary criteria to help diagnose FTLD is recommended.

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8.2. What is the differential diagnosis of dementia?

Before establishing the diagnosis of dementia, we must basically rule out all those processes that might simulate it.

Acute confusion syndrome (delirium)

Acute confusion syndrome or delirium is a severe, normally reversible, disorder that is associated with high morbidity and mortality. It is a real medical urgency, and is usually due to systemic causes. Advanced ages and neurodegenerative diseases are risk factors for this entity. Patients with dementia have a high risk of presenting acute confusion syndrome, but an initial diagnosis of dementia must not be made in the context of a confusion picture.[136]

It is clinically characterised by the disturbance of the level of consciousness, a reduction in capacity to direct and sustain attention, and fluctuating cognitive evolution deficits. The onset may be acute and the disturbances are usually reversible if the cause is detected and appropriately treated. The DSM-IV_TR criteria for diagnosing delirium are described in **Table 1**. Some characteristics that help differentiate delirium from dementia are given in **Table 2.**

Table 1. DMS-IV-TR criteria for the diagnosis of delirium (translated from APA, 2000)[16]

A.	Disturbance of consciousness (reduced clarity of awareness of the environment), with reduced ability to focus, sustain or shift attention.
B.	A change in cognition (such as memory deficit, disorientation or speech disorder) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia.
C.	The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
D.	There is evidence from the history, physical examination or complementary examinations that the disturbance is caused by the direct pathophysiological consequences of a systemic disease, intoxication, effect of drugs or by more than one cause.

Table 2. Differential diagnosis between delirium and dementia[137]

DELIRIUM	DEMENTIA
• Precise, sudden onset with identifiable date	• Gradual onset but impossible to give precise date
• Acute disease, generally lasting from days to weeks, rarely more than 1 month	• Chronic disease that typically progresses for years
• Generally reversible, often completely.	• Generally irreversible, often chronically progressive.

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• Early disorientation	• Disorientation in late phase of disease, often after months or years.
• Variability from one moment to the next, from one hour to the next, for the whole day.	• Much more stable from one day to another (unless delirium appears)
• Outstanding physiological impairments	• Less striking physiological changes
• Cloudy, altered and variable level of consciousness	• Consciousness is not obfuscated until terminal phase.
• Duration of attention strikingly short	• Duration of attention is not typically reduced.
• Disturbance of sleep-wake cycle, with variations from one to another	• Disturbance of sleep-wake cycle, with day-night inversion, with no hourly variations
• Marked psychomotor changes (hyperactive or hypoactive)	• Typically late psychomotor disturbances (unless depression appears).

The main risk factors of delirium are old age, the coexistence of neurological and psychiatric diseases and sensory deprivation. Many precipitating factors have been described, including drugs (mainly hypnotic, narcotic, alcohol or poly-drug use), different neurological diseases (such as ictus, intracranial haemorrhage or meningitis), systemic disturbances (infections, surgeries, hydroelectrolytic disturbances), fecalomas, acute urine retention, pain and changes in normal environment surrounding the patient (emotional stress, widow(er)hood, use of tethers and physical constraints, urine probes, change in place of residence or admissions into hospital). At times, an acute confusion syndrome may conceal prior cognitive disturbance.

Major depression and other psychiatric disorders

Major depression is another important element in the differential diagnosis of memory alterations. Frequently, people with depressive disorders present memory complaints, concentration difficulties or reduction of intellectual performance, which may even have an effect on the patient's global functioning. Thus, a comprehensive interrogation must be carried out, aimed at detecting depression syndromes such as sadness, anhedonia, anxiety, anorexia or sleep disorders. Patients usually highlight and insist on cognitive difficulties. It may become necessary to start anti-depression treatment and observe the evolution of anaemic and cognitive symptoms. Depression is often an early symptom in dementia, so the coexistence of both must be investigated. So much so that even when the onset of depression symptoms precedes or coincides in time with the appearance of cognitive symptoms and both are solved with antidepression treatment, up to 50% of the patients will develop mild cognitive impairment or dementia during the years following the depression episode. Likewise, patients with mild cognitive impairment who present depression episodes, may have a greater risk of developing AD. [42]Dementia must also be distinguished from dissociative or conversive disorder, which is usually expressed with patterns of cognitive deficit that are inconsistent in time and that are not the ones that are typically observed in dementia.[42]

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Mild cognitive impairment

Mild cognitive impairment (MCI), also called light cognitive impairment, is defined as an alteration of one of more cognitive domains, which must be acquired, reported by the informant and objectified in the neuropsychological assessment and which does not interfere or only does so minimally, with the patient's ability to carry out activities of daily living (ADL). The variable evolution of MCI depends on the underlying cause. In general, these patients have an increased risk of developing dementia, so the clinical evolution must be monitored every 6-12 months. Subjective complaints about memory, where the neuropsychological tests do not show a significant reduction in cognitive performance with respect to the normal values, may precede MCI by even 15 years, and they are often associated with mood disorders (anxiety and depression).[138]

8.3. What are the advantages of neuropsychological testing assessment in cognitive impairment and dementia?

The American Neurology Academy (ANA), in its 2001 recommendations, concludes that there is not enough evidence in literature to postulate about the advantages of dementia screening in asymptomatic population. Individuals with cognitive complaints, expressed by themselves or by people close to them, present an increased risk of presenting or developing dementia, so the ANA does recommend assessment and clinical monitoring of this type of individual.[139]

On the other hand, different quality CPG recommend that the diagnosis of dementia be carried out after a global evaluation of the patient including a formal objective cognitive assessment with standardised instruments,[140,25,5,136]

Diagnostic test study, 2+

The tests can assess the cognitive function either globally or by cognitive domains, so they may also give indications about the clinical form or nosology of dementia. In addition, given that they are quantitative tests, they may determine the degree and evolution of the impairment.

Cognitive tests can be classified into short screening tests, short-intermediate general assessment tests and specific tests. The short screening tests are simple tests that assess one or several cognitive fields and are designed to make a fast clinical assessment by non-specialised staff. The intermediate or specific neuropsychological assessment tests are sensitive to detect and characterise subtle cognitive disturbances, but they must be administered by specialised staff. They usually facilitate the differentiation between typical disturbances of age, mild cognitive dysfunctions and typical cognitive dysfunctions of dementia, so they are especially advantageous in stages of incipient cognitive impairment. They can indicate the risk of these dysfunctions leading to dementia in general, or into a subtype of dementia in particular.[6,141]

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In this sense, different CPG recommend performing complete neuropsychological studies via standardised and validated tests for the population under study in initial or questionable cases of dementia.[140,25,139,129,5,136]	Expert opinion, 4
The SEN[6] guideline recommends performing general brief-intermediate type evaluation tests when the aim is to make an assessment of the most important neuropsychological areas in a reasonable time. This guide also recommends performing detailed neuropsychological assessment via specific tests when there are differences between the clinical impression and the screening tests, diagnostic doubts or else when the complaints are limited to just one cognitive domain or evolve over a short period of time.	Expert opinion, 4
Despite the great advantage of neuropsychological tests, as a tool they are not sufficient to diagnose dementias and they must be interpreted as a complement to other diagnosis strategies. When these tests are administered to patients, it is advisable to bear in mind that the results may be dependent upon the age, the level of schooling, previous skills, attention levels, sensory difficulty, mental diseases, physical or neurological problems, and drugs, which form part of the personal history of each patient.[6]	Expert opinion, 4

8.4. What neuropsychological tests, questionnaires or functional evaluation scales must be performed on patients with dementia?

In individuals with cognitive complaints the ANA guideline[139] recommends applying, in order to monitor the degree of cognitive impairment, global cognition screen tests, neuropsychological test batteries, short cognitive instruments focused on specific aspects of cognition and certain structured questionnaires.	Diagnostic test study, 2++
The ANA guideline[139] considers global cognitive screen tests to be useful to detect dementia in populations with a high cognitive impairment prevalence (due to old age or the presence of memory complaints): • The mini-mental state examination (level of evidence: 2++) • Short test of mental state (level of evidence: 2–) • The memory impairment screen (MIS) (Level of evidence: 2++)	Diagnostic test study, 2++/2-

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Among the informant-based questionnaires, according to the ANA, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is useful (level of evidence: 2++), the Clinical Dementia Rating (level of evidence: 2–) and the Blessed Roth scale (level of evidence: 2+). [139] Other guidelines recommend the use of the Global Dementia Scale (GDS) (dementia) or the Functional Assessment Staging (FAST) (Alzheimer's disease)[140] as global scales to classify the level of cognitive impairment.	Diagnostic test study, 2++/2+/2-
Not all these tests have been validated in Spain. The following have been validated and recommended in our medium as global or focalised cognition screen tests: the MMSE (level of evidence: 2++), test of which there are several versions in our country: standardised version,[142] Lobo or MEC version;[143,144] the MIS (level of evidence: 2++); the 7-minute test (level of evidence: 2–); the Eurotest (level of evidence: 2+), or the Pfeiffer test (level of evidence: 2+).[6]	Diagnostic test study, 2++/2+/2-
Other short screen tests, developed in Spain, have proved useful to detect dementia and/or cognitive impairment, such as the Phototest (level of evidence: 2+)[145] or the memory alteration tests (T@M, level of evidence: 2+). [146]	Diagnostic test study, 2+
Likewise, the SEN[6] guideline recommends the neuropsychological examination via general brief-intermediate type evaluation tests such as the Alzheimer's Disease Assessment Scale (ADAS), the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX) or the abridged Barcelona test (TBA) when the aim is to make an assessment that includes the most important neuropsychological areas in a reasonable time interval.	Diagnostic test study, 2+
When specific tests are resorted to, they can be selected using a syndrome-based or modal approach, that is, within a specific neuropsychological field. The selection must be based on the psychometric characteristics of the instrument and on the existence of regulatory data in the medium where it is aimed to be used. In this sense, in the Spanish scenario, noteworthy are the NORMACODEM projects, and more recently NEURONORMA.ES, which presents co-standardisation data and validation of different cognitive and functional instruments.[6]	Expert opinion, 4
The SEN guideline also recommends the systematic functional assessment of the individual with a reliable observer, either using standardised questionnaires or else with a semi-structured interview and global functional rating.[6]	Diagnostic test study, 2++/2-

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The following functional assessment questionnaires are quoted as being useful: the Functional Activities Questionnaire (FAQ), Instrumental Activities of Daily living scale (IADL), Interview for the deterioration of Daily Living in dementia (IDDD), Bayer Activities of Daily Living scale (BAYER ADL), Informant Questionnaire on Cognitive Decline in the Elderly (informant's test) (IQCODE), Barthel's index, Katz' index, Rapid Disability Rating Scale (RDRS-2) and the Blessed Dementia Rating scale (BDRS), with no priority of any one over the others.

The Global Deterioration Scale (GDS), the Functional Assessment Scale (FAST) and the Clinical Dementia Rating (CDR) are among the most outstanding global assessment scales.

In addition, the systematic assessment of neuropsychiatric symptoms is also recommended, either through a semi-structured history or via standardised scales such as the Neuropsychiatric Inventory (NPI), the Behavioural Symptoms in Alzheimer's disease, geriatric depression scale or the Hamilton depression scale, etc

The GDS and FAST scales are described in **Appendix 1.14**

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Summary of evidence (questions 8.3 and 8.4).

2++ /2-	Global cognition screen tests, neuropsychological test batteries, short focused cognitive instruments and/or standardised structured questionnaires are valid to quantify the degree of cognitive impairment in patients with suspicion of dementia.[139]
1+	Formal cognitive assessment via validated instruments is necessary to establish a diagnosis of dementia[6,140,25,5,136]
2++	The standardised Spanish version of the MMSE[142] and the versions of Lobo or MEC,[143,144] are global cognitive screen tests that have proved to be useful in our medium to detect dementia in individuals with cognitive complaints.
2++/ 2+/2–	Other short screen tests such as the MIS,[139] the Pfeiffer test,6 the 7-minute test,[6] the clock test,[139] the Eurotest6 or the T@M[146] may also be useful in screening dementia.
2+	The neuropsychological examination using general short-intermediate type assessment tests is useful to make an evaluation of the most important neuropsychological areas in a reasonable time.[6]
4	The performance of a detailed neuropsychological assessment via specific tests is useful when there are differences between the clinical impression and the screen tests, diagnostic doubts or else when the complaints are limited to just one cognitive domain or evolve over a short period of time.[6]
2++/ 2–	When an individual with cognitive impairment is evaluated, it is useful to establish the degree of global functional impairment through specific scales.[6,139]

Recommendations (questions 8.3 and 8.4)

B	Patients with cognitive complaints must be assessed by means of global cognition screen tests, neuropsychological test batteries, short cognitive instruments focused on specific aspects of cognition and/or standardised structured questionnaires to quantify the degree of cognitive impairment.
A	The dementia diagnosis must include a formal objective cognitive assessment with validated instruments.
A	The use of the Spanish standardised version of the MMSE or the MEC is recommended to screen dementia in individuals with cognitive complaints or advanced age in our medium.
B	Other short screening tests, such as the Pfeiffer test, the MIS, the 7-minute test, the clock test, the Eurotest or the T@M can also be recommended to screen dementia in individuals who are suspected of having cognitive impairment.
B	The neuropsychological examination using general brief-intermediate type evaluation tests is recommended when the aim is to make an evaluation of the most important neuropsychological areas in a reasonable time.
D	The performance of a detailed neuropsychological assessment via specific tests is recommendable when there are differences between the clinical impression and the screening tests, diagnostic doubts or else when the complaints are limited to just one cognitive domain or evolve over a short period of time.
C	The use of specific scales is recommendable to quantify the degree of global functional impairment in individuals who are suspected of having cognitive impairment.
✔	The choice of a specific instrument must be made depending on the time available, on the clinical experience and on the availability of regulatory data in the language and in the medium where they will be applied.

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8.5. Which laboratory tests are essential in diagnosing dementia?

The main objective of laboratory tests is to rule out potentially reversible causes of dementia, comorbidities that may contribute to cognitive alterations and rule out other diagnosis such as delirium, for example. Potentially reversible causes are rare. In a SR that included 39 prospective and retrospective observational studies and a total of 7042 patients, only 9% had potentially reversible causes of dementia and only 0.6% reverted.[147]

Descriptive study, 3
Expert opinion, 4

There is no universal consensus about the appropriate test battery that must be carried out. However, the recommendations of the CPGs and consensus conferences are similar: Haemogram to rule out anaemia, TSH to rule out hypothyroidism, ionogram to rule out hyponatraemia or hypocalcaemia, glycaemia to rule out diabetes and serum levels of B_{12} to rule out deficit. [5,25,140,148,136]Folate deficit is rare and in the Canadian guideline they recommend determining levels only in cases of celiac disease or limited intake of cereals. [136]Depending on the syndromes, it is advisable to request folate levels, hepatic and renal function, GSV, luetic serology or HIV according to other CPGS.[140,25,5]

Descriptive study, 3
Expert opinion, 4

For metabolic, infectious and toxic alterations that might be associated with dementia, there is no specific evidence based on controlled RCT that their treatment reverts the cognitive symptoms.[5] Thyroid dysfunctions may cause cognitive and psychiatric symptoms and be confused with dementias, although the treatment of thyroid alterations does not always revert cognitive deficits.[149] There is no evidence that treatment with B_{12} or folate will improve cognitive functioning in patients with cognitive impairment with low levels of B_{12} or folate or high homocystein levels.[149] Luetic serology is a problem due to the difficulty in interpreting results. In the largest retrospective study with 672 patients referred due to dementia, 3% had positive serology for syphilis but only one patient had neurosyphilis. There are no prospective studies, and there was an improvement in cognitive symptoms in the cases treated. There are no quality studies that permit the recommendation of neurosyphilis screening in patients with cognitive symptoms.[149]

Descriptive study, 3
Expert opinion, 4

Biomarker analyses such as APOE genotype or tau and beta amyloid levels in CSF for AD, or 14-3-3 and specific neuronal enolase for CJD are not carried out on a routine basis, and the genetic study is only justified in those cases where there is a family history of dementia with an autosomal, dominant inheritance pattern **(question 7.1).**

Summary of evidence

3/4	The CPGs[5,25,140,148,136] recommend including: Haemogram, TSH, electrolytes, calcium and glucose as recommendable tests in general to rule out potentially reversible causes of dementia and to screen comorbidities, and determine folates, B_{12}, luetic or HIV serology when it is suspected that these may have been altered due to the clinical context.
3/4	There is RCT-based evidence that the treatment of metabolic, infections and toxic alterations associated with some patients with dementia reverts the cognitive deficits.[5,149]

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Recommendations

D	The performance of the following laboratory tests is recommended in all patients assessed for possible dementia: Haemogram, TSH, electrolytes, calcium and glucose, to rule out potentially reversible causes of dementia and to screen comorbidities.
D	The determination of folate levels can also be added, especially in patients with limited intake of cereals, and levels of B_{12}, above all in older adults.
D	Serologies are also recommended for syphilis or HIV only in patients with clinical suspicion of these infections as a potential cause of dementia or as comorbidity.
D	The determination of homocystein as a risk factor associated with cognitive impairment or AD is not recommended.

8.6. Must the determination of apolipoprotein E (apoE) be requested?

The apoE genotype is the only genotype that is clearly involved in late onset AD. The presence of the apoE allele ε4 is strongly associated with AD,[150] whilst the allele ε2 may have a protective effect.[151]

Case and control study, 2++

The Singapore guidelines,[140] of the EFNS[5] and of the SEN,[6] as well as SR of genetic association studies,[149] do not recommend the determination of the apoE genotype at a diagnostic or predictive level in healthcare practice, as it is not sensitive or specific enough.

In a large series with neuropathological confirmation, the sensitivity and specificity of the presence of the apoE allele ε4 for the diagnosis of AD was 65% and 68%. [153]It is not a good tool, either, to distinguish the different types of dementia.

With respect to other susceptibility genes, no clear conclusion is reached, and more studies would be required to establish their role in AD and be able to have enough scientific evidence to make recommendations.

SR of case and control study, 2++

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Summary of evidence

2++	The presence of the apoE allele ε4 is consistently associated with AD in case and control studies, but it has low sensitivity (65%) and specificity (68%) to diagnose AD.[153]

Recommendations

A	The determination of the APOE genotype is not recommended in healthcare practice to diagnose AD.

8.7 What are the advantages of analysing cerebrospinal fluid (CSF) in the diagnosis of dementia?

Tau and amyloid

Numerous studies have consistently found an increase in total tau (T-tau) and of phosphorylated tau (P-tau) and a reduction of amyloid Aβ-42 in the CSF of patients with AD respect to controls.[149] These markers have high sensitivity and specificity (> 80%) to differentiate AD from controls, depression and alcohol dementia, but they are not very specific to differentiate AD from other dementias.[154,25,5]

Case and control study, 2++/2+

Combining Aβ-42 and T-tau helps increase the specificity to distinguish AD from FTLD (85%), DLB (67%) or VD (48%).[5] P-tau has greater specificity to differentiate AD from other dementias and other neurological disorders. The sensitivity and specificity values are highly variable between studies and depending on the technique.[149]

There is usually an increase of T-tau and P-tau in FTLD as well, and a decrease of Aβ-42, of less magnitude than in AD. In DLB and in VD there may be an increase of T-tau and P-tau in some patients and a reduction of Aβ-42 in the majority of the cases, which is probably due to the usual presence of concomitant AD pathology in these diseases.

Case and control study, 2++/2+

In other neurological diseases, such as cerebrovascular disease without dementia, amyotrophic lateral sclerosis, PD without dementia, PSP, DCB, depression and alcohol dementia, the T-tau levels are normal or slightly high.[149]

Case and control study, 2++/2+

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With respect to CJD, the tau levels are much higher than in AD and there is a considerable increase of the T-tau/P-tau ratio in CSF, which discriminates CJD from AD and other dementias with almost 100% reliability.[149]

Some studies on patients with MCI have shown sensitivity to predict progression to AD of 80% for T-tau, 71% for Aβ-42, 79% for P-tau and 78% for the combination of T-tau and Aβ-42.[155,149]

Other biomarkers in CSF

Another possible biomarker in CSF are the heavy and light neurofilaments, which are augmented in AD, FTLD and VD, but their clinical utility is not established.[156] Protein 14-3-3 is associated with a rapid neuronal loss and is useful to help diagnosis CJD.[25]

Observational study, 2++/2+

The determination of 14-3-3 has 90-100% sensitivity and 84-96% specificity in the diagnosis of CJD, with false positives in cerebral infarction, encephalitis, tumours and rapidly progressive AD. If the suspicion of CJD is high, maximum reliability is achieved with the combination of EEG, MRI and 14-3-3.[5]

Diagnostic test study, 2+
Observational study, 2++

All of these case and control, or cohort studies, come from specialised centres and it is difficult to extrapolate the results. Furthermore, the reliability and standardisation of the tests is still not clear, and the absolute values and cut-off points to discriminate between normal and pathological values vary a great deal between studies and between laboratories. Other important limitations are that the execution of a lumbar puncture is troublesome and would not be widely accepted as a routine test among patients with dementia.[25]

The CSF analysis is obviously indicated whenever dementia secondary to an infection or encephalitic process of the central nervous system (for example neurosyphilis) is suspected.

Summary of evidence

2++/ 2+	The increase of T-tau and P-tau and the reduction of Aβ-42 in CSF have consistently shown high sensitivity and specificity to distinguish AD from controls, but insufficient specificity to distinguish AD from other dementias.[149,154,25,5]
2++/ 2+	Some studies on patients with MCI have shown sensitivity to predict progression to AD of 80% for T-tau, 71% for Aβ-42, 79% for P-tau and 78% for the combination of T-tau and Aβ-42.[155,149]

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2++/ 2+	An increase in the T-tau/P-tau ration in CSF is highly reliable to distinguish CJD from AD and other dementias.[149]
2++/ 2+	The determination of protein 14-3-3 in CSF is highly sensitive to detect CJD, but there is around 10% false positives.[5]

Recommendations

B	The determination of T-tau, Aβ-42 and P-tau in CSF can be used as an additional test in cases of doubtful differential diagnosis between AD and other dementias. Its routine use is not recommended to diagnose dementia.
B	The determination of T-tau, Aβ42 and P-tau in CSF can be used as an additional test in cases of mild cognitive impairment when the clinical, neuropsychological and evolving features lead to AD being suspected as an aetiology of such impairment.
A	The 14-3-3 protein test in CSF is recommended when CJD is suspected.
✔	The CSF analysis must always be performed whenever dementia secondary to an infection or encephalitic process is suspected.

8.8. Which is the structural neuroimaging technique of choice in the diagnostic process of dementia and its different types?

The study of structural neuroimaging has two aims: to rule out secondary causes of dementia (tumours, chronic hydrocephalia in adults, subdural haematoma) and[136] to provide useful information for the differential diagnosis of dementias, showing, for example, hippocampus atrophy in AD and vascular lesions in VD. [149]Neuroimaging is more useful in the initial stages of dementia (less than 2 years)[140], and it is a complement to other diagnosis tools.[149]

Diagnostic test study, 2+
Expert opinion, 4

The choice of one or the other depends on the clinical suspicion: Magnetic resonance (MRI) is, more sensitive to detect subcortical location vascular changes[25] and CJD. [157]

Diagnostic test study, 2+

Studies with volumetric MRI have also helped detect volume loss patterns in AD and other degenerative dementias, but its applicability in clinical practice has still not been established.[6] The coronal cuts in the MRI enable us to visualise and quantify the volume of medial temporal lobe, a reduction of which supports the diagnosis of AD.[158]
The SEN guideline[6,70] and the EFNS[5] recommend performing at least one neuroimaging test during the assessment of dementia.

Expert opinion, 4

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Summary of evidence

2+/4	Structural neuroimaging (CT or MRI) permit the diagnosis of some secondary causes of dementia and help towards the differential diagnosis between the dementia subtypes.[136,149]
2+/4	The MRI is more sensitive to the detection of vascular changes, hippocampus atrophy and CJD.[25,157,158]

Recommendations

B	Structural neuroimaging (CT and MRI) is recommended as a supplementary tool in the initial diagnosis of dementia, above all to identify lesions that can be treated by surgery and vascular diseases.
√	The MRI is recommended to detect vascular changes with greater sensitivity than the CT.
B	The execution of an MRI with diffusion sequences is recommended if CJD is suspected.

8.9. Which is the functional neuroimaging technique of choice in the diagnostic process of dementia and its different types?

Perfusion SPECT with ^{99m}Tc-HMPAO or ^{133}Xe and PET with ^{18}F-FDG are useful to measure cerebral blood flow or glucose metabolism, respectively. They are used in specialised centres as a complement to structural imaging to increase specificity in cases of difficult different diagnosis.[5]

In AD, the observation of a pattern of hypoperfusion or tempoparietal hypometabolism is typical. SPECT has 71% sensitivity and 90% specificity to distinguish AD from controls and 76% specificity for other dementias such as VD or FTLD. The diagnostic value of the PET is greater. These techniques provide greater specificity to the clinical criteria to distinguish AD from other dementias, but they do not provide advantages when the clinical diagnosis is clear.[25,5]

Observational test diagnostic, 2+

The PET with amyloid markers shows an augmented capture in AD, variable in DLB and absent in FTLD; in MCI it can be augmented or normal. [159]Its role in clinical practice still has to be determined, as well as that of other tau markers.

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The most useful technique for the differential diagnosis between AD and DLB is the ^{123}I-FP-CIT SPECT, which uses a dopamine transporter as a marker (DAT). The striatum dopaminergic loss in DLB is similar to that of PD with or without dementia. According to a stage II study, an abnormal result has 77.7% sensitivity to detect clinically probable DLB; with 90.4% specificity to rule out dementia of another cause, mainly AD. Hypocapture was also found in 38.2% of the patients with possible DLB; 13.3% of possible AD and 6.9% of probable AD. [160]False positives have been described (pathological SPECT) in 5% of major controls and false negatives (normal SPECT) in patients with typical DLB. The reliability of SPECT with dopamine transporter has been confirmed with autopsy data. DAT capture reduction was incorporated into the reviewed criteria of DLB in basal ganglia, detected via SPECT or PET, as a suggestive feature.	Diagnostic test study, 2++
Other neuroimaging examinations can help diagnose DLB but with less sensitivity and specificity: The presence of occipital hypoperfusion or hypometabolism has sensitivity and specificity of 60-65%, so its utility is limited in individual cases; the PET with ^{11}C-DTBZ (presynaptic striatum monoaminergic marker) and the cardiac SPECT with ^{123}I-MIBG (sympathetic denervation) help discriminate DLB from AD, but they have not been applied yet in large-scale large multi-centre tests;[160] the union of^{123} I-IBZM with the striatal D2 dopaminergic receivers may be reduced in DLB; but there is considerable overlapping with AD.[161]	Diagnostic test study, 2++/2+
Frontal and/or temporal hypoperfusion is typical in FTLD, in SPECT or PET, with 80% sensitivity and 65% specificity to distinguish FTLD from AD.[159]	Diagnostic test study, 2+

Summary of evidence

2+	The sensitivity of the presence of temporoparietal hypoperfusion/hypometabolism in SPECT/PET is around 71% to detect AD and 90% specificity to distinguish AD from controls and 76% to distinguish AD from VD and FTLD.[25,5]
2+	The presence of occipital hypoperfusion/hypometabolism in SPECT/PET only has 60-65% sensitivity and specificity, to diagnose DLB.[159]
2+	The presence of frontal and/or temporal hypoperfusion/hypometabolism in SPECT or PET, has 80% sensitivity and 65% specificity to distinguish FTLD from AD.[159]

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2+	The role of the PET with amyloid markers has been well-proven but its technical peculiarities mean that its application in routine clinical practice has still not been well studied.[160]
2++	The SPECT with dopamine transporter has 77.7% sensitivity to detect clinically probable DLB and 90.4% specificity to distinguish it from AD and other dementias.[161]

Recommendations

B	SPECT and PET can be used as a complement to structural neuroimaging to support the diagnosis or to help differentiate between different types of dementia when the diagnosis is uncertain. Its routine use or its use as a sole diagnosis tool is not recommended.
B	The ^{123}I-FP-CIT SPECT is recommended to support the diagnosis of DLB (as a suggestive diagnostic feature) and for the differential diagnosis between DLB/PDD and AD.

8.10. What are the advantages of EEG mapping in the diagnosis of dementia?

The electroencephalogram (EEG) and its quantitative analysis (*mapping*) are able to detect changes in the majority of patients with AD or DLB; but these are unspecific. On the other hand, a normal EEG may be perfectly compatible with some types of dementia (for example, FTLD). Therefore, neither the presence nor the absence of changes in the EEG permit diagnosing a dementia.[5,25]

Diagnostic test study, 2+

The EEG is only useful when the dementia is suspected to be due to a CJD and it may be helpful to exclude other processes such as delirium, complex partial epileptic crises or state of non-convulsive status epilepticus, which can rarely simulate a dementia. Beyond these situations, the EEG has not proven that it should be used on a routine basis to diagnosis dementia.[5,129]

The periodic sharp wave complexes are part of the clinical criteria to diagnose CJD, with 44% sensitivity and 92% specificity.[157]

Diagnostic test study, 2++

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Summary of evidence

2+	The EEG can show unspecific changes in patients with AD or DLB. It is not useful to diagnose dementia. [5,25]It is useful to distinguish it from delirium or epilepsy.[5,129].
2++	The presence of periodic sharp waves in the EEG has 44% sensitivity and 92% specificity to diagnose CJD. [157]

Recommendations

B	The execution of an EEG is recommended if the presence of delirium, complex partial epileptic crises or non-convulsive status epilepticus is suspected.
A	The use of EEG to diagnose CJD is recommended.

8.11. What are the indications for performinga cerebral biopsy in the aetiological diagnosis of dementia?

Cerebral biopsies can provide a specific histological diagnosis when the presence of a potentially treatable origin is considered, such as certain metabolic, infectious or inflammatory causes. As it is an aggressive technique with a high risk, its execution is only considered when a treatable disease, which cannot be diagnosed in any other way, is suspected.[25]	Expert opinion, 4
During one retrospective study, the execution of a biopsy on selected patients provided the diagnosis in 57% of the cases. A potentially reversible aetiology (chronic meningoencephalitis, vasculitis, Behçet, neurosarcoidosis, granulomatose encephalopathy, Whipple), was detected in only 10%. Complications were recorded such as haemorrhages or comitial crises in 11% of the cases.[162]	Retrospective observational study, 3
In general, it is advisable to approach the frontal lobe or the temporal pole of the non-dominant hemisphere and extract a sufficiently large sample (including leptomeninges and cerebral white matter) to increase the diagnostic efficacy. It must be performed in very specialised centres.[25] In situations where prion disease is suspected, special care must be taken, using disposable material or keeping the instruments in quarantine until the specific diagnosis is obtained.	Expert opinion, 4

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Biopsies of other tissues can be useful in certain conditions, for example, to analyse tonsillar tissue in the CJD variant or a skin biopsy in the CADASIL.

Summary of evidence

3/4	Cerebral biopsies have a high risk of complications and their use is limited to the suspicion of treatable diseases that cannot be diagnosed in any other way, such as chronic meningoencephalitis, vasculitis, Behçet, neurosarcoidosis, granulomatose encephalopathy or Whipple.[162]

Recommendations

D	The execution of a cerebral biopsy for diagnostic purposes must only be considered in highly selected patients when a reversible cause is suspected that cannot be diagnosed in any other way.

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9. Different healthcare level actions

Questions to be answered

9.1. What are the healthcare levels and how are they classified?
9.2. What role does primary care play in the all-round care of dementia?
  9.2.1. Must dementia screening be carried out in the general population?
  9.2.2. What are the criteria for referring to Specialist Dementia Care Teams (SDCT)?
  9.2.3. What monitoring must be carried out by primary care on patients with dementia?
9.3. Which specialised Dementia care teams are required to address dementia (SDCT) and what role do they play?
9.4. What is the role of the social-health network in a comprehensive approach to dementia?
9.5. What role do the mental health services play in the care of dementia?
9.6. Which social services are involved and what role do they play in the care of people with dementia?
9.7. How must the care continuity between the different dementia healthcare levels be coordinated and guaranteed?

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9.1. What are the healthcare levels and how are they classified?

Healthcare levels are understood as the different health care modalities that are offered to the population, ensuring optimal care in each specific situation, guaranteeing holistic and multidisciplinary care. The coordination and consensus between the different levels provide optimal healthcare quality and avoid competence-related problems.

The National Health System (Spanish Acronym, SNHS) is comprised of a series of Health Services pertaining the State Administration and Health Services pertaining to the Autonomous Communities (A.C) under the terms established in the General Law on Health. [163]It recognise two basic healthcare levels, primary care team (PCT) and specialised dementia care team (SDCT) Social Health Care (SHC) must also be mentioned, whose creation dates back to 1986, in Catalonia,[164] as it was the first autonomous community to plan and develop this healthcare modality. From the conceptual viewpoint, the SHC is included within specialised dementia care team (SDCT) although it has sufficient entity and specific characteristics for it to be considered as a third healthcare level. The SHC has already been developed in the entire national territory165 with different degrees of implementation and with the specificities typical of each autonomous community.[166,167,168,169,170,171,172,173,174,175,176,177,178,179,180]

1. Primary Care Team (PCT)

PC is the first health care level that citizens access, as individuals and members of the community. This is essential health care based on methods and practical technologies, that are scientifically based and socially acceptable, placed within the reach of all individuals and families of the community. PC forms an integral part of both the National Health System, where it plays a central role and of which it is the main core, and of the overall social and economic development of the community. This definition includes a series of health-related actions, such as prevention, diagnosis, treatment or rehabilitation, which must be carried out from a primary and local level in benefit of the community and at an acceptable cost, to be able to respond to the people's needs during each one of the stages of the disease.[181]

PC must guarantee the comprehensiveness and continuity of the care throughout the entire lives of the users, acting as a manager, coordinator of cases and regulator of flows.[182]

PC must be able to solve the majority of the health problems of people in the community, both related to diagnosis, treatment or adaptation of resources.

2. Specialised Dementia Care Team (SDCT)

SC is the second access level of citizens to healthcare. SC offers the population technical and human resources for diagnosis, treatment and rehabilitation that, due to their specialisation or nature, cannot be solved at PC level.[183]

Hospitals and their relative speciality centres comprise the health structure responsible for programmed and urgent SC, both in hospital and outpatients as well as at home, also developing health promotion functions, disease prevention, treatment and rehabilitation as well as teaching and research, in coordination with the PC level.

SC will guarantee the continuity of the comprehensive care for patients until they can continue to be cared for in PC.[184]

3. Social Health Care (SHC)

SHC follows a multi-disciplinary and comprehensive care model that guarantees care for the elderly, chronic dependent patients and people at end-of-life stage. SHC is mainly aimed at dependent, non self-sufficient people who require help, surveillance or special care,[185] as is the case of dementia.

The principles that this model is based upon are healthcare continuity, evaluation and comprehensive treatment, bearing in mind the biopsychosocial aspects, multidisciplinary intervention, attention to the family and caregiver, as well as coordination between healthcare levels. Both institutional and non-institutional resource connection and optimisation operating systems are established[186]

SHC is provided in different fields[187] and in those territories where this care is deployed, it is possible to find: In out-patients: a) specialised comprehensive evaluation teams for the diagnosis, treatment and monitoring of patients with cognitive disorders and dementia, fragile and geriatric patients; b) home palliative care (PC) teams; c) day hospitals (DH). In internment regime, we can find: a) long-stay units that offer medical care and nursing care, which cannot be provided at home or at other healthcare levels, due to their complexity and the characteristics of the patient; b) medium-stay units whose main purpose is for rehabilitation, and PC units.

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In short, the healthcare levels are different coordinated health care modalities that provide multidisciplinary and comprehensive care that adapts to the needs of people with health problems. The National Health System (SNHS) recognises two basic healthcare levels: primary care (PC) and specialised care (SC). There is also a third social health care (SHC) level, with unequal implementation in the different autonomous communities, which covers the home, hospital and outpatients care resources that permit offering continued and comprehensive care until the end-of-life stage.

Primary Care (PC): This is the first health care level that citizens have access to and where a team of professionals carry out disease prevention, detection and diagnosis work, followed by treatment, monitoring, management of resources and accompaniment until end of life.[181]

Specialised Care (SC): This is the second healthcare level and it offers specific and specialised care in the diagnosis, treatment and rehabilitation of health problems, which, due to their characteristics or technology needs, cannot be solved at PC level.[183]

Social-Health Care (SHC): Third level, based on a multidisciplinary and comprehensive care model that guarantees care for the elderly, chronic dependent patients and people at end-of-life stage.[185]

9.2. What role does primary care play in the all-round care of dementia?

The role of the PCT and SDCT is essential throughout the entire dementia process. Due to their proximity and contact with patients and families, they have the opportunity to detect cases of cognitive impairment at early stages. However, dementia is still under-diagnosed, with figures that vary between 25 and 80%,[188, 189,190,25] especially when dementia is in its mild-moderate stage. This is due to the diagnostic difficulty often derived from a deficiency in specific training in dementia and the reduced time to carry out the diagnosis.[189]

Early diagnosis reduces anxiety in patients and relatives and helps cope better with situations and problems that, in more advanced stages, will be more difficult to solve (decisions about guardianship, about assets, advance directive document, etc.).

The PCT must suspect the existence of cognitive impairment in the following situations: memory complaints corroborated by a reliable informant; observation of cognitive or behavioural changes; disorientation in time and space; persistent changes in mood, behaviour or personality; appearance of difficulties to carry out the advanced and instrumental activities of daily living, etc.[191,192,193,25]

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Summary of evidence

4	Alert signals for the suspicion of MCI or dementia are the appearance of memory complaints or other cognitive deficits; non-justified and persistent changes in mood, behaviour or personality; or difficulties to carry out advanced or instrumental activities of daily living. [191,192,193,25] It is essential for these signals to be corroborated by a reliable informant.
4	If good, fluent and two-directional communication is maintained between the PCT and their specialised care references, coordination between levels and healthcare continuity is guaranteed.

Recommendations

D	The PCT professionals must suspect the existence of cognitive impairment and/or dementia if they observe memory complaints, behavioural changes and difficulties to carry out advanced and instrumental ADL, carrying out screening tests and starting complementary examinations to be able to formulate a diagnosis and refer to the SDCT depending on the results.

9.2.1. Must dementia screening be carried out in the general population?

The aim of the screening strategies is to detect diseases in their initial stages, treat them early on and establish control and monitoring that will help improve the health results. The screening has a population approach. A screening strategy of a certain pathology is justified if a series of conditions are satisfied.[194]

1. It is a frequent and relevant health problem.
2. With sufficiently long clinical period to be able to be detected.
3. Availability of a sensitive, specific screen test at a reasonable price and with no side effects.
4. Have effective, safe and efficient treatment.

The first three conditions are satisfied in MCI and dementia: (1) high prevalence and major problem which, when it progresses, generates an important social and family burden; (2) prolonged clinical course; and (3) there are different screening tests with acceptable sensitivity and specificity, that are relatively economical, easy to apply and require little time and non-specific staff, but the fourth condition is not satisfied.

The cognitive assessment tests used have a low positive predictive value and the disadvantage of not being able to many patients due to the limitations of these tests, which may be influenced by the patient's age, sex, culture and education. The MMSE and the MEC are the most commonly used tests in PCT, and the score must be adapted according to age and study level[194] **(questions 8.3 and 8.4).**

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The result of a positive screening test does not necessarily entail the diagnosis of dementia. If cognitive or functional impairment is detected, the assessment must be extended with a detailed case history, which must also include the tests that assess the existence of functional loss in IADL.[195,25,196]	Expert opinion, 4
We do not have biochemical, genetic markers of neuroimaging tests for MCI and dementia, that have an acceptable level of sensitivity and specificity.[197,198]	Diagnostic test study, 2+

Summary of evidence

2+	Nowadays, and if the dementia does not satisfy all the requirements that would justify a population screen, this must not be carried out on people over the age of 65, as there are not treatments that effectively modify the evolution and prognosis of the more frequent dementias.[194,199,25,139]

Recommendations

C	There is not enough scientific evidence to permit the recommendation of population-based dementia screening in people over the age of 65.

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9.2.2. What are the criteria for referring to Specialist Dementia Care (SDC)?

The PCT must carry out the dementia orientation/diagnosis. The dementia subtype and its aetiology can be suspected in PCT but it will be confirmed in SDCT.[25,200,201] The criteria for referral to the SDCT are:

Early onset, familial of genetically determined dementias:

- Over the age of 65, with cognitive impairment in MCI degree or dementia.[200,202,203]
- Suspicion of familial dementia.[203]
- Indication of genetic counselling (HD, early AD, FTLD).[200]

Cohort study, 2+/2++
Descriptive, opinion 3
Expert opinion, 4

Difficulty to diagnose cognitive impairment, or define its degree:

- When there is a reasonable diagnostic doubt in a person who has cognitive impairment or dementia.[200,203]
- For assessment and early detection of degenerative dementias in people with MCI, when secondary causes have been ruled out.[25]

When severe secondary dementia is suspected:

- Cognitive and/or behavioural impairment in a person with recent past history of traumatic brain injury, neoplasia, treatment with oral anticoagulants or haemostasia disorder, when it is not possible to quickly rule out a pathology that requires rapid intervention with a neuroimaging test. [202]
- Fast evolving cognitive impairment associated with focal neurological symptoms or disturbances in the level of consciousness.[202]

Observational study, 2+
Descriptive study, 3

Suspicion of neurodegenerative disease:

- Which is accompanied by cognitive impairment and a diagnostic confirmation is required.[200,202,203]
- When the PCT requires the opinion of expert professionals; or additional examinations, services or treatments that are not available or not accessible through PCT.[25,200,203]
- Prescription of specific pharmacological for dementia.
- Participation in clinical trials with new experimental drugs.
- When a neuropsychological assessment is required that will help quantify and typify cognitive impairment, cognitive intervention, assessment of the premorbid intellectual level, assessment of behavioural symptomatology (above all from 50 years up and if there is depression that resists the usual treatment.

Expert opinion, 4

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Difficult to manage complications in dementia:

- Appearance of uncommon behavioural, cognitive and physical symptoms that appear in the evolving course of a person diagnosed with dementia.[200]
- Presence of severe BPSD, which do not respond adequately or as expected to the treatment.[25,200]
- For clinical monitoring of a dementia that is therapeutically difficult to manage and/or when a new diagnosis confirmation is required.[202,201]

Descriptive study, 3
Expert opinion, 4

The following should not be referred to SDCT:

- People with MCI or reversible secondary dementias with medical treatment or psychiatric approach, who can be diagnosed and treated by the PCT. Pluripathological patients with bad basic functional status, where the benefit that can be provided by the SDCT does not exceed the disadvantages that referral to the SDCT may represent.

Descriptive study, 3
Expert opinion, 4

Summary of evidence

2++/ 2+/3	The approach of early onset, familial, genetically determined dementia (early AD, HD, FTLD) must be carried out in SDCT.[200,202,203]
3/4	When there are doubts in the diagnosis of MCI or dementia, patients must be referred to the SDCT for a specific and multidisciplinary approach for neuropsychological assessments or specific additional and neuroimaging examinations to be carried out that can confirm the diagnosis [200,203,25]
2+/3	Secondary dementias that require urgent action via fast additional examinations and specialised therapeutic decisions must be referred for assessment to SDCT.[202,200]
4	The diagnostic confirmation of a neurodegenerative cause dementia (AD, DLB, FTLD) requires specialised, multidisciplinary assessment, which will include additional examinations and specific treatment, indicated and prescribed by specialists in dementia or the participation in clinical trials.[200,202,203,25]
3/4	People with already known dementia who present unusual, difficult to control behavioural, cognitive and physical symptoms are referred to SDCT;[200,25,200] or for clinical monitoring of cases that are therapeutically difficult to manage and/or when a new diagnosis confirmation is required.[202,201]
3/4	It is not useful to refer people to SDCT who have MCI or secondary dementias that are reversible with medical treatment or psychiatric approach, who can be diagnosed and treated by the PCT. It is not useful either to refer patients to SDCT who have a lot of pathology, a bad functional base status, in whom the disadvantages of the referral exceed the possible benefits.

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Recommendations

C	The PCT is advised to refer people to the SDCT who have: a) early, family or genetic onset dementia, b) doubts in the diagnosis of cognitive impairment, c) potentially severe secondary dementia, d) suspicion of neurodegenerative disease, e) unpredictable or difficult to manage complications in the course of already diagnosed dementia.
D	The referral of patients with MCI or secondary dementia that can be solved by the PCT, or pluripathological patients with bad functional basic status, is not recommended.

9.2.3. What monitoring must be carried out by primary care on patients with dementia?

The PCT must assume responsibility for the care and monitoring of the majority of people with dementia and for the management of the resources they require, continuously adapting to the changes in the disease as it evolves, the complexity of its treatment and the concomitant processes that appear during its evolution **(Appendix 1.14)**.[193,196]	Expert opinion, 4
Coordination between the different levels, PCT, SDCT, SHC is required, and also with the AFAs. This coordination of the different social-health, social and community levels ensures healthcare continuity and integration into society. Given the chronic nature of dementia and its high level of healthcare requirements, effective and adequate planning is required.[129,193,204,196]	Expert opinion, 4
Effective monitoring of dementia must consider actions that address the person affected and the care-giving family, carrying out a comprehensive approach that contemplates prevention measures of the vascular risk factors and progression of the dementia risk prevention, basic neurological and systemic assessment, assessment of the cognitive, behavioural, affective and functional functions, as well as the execution of any additional examinations required.[202,196] Changes in the evolution of the dementia, complications and the possible existence of abuse towards the patient must also be detected. The work load and the needs of the family must be assessed, as well as the state of physical, psychological and mental health of the caregiver.[25,205,202,196]	Observational study, 2++
A control must be carried out to ensure that the benefit, tolerability and adverse effects of the treatments used in dementia are specific or symptomatic, as well as a follow-up of other concomitant pathologies. The most representative symptoms will be specified, as well as the actions and recommendations to be made.[202,196]	Observational study, 2++

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The comprehensive care of dementia entails respect for dignity and defence of the patient's rights (privacy, social participation, freedom and autonomy in decision-making).[206]	Expert opinion, 4
If unexpected changes, alarm signals or behavioural crises occur, or other manifestations appear, fast attention must be provided in agreement with the requirements, guidelines and circuits established. Under normal conditions, if the process remains relatively stable or worsens in agreement with the forecasts, periodic monitoring controls of the natural progression of the dementia are recommended.[129,193]	Descriptive study, 3
The PCT must offer a care plan and support to the caregiver of the person affected by dementia, contemplating information and training aspects, accessibility and support to provide the patient with care and attention. PCT must manage the indication and access to health resources, such as home care programmes, day hospital (DH) and/or social programmes, such as the day centre (DC), admissions for rest or to control symptoms. [193]	Expert opinion, 4

Summary of evidence

4	The PCT must assume responsibility for the care and monitoring of the majority of people with dementia and for the management of the resources they require **(Appendix 1.14)**.[193,196]
4	Coordination and communication between PCT, SDCT, SHC and AFA guarantees healthcare continuity throughout the entire process.[129,193,204,196]
2++	Actions aimed at the person affected and the caregiving family must be carried out; via a comprehensive approach, pharmacological and non-pharmacological treatment, psychological and social support, detecting changes, alarm signals, complications, concomitant diseases, analysis of the suspicion of abuse, evaluation of the burden of caregivers, of their needs, and their physical, psychological and mental state of health.[25,205,202,196]
3	If unexpected changes, alarm signals or behavioural crises occur, or other manifestations, fast attention must be provided in agreement with the guidelines and circuits established. If the process remains relatively stable or predictable, the normal controls will be carried out.[129,193]
4	The PCT must provide caregivers with information, offering them support in their care work and managing the appropriate health and social resources.[193]

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Recommendations

D	The PCT must assume responsibility for the management, care and monitoring of people with dementia and of their caregivers.
D	People with predictable evolution must be periodically controlled by the PCT. If there is unexpected worsening, alarm signals, behavioural crises, etc. they must be quickly attended by PCT, and they are difficult to control, they must be referred to the SDCT.
D	Coordination and communication between PCT, SDCT, SHC and AEA must be established to guarantee healthcare continuity throughout the entire process.

9.3. Which specialised care teams are required to address dementia (SDCT) and what role do they play?

The SDCT are multidisciplinary teams of reference who carry out a comprehensive and specialised evaluation of AD and other dementias.

Each team must be made up of an expert physician in the management of dementia (neurologist, geriatrician or psychiatrist), a psychologist/neuropsychologist, a nursing professional, a social worker and administrative staff. The SDCT can be located inside or outside the hospital and must have access to all the necessary technical means to make a diagnostic assessment of syndrome, familial and social dementia. They provide healthcare, teaching, research and management functions.[6,207]

After carrying out the individual assessment, establishing the diagnosis and treatment strategy to follow, the person affected and the family must be informed about the diagnostic guideline, therapeutic possibilities, probable evolution, monitoring and social-health and community resources available **(questions 10.1.1 and 10.1.2).** All of this information will be summed up and compiled in a healthcare report addressed to the patient and/or family and to the referring practitioner from the PCT.

Summary of evidence

4	The SDCT is a multidisciplinary team of reference for a specific territorial area, which carries out a comprehensive and specialised approach for people affected by dementia.
4	The SDCT must be comprised of: an expert physician in the management of dementias (neurologist, geriatrician or psychiatrist), a psychologist/ neuropsychologist, a nurse, a social worker and administrative staff. This SDCT must have access to technical means to be able to confirm the diagnostic guideline and with healthcare, teaching, research and management objectives.[6,207]

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4	The patient and his/her family must be informed about the diagnosis and strategy to be followed **(questions 10.1.1 and 10.1.2).**
4	The patient and/or family must be given a written report listing all the examinations carried out, the diagnosis and treatment, and monitoring plan. This information must be given to the referring practitioner so that they can carry out the most appropriate control. Shared control between the PCT and the SDCT will be carried out in complicated patients.

Recommendations

D	It is recommendable for the multidisciplinary team of the SDCT to include an expert specialist physician in dementia (neurologist, geriatrician or psychiatrist), a psychologist/neuropsychologist, a nursing professional, a social worker and administrative staff. The SDCT must have access to diagnosis means to be able to design treatment, monitor strategies and satisfy their healthcare, teaching, research and management objectives.
D	Patients and/or their families must be informed about the diagnosis, the prognosis and the strategy to be followed.
D	Patients and/or their families must receive a written report listing all the examinations carried out, the diagnostic guideline and treatment, and monitoring plan. This information must be given to the PCT and/or to the referring practitioner.

9.4. What is the role of the social-health network in a comprehensive approach to dementia?

Dementia is a progressive impairment of all the functions, with different characteristics and needs depending on the stages of evolution of the disease, which include progressive dependence for ADL, behavioural alterations, added comorbidity and strain in the caregiver. To respond to these needs and guarantee healthcare continuity, a healthcare network with well-developed and planned expert professionals is essential, to provide a comprehensive, multidisciplinary and coordinated approach to dementia.[208,192,209]

Some autonomous communities have a social-health network that has different types of resources to care for people with dementia.

Dementia diagnosis and treatment units (question 9.3). They may or may not be framed within the SHC, but they are characterised by a work methodology based on comprehensive evaluation, the existence of a specialised multidisciplinary team, the integration of health care and social care, coordination with the different healthcare resources and healthcare continuity.

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Outpatient Services of Centres: They attend to in people with cognitive impairment without having to admit them. Access and registration in this type of resource must be agreed upon in each territory:[185,186]

- **Day Hospital (DH):** Its objectives are to apply non-pharmacological therapeutic measures, maintain autonomy and functional capacity with respect to the activities of daily living, physical rehabilitation, prevention and treatment of added comorbidity, health education, information, training and s to patients and to their relatives, as well a to reduce the caregiver's burden. Patients attended in DH are people with MCI or mild or moderate degree of dementia. [167]There is a multidisciplinary team at these DH that is usually comprised of an expert physician, psychologist/neuropsychologist, occupational therapist, physiotherapist, nursing staff, etc.
- **Day Centres (DC):** The aim of this type of resource, which often depends on the social area, is to maintain the ADL, behaviour control, cognition, physical functionality and attention to other social aspects of dementia patients, as well as to decrease the burden of usual caregivers. It is the most adequate resource for advanced stages of the disease. They must have expert professionals in non-pharmacological, cognitive intervention treatments and other therapeutic type activities, adapted to the more advanced stages of dementia.
- **Night care centres (NCC):** These are not very common in Spain. This is a resource whose aim is to control and treat sleep disorders and remove the burden from the caregiver during this time period.

Internment care services:

- **Medium-stay psychogeriatric units**
  Limited duration internment, whose main aim is to treat BPSD that are difficult to control out of hospital and which cause stress and strain on the caregiver. They are also used to adapt the pharmacological treatment, which cannot be done outside the hospital, to solve serious family crises, rest or convalescence of the caregiver. The care team i multidisciplinary, with expert professionals in the comprehensive approach to dementias. This type of unit is a resource that exists in the Autonomous Community of Catalonia.[181,184,182,183]

- **Long-stay psychogeriatric units**
  They offer care to patients with dementia with different levels of dependence and degrees of clinical complexity, who require continuous health care and which cannot be provided at the home or at other healthcare levels.[184]

Other resources:

There are other types of resources to care for people with dementia, the ones that merit special attention being residential centres, which are normally centres managed by the social services.

There are other resources available, which the health professionals must be aware of; these are telecare, home support teams of the social services, etc.[185]

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Summary of evidence

4	Dementia generates a series of needs that require a social health resources network with expert professionals who can respond to these needs, and guarantee healthcare continuity, ensuring a comprehensive, multidisciplinary and coordinated approach of each case.[208,192,209]
4	The social health resources in those territories that have this type of care can include: dementia diagnosis and treatment units (question 9.3); outpatient services: Day Hospital (DH); Night care centres (NCC); internment services: Medium-stay psychogeriatric units; Long-stay psychogeriatric units. Other resources: Telecare, home support social teams.[185,181,184,182,183]

Recommendations

D	The existence of specific resources is recommendable to care for people with dementia, and the SHC network must have specific resources that adapt to each stage of the disease.
✔	To optimise the comprehensive treatment of dementia, it is recommendable for there to be referral, admission and discharge criteria for each healthcare resource.
D	Treatment in specific day hospitals for dementia is recommended in mild and moderate phases of dementia.

9.5. What role do the mental health services play in the care of dementia?

There are no documents that provide scientific evidence to define the role of the mental health services in the care of dementia.

The Mental Health Strategy of the SNHS (2007),[210] published by the Ministry of Health and Consumer Affairs, indicates that the development of specific care systems for mental disorders in elderly people present a diversity that is linked to the territorial organisation of the State, and underlines as a critical point, the scarcity of specific multidisciplinary programmes to provide mental health care for elderly people, and includes dementia among these mental disorders

Today, the majority of autonomous communities have incorporated healthcare objectives into their mental health or gerontological health plans, aimed at elderly people with mental health problems in general and with dementia in particular.

The Spanish Consensus on Dementia, whose second edition was published in 2005,[167] dedicates a chapter to the management of patients with dementia, including several considerations about care for people with dementia made by the different mental health systems.

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Mental health care evolves around a central axis: The multidisciplinary and comprehensive evaluation mental health teams that have a clear community vocation. These are teams that are closely related to PCT, from whom they receive demands to evaluate cases where cognitive impairment is suspected, above all when these are accompanied by psychological and/or behavioural disorders (depression, psychotic symptoms, premorbid personality changes) or atypical disorders (in the case of young people who start with psychological and/or behavioural disorders prior to the manifestation of cognitive impairment), and in the assessment and differential diagnosis with psychiatric diseases.

The SDCT should have the systematic collaboration of psychiatry professionals. These play an outstanding role in the evaluation of behavioural and psychological manifestations of dementia, as well as in the pharmacological treatment of the associated pathopsychology and in drawing up, together with the rest of the team, the non-pharmacological intervention plan. Community and comprehensive guidance is very important to evaluate the caregiver's situation of strain and to plan interventions aimed at treating and preventing it.

Another area of care is hospitalisation in psychiatric units of general hospitals. The main admission criteria in these units are defined as: Risk of suicide, severe disruptive behaviour that cannot be controlled in community environments, the appearance of an acute/sub-acute cognitive impairment with no apparent cause and the need to carry out additional and complicated examinations, The aim of the admission is to stabilise the acute symptoms and control the psychological and behavioural symptoms.[192]

The length of the stay, which may be necessary due to different circumstances, justifies the existence of convalescence or medium-stay units, whose aim is to provide care in a hospitalisation regime for people who are suffering from crisis situations such as those described above, but whose clinical situation (normally sub-acute) requires specific care that is difficult to solve within the community.[192]

Summary of evidence

4	There are no documents that provide scientific evidence to define the role of the mental health services in the care of dementia.
4	The Mental Health Strategy of the SNS (2007) indicates that there are limited specific multidisciplinary programmes to provide mental health care for people with dementia.[210]
4	The majority of autonomous communities have published mental health plans that have healthcare objectives aimed at people with dementia.
4	The mental health teams carry out a comprehensive and multidisciplinary evaluation of people with dementia that present BPSD, as well as the differential diagnosis with psychiatric diseases.[167]
4	Hospitalisation in psychiatric units of general hospitals permits the admission of people with dementia when the BPSD are severe and difficult to control.[192]

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4	The convalescence or medium-stage unit permit a better and more prolonged control, if necessary, of the crisis situations that require specific care, that are difficult to solve in the community.[192]

Recommendations

√	It must be taken into account that the mental health services carry out an essential role in the care of people with dementia, as they contribute to the aetiological diagnosis, the treatment and hospitalised care if severe BPSD appear. They provide coordinated, comprehensive and multi-disciplinary care.

9.6. Which social services are involved and what role do they play in the care of people with dementia?

Social services are a series of resources, benefits, activities, programmes, material and amenities that are aimed at providing the population with social care. Their aim is to respond to the social needs of families, to complement the economic benefits and at the same time strive to achieve an improvement in the living conditions of the beneficiaries, reducing, insofar as possible, the personal limitations caused by age or disability.[211]

The Public Care Social Services Network is comprised of public and private social services that are accredited and approved by the Administration. It is governed by the principles of universality, equality, public responsibility, solidarity, civic participation, globality, subsidiarity, prevention and community dimension, promotion of social cohesion, standardisation, coordination, personalised and comprehensive care, respect for the rights of people, promotion of personal autonomy, economy, efficacy and effectiveness, quality of the services and continuity of services.[212,213]

The demand for social services is progressively increasing in agreement with the increasing number of people affected by dementia; this fact is favoured by changes that occur in the family structure, especially due to the majority participation of women in the labour world and the respective reduction of their caregiving activity.

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People affected by dementia are usually cared for by the family. The prevalence of family caregivers increases with age; it is 15% when the sick person is between 65 and 69 years old; it increases to 27% between the ages of 75 and 79 and reaches 47% when the patient is over 84 years old. 60% of dependent elderly people live in their own homes; 19% of them live in the homes of their closest relatives and 77% of them live in the same home in a stable manner and with the same family caregiver.[214]	Observational study, 2++
Relatives, friends and neighbours share 85% of home care and carry out administrative formalities (93.2%), help in hygiene and showering (75.6%), in using the toilet (65.1%), bathing (46.4%), changing nappies due to urinary incontinence (35.4%) or faecal incontinence (31.1%), or else they help them eat (30%).[214]	Observational study, 2++
More than half the caregivers spend an average of 4 to 5 hours a day, seven days a week. The average time dedicated to patients with dementia amounts to 60 to 75 hours a week.[214,215]	Observational study, 2++
The annual cost of the care of a person with AD in Spain may vary, depending on the stage of evolution, between 12,000 and 22,000 Euros.[216] In a prospective multicentre cohort study, with one year control, with a sample of 560 patients with possible/probable AD, the monthly cost was 1425.73 Euro. Of this amount, 74.3% (1059 Euro) were earmarked for overall costs and 88% (1,244.22 Euro) were assumed by the family. A SR that included 16 studies on the cost of AD in Europe showed an average expenditure of 28,000 Euro, with a marked variability between countries, varying between a minimum of 6614 Euro up to a maximum of 64,426 Euro.[218]	Observational study, 2++
Spanish families express their preferences of caring for their relatives with dementia themselves; however, there are more and more caregivers (13.6 to 24.6%) who request external aid from professionals and institutions.[214]	Observational study, 2++

The relatives of patients with dementia can access the public social care services network through the district, municipality, region, PCT, SDCT, hospitals or else other social health resources. Information, guidance and counselling are offered at any of these points of the network, and social diagnoses are carried out that permit access to the different basic and specialised social benefits.

All people diagnosed with dementia who are registered in a municipality are entitled to access the public social services network. Those who do not satisfy this requirement but are in precarious situations, may have access to them, in agreement with that established in the applicable legislation on aliens.

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The social services portfolio is organised differently with different characteristics in each territory or autonomous community so it will not be described in this guideline. By way of example:

Grassroots social services: These are the gateway to the network and accessible for the entire population. The professionals who provide them and manage them hold diplomas in social work and social education, and they are responsible for informing, counselling, making diagnoses and evaluations, prescribing services, detecting risk situations that require preventive action, and carrying out community projects for the social integration of risk groups and people.

Specialised social services: They respond to situations or needs that require technical specialisation or the availability of special resources. They provide technical support and collaboration to the grassroots social services in matters of their competence.

Provision of services: Activities aimed at prevention, diagnosis, evaluation, protection, promotion, care and social insertion. These can be grassroots or specialised social services.

Information and social support: to prevent and improve the burden related to the action of caring. Cohort study, 2+/2++

- **Psycho-educational interventions:** They inform the family about existing resources that will enable them to plan the strategy to be followed during each stage of evolution of dementia. These programmes can be applied to a family individually or to a group of them, as they provide them with tools and skills to cope better with the problems, enabling them to take care of themselves and care better.[215,219]

- **Psychological interventions:** They help improve the burden of the caregiver and facilitate their adaptation to it. There are therapeutic aid programmes for one single family or for several families at the same time. The most effective interventions are those that adapt to the needs of each case, and combine information, learning skills and emotional support in several sessions.[220,221]

Social resources: These can be outpatient or part-time (a few hours and days of the week), residential or permanent, and short holiday periods.

- **Outpatient:** Day Centres (DC); Night care centres (NCC) **(question 9.4).**

- **Residential centres:** Establishments designed as permanent residences, where comprehensive and continuing health care is provided to those people affected by dementia that cannot be adequately cared for in their homes, either because they live alone or because their caregivers have not got the skills to care for them in a satisfactory manner.

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- **Therapeutic holidays for people with dementia:** This resource is limited; it provides people with dementia and their relatives with the possibility of enjoying holidays with therapeutic, training, respite, socialisation and free time activities. They can be carried out at spas, at hotels, country holiday houses, etc. There is always a multidisciplinary team of professionals, who act as a therapeutic, animation and care team.

Economic benefits: Monetary aid provided by the Administration to help people who are specifically in a situation of social need, including retirement, disability pension, grant related to the Law of Dependence, contract for the caregiver and other economic subsidies.

They can be granted by way of subjective right, right of attendance or social emergency and they are governed by Law 13/2006, 27 July, on economic social benefits.[222]

Home aid: They may or may not be instrumental. Their aim is to favour and prolong the time people with dementia can remain in their homes. It contemplates family worker measures for personal hygiene, eating or controlling medication, accompaniment, volunteerism, physiotherapy, speech therapy, cognitive intervention, nursing, meals on wheels service, home care service (HCS), adaptation of the home, telecare, intervention and communication techniques (ICT), etc.

The social services resources or helpful aids for people with dementia and their families are summed up in **Table 3.**[223,224]

Table 3. Social-health resources in the care of dementia[223,224]

Resources	Person with dementia	Relatives
Provision of services	• Prevention • Diagnosis • Evaluation • Protection	• Prevention • Diagnosis • Evaluation • Protection • Promotion • Care
Information and social support	• Information • Psychological support	• Information • Counselling – Legal – Resources – Aid • Care management • Psychological support • Therapeutic aid groups (TAG) • Mutual aid groups (MAG)

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Services such associal resources	• Day Centres • Night care centre • Family respite • Residential centres • Sheltered homes • Community canteens • Adapted transport • Therapeutic holidays	• Family associations • Family rest • Therapeutic aid groups (TAG) • Therapeutic holidays • Information material • Training programmes • ICT
Economic benefits or aid	• Disability pension • Retirement • Law of Dependence	• Caregiver contract-dependence law • Economic aid
Home benefits or aid	• Family worker • Companion/volunteer • Canteen service • Physiotherapy • Speech therapy • Neuropsychology • Nursing cures • HCS • Telecare • ICT	• Family worker • Adaptation of the home • Accompaniment • Care to grief

Summary of evidence

4	The demand for social services increases as the number of people affected by dementia increases.
2+	The family usually cares for people with dementia. The number of caregivers increases with the age of the people: 15% (65 to 69 years), 27% (75 to 79 years), 47% (over 84 years). 60% of dependent elderly people live in their own homes, 19% in the homes of relatives and 77% live in the same home as the family caregiver.[214]
2+	The most common tasks of the caregivers of people with dementia include: Carrying out administrative formalities, helping in hygiene, cleanliness, showering and use of the bathroom, changing nappies and helping them eat (30%).[214]
2+	More than half the caregivers of people with dementia spend an average of 4 to 5 hours a day, 7 days a week, in their task of caring, Dedication reaches 60 to 75 hours a week.[214,215]
2+/ 2++	The annual cost of a person with AD in Spain may vary, depending on the stage of evolution, between 12,700 and 22,000 Euro. [216]In a prospective cohort study, with one year control, on 560 patients with AD, the monthly cost was 1425.73 Euro: 74.3% (1059 Euro) earmarked for overall costs. 88% of the total cost (1,244.22 Euro) was assumed by the family.[217]
2+	A SR that included 16 studies on the cost of AD in Europe showed an average expenditure of 28,000 Euro, with marked variability between countries, varying varied between a minimum of 6,614 Euro up to a maximum of 64,426 Euro.[218]

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2+	Spanish families prefer to care for their relatives with dementia themselves; however, there are more and more caregivers (13.6 to 24.6%) who request external aid from professionals and institutions.[214]
4	All families affected by dementia may access the social services network. There they are offered information, counselling, advice and social diagnosis, and access is provided to social benefits.
4	The Social Services Network of the Public Administration (Spanish acronym RSSAP) includes a services portfolio that may vary from one territory to another.

Recommendations

D	It is recommendable for health and social services professionals to have a knowledge of the problems that affect their dementia patients to be able to provide an answer to their demands and know what tasks caregivers must carry out, the time they spend, the environment where they live, and the cost it represents for the family.
D	The Administration, through its social services network, must adapt to the increase in demand for care and services for people with dementia.
D	Favouring access to social services is recommendable as well as providing the services to give adequate support to the task of caring of families that care for people with dementia.
D	It is recommendable to step up the support measures to make it easier for people with dementia to remain at home.
C	Psychological support and psychoeducational interventions geared towards families with people with dementia are recommendable, in order to favour their task of caring, reduce the care burden and improve the quality of life.
D	In each case and depending on the moment of evolution of the dementia, it is recommendable to dynamically select the best social service resource that must be provided to a family caring for a person with dementia.

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9.7. How must the care continuity between the different dementia healthcare levels be coordinated and guaranteed?

The PCT will make the referral to the SDCT when the referral criteria established are fulfilled **(question 9.2.2)**. Communications between both levels must be quick and effective, avoiding continuity solutions or unnecessary repetitions that may cause problems in those affected or additional costs.[25,6,207]	Expert opinion, 4
The multidisciplinary assessment by the SDCT must be carried out as soon as possible and in a coordinated manner. Once the diagnosis has been carried out and after establishing the therapeutic proposal it must be transmitted, with a detailed report, to the referring PCT, for them to put into motion the decisions and strategies established.[25,6,207]	
There must be coordination in the use of the resources, avoiding unjustified delays that might alter the efficacy of early use, optimising times and contents, satisfying the admission and discharge criteria of each resource and facilitating the formalities and access to them.[25]	
The continuity of care for patients and their families must be crosscutting and longitudinal, ensuring that there are no losses when the resources are changed and that the family never feels neglected. These measures must be stepped up in the most advanced stages of dementia, at the actual home and at the relative internment centre.[25]	Descriptive study, 3 Expert opinion, 4
It is important for all the professionals, of the different healthcare and social services levels, to continue collaborating in the post mortem stage, to collect biological samples and neurological tissues to be able to carry out a fail-safe diagnosis of the type of dementia.[25,6]	Expert opinion, 4
Coordinated and multidirectional action must contemplate the comprehensive nature of resources available at social health level and of the community, including the AFA and other institutions/foundations that work to improve the quality of care of people with dementia.	Expert opinion, 4

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This coordination between healthcare levels must be adapted individually to each person and family and must be extended to joint coordination or work among the different SDCT.

This must also be extended to collaboration in teaching and research between the different levels, and the University, the pharmaceutical industry and other institutions that earmark resources for research in basic, clinical and social aspects in the field of dementia.[25]

One element that may favour coordination is the supply, storage and exploitation of the data of a common and shared record of data available on prevalent cases of dementia. All the professionals from the different levels can collaborate in compiling information, maximising the personal requirement for quality data. This information is helpful for health and social planning.[225]

Expert opinion, 4

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Summary of evidence

4	The PCT must refer to the SDCT when the referral criteria established are fulfilled **(question 9.2.2).** The coordination between both levels permits healthcare continuity and avoids repeating examinations and thus reduces problems or additional costs.[25,6,207]
4	The SDCT carries out a multidisciplinary assessment to reach the diagnosis, designs treatment and monitoring strategies, and transmits a detailed report to the PCT, for them to put the established strategies into motion.[25]
4	In the care of people with dementia, there must be coordination in the use of the resources, according to admission and discharge criteria, and avoid delays that might alter the efficacy, optimising the duration and the interventions, facilitating formalities and access.[25]
4	The continuity in care of people with dementia and their families is longitudinal to guarantee that the family never feels neglected. These measures must be stepped up in the more advanced stages of dementia.[25]
4	To guarantee the diagnosis of people with dementia, there should be collaboration between the health professionals from the different levels and those of the social services who intervene in the process. This collaboration must continue in the post-mortem phases to facilitate the collection of biological samples and neurological tissues.[25]
4	The desirable coordination between the different SDCTs must be related to care (common criteria, action protocols), in teaching and research, and it will be reinforced by establishing links with the university, pharmaceutical industry and institutions that earmark resources to basic clinical and social research in dementia.[25]

4	The selection and storage, by the professionals who intervene in the process, of minimum quality data of the people affected by dementia and their relatives in a common centralised record favours coordination between the three levels (PCT, SDCT, SHC). The exploitation and analysis of the data available in the record permits improving knowledge of dementia and planning health and social improvement strategies and policies.[225]

Recommendations

D	To ensure seamless social and health care in the care of people with dementia and their families, it is recommendable, throughout the entire process, for there to be coordination between the different care levels, social services and community resources.
D	To favour the comprehensive care of the person/family with dementia, it is recommendable for the communication and coordination between the different levels (health, social and community) to be fast, efficient, effective and multidirectional.
D	It is recommendable for all the care levels to collaborate in obtaining a fail-safe diagnosis, favouring the obtaining of biological and neurological tissue samples.
D	Coordination at the different healthcare levels is recommendable in order to favour respect for the rights and freedoms of patients in decision-making (advance directives).
D	Coordination between the healthcare levels, the SDCT, universities, pharmaceutical industry, teaching and research institutions and the AFA is recommendable to favour an increase in knowledge (training and research) of dementias (health, social, community aspects).
D	It is recommendable for the different professionals who intervene in the care of dementia to collaborate in drawing up a record of dementias to have a better knowledge of reality and rationally plan new intervention strategies.

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10. Dementia treatment

10.1. General measures

Questions to be answered

10.1.1. When and how must patients and their families be informed of the dementia diagnosis?
10.1.2. What basic content must the information given to patients and family have?

10.1.1. When and how must patients and their families be informed of the dementia diagnosis?

98% of families want the patient to be informed.[226] 92% of the patients want to know the diagnosis. There are families that hide information from the patients arguing that they want to protect them and minimise the impact that the information about the disease may generate. It has been demonstrated that the information received does not predispose or generate an affective disorder or depression in the person affected.[227,228,229]	Descriptive study, 3
Patients and their families must be informed about the dementia diagnosis when we have a reasonable suspicion of the diagnosis. Normally it is the family of the person affected that fosters the consultation with the practitioner, alarmed by the uncertainty generated by detecting the changes observed in the relative affected. In these cases, the families and people affected need information that will enable them to understand the current problem and be able to cope with future problems. Patients and/or families must be informed by the physician from the SDCT and/or PCT.	Expert opinion, 4
There are patients who wish to be informed and others that do not wish to receive information, on their own volition or because they are unable to assume it, due to the actual disease. This right must be respected whenever it does not harm them.[140,230,231]	Expert opinion, 4

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Patients and/or their families must be informed of the diagnosis with caution, without haste, and in appropriately intimate and comfortable conditions and environment. A professional/patient/family relationship must be created based on a commitment of respect and trust. The dialogue will be aimed at helping them understand the diagnosis and favour decision-making, and it must be empathic, simple and two-way, listening to the patients' and their families' opinions, and facilitating an exchange of questions and answers. Individually adapt the information offered to patients and families so that it is understood, bearing in mind the patient's cognitive impairment, age, sex, race, education level, culture and religion. If there are language barriers, communication must be facilitated through an independent cultural mediator.[193]	Expert opinion, 4
It is advisable to give the information progressively, devoting the necessary time. The information offered must be true and non-alarmist, not allowing for doubts or creating false expectations.[140]	Descriptive study, 3 Expert opinion, 4
Notifying the diagnosis may cause a great impact on patients and their families, to the extent that the session has to be interrupted and offering time for thought. In these cases, the information must be extended during control visits and/or with the subsequent participation in information sessions carried out by the SDCT and/or PCT and complemented in the associations of families of people affected by dementia (AFA).[193]	Expert opinion, 4
Further information or verbal communication may be provided through explanatory leaflets, videos and other audiovisual means aimed at helping understand the diagnosis. Further information can also be provided through recommended websites, books, AFA.[232]	Descriptive study, 3-

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Summary of evidence

3	The majority of patients and families wish to be informed.[226] However, there are families that hide information from the patients to protect them and minimise the impact of the process. It has been shown that receiving information does not generate affective disorders or depression.[227,228,229]
4	To favour the comprehensive care of the person/family with dementia, it is recommendable for the communication and coordination between the different levels (health, social and community) to be fast, efficient, effective and multidirectional.

4	The patient's right to be informed must be respected, especially in the onset stage of dementia, when they can maintain their memory, capacity to understand, assimilate information, be aware of the scope and impacts, and be able to decide on who they wish to inform about the process (family, friends). The right to not want to be informed must be respected.[140,206]
4	The information about dementia to be transmitted to patients and their families must be reasonable, individualised, respectful, empathic, simple, understandable and two-way. It must be transmitted in appropriately private and comfortable conditions and environment, aimed at helping understand the disease and decision-making. This will facilitate the exchange of questions and answers. If there are language barriers, the intervention of an independent cultural mediator will be provided.[193]
4	It is advisable to give the information progressively, if necessary, devoting the necessary time, with true, non-alarmist content and not leaving any doubts or creating false expectations.[140]
4	Communicating the diagnosis of dementia may produce a great impact on patients and their families. It may be necessary to interrupt the information session and offer time for thought. The information must be updated and/or further information provided during successive visits, with information sessions organised by the SDCT and/or PCT and complemented at the AFA.[193]
3	Further verbal information may be provided through explanatory leaflets, videos, DVD and other audiovisual means, if necessary, to help understand the diagnosis. Further information can also be provided through recommended websites, books, AFA.[232]

Recommendations

D	Informing patients and their families of the dementia diagnosis is recommended when there is reasonable suspicion of dementia. The SDCT physician and/or PCT are the people who must inform.
C	Informing patients who request this and their families of the diagnosis is recommended; as it has been proven that the information received does not predispose or generate a disorder in the person affected.
D	The patients' right to be informed or not must be respected, as well as their right, if they are capacitated to do so, to choose those people around them who must be informed of the process.

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C	Offering information via understandable, sensible, respectful, empathic, verbal communication, and an adequate environment and conditions is recommended, to facilitate two-way dialogue. To make it easy to understand the diagnosis and its consequences, further information can be provided via information leaflets, booklets, videos, Internet and other audiovisual means and associations of families of dementia patients (AFA). If there are language barriers, communication must be facilitated through an independent cultural mediator.
D	The individual evaluation of the possible impact that communicating the diagnosis may generate is recommended, as well as doing so in instalments if necessary, providing further information during successive visits and in information sessions (SDCT, PCT, AFA).

10.1.2. What basic content must the information given to patients and family have?

The basic information received by patients and their families must be comprised of:[129] — Expert opinion, 4

- Diagnosis of the disease
- Type of dementia
- Stage in the evolution of dementia that the patient is in.
- Probable prognosis
- Treatment to follow
  - Drugs: Benefits and adverse effects
  - Non-pharmacological interventions
  - Guidelines and recommendations
- Guidance about successive controls and emerging alarm signals that require urgent attention.
- Information about available resources and their accessibility.

The information given must enable patients and their families to:

- Plan their future
- Decide on the guardian to take decisions
- Reorganise and take decisions about economic and legal questions.
- Accept the treatment proposed or not, weighing up risks and benefits.
- Accept participation in research programmes or not.

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Information can be offered to patients with mild dementia who can understand the explanations, express their concerns and comment on the difficulties to plan the future with the aid of relatives and professionals. Expert opinion, 4

Knowing the prognosis of the disease will give them the chance to be able to plan their future, exercising their right to decide (advance directive documents, appoint a guardian).[233,42]

The group information sessions aimed at the families must contemplate the following aspects: Expert opinion, 4

- Inform about basic aspects of the disease and its evolution stages.
- Differentiate cognitive, behavioural and functional symptoms.
- Impact of the loss of autonomy.
- Involvement of the different professionals (PCT, SDCT, SHC).
- Foster comprehensive and multidisciplinary treatment
- Foster help to the caregiver and to the family.
- Advise about the prognosis and future prospects.
- Inform about the social health and social resources available.
- Advise about basic legal aspects.
- Management and attitudes to be adopted to cope with emerging problems.
- Evaluate the needs, burdens, demands, risks or repercussion of the caregiver.
- Help implement a solid family support network.
- Inform the caregiver about support resources.

The basic information about dementia must be complemented with more specific contributions, for those families with patients in very advanced stages of dementia, whatever the aetiology, or when they live with people affected by DLB, FTLD or VD, and they pose different problems to the normal ones of AD.

Training health practitioners, social services professionals and professional volunteers is necessary so that they can manage a group of MAG or TAG. This training programme can be carried out at any of the healthcare levels, or at the AFA.140 it is advisable for the primary caregivers (relatives or professionals) to receive training that will empower them to manage dementia and carry out non-pharmacological interventions. Training provides useful competence to carry out the non-pharmacological interventions indicated by the SDCT or PCT professionals, at home or in a nursing home.[193] Expert opinion, 4

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Summary of evidence

4	Patients with mild or moderate dementia can be informed. This information can be beneficial as it will enable patients to express their concerns, doubts and be able to cope better with daily difficulties. Knowing the prognosis of their disease may help them take decisions and plan their future.[233,42]
4	The basic information for patients and their families must be comprised of: Diagnosis of the disease, type of dementia, evolution stage, prognosis, pharmacological treatment, non-pharmacological treatment, monitoring and available resources.[129]
4	The information will enable patients and their families to plan for the future, decide on the guardian, reorganise financial and legal questions, evaluate pharmacological and non-pharmacological treatment, and decide upon their participation in research programmes.[129]
4	Information sessions aimed at families must contemplate basic aspects of the disease, dementia stages, diagnosis, involvement of different professionals and healthcare levels (PCT, SDCT, SHC), comprehensive multidisciplinary treatment, social health and social resources available, legal advice and economic aid.[193]
4	The information sessions to relatives offer instruments to manage emerging problems during the evolution of the disease. They inform about the burden and support measures for the caregiver, risks and repercussions, and the usefulness of creating a solid family support network to help the caregiver.[193]
4	In very advanced stages of dementia or in DLB, FTLD and VC more specific aid and information programmes must be offered to the family.[193]
4	Health practitioners, social services and professional volunteers can collaborate as MAG or TAG group leaders, after having received sufficient training in this regard. These programmes may be carried out in SPD, PC or else in the AFA.[140]
4	The primary caregivers can receive training that enables them to collaborate as co-therapists in non-pharmacological interventions of dementia.[193]

Recommendations

C	Giving information to patients and families about dementia is recommended, as well as about its evolution, clinical manifestations, comprehensive treatment and support to the caregiver, which will enable them to plan their future.
D	It is advisable for the group information sessions aimed at families to contemplate basic aspects of dementia; function of the different professionals and healthcare levels; comprehensive treatment and available resources; management of emerging problems; detection of burdens derived from the task of caring, and support to the caregiver.

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D	The execution of specific training programmes for families who live with people affected by DLB, FTLD or VC and in advanced or terminal dementia stages is recommended.
D	Training health practitioners, social services professionals and volunteers/professionals is recommended so that they can manage a group of patients and/or families affected by dementia.
D	It is recommendable to train caregivers (families or professionals) to empower them to manage non-pharmacological interventions of dementia.

10.2. Specific pharmacological treatment of dementia

Questions to be answered

10.2.1. When and how must patients and their families be informed of the dementia diagnosis?
10.2.2. Is there a specific pharmacological treatment for dementia?
10.2.3. Is the specific pharmacological treatment equally effective in all people?

Alzheimer's Disease

10.2.3. Which pharmacological treatment is effective in the treatment of mild, moderate and severe Alzheimer's disease?
10.2.4. Which specific pharmacological treatment is effective in cognitive, behavioural, functional manifestations and/or quality of life in AD?
10.2.5. What adverse effects and contraindications exist for the specific pharmacological treatment in Alzheimer's disease?
10.2.6. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe Alzheimer's disease?
10.2.7. When must specific treatment in Alzheimer's disease end?

Parkinson's disease dementia

10.2.8. Which specific pharmacological treatment is effective in Parkinson's disease dementia?
10.2.9. What adverse effects and contraindications exist in the pharmacological treatment of Parkinson's disease dementia?
10.2.10. How effective and safe is the combination of two or more specific drugs in Parkinson's disease dementia?

Dementia with Lewy bodies

10.2.11. Which specific pharmacological treatment is effective in dementia with Lewy bodies?
10.2.12. What adverse effects and contraindications exist in the specific pharmacological treatment of dementia with Lewy bodies?

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10.2.13. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe dementia with Lewy bodies?

10.2.14. How useful are drugs with dopaminergic action in dementia with Lewy bodies?

Frontotemporal lobar degeneration

10.2.15. Which pharmacological treatment is effective in cognitive and behavioural manifestations of frontotemporal lobar degeneration?

Vascular Dementia

10.2.16. Which pharmacological treatment is effective in mild, moderate and severe vascular dementia?

10.2.17. What influence does pharmacological treatment have on vascular dementia with respect to cognitive, behavioural, functional manifestations and/or quality of life?

10.2.18. What adverse effects and contraindications exist in the pharmacological treatment of vascular dementia

Other pharmacological treatments

10.2.19. Are any other types of drugs effective in cognitive and functional manifestations in people affected by any type of dementia?

10.2.1. Is there a specific pharmacological treatment for dementia?

There are currently two types of specific drugs for the symptomatic treatment of Alzheimer's disease (AD): a) acetylcholinerasterase enzyme inhibitors (ACE inhibitors): donepezil, rivastigmine and galantamine; b) a non-competitive N-methyl D-Aspartic receptor antagonist (NMDA): Memantine.

ACE inhibitors have been recommended for the treatment of patients diagnosed with mild to moderate AD.[5,234,140,42,235]	RCT, 1++/ 1+
ACE inhibitors have also proved beneficial to manage mild to moderate VD and in DLB and PDD.[140,42,5]	RCT, 1+
In RCT, patients who have been treated with ACE inhibitors have shown less cognitive, functional and behavioural impairment than those treated with placebo. [140,42,5]	RCT, 1+
The efficacy and safety profiles for the three ACE inhibitors are similar.	RCT, 1++/ 1+
Memantine has proved to be effective in the treatment of moderate to severe AD, administered in mono-therapy or combined with ACE inhibitors.[5,140,42]	RCT, 1++/ 1+

There are no specific treatments for FTLD.[5,6,52]

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Summary of evidence

1++/ 1+	ACE inhibitors have proved beneficial compared to placebo in the treatment of mild to moderate AD.[5,234,140,42,235]
1+	ACE inhibitors have proved beneficial to treat mild to moderate VD and in DLB and PDD.[140,42,5]
1++/ 1+	The efficacy and safety profiles for the three ACE inhibitors are similar.[140]
1++/ 1+	Memantine has proved beneficial compared to placebo in the treatment of moderate to severe AD, in mono-therapy or combined with ACE inhibitors.[5,140,42]
-	There is no specific pharmacological treatment for FTLD.[5,6,52]

Recommendations

A	ACE inhibitors are recommended for the specific and symptomatic treatment of mild to moderate AD.
A	Treatment with ACE inhibitors is recommended to manage mild to moderate VD.
B	ACE inhibitors have proved to be beneficial in dementia by DLB and PDD.
B	No differences have been shown regarding different ACE inhibitors (donepezil, rivastigmine and galantamine) in respect of efficacy and safety
A	Memantine is recommended as specific treatment for moderate to severe AD in mono-therapy or combined with ACE inhibitors.

10.2.2. Is the specific pharmacological treatment equally effective in all people?

Some RCT have shown differing efficacy of pharmacological treatment in people treated. In one RCT,[236] which included 240 patients with mild-to-moderate AD treated with galantamine, during a 48-month control, different degrees of cognitive decline were observed according to scores obtained in the ADAS-Cog scale, and it was possible to identify three subgroups: In the first group (82 patients) with less decline, the average score on the ADAS-Cog scale was 15+/-8, with respect to the basal, whilst in the other group (75 patients) with persistent progression, the score was 30+/-9, and in the third group (82 patients) with intermediate evolution, from 20+/-9. In general, patients who obtained a higher score on the basal ADAS-Cog scale experienced less impairment.	RCT, 1+

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

The other group of patients experienced considerable impairment and the other subgroup showed an intermediate degree of impairment, between the other two. The authors of this study conclude that they do not provide any indicative data that certain epidemiological, cognitive or genetic characteristics are correlated to greater efficacy of the treatment, so it is not possible to identify patients who will respond to the treatment a priori.

In the case of VD, slight differences in response to the treatment have been found, depending on the type of vascular lesion (cortical, subcortical or small vessel)237 and depending on age (older people have a greater probability of having associated AD).[238]

RCT, 1++/ 1+

Summary of evidence

1+	In an extension study of two RCTs with galantamine, the decline in the score on the ADAS-Cog scale after 2 years with respect to the basal was 15+/-8 points on average in one third of the patients, 20+/-9 points in another third and 30+/-10 points in the remain third of the patients.[236]
1++/ 1+	Modest response differences to the treatment have been observed in VD depending on the type of vascular lesion and on the age.[237,238]

Recommendations

-	We have little evidence about whether specific pharmacological treatment is just as effective in all people due to the lack of studies that assess the individual response to different drugs.

Alzheimer's Disease

10.2.3. Which specific pharmacological treatment is effective in the treatment of mild, moderate and severe Alzheimer's disease?

ACE inhibitors

ACE inhibitors are approved in Spain for mild or moderate AD. Memantine is approved for moderate and severe AD.

A Cochrane SR[239] performed a MA of 13 multi-centre, double blind RCT, on parallel groups, with 7,298 participants (2,228 receiving treatment with donepezil, 2,267 receiving treatment with galantamine and 2,803 receiving treatment with rivastigmine) to assess the efficacy (cognitive, functional and global) and safety of the ACE inhibitors in AD.

MA of RCT, 1++

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

The MA revealed benefits associated with ACE inhibitors compared with placebo in cognitive function, according to the improvement observed in the scores of the ADAS-Cog (-2.7 points) and MMSE scales, a beneficial effect on ADL, according to scores on the PDS scale, and modest efficacy on behavioural disorder (apathy, anxiety and depression), according to score of the NPI-total scale. With respect to quality of life, there is no evidence of a benefit, assessed using quality of life scales after 12 and 24 weeks.[240,241]

There are very few comparative studies between the different ACE inhibitors. One Cochrane SR[239] identified four comparative studies. Two of them, simple blind, compared donepezil and galantamine: One of them showed a greater benefit in cognitive function after 12 weeks (-2.5 points on average on the ADAS-Cog scale, with no differences in MMSE) and in ADL (2.10 points in DAD) in patients treated with donepezil, which was not corroborated by the other more prolonged study, lasting for 52 weeks,[242] and which did not show any differences between the two drugs according to scores on the ADAS-Cog, MMSE and ADL scales. The other two studies that compared donepezil and rivastigmine, one 12-week single blind[243] and another 2-year double-blind one,[244] did not find any differences with respect to cognitive function, behavioural disorders, ADL or global functioning, assessed by means of the SIB, GDS, ADAS-Cog, ADCS-ADL, MMSE and NPI scales. Despite the slight variations in the action mechanism of the three ACE inhibitors, current evidence does not provide proof of any significant difference in efficacy and safety profile between them.

Comparative studies, 1++

The majority of the available RCTs last for 6 months The effect of the ACE inhibitors cannot be demonstrated in a longer term, although there are observational studies that show that the long-term benefit continues after the control year.

Patients treated with ACE inhibitors have a probability of 2.5 points more than those not treated of progressing more slowly during a 2-year observation period.[245]

Observational study, 2++

In a SR of 22 RCT[241] (12 studies with donepezil, six with galantamine and four with rivastigmine) with 9,883 participants who presented mild to moderate AD, the results showed an improvement or maintenance of the cognitive function for all three drugs, compared with placebo and a favourable effect in ADL

SR of RCT, 1+

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

Donepezil

Donepezil has proven to be effective in patients with mild, moderate and severe AD. The recommended starting dose is 5mg/day for 4 weeks, increasing afterwards to 10 mg/day.[246,235] the duration of the majority of the RCT has been 12-24 weeks, except for two lasting for 12 months and another that lasted for more than 24 months. The majority were carried out on patients with mild to moderate AD (MMSE: 10-26 points), two with moderate to severe AD (MMSE: 5-17 points), and one with mild AD (MMSE: 21-26 points).

RCT, 1++

In a Cochrane SR[240] until 2005, 23 multi-centre, double blind RCT were included in a MA, all of them with parallel groups, except for one crossed[247] and another with one part crossed and another with parallel groups[248], with a total of 5,272 participants, to assess the benefit of donepezil after 12, 24 and 52 weeks. The results of the MA based on 14 RCT were as follows: 1) cognition: Donepezil showed a statistically significant improvement with respect to placebo in the ADAS-Cog scale after 24 weeks, both with 5 mg/day (-2.01 points) and with 10 mg/day (-2.80 points). An improvement was also observed in MMSE after 52 weeks with 10 mg/day (1.84 points); 2) global clinical status: The number of patients with mild or moderate AD who showed an improvement in score on the CIBIC-plus scale after 24 weeks was greater in patients treated with donepezil, 5 mg/day (OR = 2.18) and 10 mg/day (OR = 2.38) than with placebo; 3) ADL: Donepezil has shown an improvement in ADL with respect to placebo.

SR and MA of RCT, 1++

In a study [249] on patients treated with donepezil at a dose of 10 mg/day, an improvement was observed in functionality according to the PDS scale (3.8 points) after 52 weeks. In one of the studies, a decrease was observed in the open phase, in the score of the total NPI scale after 6 to 12 weeks with respect to the basal; patients who had received donepezil continued to improve whilst those who had received placebo got worse. The benefit of donepezil on the NPI has been observed both in outpatient and institutionalised patients. [251]

RCT, 1+/1-

Donepezil showed a delay in institutionalisation of patients in one study but not in the other, both with limited methodological quality.[42]

RCT, 1-

According to a RCT performed on patients with mild or moderate AD,[248] the modest improvement in cognitive function of patients treated with donepezil is maintained for 2 years, although a reduction in the institutionalisation rate is not observed. In this study no significant differences were observed either between donepezil and placebo with respect to the BPSD and the adverse effects.

RCT, 1+

More than 5 years have passed since the publication of the Clinical Practice Guideline and its validity has not been reviewed

The dose of 10 mg/day showed a greater benefit than the dose of 5 mg/day on the symptoms of AD in the majority of the studies. The evidence of correlation between the dose and the effect of the donepezil is weak. [240]

RCT, 1+

Rivastigmine

Rivastigmine has confirmed its efficacy in patients with mild and moderate AD. The recommended dose is 6-12 mg/day (oral), starting treatment with 1.5 mg/12 h and increasing to 1.5 mg/12 h every 4 weeks. The recommended dose via transdermal route is 4.6-9.5 mg/day starting with 4.6 mg for 4 weeks and then increasing to 9.5 mg.[246,235]

RCT, 1+

A Cochrane SR[239] until 2008 included nine RCT, with a total of 4,775 patients with mild to moderate AD, in outpatient regime, with maximum control of 26 weeks, except for one that lasted for 12 months, and it showed the following results: 1) cognition: Rivastigmine at a dose of 6 to 12 mg/day showed an average improvement of -1.99 points on the ADAS-Cog scale compared with placebo at 26 weeks. Two SR[252,253] showed a benefit in cognitive function in patients treated with rivastigmine. One CPG[235] referred to the existence of a benefit with rivastigmine in cognitive function; 2) global clinical status: rivastigmine at a dose of 6 to 12 mg/day showed a slight statistically significant improvement in global function, assessed by means of the CIBIC-plus, CGIC or GDS scales[254]; ADL: rivastigmine at a dose of 6 to 12 mg/day was associated with an average improvement of 2.15 points on the PDS scale after 26 weeks, which was not observed at a dose of 4 mg/day. the same CPG[235] refers to the existence of a modest benefit for ADL; 4) behavioural alterations: No significant benefit compared with placebo was shown in two studies that assessed mood and behaviour measures.[254]

SR of RCT, 1++/1+

Galantamine

Galantamine has proved to be effective in patients with mild and moderate AD. The recommended dose is from 16 to 24 mg/day, starting treatment with a dose of 8 mg/day (non-therapeutic dose) and increasing 8 mg/day every 4 weeks.[246,235] Available in tablets (taken twice a day) or capsules of extended release (taken once a day) with similar efficacy.

RCT, 1++

More than 5 years have passed since the publication of this clinical practice guideline, and its validity has not been reviewed

A Cochrane SR[253] until 2005 that included 10 RCTs, with a total of 6805 patients, observed a favourable effect of the treatments with galantamine, at doses of between 16 and 36 mg/day, in outpatients with mild-to-moderate AD compared with placebo, assessed after 3 and 6 months. The benefit was observed for doses of 16 to 24 mg/day with no significant difference between both doses, but this was not observed for the dose of 8 mg/day, according to the following results: 1) cognition: Galantamine proved to be beneficial in patients with mild-to-moderate AD, on the cognitive function (a dose of 16 mg/day) after 6 months:[253,241,5,235] 2) global clinical status: The number of patients with an improved score or with no change on the CIBIC-plus or ADCS-CGIC scale was greater with galantamine than with placebo with all doses except for 8 mg/day (or = 1.6-1.8 at dose of 16 to 36 mg/day) after 6 months; 3) ADL: Galantamine showed a lower decrease in the ADCS-ADL score with respect to placebo for 16 mg/day (3.1 points) and for 24 mg/day (2.3 Points) after 6 months. An improvement was also observed in DAD disability scale of 3.7 points with the dose of 24 mg/day; 4) behavioural alterations: An RCT that assessed the change in score of the NPI after 3 months showed no effect of the treatment with galantamine at doses of 24 and 32 mg/day. In three RCTs lasting for 6 months, an average reduction was observed of 2.1 points on the NPI scale with doses of 16 mg/day, but not with doses of 16 to 24 mg/day.

SR of RCT, 1++/1+

The effect of galantamine on severe AD has been recently assessed in a RCT[255] that included 407 institutionalised patients (MMSE 5-12 points), who received 24 mg/day galantamine or placebo for 3 years. The average score on the SIB scale improved by 1.9 points, especially in memory, Praxis and visual spatial capacity, in the group treated with galantamine and it worsened by three points in the group treated with placebo. The average score in MDS-ADL worsened by 1.2 points in the galantamine group and 1.6 points in the placebo group.

RCT, 1+

Memantine

Memantine has proved to be effective in patients with moderate and severe AD. The recommended dose is 20 mg/day, starting treatment with 5 mg/day and increasing 5 mg/every week.[246,235]

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

One Cochrane SR[256] on patients with moderate to severe AD treated with memantine at doses of 20 mg/day showed a significant difference in cognitive function assessed via the SIB scale, in the global function according to the CIBIC-Plus scale, in ADL according to ADCS-ADL scale and in mood and behaviour according to NPI scale, after 24 and 28 weeks. Out of five RCT that assessed behavioural alteration, only two showed statistically significant differences with respect to placebo. Three RCT carried out on patients with mild to moderate AD, treated with memantine, showed significant differences in cognitive function (ADAS-Cog scale), global function (CIBIC-Plus scale), and no differences were found with respect to mood and behaviour (NPI scale).

SR of RCT, 1+

The data of three RCTs lasting for 6 months on patients with MMSE between 10-24, showed a minimal benefit of memantine 20 mg/day compared to placebo, in cognition (average improvement of 0.99 points in ADAS-Cog scale) and in global clinical status (average improvement of 0.13 points of CIBIC-plus), clinically not relevant. No effect was observed on ADL or on behavioural alterations.[256]

Not many studies have been carried out on patients with moderate and severe dementia. The data from three RCT lasting for 6 months on patients with MMSE between 3-15 showed the benefit with memantine 20 mg/day over placebo in the following aspects: 1) cognition: Average improvement of 2.97 points on the SIB scale. One study[257] also assessed the change in the MMSE scale and no significant differences were observed between memantine and placebo; 2) global clinical status: Average improvement of 0.28 points on the CIBIC-plus scale; ADL: average improvement of 1.27 points on the ADCS-ADLsev scale; behavioural alterations: improvement of 2.76 points on average in the total NPI. Patients who received memantine proved to have a slightly less probability of experiencing agitation, but there is no proof of an effect on already existent agitation.

RCT, 1++

One MA that included 1,826 patients belonging to six RCTs[258] with moderate to severe AD treated with memantine or placebo showed the benefit of the group treated with memantine according to a score in the total NPI.

MA of RCT, 1++

Summary of evidence

ACE inhibitors	
1++	The effect of the ACE inhibitors on the cognitive functions in mild to moderate AD is similar, with an improvement compared to placebo of 1 point in MMSE and 2.70 points on the ADAS-Cog scale after 6 months.[239]

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1++	No significant differences have been observed with respect to efficacy in comparative studies between donepezil and galantamine[239,242] or between donepezil and rivastigmine.[244,243]
Donepezil	
1++	In one Cochrane SR, on patients with mild to moderate AD, donepezil showed a statistically significant improvement compared to placebo in the ADAS-Cog scale after 24 weeks, with 5 mg/day (-2.01 points) and with 10 mg/day (-2.80 points), and in the MMSE after 52 weeks with 10 mg/day (1.84 points).[246,235]
1++	The number of patients with mild or moderate AD who showed an improvement in score on the CIBIC-plus scale after 24 weeks was greater in those treated with donepezil than with placebo, both for 5 mg/day (OR = 2.18) y 10 mg/day (OR = 2.38)[240,247,248]
1+/1-	Donepezil showed an improvement compared to placebo in ADL of 3.8 points on the PDS scale with a dose of 10 mg/day at 52 weeks in one study.[249] In another study,[250] a longer period of time was observed until impairment was clinically observable in functionality, with donepezil 10 mg/day at 54 weeks.
1+/1-	Donepezil 10 mg/day showed an average improvement in total NPI at 6 weeks (6.2 points) and at 24 weeks (-3.26 points).[249,250]
1+/1-	In the open phase of one study, patients who continued treatment with donepezil maintained the decrease of NPI whilst the change to placebo produced a worsening.[249,250]
1+	The benefit of donepezil according to the NPI scale has been observed in outpatient and institutionalised patients.[259]
1+	Donepezil showed no benefit in quality of life of the patient either after 12 or after 24 weeks. The quality of life has not been assessed with other drugs.[248]
1+	Treatment with donepezil did not show a delay in institutionalisation patients with AD. [248]
1+	The dose of 10 mg/day showed a slightly greater benefit over the symptoms of AD than the dose of 5 mg/day, in the majority of studies.[240]
Rivastigmine	
1++/ 1+	Rivastigmine at a dose of 6 to 12 mg/day was associated with an average improvement of 0.99 points on the ADAS-Cog scale compared with placebo at 26 weeks in patients with mild to moderate AD, in a Cochrane SR.[239,252,253,235]
1++/ 1+	Rivastigmine 6 to 12 mg/day showed a slightly significant improvement in global function, assessed by means of the CIBIC-plus, CGIC or GDS scales.[239,254]
1++/ 1+	Rivastigmine 6 to 12 mg/day was associated with an average improvement of 2.15 points on the PDS scale of ADL after 26 weeks.[239,235]
1+	Rivastigmine showed no significant benefit compared to placebo in two studies that assessed mood and behaviour measures.[239,254]

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Galantamine	
1++	Galantamine at doses of 24 mg/day showed an improvement of 3.7 points on the DAD scale.[253]
1++	Changes have been observed in the NPI score in one RCT receiving treatment with galantamine at doses of 24 and 32 mg/day, after 3 months.[253]
1++	The dose of galantamine 8 mg/day is not effective.[246,235]
1+	In one RCT on patients with severe AD, galantamine at a dose of 24 mg/day improved 1.9 points on the SIB scale compared with a worsening of 3 points with placebo, after 3 years.[255]
Memantine	
1++	Memantine at a dose of 20 mg/day was associated with an average improvement of 2.97 points on the SIB scale compared with placebo at 6 weeks in patients with moderate to severe AD, in a Cochrane SR.[256] No differences in score were observed in MMSE
1++	Memantine 20 mg/day showed an average improvement of 0.28 points in CIBIC-plus after 6 months on patients with moderate to severe AD.[256]
1++	Memantine 20 mg/day showed an average improvement of 1.27 points in ADCS-ADLsev after 6 months on patients with moderate to severe AD.[256]
1++	Memantine 20 mg/day showed an average improvement of 2.76 points in total NPI after 6 months on patients with moderate to severe AD. A slightly higher percentage of patients remained free from agitation, delusions and disinhibition.[256,258]
1++	In patients with mild to moderate AD, memantine 20 mg/day showed an average improvement compared to placebo in ADAD-Cog and CIBIC-plus at 6 months no benefit in ADL or behaviour Was observed. [256]

Recommendations

A	Treatment is recommended with ACE inhibitors (donepezil 5-10 mg/day, galantamine 16-24 mg/day or rivastigmine 6-12 mg/day oral/4.6-9.5 mg/day transdermal) in patients with mild or moderate AD.
B	An ACE inhibitor can be used (donepezil or galantamine) in severe AD, although there is less evidence of its benefit.
A	Treatment with memantine is recommended, at a dose of 20 mg/day in patients with moderate to severe AD.

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10.2.4. Which specific pharmacological treatment is effective in cognitive, behavioural, functional manifestations and/or quality of life in AD?

Specific pharmacological treatment (ACE inhibitors and memantine), in AD, has a different effect depending on the stage of the disease (mild, moderate or severe) and according to the manifestations of the AD (cognitive, behavioural, functional and/or quality of life) as recorded in several CPG[5,25,140,42,235] y SR.[239,240,241]

Cognitive manifestations

The effect of the ACE inhibitors on the cognitive functions in AD has been statistically significant in the different RCT performed; an improvement has been observed of 1 point in MMSE scale and 3 points in the ADAS-Cog scale, compared with placebo.[42]

Donepezil

According to one MA of RCT included until 2005, in a Cochrane SR, donepezil showed a statistically significant improvement compared to placebo in patients with mild to moderate AD according to the ADAS-Cog scale after 24 weeks, with 5 mg/day (-2.01 points) and with 10 mg/day (-2.80 points). An improvement was also observed in the MMSE score (1.84 points) after 52 weeks with 10 mg/day.

MA of RCT, 1++

Rivastigmine

According to one MA of RCTs included until 2005, in a Cochrane SR[239] rivastigmine at a dose of 6 to 12 mg/day showed an average improvement of 1.99 points on the ADAS-Cog scale compared with placebo at 26 weeks in patients with mild to moderate AD.

MA of RCT, 1++

Galantamine

According to one MA of RCT included until 2005, in a Cochrane SR252 galantamine at a dose of 16-24 mg/day in patients with mild to moderate AD showed an average decrease of 3.1 points on the ADAS-Cog scale compared to placebo after 6 months.

MA of RCT, 1++

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

Memantine

According to one MA of studies included until 2006, in a Cochrane SR,[256] memantine at a dose of 20 mg/day showed an average improvement of 2.97 points on the SIB scale compared to placebo in patients with moderate to severe AD after 6 months. — MA of RCT, 1++

In one RCT, no significant differences were observed between memantine and placebo, according to assessment using the MMSE scale.[254] In patients with mild-moderate AD there was an average improvement of 0.99 points in ADAS-Cog.[256] — RCT, 1++

Behavioural manifestations

Donepezil

In a Cochrane MA[240] donepezil at a dose of 10 mg/day showed an improvement in total NPI at 6 weeks (-6.2 points) and at 24 weeks (-3.26 points). In the open phase of one of the RCTs, a decrease was observed in the score of the total NPI scale after 6 and 12 weeks with respect to the basal; patients who received donepezil in this stage continued to improve and those who had received placebo got worse. The benefit of donepezil assessed by means of NPI has been observed both in outpatient and institutionalised patients. [251] — MA of RCT, 1++

Rivastigmine

No significant benefit compared with placebo was shown in two studies that assessed mood and behaviour.[254] — RCT, 1++

Galantamine

According to three RCTs of a Cochrane MA[253], galantamine only showed a reduction of the NPI score (average of 2.1 points) after 6 months with doses of 16 mg/day, but not with doses of 16 to 24 mg/day. In another RCT no changes were shown in NPI at doses of 16 or 24 mg/day after 5 months. — SR and MA of RCT, 1++

Memantine

In patients with moderate to severe AD, treatment with memantine at doses of 20 mg/day showed an average improvement of 2.76 points in the total NPI after six months.256 Patients who received memantine showed they had a slightly less likelihood of experiencing agitation, but no effect of memantine has been observed on already existing agitation. — RCT, 1++

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One MA that included 1,826 patients belonging to six RCT[258] with moderate to severe AD, treated with memantine vs. placebo, showed a benefit of memantine in the total NPI score. Fewer symptoms (agitation/aggressiveness, delusions and disinhibition) were observed in patients at week 12, and fewer symptoms (agitation/aggressiveness, irritability/lability and disturbed nocturnal behaviour) at week 24/28. No item was worse with memantine than with placebo.

MA of RCT, 1++

Functionality

Donepezil

According to a Cochrane SR[240], one RCT showed an improvement on the PDS scale (3.8 points) with 10 mg/day after 52 weeks. A reduction in the time elapsed until clinically observable impairment was also observed, with donepezil at doses of 10 mg/day at 54 weeks in another RCT. The number of patients with mild or moderate AD who showed an improvement on the CIBIC-plus scale was greater in patients treated with donepezil at a dose of 5 mg/day (OR = 2.18) and 10 mg/day (OR = 2.38) than with placebo after 24 weeks.

RCT, 1++

Rivastigmine

At a dose of 6 to 12 mg/day there was a slightly significant improvement in global functioning according to assessment via CIBIC-plus, CGIC or GDS,[254] and an improvement of 2.15 points on the PDS scale, which was not observed at a dose of 4 mg/day,[239] after 26 weeks.

RCT, 1++

Galantamine

According to a Cochrane MA,[253] galantamine showed a lower decrease in the ADCS-ADL score at a dose of 16 mg/day (3.1 points) and at a dose of 24 mg/day (2.3 Points) compared with placebo. An improvement was observed in DAD scale of 3.7 points with a dose of 24 mg/day after 6 months. The number of patients with an improved score or with no change on the CIBIC-plus or ADCS-CGIC scale was greater in those treated with galantamine at a dose of 16 to 36 mg/day, than in the placebo group (OR = 1.6-1.8).

SR and MA of RCT, 1++

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

Memantine

In patients with moderate to severe AD[256] treated with memantine at a dose of 20 mg/day, an average improvement of 0.28 points on the SIB scale and 1.27 points on ADCS-ADL was observed, after 6 months. In patients with mild-moderate AD, the improvement in the average score of 0.13 points of CIBIC-plus was statistically significant but clinically not relevant.

RCT, 1++

Quality of life

Donepezil

Quality of life has only been assessed in studies performed with donepezil, and no benefit was observed on quality of life with a dose of 5 or 10 mg/day, either at 12 or at 24 weeks.[240]

RCT, 1++

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

Summary of evidence

Cognitive manifestations	
1++	One Cochrane MA[240] on patients with mild to moderate AD, receiving treatment with donepezil showed a statistically significant improvement in cognitive function according to assessment via the ADAS-Cog scale after 24 weeks, with 5 mg/day (-2.01 points) and with 10 mg/day (-2.80 points), and in the MMSE after 52 weeks with 10 mg/day (1.84 points).
1++	One Cochrane MA[239] on patients with mild to moderate AD receiving treatment with rivastigmine at a dose of 6 to 12 mg/day showed an improvement in cognitive function (-1.99 points in ADAS-Cog) compared to placebo at 26 weeks.
1++	One Cochrane MA[253] on patients with mild to moderate AD receiving treatment with galantamine at a dose of 16 to 24 mg/day showed an improvement in cognitive function (-3.1 points in ADAS-Cog) compared to placebo at 6 months.
1++	One Cochrane MA[256] of patients with moderate to severe AD receiving treatment with memantine at a dose of 20 mg/day showed an average improvement of 2.97 points on the SIB scale compared to placebo in after 6 months. No score differences were observed in MMSE.[257,254]
Behavioural manifestations	
1++	According to one Cochrane MA[240] treatment with donepezil at a dose of 10 mg/day showed an average improvement in total NPI (-6.2 points) after 6 weeks and -3.26 points after 24 weeks
1++	Rivastigmine showed no significant benefit compared with placebo in two studies that assessed mood and behaviour measures.[239,254]

1++	One Cochrane MA of three RCT[253], on patients receiving treatment with galantamine at a dose of 16 mg/day showed an average reduction of the NPI score of 2.1 points after 6 months, which was not observed at doses of 16.24 mg/day, or in another RCT at doses of 24 and 32 mg/day.
1++	Memantine 20 mg/day showed an average improvement of 2.76 points in total NPI on patients with moderate to severe AD after 6 months.[256,258]
Functionality	
1++	In patients with mild or moderate AD treated with donepezil, an improvement in functionality according to the CIBIC-plus scale was observed at a dose of 5 mg/day (OR = 2.18) and 10 mg/day (OR = 2.38) after 24 weeks.[240]
1++	Treatment with rivastigmine at a dose of 6 to 12 mg/day was associated with an average improvement of 2.15 points on the PDS scale of ADL after 26 weeks.[254,239]
1++	The number of patients treated with galantamine at a dose of 16 to 36 mg/day, who showed an improved score or with no change on the CIBIC-plus or ADCS-CGIC scale, was greater than the number of patients treated with placebo (OR = 1.6-1.8) after 6 months.[53]
1++	In patients with moderate to severe AD, treatment with memantine at a dose of 20 mg/day showed an average improvement of 1.27 points on the ADCS-ADLsev scale after 6 months.[56]
Quality of life	
1++	Quality of life has only been assessed in one study with donepezil, and no benefit was observed on the quality of life of the patient either at 12 or at 24 weeks.[240]

Recommendations

A	Treatment with ACE inhibitors is recommended in patients with mild to moderate AD, to manage the cognitive and functional symptoms.
A	Treatment with ACE inhibitors is recommended in patients with mild to moderate AD, to manage behavioural alterations (apathy, anxiety and depression), despite the benefit being modest.
A	Treatment with memantine is recommended in patients with moderate to severe AD, to manage the cognitive and functional symptoms.
B	There is no evidence to recommend treatment with ACE inhibitors to improve the quality of life of patients with AD.

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10.2.5. What adverse effects and contraindications exist for the specific pharmacological treatment in Alzheimer's disease?

Adverse effects

Pharmacological treatment with ACE inhibitors is well-tolerated.[5,140,252,239]	RCT, 1++/ 1+
According to several SR[240,260,256,253,254,241,261,262,263,264,265,149], the most common side effects of treatment with ACE inhibitors are gastrointestinal ones (nausea, vomiting and diarrhoea). The following appear less frequently: Abdominal pain, anorexia, weight loss, sleep disorders, muscle cramps, urinary incontinence, bradycardia and syncope. Donepezil at a dose of 10 mg/day. nausea (9%), vomiting (3%), diarrhoea (3%), insomnia (3%), fatigue (5%), anorexia and muscle cramp. Rivastigmine at a dose of 6-12 mg/day. nausea (9%), vomiting (4%), diarrhoea (3%), fatigue (14%), muscle cramps (10%), anorexia, drowsiness and insomnia. With galantamine at a dose of 8 mg/day, the side effects were not statistically significant compared with placebo. At a dose of 16 mg/day. nausea (4%), vomiting (2%), diarrhoea (5%), and anorexia (2%). At a dose of 24 mg/day. nausea, vomiting, dizziness, weight loss, anorexia, tremors and headaches. At a dose of 32 mg/day. The same as with doses of 24 mg and also abdominal pain.	SR of RCT, 1++/1+
A MA of 16 RCT and a total of 7,954 patients that assessed adverse effects of the different ACE inhibitors showed 6% of adverse effects with donepezil, 8% with rivastigmine and 12% with galantamine compared to placebo.	MA of RCT, 1+
The main side effects of memantine are: nausea (2.8%), vomiting (3%), dizziness (6.9%), confusion (7.9%), fatigue (2.3%), headache and hallucinations.[246] In the RCTs, the percentage of side effects that appeared in patients treated with memantine was similar to that observed in the placebo group.[256]	RCT, 1++
In general, some of the side effects are mild, transient or dose-dependent. Their appearance can be prevented or minimised by starting treatment with low doses and administering progressive ascending doses of each drug until the optimal tolerated therapeutic dose is reached.	Technical data sheet

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The recommended starting dose for donepezil is 5 mg/day for 4 weeks, progressively increasing to 10 mg/día;[246,235] for rivastigmine it is 6-12 mg/day (oral), starting treatment with 1.5 mg/12 h and increasing 1.5 mg/12 h every 4 weeks. Via transdermal route it is from 4.6-9.5 mg/day, starting treatment with 4.6 mg for 4 weeks and increasing to 9.5 later on.[235,246] For galantamine the recommended dose is 16 to 24 mg/day, starting treatment with a dose of 8 mg/day (non-therapeutic dose) and increasing 8 mg/day every 4 weeks.[246,235] The recommended dose for memantine is 20 mg/day started the treatment with 5 mg/day and increasing 5 mg/day every week.[246,235]

Domperidone can be used to treat mild gastrointestinal side effects of ACE inhibitors, as recommended by experts in CPG of the Junta of Castile and Leon.[234]	Expert opinion, 4

Contraindications

ACE inhibitors:

Epilepsy, asthma or chronic obstructive lung disease, arrhythmias, (with the exception of auricular fibrillation), past history of syncopes, third-degree atrioventricular blocks, sinus node disease, low blood pressure, presence of bradycardia or long QT, active peptic ulcer and urinary retention. They must be used with caution in the case of renal or hepatic insufficiency.[246,140]

Memantine: There are no absolute contraindications for its use, but it must be used with caution in cases of epilepsy, renal insufficiency or urinary retention.[246,140]

Summary of evidence

1++	Treatment with ACE inhibitors is generally well tolerated.5,140,252,239 The most common adverse effects are gastrointestinal, and other less frequent ones are anorexia, weight loss, sleep disorders, muscle cramps, urinary incontinence, bradycardia and syncope. The adverse effects are usually mild, transient and dose-dependent.[260,256,253,254,241,264,265,149]
1++	The percentage of side effects of memantine in the RCTs was similar to placebo.[256]
4	To prevent the appearance or to minimise adverse effects, progressive ascending doses of all ACE inhibitors and memantine are recommended.[234]
4	Domperidone can be used to treat mild gastrointestinal effects secondary to ACE inhibitors.[234]

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Recommendations

✓	Following the indications of the technical data sheet of the drug it is recommended to assess adverse effects and contraindications of the ACE inhibitors and memantine.
D	The administration of a progressive dose of the drug is recommended to avoid or reduce the adverse effects of the ACE inhibitors, starting the treatment at low doses, to reach the optimal tolerated therapeutic dose.
D	ACE inhibitors must be use with caution in patients with a background of epilepsy, asthma or obstructive lung disease, arrhythmias, syncopes, low blood pressure, presence of bradycardia or long QT, active peptic ulcer, urinary retention, renal or hepatic insufficiency. Memantine must be used with caution in patients with a background of epilepsy, renal insufficiency and urinary retention.
D	Domperidone can be used to treat mild gastrointestinal effects secondary to ACE inhibitors.

10.2.6. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe Alzheimer's disease?

In a RCT that included 404 patients with moderately severe or severe AD (MMSE 5-14) who received treatment with donepezil at a dose of 5-10 mg/day, memantine was added at a dose of 20 mg/day for 24 weeks to half of the patients. The combination of memantine and donepezil was associated with a significant improvement of the cognitive function (0.9 vs. -2.5 on the SIB scale), with less impairment of ADL (-2.0 vs. -3.4 on the ADCS-ADL scale 54 points) and an improvement in global clinical status (4.41 vs. 4.66 on the CIBIC-plus scale of 1 to 7), compared to those treated only with donepezil. The results were statistically significant but with little or no clinical relevance. [266,215,267]In a subsequent analysis of this RCT, it was observed that treatment with memantine improved the scores in agitation and irritability on the NPI scale after 24 weeks.[268]	RCT, 1+
A SR of RCT,[149] two CPG,[140] and consensus of experts[269] recommend the addition of memantine in patients with moderate to severe AD who received treatment with stable doses of donepezil to provide a greater beneficial effect in cognitive and functional symptoms.	SR of RCT, 1+ Expert opinion, 4

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A RCT[270] performed with 433 patients with mild-moderate AD and MMSE between 10-22 receiving stable treatment with any one of the three ACE inhibitors, received 20 mg/day of memantine vs. placebo for 24 weeks. No significant differences were observed between the group with the addition of memantine and the placebo group in any of the variables analysed (ADAS-Cog, CIBIC-plus, ADCS-ADL, NPI and MMSE).	RCT, 1+

Summary of evidence

1+	In a RCT on patients with moderately severe or severe AD treated with donepezil, the addition of memantine produced a minimal improvement compared to placebo, in cognitive scales (SIB), of ADL (ADCS-ACL), impression of change (CIBIC-plus) and some items of the statistically significant NPI, but with no clinical relevance, after 6 months.[6]
1++/4	A SR of RCT,[149] recommends the addition of memantine in patients with moderate-severe AD who receive treatment with stable doses of donepezil to provide a greater beneficial effect in cognitive and functional symptoms. That same recommendation is formulated in two CPG,[140] and in an expert consensus document.[269]
1+	In a RCT on patients with mild to moderate AD, treated with ACE inhibitors, the addition of memantine did not give rise to any change after 6 months in any variable (ADASCog, CIBIC-plus, ADCS-ADL, NPI or MMSE).[270]

Recommendations

B	The addition of memantine is recommended in patients with moderate to severe AD, treated with donepezil at stable doses in combined therapy.
B	The addition of memantine to donepezil is not recommended to treat patients with mild to moderate AD.

10.2.7. When must specific pharmacological treatment in Alzheimer's disease end?

There is no scientific evidence about the recommended duration of specific pharmacological treatment in AD, as there are no RCT that assess this item, and therefore the maintenance of the treatment or its suspension cannot be recommended, beyond the period studied in the RCT.

In a study where donepezil was interrupted for 6 weeks and was started up again later, neither cognition nor function returned to the level achieved before the interruption.[271]	RCT 1+

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Bearing in mind that the disease gets worse in some patients when the specific pharmacological treatment is withdrawn, this suspension must be assessed individually, unless there is evidence available.	Expert opinion, 4

Summary of evidence

-	There are no RCT that assess the duration of specific pharmacological treatment in AD.
1+	In one study where treatment with donepezil was interrupted for 6 weeks and was started up again later, neither cognition nor function returned to the level achieved before the interruption.[271]

Recommendations

✓	Individual assessment of the suspension of specific pharmacological treatment is recommended, as we have no studies that assess this item, and in the only study where the treatment with donepezil was interrupted, neither cognition nor function returned to the level achieved before the interruption.

Parkinson's disease dementia

10.2.8. What specific pharmacological treatment is effective in Parkinson's disease dementia?

There are studies with the three ACE inhibitors in PDD, but the majority are open-ended and small in size (<30 patients).[5]	RCT, 1+
There is only one RCT[272] with rivastigmine, which included 541 patients with Parkinson's disease and mild or moderate dementia. Patients treated with rivastigmine presented an average improvement of -2.1 points on the ADAS-Cog scale compared with placebo group (0.7 points) after 6 months. Significant improvements were observed in the scores of ADCS-CGIC in 19.8% of the patients of the group treated with rivastigmine and in 14.5% of the group treated with placebo. A significant improvement was also observed in all secondary variables including NPI and ADAS-ADL The differences were moderate and similar to the trials with rivastigmine in AD. The benefit was maintained in the extension study for another 6 months.	

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There are three small sized RCT with donepezil: One crossed pilot trial with donepezil in two 10-week periods on 14 patients with PDD[273] showed an improvement in 42% of the patients treated with donepezil on the CIBIC-plus scale, and an improvement of 17% in the placebo group An improvement of 2.1 points was observed on the MMSE scale. No changes were observed in the NPI scale.	RCT, 1-
In another RCT with 16 patients treated with donepezil an improvement was observed in the memory subscale of the Dementia Rating Scale after 15 weeks, but not in other scales.[274]	RCT, 1+
In another crossed trial in two 10-week periods with 22 patients, a significant improvement of 2 points was observed in MMSE and 0.37 points in CGI in the group treated with donepezil, with no significant improvement in ADAS-Cog, Mattis Dementia Rating Scale or Brief Psychiatric Rating Scale.[275]	RCT, 1+
In an RCT on PDD (n = 40) and DLB (n = 32) patients to assess the effect of memantine at a dose of 10-20 mg/day, a slight but significant improvement was observed in the CGI-C scale. No differences were observed in any of the cognitive, behavioural or functional scales used (MMSE, NPI, DAD).[276]	RCT, 1-

Summary of evidence

1+	In one RCT that included 541 patients with PDD, rivastigmine has shown an improvement of cognitive function (-2.1 points in ADAS-Cog *vs*. +0.7 points in the placebo group), and a modest improvement in ADCS-CGIC, NPI and ADCS-ADL, after 6 months. The results are similar to the studies in AD.[272]
1+/1-	In three RCTs with the reduced number of patients and short duration,[273,274,275] donepezil has proved to be beneficial in some variables but not in a consistent manner.
1-	In one RCT that included 40 patients with PDD and 32 with DLB,[276] memantine only showed a slight improvement in CGI-G.

Recommendations

B	The use of rivastigmine is recommended in PDD.
B	The use of donepezil may be considered to treat cognitive and functional symptoms in PDD.
C	There is not enough evidence to recommend the use of memantine in PDD.

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10.2.9. What adverse effects and contraindications exist in the specific pharmacological treatment of Parkinson's disease dementia?

In one RCT, patients treated with rivastigmine presented a higher percentage of nausea, vomiting, dizziness and increase in the intensity of tremors (10.3%), than those of the placebo group. A lower mortality rate was observed in the group treated with rivastigmine.[272]	RCT, 1+
In one RCT with a reduced number of patients treated with donepezil, the rate of adverse effects was similar to the placebo group and no worsening of the parkinsonism was observed.[274,273,275]	RCT, 1+
In one RCT with memantine, the rate of side effects observed in the group treated with memantine, was similar to the placebo group[276]	RCT, 1+

Summary of evidence

1+	In one RCT on patients with PDD and treated with rivastigmine a greater incidence of adverse effects was observed as well as an increase in tremors and a lower rate of mortality compared with the placebo group.[272]
1+	In one RCT with donepezil, the rate of adverse effects were similar to the placebo group and no worsening of parkinsonism was observed.[274,273,275]
1+	In RCT with memantine, the rate of adverse effects was similar to the placebo.[276]

Recommendations

B	In patients affected by PDD, treatment with donepezil and memantine is associated with a rate of adverse effects similar to the placebo group, unlike with rivastigmine, which showed a higher rate of side effects, an increase in tremors and a lower rate of mortality than the placebo group.

10.2.10. How effective and safe is the combination of two or more specific drugs in Parkinson's disease dementia?

No RCT has been published in literature that has evaluated the efficacy and safety[o] of combining two or more specific drugs in Parkinson's disease dementia.

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Dementia with Lewy bodies

10.2.11. What specific pharmacological treatment is effective in dementia with Lewy bodies?

One RCT that included 120 patients with DLB treated with rivastigmine at a dose of 6-12 mg for 20 weeks showed a modest improvement in the "cognitive velocity" variable and in the NIP-4 variable (delusions, hallucinations, apathy and depression). 40% of the patients treated and 20% of the placebo group showed more than a 30% reduction of the score in NPI-4 and in other scores of NPI 10. There were no significant differences between both groups on the MMSE scale and no worsening was observed in the motor scale of UPDRS.[277]	RCT, 1-
Another RCT lasting for 20 weeks that included 92 patients showed an improvement in attention, work memory and episodic memory assessed according to the Cognitive Drug Research Computerized Cognitive Assessment. [278]The benefit observed reverted to the suspension of treatment.	
Open-ended studies with donepezil and galantamine have shown an improvement in cognitive function and BPSD.[279,280]	RCT, 1-
In the only RCT performed with memantine, which included 72 patients (40 with PDD and 32 with DLB) 34 of whom received memantine at a dose of 20 mg/day and 38 with placebo for 6 months, the group with memantine showed an improvement on the CGIC scale in the group of patients with PDD, but this was not statistically significant in the group of patients with DLB. The results are not conclusive.	RCT, 1-

Studies on treatment of DLB, with the exception of the McKeith RCT, are scarce, of limited methodological quality and low evidence level.[277] There are no specifically designed studies to determine when treatment must be suspended

Summary of evidence

1+	Two RCT with rivastigmine at a dose of 6-12 mg/day, lasting for 20 weeks, showed an improvement in cognitive velocity, attention, work memory, episodic memory and in BPSD: Delusions, hallucinations, apathy and depression, assessed according to the NPI scale.[277,278]
1-	In open-ended studies, donepezil and galantamine have shown an improvement in BPSD and cognitive function.[279,280]
1-	In one RS T that included a reduced number of patients with PDD and DLB, treatment with memantine did not show any clinical improvement.[276]

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Recommendations

B	The use of rivastigmine is recommended to treat BPSD in DLB.
C	The use of donepezil or galantamine may be considered to treat cognitive symptoms and BPSD in DLB.
C	There is no evidence to recommend the use of memantine in DLB.

10.2.12. What adverse effects and contraindications exist in the specific pharmacological treatment of dementia with Lewy bodies?

In one RCT with rivastigmine,[277] 92% of the patients with DLB who received an active drug and 75% of those that received placebo presented adverse effects. The most frequent were nausea (37%), vomiting (25%), weight loss (19%) and drowsiness (9%). In the group treated with rivastigmine, there were more dropouts (30% vs. 16%) than in the placebo group.	RCT, 1+
In one RCT with patients with DLB treated with memantine[276] the number of adverse effects and dropouts was not greater compared with the placebo group, nor was there any worsening of the motor symptoms	RCT, 1+

Summary of evidence

1+	One RCT with rivastigmine,[277] showed adverse effects in 92% of the patients with DLB who received an active drug and 75% of those that received placebo. In the group treated with rivastigmine there were more dropouts (30% vs. 16%).
1+	In one RCT with patients with DLB treated with memantine276 the number of adverse effects and dropouts was not greater, compared with the placebo group, nor was there any worsening of the motor symptoms.

Recommendations

✓	The most frequent adverse effects observed in treated patients with DLB are: nausea, vomiting, weight loss and drowsiness. These were more frequent in patients treated with rivastigmine compared to placebo.Those treated with memantine compared to placebo had the same adverse effects. The potential adverse effects of rivastigmine must be detected and monitored during treatment.

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10.2.13. How effective and safe is the combination of two or more specific drugs in mild, moderate and severe DLB?

There are no studies that assess the effect of the combination of several specific drugs in patients with DLB.

10.2.14. How useful are drugs with dopaminergic action in dementia with Lewy bodies?

The efficacy of levodopa on extrapyramidal symptoms in DLB has not been assessed in methodological quality studies. In retrospective observational studies, both a lack of response to levodopa or a limited response as well as a marked response have been described; the results are difficult to interpret.[281] In the few open-ended prospective studies that exist, with a reduced number of patients, the motor benefit associated with the levodopa in DLB is modest.[281]	Observational study, 2-
In a study that included patients with DLB (n = 20), PD and PDD, the response to the levodopa test (200 mg) was similar in the three groups; however, the proportion of responders in the DLB group was less. The good response to the levodopa test was indicative of the greater efficacy of treatment with the levodopa (0.4-3 years control).[282]	Observational study, 2-
In another study,[281] a levodopa test was performed (100 mg) on 14 patients with DLB, and an average improvement of 13.8% was observed in the UPDRS III (less than 20.5V% in PD and 23% in PDD). In 36% of the patients with DLB, a response was observed.	Observational study, 2-
In another study with 19 patients and an average control of 3 months with low doses of levodopa (368 mg), only one third of the patients obtained a motor improvement (defined as an improvement > 10% in UPDRS) and only four patients (22%) showed a motor improvement without exacerbation of psychosis.[283]	Observational study, 2-
There are no RCTs that assessed the use of dopaminergic agonists in DLB. The use of dopaminergic and anticholinergic agonists in DLB can be associated with a worsening of the cognitive and psychotic symptoms and the production of sleep alterations and orthostatic hypotension.[6,47]	Expert opinion, 4

Summary of evidence

2-	In open-ended studies with a limited number of patients, levodopa has shown a varying degree of improvement on motor symptoms in approximately one third of patients with DLB.[283]

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4	There are no RCT that assess the use of dopaminergic agonists in DLB. According to experts, the use of dopaminergic agonists and anticholinergics in DLB can be associated with a worsening of the cognitive and psychotic symptoms, producing sleep disorders and orthostatic hypotension.[6,47]

Recommendations

C	Levodopa can be used in monotherapy to treat the motor symptoms of DLB.
D	It is advisable to avoid the use of dopaminergic and anticholinergic agonists in DLB due to their potential effect of worsening the cognitive and psychotic symptoms and producing sleep alterations and orthostatic hypotension.

Frontotemporal lobar degeneration

10.2.15. Which pharmacological treatment is effective in cognitive and behavioural manifestations of frontotemporal lobar degeneration?

No drug has been specifically approved today by the European Medicines Agency (AGEMED) or the American Food and Drug Administration (FDA) to treat patients with FTLD. No RCT has been published with large samples of patients.

In the three SR,[149,284,285] that included RCT, open-ended studies and case series published until June 2008, none of the drugs assessed, which included donepezil (an open-ended study), galantamine (an open-ended study), rivastigmine (an open-ended study), selegiline (an open-ended study), methylphenidate (a RCT), selective serotonin reuptake inhibitors (SSRI) (two RCTs, four open-ended studies), trazodone and atypical neuroleptics, showed a beneficial effect on the stabilisation or improvement of cognition of patients with FTLD.

SR of RCT, 1+/1-

One randomised open-ended study[286] did not show any cognitive improvement with donepezil and a reversible improvement of the behavioural symptoms was observed.

RCT, 1-

Three studies performed with memantine (two open-ended studies)[285,287] and a series of cases[285] did not prove to be effective on cognition, and showed diverging results on behaviour.

RCT, 1-
Series of cases, 3

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With respect to behavioural alterations, two SR[284,285] and the experts support the use of SSRI (three open-ended studies, one RCT), trazodone (one RCT) and atypical neuroleptics (one open-ended study) for the symptomatic treatment of behavioural disorders in FTLD, especially in the treatment of inappropriate, compulsive behaviour, stereotypies and agitation. The SSRI could be considered as first-line drugs to treat behavioural alterations as they have a low percentage of side effects. Trazodone may produce hyper-drowsiness and atypical neuroleptics, hyper-drowsiness, weight increase and extrapyramidal effects.	SR of RCT, 1+/1-
One open-ended study with rivastigmine showed a slight behavioural improvement and cognitive worsening.[284]	RCT, 1-

Summary of evidence

1+/1-	ACE inhibitors or memantine are not effective to treat cognitive-behavioural symptoms of patients with FTLD.[149,284,286]
1+/1-	ACE inhibitors, trazodone and atypical neuroleptics are effective to treat agitation, inappropriate behaviours, compulsions or stereotypies in patients with FTLD.[284,285]

Recommendations

B	The use of ACE inhibitors or memantine to treat cognitive-behavioural symptoms of patients with FTLD is not recommended.
B	The use of selective serotonin reuptake inhibitors, trazodone or atypical neuroleptics is recommended to treat agitation, inappropriate behaviour, compulsions or stereotypies in patients with FTLD

Vascular Dementia

10.2.16. Which specific pharmacological treatment is effective in mild, moderate and severe vascular dementia?

It has been observed that ACE inhibitors may improve the cognitive symptoms of VD and mild to moderate dementia with vascular brain lesions, although they are not authorised by the FDA or by the EMEA for this indication.

One SR[288] on the treatment of VD with ACE inhibitors showed that donepezil was the most effective and best tolerated treatment. Galantamine was also effective but worse tolerated. Rivastigmine has proven to have a beneficial effect in patients with dementia and high scores on the Hachinski scale, as well as an improvement in some scales in patients with VD diagnosed according to NINDS-AIREN criteria. Memantine has not proved to be effective in cognitive functions or in global clinical function and it is well tolerated.

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Different vascular pathologies are included under the title of VD, with lesions at different levels and a different therapeutic response and course of evolution. Two RCT with donepezil[289,290] proved to be more beneficial in patients with VD who had cortical or multi-territorial lesions compared with those who had subcortical lesions.

The studies carried out are short in duration and include an heterogeneous population (patients with AD, VD or mixed), and they do not assess either behavioural disorders or quality of life.[140]

Donepezil

In two RCT with donepezil on mild-to-moderate VD, lasting for 6 months, one of them[289] with 603 patients. treated with donepezil, showed an improvement on the ADAS-Cog scale compared to placebo (5 mg/day,-1.90 points; 10 mg day,-2.33 points); with respect to global function, an improvement was observed in the CIBIC-plus for 5 mg/day and in the CDR for 10 mg/day; a benefit was observed compared to placebo in ADL (average difference in ADFACS: 5 mg/day, –1,31 points; 10 mg/day, –1,31 points).[289,290] In the other RCT 290 with 616 patients, donepezil showed an improvement in ADAS-Cog (5 mg/day, –1,65 points; 10 mg/day, –2,09 points) and in the CIBIC-plus (25% improvement of the placebo group, 39% of the group of 5 mg/day and 32% of the group of 10 mg/day).	RCT, 1+
A Cochrane RS, in a study with donepezil observed a cognitive benefit but inconsistent effects on global measures and on ADL[291]. Donepezil showed an improvement in cognitive scales after 12 and 24 weeks with 5-10 mg/day (ADAS-Cog, MMSE), in global clinical impression (CDR-SB after 24 weeks with 10 mg > 5 mg > placebo, CIBIC-plus only with 5 mg/day) and in functional capacity (improvement in IADL with the dose of 10 mg/day, ADFACS with 5 10 mg/day), with good tolerance.[291,140,5]	
Another RCT with 974 patients with VD showed the efficacy of donepezil in cognitive scales (V-ADAS-Cog), but not in the other variables.[292]	RCT, 1+
In an open-ended study, on patients treated with donepezil at doses of 5 and 10 mg/day, during a period of up to 156 weeks, the improvement or stabilisation of VD was heterogeneous without reaching statistical significance.[252]	RCT, 1-
In a RCT with 168 patients with CADASIL a beneficial effect of donepezil was observed in secondary variables (tracking test, executive functions), but not on the main variable ((V-ADASCog).[293]	RCT, 1+

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Rivastigmine

In one single RCT performed with rivastigmine on VD[238] with the participation of 710 patients, rivastigmine was effective to exclusively improve cognitive symptoms (ADAS-Cog, VADAS, MMSE) after 6 months. This improvement was only observed in older patients who supposedly had more possibility of having concomitant AD. RCT, 1+

In a RCT on 208 patients with VD with subcortical lesions treated with rivastigmine vs. acetylsalicylic acid, a benefit on cognition was observed according to MMSE and clock test; behaviour assessed with BEHAVE-AD and depression.[294] RCT, 1-

Galantamine

Two RCT on VD that included 592 patients with dementia and cerebrovascular disease, receiving treatment with galantamine at a dose of 16-24 mg/day showed a benefit, at 24 weeks, in coordination (ADAS-Cog DMP -2.29 points), in global clinical status (CIBIC-plus: Number of patients without changes or worse OR = 1.97), in ADL (DAD DMP 4.1 points) and behaviour (NPI DMP –2.06 points). This effect was maintained after 12 months in an open-ended extension study. [295]It was not possible to demonstrate this benefit in the subanalysis of the patients that would satisfy NINDS-AIREN criteria for VD. In the subgroup of patients with probable VD (188 patients), the scores on the ADAS-Cog improved by 2.4 points vs. 0.4 points in the placebo group, and the proportion of improved scores on the CIBIC-plus was 31% in the galantamine group and 23% in the placebo group.[296,297,295] RCT, 1+/1-

786 patients were included in the other study.[298] Galantamine was effective for cognition at 26 weeks (improvement of -1.8 points on the ADAS-Cog scale,-0.3 points in the placebo group), with no significant difference in the percentage of patients who responded (ADAS-Cog and ADCS-ADL), or in the CIBIC-plus or NPI score. A slight improvement in cognitive function was detected (2.4 points on the EXIT-25 scale in the galantamine group compared with -1.4 in the placebo group. RCT, 1+

Another two RCTs assessed the effect of galantamine at a dose of 16-24 mg/day in patients with VD or with AD associated with cerebrovascular disease. One of them with 396 patients in the active group and 196 in the placebo group[299] and another study with 740 patients, treated for 26 weeks,[298] show that galantamine was effective for cognition (ADAS-Cog) and that it stabilised or slightly improved the CIBIC-plus. RCT, 1+

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According to a Cochrane MA[300], galantamine can be useful in VD, although with a reduced benefit, and it is associated with a high percentage of adverse effects and drop-outs. RCT, 1+

Memantine

In a Cochrane SR,[256] the data of two studies performed on patients with mild to moderate VD treated with memantine at a dose of 20 mg/day, for 28 weeks, showed a slight beneficial effect on cognition (1.85 points in ADAS-Cog) and on behaviour (less cases of agitation than in the placebo group, 4.3% vs. 7.7%, OR = 0.54). No benefit was observed in global function. In the first study[301] with 321 patients, a significant improvement in ADAS-Cog was achieved at 7 months (0.4 points compared with -1 point in the placebo group). The response rate for CIBIC-plus, defined as improvement or stability, was not different in either group. In the other study[302] with 579 patients, an improvement was also observed in ADAS-Cog at 7 months (-1.75 points), but not in CGI-C or in functional capacity variables (CGB, NOSGER). A post hoc analysis of both studies suggests that memantine may be more effective in people with small vessel VD.[303,279] RCT, 1+

One RCT MA concludes that patients with mild to moderate VD who received memantine suffered less cognitive impairment at 28 weeks, but the effects were not clinically relevant.[237] MA of RCT, 1++

Summary of evidence

1+	Donepezil 5-10 mg/day has shown an improvement with respect to placebo in cognitive scales, global clinical impression and in functional capacity at 12 and 24 weeks in patients with VD.[292,289,290]
1+	In a study of patients with CADASIL, donepezil did not prove to be beneficial in the V-ADAS-Cog score.[292,293]
1+	Rivastigmine only improved the cognitive symptoms in a study on patients with VD.[238]
1+	In patients with VD, galantamine has shown an improvement at 6 months with respect to placebo in cognitive symptoms (ADAS-Cog), and stability or slight improvement in global clinical impression.[298,295,297,296]
1+	Galantamine has not proved to be beneficial in ADL or behaviour in patients with VD.[296,298]
4	According to the opinion of the authors of the RCT, the benefit of all ACE inhibitors on VD could be due to the associated AD component.[299,298,300]

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1+	Memantine has shown an improvement at 6 months with respect to placebo in patients with VD, only in cognitive symptoms (ADAS-Cog).[301,256,279]
1++	The ACE inhibitors and memantine have proved to be effective on cognitive improvement in VD.[237,289,290,292,301,302,256]

Recommendations

A	The use of ACE inhibitors is recommended in mild to moderate VD.
A	ACE inhibitors are recommended to improve the cognitive symptoms of mild to moderate VD.
A	Donepezil is recommended to improve the global clinical impression and functional deficiencies (ADL) in VD.
A	The use of galantamine is recommended to treat cognitive symptoms, functional deficiency and BPSD in patients with mild to moderate VD, mixed dementia and/or AD with cerebrovascular disease.
C	Rivastigmine may be used to improve cognition in VD.
A	Memantine may be used to treat cognitive symptoms of moderate and severe VD.

10.2.17. What influence does specific pharmacological treatment have on vascular dementia with respect to cognitive, behavioural, functional manifestations and/or quality of life?

In studies of VD, treated with ACE inhibitors or memantine, the beneficial results are conclusive with respect to its action on cognitive manifestations. The benefit on cognition and in these patients has been assessed via the ADAS-Cog scale and a change has been observed of -2.17 points for donepezil, -1.18 points for memantine, -1.60 points for galantamine and-1.10 points for rivastigmine. Donepezil at a dose of 5 mg/day did not show any benefit in the ADL assessed using the ADCS-ADL, DAD, ADFACS scales. At a dose of 10 mg/day the benefit was limited [256,289,290,292,301,302]

RCT, 1+

The quality of life of patients with VD and of their caregivers was not assessed in any study.

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Summary of evidence

1+	In VD, the cognitive improvement assessed with the ADAS-Cog scale was -2.17 points for donepezil, -1.60 points for galantamine, -1.10 points for rivastigmine and -1.88 points for memantine.[256,289,290,292,301,302]
1+	In VD, neither ACE inhibitors nor memantine have shown an improvement in behavioural symptoms.[289,290,292,301,302,256]
1+	Donepezil showed an improvement or no change on the CIBIC-plus scale of clinical impression at a dose of 5 mg/day, and an improvement of ADL at a dose of 10 mg/day, in two of the three available studies.[302,289,292]
-	There is no evidence in VD of the influence of ACE inhibitors and/or memantine on the quality of life of patients and of their caregivers.

Recommendations

B	ACE inhibitors may be used to treat cognitive symptoms of VD.
B	ACE inhibitors and/or memantine are not recommended to manage behavioural symptoms in VD.

10.2.18. What adverse effects and contraindications exist in the pharmacological treatment of vascular dementia?

The adverse effects and contraindications of all ACE inhibitors and/or memantine in VD, mixed dementia or AD associated with cerebrovascular disease are the same as commented in the chapter on specific pharmacological treatment of AD **(question 10.2.5)**. However, patients with VD usually have more vascular risk factors and the treatment of these factors increases the possibility of pharmacological interactions.

In the RCTs of VD, patients treated with ACE inhibitors (donepezil, galantamine, rivastigmine) presented more adverse effects than in the placebo group. In general they were slight, they went away when treatment was withdrawn, and it was rarely necessary to discontinue it.[300]

RCT, 1++

In one RCT, 21.8% of dropouts was observed due to the appearance of adverse effects on patients treated with donepezil at a dose of 10 mg/day vs. 11.1% of dropouts in the placebo group.[289] In another RCT, 8.8% were withdrawn due to adverse effects with donepezil at a dose of 5 mg/day and 16.3% at a dose of 10 mg/day *vs*. 10.1% in the placebo group.[290]

RCT, 1++

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The percentage of people treated with donepezil at a dose of 10 mg/day, who dropped out, was 26.3% compared with placebo (15.8%), in those treated with galantamine (24.4%) with respect to placebo (15.7%) and with rivastigmine (24.7%) compared with placebo (13.9%). There were no differences in the percentage of dropouts between those treated with donepezil 5 mg/day placebo or between those treated with memantine and placebo.[300]	
The most serious adverse effects were syncopes, bradycardia and the possibility of a stroke. Deaths attributed to donepezil in patients with VD are rare and controversial. [42]Bearing in mind that patients with VD usually have a high cardiovascular risk, the possibility of the ACE inhibitors being able to cause potentially serious effects requires caution in their use and stepping up surveillance in their management	RCT, 1++
In patients with mild to moderate VD who received 20 mg/day of memantine for 28 weeks, the dropout rates and the number of people with adverse events of any type, dizziness or confusion, were similar in the treatment and placebo groups.[256]	RCT, 1++

Summary of evidence

1++	The adverse effects of ACE inhibitors and memantine on patients with VD are similar to those observed in patients with AD.[256]
1++	The number of dropouts from the treatment in the RCT for VD was higher with ACE inhibitors (around 25%) than with placebo (around 15%) for a dose of 10 mg/day.[300]
1++	In people with VD treated with specific drugs, there were no differences in the percentage of dropouts between those treated with donepezil 5 mg/day and placebo or between those treated with memantine and placebo.[300]
1++	In VD treated with all ACE inhibitors, serious adverse effects (syncope, bradycardia, stroke) are not very frequent.[42]
1++	Patients with mild to moderate VD treated with 20 g/day of memantine, for 28 weeks, presented the same rate of dropouts and adverse effects as the group treated with placebo.[256]

Recommendations

✓	Bearing in mind that patients with VD usually suffer a high cardiovascular risk, treatment with ACE inhibitors should be assessed individually, paying special attention to how the treatment is managed.
✓	It is advisable to follow the indications given in the product technical data sheet.

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Other pharmacological treatments

10.2.19. Are any other pharmacological treatments effective to treat cognitive and function al functions in people affected by any type of dementia?

Drugs placed on the market today have been included in this section and whose efficacy in AD or any other type of dementia has been proven in quality RCT, and which have not been included in any other sections of this guideline. Drugs that have been exclusively approved in clinical trial context (current or past) have not been included.

Hormone treatments

Therapy with adrenocorticotropic hormone analogues (ACTH) and prednisone has not proved to be effective in the treatment of AD.[304] — RCT, 1++

Two CPGs[5,235] conclude that there is no evidence of the efficacy of oestrogen treatment or hormonal replacement therapy (HRT) to treat or prevent AD, and some studies even suggest an increased risk of cognitive impairment associated with their use.

One SR[149] concluded that the available evidence did not support the efficacy of dehydroepiandrosterone in improving memory or other cognitive aspects in healthy elderly people, although there are no quality studies that assess its efficacy in individuals with dementia. — SR of RCT, 1++

Non-steroid Anti-inflammatory drugs (NSAID)

One SR[149] concluded that there is evidence about the lack of efficacy of ibuprofen, indometacine or low doses of naproxen in the treatment of AD. — SR of RCT, 1++

Piracetam

One SR[149] assessed the efficacy of the treatment with piracetam in AD and other types of dementia, analysing 68 studies. Only three were controlled over a period of more than 3 months and many of them had low methodological quality. The conclusion of the reviewers was that the results did not support the use of piracetam in dementia or in MCI, as the benefit on the global change impression was small and not confirmed in more specific measures. — SR of RCT, 1++

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Propentofylline

One SR[149], which included four RCT published until February 2003, concluded that propentofylline did not show any benefit in the treatment of cognition, global function or ADL in patients with AD or VD.	SR and MA of RCT, 1++

Nimodipine

One Cochrane SR[305] that included studies published until August 2001 on the efficacy of nimodipine in the treatment of AD or VD, concluded that it may be beneficial at a dose of 90 mg/day, in global cognitive function at 12 weeks. Its benefit in functionality could not be demonstrated due to a lack of data.	SR of RCT, 1+
A later RCT with VD[306] did not show any benefit either at 52 weeks.	RCT, 1+

Selegiline

One RCT that assessed the efficacy of selegiline in AD showed certain efficacy at 3 months, which was not corroborated in subsequent RCT at 6 months or 2 years. [304]The EFNS CPG5 concludes that there is not enough evidence or literature to recommend the use of selegiline in the treatment of AD.	RCT, 1++

Idebenone

One RCT that assessed the efficacy of idebenone in AD showed no relevant efficacy in delaying cognitive impairment in the treatment of AD.[152]	RCT, 1++

Dihydroergotoxine mesylate

One Cochrane RS[307] that included 19 RCT published until November 2000 concluded that although mesylate dihydroergotoxine showed benefit when assessed with global impression scales, due to the fact that the majority of the studies were old, with not very specific assessment or diagnosis criteria, a beneficial effect of mesylate dihydroergotoxine on the treatment of dementia in general and on certain subtypes (AD or VD) in particular could not be concluded.	SR of RCT, 1++/1+

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Citicholine or Citidindiphosphocholine (CDP-choline)

SR OF RCT, 1+

One Cochrane SR[308] assessed 14 RCT published until 2004 on the efficacy of citicholine in the treatment of cognitive alterations in patients with vascular cognitive impairment of different degrees, although some of them are not valid for analysis, given that they included a small number of individuals and only one presented a control of less than 3 months. A second benefit of citicholine was objectified in memory, behaviour and global change impression, although this conclusion was limited by the short duration of the studies, the different dosages and administration pathways (5 intravenous, 5 intramuscular and 4 oral), inclusion criteria and methodology.

The only RCT at 12 months included in the Cochrane SR[308] did not objectify any benefit of citicholine administered orally in the treatment of VD, although the number of individuals included in the study was small. No relevant side effects were observed, but it must be highlighted that the tolerability and applicability of the parenteral administration pathways limits its prolonged use both in research and in clinical practice.

No quality studies have been found that assess the efficacy of citicholine in the treatment of AD or other degenerative dimensions.

Summary of evidence

Hormone treatments	
1++	Hormone treatments, ACTH, prednisone[304], oestrogens[304] and dehydroepiandrosterone[149] are not effective in AD and may have harmful effects.[5,235,149,304]
NSAID	
1++	Neither ibuprofen, indometacine nor low doses of naproxen are effective in the treatment of AD.[149]
Piracetam	
1++	Piracetam has not proved to be effective in the treatment of AD.[149]
Propentofylline	
1++	Propentofylline is not effective in the treatment of AD or VD.[149]
Nimodipine	
1+	Nimodipine is not effective in the treatment of VD.[305,306]
Selegiline	
1++	Selegiline is not effective in the treatment of AD.[304,5]

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Ibedenone	
1++	Ibedenone is not effective in the treatment of AD.[152]
Dihydroergotoxine mesylate	
1++/ 1+	Dihydroergotoxine mesylate has not proved to be effective in the treatment of dementia in general or on subtypes (AD or VD).[307]
Citicholine or CDP-choline	
1+	The oral administration of citicholine or CDP-choline is not effective in the treatment of VD.[308]
1+	The parenteral administration of citicholine or CDP-choline could have a certain beneficial effect on the treatment of vascular cognitive impairment in the short-term [308]
4	Parenteral administration limits the use of citicholine or CDP-choline in clinical practice in the treatment of vascular cognitive impairment.[308]

Recommendations

Hormone treatments	
A	Hormonal therapies (ACTH, prednisone, oestrogens, dehydroepiandrosterone) are not recommended as treatment of AD.
NSAID	
A	Neither ibuprofen, indometacine nor low doses of naproxen are recommended to treat AD.
Piracetam	
A	Piracetam is not recommended to treat AD.
Propentofylline	
A	Propentofylline is not recommended to treat AD or VD.
Nimodipine	
B	Nimodipine is not recommended to treat VD.
Selegiline	
A	Selegiline is not recommended to treat AD.
Ibedenone	
A	Ibedenone is not recommended to treat AD.
Dihydroergotoxine mesylate	
B	Dihydroergotoxine mesylate is not recommended to treat AD or VD.

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Citicholine or CDP-choline	
B	The oral administration of neither citicoline nor CDP-choline are recommended to treat VD.
D	The parenteral administration of neither citicoline nor CDP-choline are recommended to treat vascular cognitive impairment..

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10.3. Non-pharmacological treatment of dementias

Questions to be answered

Cognitive intervention or stimulation

10.3.1. What is cognitive intervention or stimulation?
10.3.2. What types of cognitive intervention exist?
10.3.3. Are cognitive intervention programmes effective in dementia?
10.3.4. Are computer-based cognitive intervention programmes effective in patients with Alzheimer's disease?
10.3.5. Are cognitive intervention programmes indicated in illiterate individuals or in patients with severe sensory limitations?
10.3.6. Are individual cognitive interventions recommendable?

Intervention programmes on activities of daily living

10.3.7. What do intervention programmes on activities of daily living consist of in patients with dementia?
10.3.8. Do intervention programmes on activities of daily living improve the functionality of people with dementia?

Physical activity programmes

10.3.9. Are physical activity programmes effective in improving or stabilising the functional capacity and cognitive functions of patients affected by dementia?

Other non-pharmacological treatments

10.3.10. Are there any other non-pharmacological treatments that are effective in cognitive, functional, motor and/or quality of life manifestations in dementias?

Safety of non-pharmacological treatments

10.3.11. May non-pharmacological treatments used in dementia have harmful effects?

Cognitive intervention or stimulation

10.3.1. What is cognitive intervention or stimulation?

There is no agreement in literature about the most appropriate nomenclature to name those activities that promote the fostering, maintenance or recuperation of cognitive skills and/or favour independence for ADL and socialisation. The most common terms are cognitive intervention,[309] cognitive stimulation,[6] psycho-cognitive therapy or psychosocial therapies.[25] In this guideline we will use the term cognitive intervention.

10.3.2. What types of cognitive intervention exist?

The NICE CPG classifies psycho-cognitive therapies into cognitive stimulation, cognitive rehabilitation and cognitive training. Cognitive stimulation in this sense would include those therapies that entail exposure and participation in activities and materials that require a type of general cognitive processing and which is normally done in a group with a social context. On the other hand, cognitive training would include those therapies focused on one single cognitive domain and cognitive rehabilitation would refer to those therapies specifically designed to cover the needs of a specific individual, and therefore are done individually.

Other authors[310] classify cognitive interventions into compensatory and restorative therapies. Compensatory strategies would be those whose objective is to teach new ways of carrying out cognitive tasks. They can use internal strategies, such as organising information, classifying or visualising information to remember, encoding through multiple sensory channels, asking and paraphrasing during learning, and focusing on one single task or else external strategies such as details of the environment, memory notebooks, calendars or agendas. Training in procedures can also be used to be able to carry out complex behaviours mediated by higher-order cognitive processes. Restoration strategies seek to improve functioning in specific domains in order to recuperate the functioning of these domains at premorbid level.

More specifically, the main cognitive intervention techniques described in literature are reality counselling techniques, reminiscence, validation, memory training or other basic cognitive functions, sensory stimulation and ADL training **(question 10.3.9.)**[6,311]

Reality therapy counselling: This is a group technique that aims to improve the patient' cognitive and behavioural deficits, using all possible sensory modalities to provide updated and true information about the patient and his or her environment.

Reminiscence therapy: This is based on the fact that by reviewing patients' own past with the help of significant stimuli, this will foster their coherence and adjustment to their environment. Its aim is to improve memory, favour creativity and increase the re-socialisation of patients, stimulating conversation. It also aims to increase self-esteem, personal satisfaction, well-being and satisfaction with life.

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Validation therapy: It purports to establish a communication with patients with dementia by means of accepting reality and convictions as these are experienced by the patient.

Cognitive training: This consists in the supervised repetition of a series of activities designed to exercise a specific cognitive function, such as memory, attention or planning, and it can be carried out in different environments and formats (individual, group, computer-based, etc). Cognitive training is based on the hypothesis that the repetition of an activity can improve or maintain the functional capacity in the area trained, going beyond the actual training session.

Sensory stimulation: It purports to offer sensory stimuli, either of a certain sensory modality (music therapy, aromatherapy, massages, etc), or in a multisensory way (snoezelen), to patients with dementia to favour their cognitive activity.

10.3.3. Are cognitive intervention programmes effective in dementia?

A series of limitations can be seen in the review of literature, which make it difficult to answer the question formulated. One of these limitations is the small number of high-quality methodological studies, as well as the use of different terminology and of programmes that include different combined cognitive interventions (so it is not possible to assess each one of them separately), different measurement instruments, and the possibility of the existence of a publication bias towards the studies that prove to be effective.

A MA of RCT[310] that assessed 19 controlled studies carried out until December 2004, of which only five were considered "quality", on different cognitive interventions in patients with AD or dementia in general, in mild or moderate stages, concluded that cognitive interventions can improve the cognition and functionality of patients with AD or dementia in mild or moderate stages, although the magnitude of the effect is very variable among the different aspects assessed and the different studies.

MA of RCT, 1+

The greatest benefit was detected in the executive capacity, in verbal and visual learning and in ADL. This MA found differences in the results of different cognitive interventions. Four of the five interventions that turned out to be more beneficial used general cognitive stimulation techniques, which, according to the authors, supports the idea that maintaining high mental activity levels can have a beneficial effect. The restorative techniques presented a greater effect, although not a significant one, than compensatory therapies, but this difference was not noticed when restricted to the five studies with the greatest methodological rigour.

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This MA underlines that the magnitudes of the effects of the intervention were greater in those studies that used individuals on the waiting list, respect to those that used placebo intervention (higher quality studies), and it suggests that part of the effect of the intervention may be mediated by the attention received and the social interaction programme rather than by the actual cognitive intervention. These studies, which provided control data following the interruption of the therapy, showed a positive effect up to 4.5 months.

The NICE CPG[25] included 19 RCT in its review on the topic (until 2006), in six of which cognitive intervention entailed reality counselling, in six reminiscence therapy, in six memory training, cognitive rehabilitation in one and multisensory therapy in 1 study. All of them were carried out on patients with dementia, mainly AD in mild or moderate stages. Only the multisensory therapy study included patients in severe stage. SR of RCT, 1+/1-

Four of the RCT included, specifically compared the effect of the stable therapy with ACE inhibitors (donepezil or rivastigmine) combined with cognitive stimulation compared with treatment with ACE inhibitors in an isolated manner,25 three of which showed improvements or cognitive stabilisation in those individuals who received combined treatment compared with those that only received the drug, whilst the only study that did not notice any differences was, on the other hand, the only one that used a cognitive activity as control. The authors concluded that there was reasonable evidence to support the use of cognitive intervention programmes in people with mild to moderate dementia, mainly AD, due to signs of improvement in quality of life that accompanied the modest improvements in cognitive function. They conclude, too, that cognitive training does not appear to be associated with benefits beyond the tasks trained, and that there is not enough evidence to assess the effects of reminiscence therapy and of cognitive rehabilitation in connection with the cognitive function in patients with dementia.

The CPG of the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD) of 2007,[152] after reviewing three RCT, concludes that there is not enough evidence to make a recommendation (grade C) on cognitive training or cognitive rehabilitation with reference to cognitive or functional performance in people with mild-to-moderate dementia. RCT, 1+

One RCT carried out in Spain[312] objectified cognitive stabilisation at six months in patients with AD in mild or moderate stages receiving stable treatment with ACE inhibitors after carrying out a combined activity programme that included cognitive stimulation, physical exercise and social activities with respect to controls that only received psychosocial support. RCT, 1+

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The CCCDTD 2007,[152] based on a RCT, considers that there was not enough evidence to recommend the execution of cognitive interventions in VD. A later RCT[313] did not demonstrate the efficacy of cognitive stimulation in VD. Similar cognitive interventions were applied in these two studies to those carried out on individuals with AD.	RCT, 1+
Several low quality methodological studies (case or series of clinical cases due to the low frequency of the disease) suggests that cognitive training can be effective in re-learning words in semantic dementia, although they did not assess the possible relevance of these improvements on the nomination for daily living of the patients.[314]	Descriptive study, 3

There is no RCT on the efficacy of cognitive interventions in other dementias not named in this section.

Summary of evidence

1+	Cognitive intervention programmes are effective with mild or moderate AD, to maintain their cognitive function, their functionality and quality of life, although the magnitude of the effect attributable to the actual cognitive intervention is not well established.[310]
1+	There is no direct evidence about whether one cognitive intervention is more effective than another in patients with mild or moderate AD, although interventions that require a general processing type seem to have a greater overall benefit than those where cognitive training of specific functions is carried out.[152]
1+	There is no evidence about the efficacy of cognitive stimulation programmes in patients with VD.[152,313]

Recommendations

B	The participation in cognitive intervention programmes is recommendable in patients with mild or moderate AD, to maintain their cognitive function, their functionality and quality of life, although the magnitude of the effect attributable to the actual cognitive intervention is not well established.
C	There is currently no evidence of the efficacy of cognitive stimulation in individuals with VD to recommend its use in this dementia subtype.
–	A type of specific cognitive intervention cannot be recommended at the present time, based on the degree of efficacy in patients with mild or moderate AD, although interventions that require a general processing type seem to have a greater overall benefit than those where cognitive training of specific functions is carried out.

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10.3.4. Are computer-based cognitive intervention programmes effective in patients with Alzheimer's disease?

Several studies in literature use computer support as part of a broader cognitive stimulation programme, but only three RCT have been detected that assessed the usefulness of computer-based cognitive stimulation in an isolated way.[25]

One of them[315] did not show any benefit of a memory training programme compared with the social support programme.	RCT, 1-
Another of these RCT[316] observed a slight improvement in global cognitive functions over a 24 week period when comparing the effect of a multimedia programme associated with a global cognitive intervention programme, and ACE inhibitors compared with the stimulation programme with ACE inhibitors or ACE inhibitors alone in initial AD.	RCT, 1-
A third RCT did not show significant benefits on comparing an intensive computer-based intervention programme with passive computer-based activity on individuals with mild cognitive impairment.[317]	RCT, 1-

Summary of evidence

1-	There is contradictory evidence about the benefits of computer-based cognitive intervention programmes in initial AD or mild cognitive impairment.[315,316,317]

Recommendation

C	The use of computer-based cognitive intervention programmes in initial AD or mild cognitive impairment cannot be recommended at the present time.

10.3.5. Are cognitive intervention programmes indicated in illiterate individuals or in patients with severe sensory limitations?

The majority of the studies exclude those individuals with sensory deficits in the stimulus presentation modalities or those for whom the intervention result measurement instruments are not valid. However, no evidence has been found in literature to answer this question.

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10.3.6. Are individual cognitive interventions recommendable?

An MA of RCT[310] that assessed 19 controlled studies on cognitive interventions in AD carried out until December 2004, show that the studies that assessed individualised interventions (eight studies) presented a positive effect with respect to control intervention, with a small effect magnitude, although this was greater when the control condition was the waiting list than when it was a programmed activity. The individual interventions also presented a greater positive effect magnitude, although not a significant one, than studies on group interventions (10 studies), although this difference appeared when the five higher quality methodological studies were analysed. This MA concludes that it cannot be established if the possible greater effect of individual therapy is due to greater individual attention or to the design of the most appropriate therapy for the individual. The authors point out that whatever the reason, this finding provides evidence of the potential therapeutic effect of individualised attention to patients, administered by their relatives on the patients' cognition and functionality.

MA of RCT, 1++/1+

Summary of evidence

1++/ 1+	Individual cognitive interventions are effective to stabilise the cognitive function and functionality of individuals with AD.
1–	There is not enough evidence to establish if individual interventions are more effective than group interventions or vice versa.

Recommendation

B	Individual cognitive interventions are recommendable to stabilise the cognitive function and functionality of individuals with AD.
-	The use of individual interventions rather than group interventions cannot be recommended or vice versa.

Intervention programmes on activities of daily living

10.3.7 What do intervention programmes on daily living consist of in patients with dementia?

Activities of daily living (ADL) are the series of actions that people execute every day or almost on an everyday basis to live autonomously and integrated into their environment and play their social role.[318,319]

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The most normal way of classifying ADL[320] is into basic activities (BADL), instrumental activities (IADL) and advanced activities (AADL).[318,319] ADL have a hierarchical structure and increase in complexity as the level increases and, in the majority of the cases, if the activities of one level can be carried out, this means that those of the lower levels can also be carried out. Thus, BADL are essential to survive, IADL are necessary to live independently and AADL are necessary for a socially satisfactory life. [321]

Intervention programmes on ADL are actions whose aim is to maximise the autonomy of patients in their daily lives. These programmes are based on the statement that functional dependence is a multi-cause phenomenon and they cannot only be attributed to the organic conditioning factors of the disease, but that they must also take into account the psychological and contextual factors (physical and social environment) which may contribute to maintaining it and increasing it.

Excess disability refers to the impairment caused by the lack of use of preserved capacities that are not the direct consequence of a state of physical fragility or disease and which have a reversible nature. Thus, excess disability means attributing dependence behaviours to the disease when, in fact, they are also derived from another more benign source which is reversible. [322]It must also be taken into account that excess care also fosters excess disability: Providing unnecessary aid eliminates opportunities to stimulate, exercise and practice self-care skills. [323]Based on all of this, the intervention programmes on ADL consist of giving caregivers adequate strategies to maximise the functional independence behaviours of people with dementia. These strategies are:

The graded assistance technique:[324] this covers a whole spectrum of assistance for people with dementia, consisting in providing the minimal aid that the person needs at a given moment of the evolution, to thus be able to develop their activities of daily living. This spectrum of actions contemplates the following grades, which go from minimum to maximum care. a) verbal guidelines; b) demonstration of the activity; c) physical guideline; d) partial physical assistance; e) full physical assistance.

Functionality retraining sessions: An individual intervention where objective behaviours are established and the person is asked to practice them at different times of the day, applying positive reinforcement and using the techniques of intensive practice, repetition and graded assistance.

Use of compensatory strategies: Used to adapt the activities of daily living to the patients' disabilities (use of agendas, alarms, notebooks, etc).

Environmental modifications: Changes made in the physical environment to minimise the disability.

Training the caregiver: To increase their perception of competence and control over the situations.

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Occupational therapists play an outstanding role in ADL intervention programmes, both in the assessment of needs and in the design of the intervention programme.

10.3.8. Do intervention programmes on activities of daily living improve the functionality of people with dementia?

There are very few studies that analyse the effects of intervention programmes of ADL. Two RCTs have been identified that use different populations of individuals: People with dementia who live at home with a caregiver[325] compared with people with dementia that live in geriatric homes.[326] Different types of interventions were used in both studies: Group training in ADL for 20 weeks[326], and individual intervention that consisted of teaching compensatory strategies and environmental modifications, and training for the caregiver for 5 weeks.[325]

RCT, 1+

Both studies showed an improvement in the individuals' functionality, which was maintained in the Graff study[325] after suspending the intervention, and they pointed out that it is possible to improve functionality if direct action is taken on the ADL and this is consistent with the theory of excess disability. Both studies also highlight the importance of training the caregivers (formal or informal) in the acquisition of adequate strategies to maximise functional independence behaviours and reduce the perception of emotional strain.

Summary of evidence

1+	The execution of intervention programmes on activities of daily living is effective to improve the functionality of patients with dementia and decrease the strain on the caregiver in the medium term, both in institutionalised individuals and individuals who live in the family home.[325,326]

Recommendation

B	Intervention programmes on activities of daily living are recommended to improve the functionality of patients with dementia and decrease the strain on the caregiver in the medium term, both in institutionalised individuals and individuals who live in their family homes.

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Physical activity programmes

10.3.9. Are physical activity programmes effective in improving or stabilising the functional capacity and cognitive functions of patients with dementia?

One SR that includes six studies of different designs published between the years 1974 in 2005[327] concludes that physical activity programmes can have a beneficial effect on the functional activity of institutionalised individuals with dementia, but only when a long-term physical activity programme is carried out.

SR of different designs, 1+/2+

A later RCT[328] analysed the effects of a physical activity programme lasting for one hour twice a week for 1 year on institutionalised patients with dementia, and it found a slighter decline in the functionality of patients treated.

RCT, 1+

There are no RCT on the effect of physical activity on cognitive functions or on the functionality of individuals living at home.

Summary of evidence

1+/2+	Long-term physical activity programmes are effective to maintain the functionality of institutionalised patients with dementia.[327,328]

Recommendation

B	Long-term physical activity programmes are recommended to maintain the functionality of institutionalised patients with dementia.

Other non-pharmacological treatments

10.3.10. Are there any other non-pharmacological treatments that are effective in cognitive, functional, motor and/or quality of life manifestations in dementias?

Therapeutic touches massages

In one Cochrane SR[329] about the use of therapeutic touch massages on patients with dementia, which identified 34 references in the initial searches, of which only seven were RCT and only two satisfied the requirements of the series of minimum methodological criteria, no data regarding the efficacy of this intervention on cognition or functionality of patients with dementia were found, although in the majority of these studies, the main objective was to study behavioural disorders.

SR of RCT, 1-

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Transcutaneous electrical nerve stimulation

Another SR[330] on the use of transcutaneous electrical nerve stimulation in AD and VD in mild stage, included eight RCT, although complete data were only available in three. The conclusions of the review were that transcutaneous electrical nerve stimulation could have a beneficial effect on memory, recognition of faces or motivation immediately after the application of the therapy, but it had no effects on other cognitive functions and its effect was not maintained in time, although the small number of individuals included in each study and the non-availability of all the data of all the studies made it difficult to draw conclusions.

SR of RCT, 1-

Music therapy

One SR on the use of music therapy in dementia[331] carried out until January 2006 included five RCT and concluded that the methodological quality and the results shown were poor, which did not permit drawing conclusions. Only one of the RCT assessed the cognitive function of the patients included, and compared a music therapy session with a conversation session. The authors of this RCT referred to an improvement in verbal fluency and in the contents of the discourse, with no improvement in the MMSE or in other language tests. The authors of the SR pointed to defects in the methodology and in the presentation of results, which places doubt upon the validity of the results.

SR of RCT, 1-

Multi-sensory stimulation

One SR[332] on multi-sensory stimulation (*snoezelen*) on individuals with dementia, which selected six randomised or quasi-randomised controlled studies of' 23 published until June 2006, concluded that there was no evidence about the efficacy of multi-sensory stimulation to treat dementia, including cognitive and functional data, although it was not possible to carry out a MA due to the limited number of the study and the heterogeneity of the methods used.

SR of RCT/ quasi randomised, 1+

Behavioural change, programmed hygiene and induced urination

In the CPG of the AAN[304] on the management of dementia, two RCT were reviewed that showed that behavioural change, programmed hygiene and induced urination could reduce urinary incontinence, so these practices were recommended.

RCT, 1+

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Summary of evidence

1–/1+	The use of therapeutic touch massages,[329] transcutaneous electrical nervous stimulation,[330] music therapy[331] or multi-sensory therapy[332] have not proven to be effective to treat cognitive or functional manifestations in patients with dementia or specifically with AD.
1+	Behavioural changes, programmed hygiene and induced urination are efficient to reduce urinary incontinence.[304]

Recommendation

C	The use of therapeutic touch massages, transcutaneous electrical nervous stimulation, music therapy or multi-sensory therapy cannot be recommended at the present time to treat cognitive or functional manifestations in patients with dementia or specifically with AD.
B	Behavioural changes, programmed hygiene and induced urination are recommendable to reduce urinary incontinence in individuals with dementia.

Safety of non-pharmacological treatments

10.3.11 May non-pharmacological treatments used in dementia have harmful effects?

Short-term adverse emotional consequences of cognitive interventions have been described in narrative reviews.[309] Reactions of anger against the caregiver, frustration and depression have especially been described with reality counselling therapies and frustration reactions for the patient and the caregiver with cognitive training therapies, although these are not normally reflected in clinical studies or MA on the efficacy of these therapies.

Expert opinion, 4

Summary of evidence

4	Cognitive interventions may have adverse emotional reactions when they do not adapt to the patient's context and possibilities.[309]

Recommendation

✔	Cognitive intervention programmes, especially those based on reality counselling therapies and cognitive training, must be adapted to the cognitive skills and to the emotional tolerance of each patient, in order to avoid adverse emotional consequences.

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10.4. Treatment of behavioural and psychological symptoms of dementiaQuestions to answer:

Questions to be answered

10.4.1. What do we understand by behavioural and psychological symptoms of dementia?
10.4.2. Why are BPSD important in dementia?
10.4.3. How can the intensity and frequency of BPSD be quantified?
10.4.4. At what moment in time do BPSD appear in the evolution of dementia?
10.4.5. Are there some BPSD that are characteristic of some types of dementia? 10.4.6. Which non-pharmacological measures are indicated in each BPSD in dementia?
10.4.7. What are the general recommendations for the pharmacological treatment of BPSD?
10.4.8. What is the optimal pharmacological treatment for each BPSD?
10.4.9. What adverse effects and contraindications do drugs used to control BPSD have?
10.4.10. How effective is it to combine pharmacological and non-pharmacological treatment to treat behavioural and psychological symptoms in mild, moderate and severe dementia?
10.4.11. Which are the most effective recommendations to avoid BPSD in patients with dementia?
10.4.12. How must BPSD, which are difficult to monitor in outpatient, be treated?
10.4.13. What attitudes must the caregiver satisfy to deal with patients with BPSD?

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10.4.1. What do we understand by behavioural and psychological symptoms of dementia?

In 1996, the IPA (International Psychogeriatric Association) proposed using the expression Behavioural and Psychological Symptoms of Dementia to define a series of symptoms related to the alteration of perception, the content of thought, mood and behaviour that can appear in people affected with dementia, and which form part of the expression of the disease.[333,5]

In some CPG and manuals, they are called neuropsychiatric symptoms or neuropsychiatric and behavioural disorders. In this guideline, we will refer to them by calling them, as in the majority of recommended CPGs, behavioural and psychological symptoms of dementia (BPSD).

BPSD are complex symptoms with multifactor aetiology (genetic, neurochemical, neuropathological and biopsychosocial factors) influenced by the prior personality and interaction with the environment. [334,333,335]The existence of other causes that might generate the appearance of behavioural systems must be considered, such as: The presence of pain, decompensated heart disease, dehydration, infections, the effect of some drugs or an inadequate environment.[5]

The presence of BPSD in AD, FTLD, DLB, PDD and VD is very frequent. They vary a great deal in their presentation and the stage of dementia when they appear. Knowing the triggering factors enables us to manage, implement and develop the interventions better.[5,25]

People with dementia can present three main types of BPSD:

- Mood disorders (depression, anxiety and apathy).
- Agitation (aggressiveness, irritability, unrest, shouting and erratic wandering).
- Psychotic symptoms (visual, auditory hallucinations and delusions).

In the study carried out by the European Alzheimer Disease Consortium,[336] whose objective was to identify possible neuropsychiatric syndromes in a broad sample of patients with AD, 2,354 patients were included from 12 European centres who were assessed via the NPI scale. A group of 12 symptoms from the NPI was observed in four factors that explained 51.8% of the total variance:

- The first factor, "hyperactivity" (23.1% of the total variance), included an increase in the scores on agitation, disinhibition, irritability and aberrant motor behaviour.
- The second factor, "psychosis" (10.5% of the total variance), included delusions, hallucinations and disruptive behaviour during the night.
- The third factor, "affective" (9.3% of the total variance), with an increase in score of the depression and anxiety items..
- The fourth factor, "apathy" (8.9% of the total variance), with an increase in score in the apathy and changes in intake items.

The most common of the symptoms was apathy (65%), followed by hyperactivity (64%), affective (59%) and finally psychosis (30%). The combination of the hyperactivity and psychosis syndromes occurred in 28%; the combination of hyperactivity and affective in 38%; hyperactivity and apathy in 42%; psychosis and affective in 24%; psychosis and apathy in 25%; and affective and apathy in 37% of the patients.

Apathy

This is the most frequent syndrome among the BPSD. [336,25,337,335]By apathy we understand the absence or loss of feelings, emotions or interest in the environment This lack of activity can be caused by a combination of different factors: a) cognitive: cognitive impairment and feeling of fatigue faced with the effort represented by mental activity, b) volitional: Lack of willingness to start an activity, c) motor: Akinesia or tendency towards psychomotor slowdown, d) emotional: Anhedonia and emotional poverty.

It can appear in early stages of the disease and is normally gets worse as AD evolves and it can give rise to a greater impairment in patients suffering from it.338,336 It usually generates a great impact on patients and their surroundings, possibly with respect to the loss of self-care and the disappearance of the emotional transmission with their caregivers increasing the risk of family claudication and institutionalisation Apathy is related to the affectation of the anterior cingulate medial prefrontal cortex and dorsolateral prefrontal cortex.

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Depressed mood

This is characterised by sadness, decrease of reactivity towards external stimulation, decrease of interpersonal contact, sleep alterations, feeling of uselessness, delusions, psychomotor slowdown, decrease of mime, limited dialogue initiative, monosyllable answers and rather unhelpful attitude. Irritability is also frequent and this can turn into psychomotor agitation and carrying outbursts. There is usually an abandonment of self-care, loss of appetite, tendency to reject intake, as well as avoidance behaviour, above all of social contact. Patients with dementia and depression symptoms are more susceptible to presenting more behavioural alterations, agitation and alterations of sensory perception than those who do not present depression.[339,25,338,340]

Anxiety

Anxiety is more frequent in the initial stages of AD than in the geriatric population without dementia. Its range of appearance varies between 0 and 50% with an average frequency of 32%.[269] Anxiety may arise as a result of patients realising their deficiency and when they have to cope with unknown circumstances.[341]

Aggressiveness

There are several degrees of aggressiveness that go from irritability, verbal and/or gestural aggressiveness, to psychomotor agitation with aggressiveness. It is often the result of the presence of paranoid type delusions, threatening hallucinating states and depressive-anxious pictures.

Delusions

This is an idea whose content is perceived by the patient as real, departing from objective reality, with a trait of persistence and non-influenceability, despite an external attempt to confront reality. 10 to 73% of patients with dementia developed delusions. In AD this percentage is 19.4%.[336,337]

The most common delusions in dementia and in AD are:[342,339]

- **Paranoid delirium:** The most frequent. Patients believe they are being conspired against, being robbed, deceived, spied upon, pursued, poisoned, drugged, harassed or obstructed in achieving their objectives. Here we include abandonment delirium, when patients believe that their caregivers want to get rid of them.
- **Self-referential delirium:** This is a delirious interpretation of a feeling that reaches them from their immediate environment. Feelings that would normally go unnoticed or would cause a neutral feeling, take on a new meaning and have an impact on the person. The intensity may vary from the feeling that something of what is happening around them is vaguely related to them, or interpreting certain signals in a clearly delirious manner, such as reference being made on the television to them or that somebody is weaving a plan against them.
- **Delusional delirium** (Othello syndrome or spouse paranoia): Delirious and unjustified conviction of the spouse's infidelity. More frequent in dimensions associated with binge drinking.

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- **Somatic delirium:** Delirious conviction of suffering from a disease. On other occasions, patients even believe that certain parts of their bodies do not work properly (nihilist delirium or Cotard's syndrome).

Hallucinations

These are perceptions without an object. They involve any sensory path, but in dementia, the most frequent is visual. Generally speaking, the hallucinations are threatening, terrifying and they can cause anxiety, fear, distress, flight or aggression.

Identification alterations.

These are a type of illusion associated with a secondary delirium. In AD, we can observe:

- **Errors of own identification:** Patients do not recognise themselves in the mirror, which normally generates a feeling of intrusion, discomfort, fear and even aggressiveness.
- **Self-referentiality:** Patients believe that the people on the television are really in their homes and that what they say has a direct relationship with them.
- **Capgras or sosias syndrome:** Patients believe that a person, normally their spouse, has been replaced by an imposter, which fosters fear, rejection, paranoid attitudes, aggressiveness, agitation, etc.
- **Reduplicative paramnesia:** This is the belief that a certain place has been duplicated and exists in two or more places at the same time. It is not very common in AD; it is more frequent in vascular dementia and is associated with simultaneous lesions in the right hemisphere and frontal lobe.

10.4.2. Why are BPSD important in dementia?

BPSD are important due to:

- Frequency in appearance: 92% of the patients presented at least one BPSD when assessed with the NPI scale.[334,335]
- The presence of these symptoms may facilitate the differential diagnosis of the different types of dementia; in some dementias it forms part of the diagnosis criteria (visual hallucinations in dementia with Lewy bodies, disinhibition in FTLD).[25,5]
- Certain BPSD permit a predictive approach of the cognitive alteration.[5]
- Their presence must be taken into account when the healthcare plan is structured.[343]
- The persistence or intensification of some BPSD such as agitation, aggression or hallucinations usually require urgent healthcare.
- The appearance of BPSD increases caregivers' stress and burden, it predisposes them to depression and is usually the most frequent reason for family claudication and early institutionalisation.[344,215]
- Emerging BPSD may indicate the existence of concomitant diseases, so they must be systematically detected, assessed and treated.[215,5]

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Summary of evidence

-	There is no scientific evidence that enables us to formulate evidence-based recommendations but a series of recommendations can be drawn up as points of good practice based on the above.

Recommendation

✔	The systematic assessment of the presence of BPSD is recommended as it is a fundamental component of the clinical picture, it appears very frequently, it is difficult to manage, it has an impact on the quality of life and is a frequent reason for urgent care, family claudication and institutionalisation.

10.4.3. How can the intensity and frequency of BPSD be quantified?

The diagnosis and treatment of dementia must include identification, quantification and recording of the BPSD using appropriate documentation. There are different instruments or scales to quantify the intensity and frequency of BPSD:

- General dementia assessment scales, which include items that evaluate BPSD, among others.
- Specific assessment scales for several BPSD.
- Scales that evaluate one single BPSD.

General assessment scales that include several BPSD:

- **Cambridge mental disorders of the elderly examination** (CAMDEX): This is a scale aimed at diagnosing dementia, comprised of [344] items distributed into eight sections. Sections A, C and H assess the psychopsychological status of the patient via a structured interview. It is a useful instrument in clinical and epidemiological studies, but the time required makes it difficult to apply in other fields.[345,346]
- **Geriatric mental state** (GMS-AGECAT): This is a standardised clinical interview comprised of 154 items grouped into 30 sections and its applicability is focused on clinical and epidemiological studies.[340,347]
- **Alzheimer's disease Assessment Scale** (ADAS): The ADAS is a test that assesses cognitive changes and behavioural disorders in patients with AD. It comprises 21 items divided into two subscales: Cognitive (ADAS-Cog) and behavioural (ADAS-Noncog), with 11 and 10 items respectively, whose information is obtained through the actual patient and relative or caregiver. In practice, the administration of the ADAS-Cog has become very popular, so the ADAS-Noncog has been relegated due to the existence of more accurate behavioural scales.[8,349,350]

Specific assessment scales for several BPSD:

- Neurobehavioral Rating Scale (NRS): This scale assesses the presence of different BPSD. It comprises 27 items that are scored in an intensity from 1 to 7.[351,352]

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- **Behaviour pathology in Alzheimer's Disease Rating Scale** (BEHAVE-AD): This scale assesses psychiatric disorders in patients with AD and their impact on the caregivers. 25 symptoms are scored based on seven neuropsychiatric symptomatology domains. It provides a global score of non-cognitive symptomatology.[353,354]
- **Neuropsychiatric Inventory** (NPI): the NPI[335] is the most commonly used instrument to assess behavioural and psychological symptoms in patients with dementia. It assesses frequency and severity of each one of the behavioural disorders and symptoms. It is comprised of 12 items to evaluate frequency (on a scale from 0 to 4) and severity (on a scale from 1 to 3) of the symptoms: Delusion, hallucinations, agitation, depression/dysphoria, anxiety, euphoria/jubilation and, apathy/indifference, disinhibition, irritability/lability, motor behaviour without a purpose, sleep alteration and eating disorder. Subscales of depression and agitation/aggressiveness can also be obtained. It is available in Spanish version[355,356,350,342,335,357,152] and abridged versions (NPI-Q) or Neuropsychiatry Inventory-Nursing Home (NPI-NH). [358,359]
- **Cohen Mansfield Agitation Inventory** (CMAI): This is considered to be the standard instrument to assess agitation. It comprises 29 items that assess the presence of anomalous behaviours, organised around four behaviour components: Agitation, aggression, non-aggressive motor alterations and recollection of objects. Each item is scored on a scale of 7 points according to the severity and frequency of the altered behaviour.[340,347]
- **Hamilton Anxiety Depression** (HAD): This is an assessment instrument that quantifies anxiety and depression.[360,361,362]

Scales that evaluate one single BPSD:

- **Cornell Scale for Depression in Dementia** (CSDD): This scale permits making a diagnosis of major depression according to DSM-IV criteria; it is the most commonly used instrument for this indication. It comprises 19 items and it has a maximum score of 38. It is based on an interview held with the patient and caregiver; the opinion of the latter prevails if there are differences between the two.[345,346] It is available in Spanish version.[363]
- **Yesavage Geriatric Depression Scale:** Comprised of 30 items with an abridged version of the Yesavage geriatric depression scale of 15 items.[364,365,366]
- **Rating of Aggressive behaviour in the elderly** (RAGE): This is a scale to assess aggressiveness, comprised of 23 items, the majority of which are evaluated on a scale of 4 points according to frequency.[367] It is available in Spanish version.[368]

Summary of evidence

4	There are general scales to assess BPSD: el CAMDEX (Cambridge mental disorders of the elderly examination), with 344 items it is a useful instrument in clinical-epidemiological studies;[345,346] the Geriatric mental state (GMSAGECAT) is a standardised clinical interview comprised of 154 items, applicable in clinical and epidemiological studies;[340,347] the behavioural subscale (ADAS-Noncog) of the Alzheimer's disease Assessment Scale (ADAS), with 10 items.[348,349,350]

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4	There are specific scales to assess several BPSD, such as the Neurobehavioral Rating Scale (NRS), with 27 items that score in an intensity from 1 to 7.[351,352] The Behaviour pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) assesses psychiatric disorders in patients with AD and their impact on the caregivers; 25 symptoms are scored based on seven neuropsychiatric symptomatology domains, and it provides a global score of non-cognitive symptomatology.[353,354] The Neuropsychiatric Inventory (NPI)[335] is the most commonly used instrument; it assesses frequency and severity of 12 items: Delirium, hallucinations, agitation, depression/dysphoria, anxiety, euphoria/jubilation and, apathy/indifference, disinhibition, irritability/lability, motor behaviour without purpose, sleep alteration, eating disorder. There is an abridged version (NPI-Q) or Neuropsychiatry Inventory-Nursing Home (NPI-NH).[358,359]
4	The Cohen Mansfield Agitation Inventory (CMAI): This is the standard instrument to assess agitation, with 29 items and for behavioural components: Agitation, aggression, non-aggressive motor alterations and recollection of objects.[340,347]
4	The Hamilton Anxiety Depression (HAD) is an assessment instrument that quantifies anxiety and depression.[360,361,362]
4	The most commonly used instrument to assess depression in dementia is the Cornell Scale for Depression in Dementia (CSDD), which comprises 19 items and a maximum score of 38. It is based on an interview held with the patient and caregiver.[345,346,363] The Yesavage Geriatric Depression Scale is also useful, with two versions of 30 and 15 items.[364,365,366]
4	The Rating of Aggressive behaviour in the elderly (RAGE): This is a scale to assess aggressiveness, with 23 items that are evaluated on a scale of 4 points according to frequency.[367]

Recommendation

✔	The use of specifically designed instruments is recommended to evaluate BPSD in dementia independently from cognitive and functional alterations.
✔	NPI (Neuropsychiatric Inventory) is recommended as an instrument to assess the intensity and frequency of BPSD, the CSDD scale (Cornell Scale for Depression in Dementia) to assess depressive symptomatology and CMAI (Cohen Mansfield Agitation Inventory) to assess agitation.

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10.4.4. At what moment in time do BPSD appear in the evolution of dementia?

BPSD can appear at any stage of the disease. Sometimes it is the appearance of the BPSD that alert the family and lead them to consult the PCT. If one of these symptoms is found, the existence of other BPSD must be explored, which may go unnoticed if the intensity is light.[370]

A door to door epidemiological study, evaluating 108 people with dementia, showed that 76.9% presented at least one BPSD. In AD the percentage was 73.5%, in the DLB/PDD group, 80%, in VD, 78.6%, and 100% in FTLD.[371] — Descriptive study, 3

BPSD (apathy, depression, anxiety) may appear in the initial stages of dementia, which may help us differentiate between AD, VD, FTLD, DLB and PDD.

There are certain BPSD in FTLD and in DLB that, due to their prevalence, form part of their diagnostic criteria.[51,6] There are usually multiple BPSD in the different types of dementia, unlike idiopathic psychiatric diseases where psychosis or depression appear exclusively.

As the dementia progresses, the prevalence and intensity of the BPSD increases. In the mild to moderate dementia stage, parallel to the impairment of IADL, sleep disorders and eating and sexual disinhibition behaviours appear.[372]

In a cohort study on people with moderate to severe dementia, the presence of BPSD was significantly correlated to the scores on the functional scales ($p = 0.039$).[372] — Cohort study, 2++

In more advanced stages of AD, delusions, hallucinations and agitation may appear. All the degenerative dementias occur with BPSD; in AD they have been observed in 73.5-94.6%; in VD, in 78.6-96.4%; in FTLD, in 100% of those affected, and in DLB and PDD dementia, the percentage reaches 80%.[5,25,373] — Cohort study, 2++

Apathy is the most prevalent BPSD in all types of dementia (53.70%). In AD, 51.3-64.6% is observed; in VD, in 42.9%; in FTLD in 100%, and in DLB and PDD, 50%.[374,371] — Cohort study, 2++

In a prospective cohort study with 91 people with MCI, 344 with AD (99 mild, 245 moderate, 45 moderate-severe) and 50 healthy controls, depression is found in 8% of the healthy controls, 33% of the MCI, 41.4% in mild AD and 44.1% in moderate to severe AD.[372] In another study by the same authors, depression was present in 49.60% of those affected by AD, and in 42.9% of VD.[374,371] — Cohort study, 2++

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In another study, depression was present in 18.4% of the normal population; in 44.1% of people with MCI and in 19.5% of those with AD.[375] In another prospective study with 119 patients with AD, 126 with MCI, depression was observed in 49.6% of the people with AD and in 44.1% of the people with MCI.[376]	Cohort study, 2++
The frequency of anxiety in the normal population may vary between 4.0-24.9%.[375] In cohort studies people with MCI presented anxiety in 46.8% of the cases, and with dementia in 35.2%.374,371 In AD this may vary between 16.3 and 32.10%. 375,374,371 In VD it is present in 42.9%[374,371] and in FTLD it reaches 100%.[374,371]	Cohort study, 2++
Other frequent BPSD in MCI and dementia are: Agitation, irritability, sleep alterations and eating behaviour disorders. Irritability was observed in 15% of patients with MCI and in 30% of those affected by AD. Agitation, in 50% of the patients with Parkinson's disease dementia (DLB-PDD).[374,371]	Cohort study, 2++
Aberrant motor activity appears in moderate and advanced stages of dementia; in 24.3% of people with AD, it is not normal in VD and appears in practically all the cases of FTLD.[374,371,38] When it appears at early stages of AD, it is due to dysfunction of the frontal lobe.[377]	Cohort study, 2++
Disturbances of the sleep-wake cycle may be present in normal population, according to different studies, between 3.6 and 55.7% of people.[378] In dementias, it appears in 30.4%.[374,371]	Cohort study, 2++
A cohort study with 155 people with AD and 420 healthy controls, using the Mayo Sleep Questionnaire and the NPI, show that 71% of people with AD presented some type of sleep disturbance.[378]	Cohort study, 2++
Others studies showed sleep disorders in 3.6% of people in VD, and in 50% of those affected by DLB and PDD.[374,371,378,379]	Cohort study, 2++
The most frequent sleep disorders in mild dementia were insomnia (29.9%), night cramps (24.1%) daytime drowsiness (22.6%), restless legs syndrome (20.7%) and REM sleep behaviour disorders (18.5%).[378,379]	Cohort study, 2++
In DLB, REM sleep behaviour disorders can precede the onset of dementia by many years. Sudden sleep erises are more frequent in PDD.[379]	Cohort study, 2++

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There is little information about sleep alterations in FTLD. A control study of 13 people with FTLD, controlled with a sleep diary and prolonged actigraphic recording, and compared with the normal population and with patients with AD, showed disturbances of wake-sleep cycle characterised by ineffective sleep, increase of nocturnal activity, shortening of sleep duration and decrease of morning activity. These are early disturbances in the evolution of the disease and enable it to be differentiated from AD.[250]	Case series, 3
Sleep disorders increase in parallel with the severity of dementia and they are one of the factors that favour institutionalisation.[379]	Cohort study, 2++
A door to door epidemiological study showed the existence of eating disorders in 37.8% of patients with AD, in 14.3% of those affected by VD, and in 50% of people with DLB/PDD.[371,374]	Descriptive study, 3
Delirium is exceptional in healthy population (0.4%); it is observed in 3.4% of MCI, it is more frequent in the initial stages of FTLD and it may appear in moderate to severe stages of AD.[5,25,373]	Cohort study, 2+

Summary of evidence

2++	BPSD can appear at any stage of the evolution of dementia and it may be the first manifestation.
2++	A door to door epidemiological study, which included 108 people with dementia, showed that 76.9% presented at least one BPSD. In AD, 73.50%, in the DLB/PDD group, 80%, in VD, 78.60%, and 100% in FTLD.[371,374]
2++	There are some BPSD in FTLD and in DLB that form part of the diagnostic criteria of both diseases. Delusions and hallucinations usually appear in the earlier stages in FTLD and DLB.[51,6]
2++	As the dementia progresses, the prevalence of BPSD increases, new BPSD appear or the already existing ones increase in intensity.[372] In the mild to moderate dementia stage, parallel to the impairment of IADL, sleep disorders and eating and sexual disinhibition behaviours appear. The presence of BPSD is significantly correlated to the scores on the functional scales (P = 0.039) in moderate-severe dementia.[372] Delusions, hallucinations and agitation may appear in more advanced stages in AD.[5,25,373]
2++	Apathy is the most frequent BPSD of dementia from the onset: 51.3- 64.6% in mild AD; 78.4% in moderate to severe AD; 42.9% in VD; 100% in FTLD, and more than 50% of DLB and PDD.[371,374,372,376]

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2++	Depression appears in 41.4% of people with mild AD, 44.1% in moderate to severe AD.[372] In another study by the same authors depression appears in 49.6% of people with AD and in 42.9% of VD.[371,374] In other series, the depression percentage varied between 19.5 and 49.6%. [376]
2++	Anxiety occurs in dementia in 35.2% of the cases. [371,374] In AD it varies between 16.3 and 32.10%.[375,371,374] In VD it appears in 42.9%371,374 and in FTLD in 100% of the cases[371,374]
2++	Other frequent BPSD in dementia are irritability, agitation, sleep disturbances and eating behaviour disorders.[376] Irritability in 30% of people with AD; agitation in 50% of people with Parkinson's disease dementia.[371,374]
2++	Aberrant motor activity appears in moderate and advanced stages of dementia. 24.3% of people with AD; it is not normal in VD, and it appears in all FTLD.[371,374,38,377]
2++	Disturbances of the wake-sleep cycle appear in 30.4% of people with dementia.[378,371,374] A cohort study using the Mayo Sleep Questionnaire and the NPI, show that 71% of people with AD presented some type of sleep disturbance.[378]
2++	In VD, sleep disorders appear in 3.6% of those affected; in DLB and PDD they are more intense and appear in 50% of the cases.[371,374,378,379]
2++	The most frequent sleep disorder in mild dementia is insomnia (29.9%), night cramps (24.1%) daytime drowsiness (22.6%), restless legs syndrome (20.7%) and REM sleep behaviour disorders (18.5%).[378,379]
2++	In DLB, REM sleep behaviour disorders can precede the onset of dementia by many years. Sudden sleep crises are more frequent in PDD.[379]
3	A control of 13 people with FTLD, compared with the normal population and with patients with AD, showed ineffective sleep in FTLD, with an increase of nocturnal activity and morning tiredness, early disturbances that permit differentiating it from AD.[380]
2++	Sleep disorders increase with the severity of dementia and they favour institutionalisation.[379]
2++	Eating disorders were observed in 37.8% of patients with AD; 14.3% in VD, and in 50% of people with DLB and PDD.[371,374]
2+	Delirium is exceptional, in healthy population (0.4%), rare in 3.4% of people with MCI, frequent in the initial stages of FTLD and it may appear in moderate to severe stages of AD.[5,25,373]

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Recommendation

B	It is advisable to bear in mind that BPSD may appear at any time during the evolution of dementia, whatever its aetiology, and it is not unusual for it to be the first manifestation.
B	If delusions and hallucinations appear in a person with early stage dementia, FTLD or DLB must be suspected. If there are REM sleep behaviour disorders, the first suspicion will be DLB.

10.4.5. Are there some BPSD that are characteristic of some types of dementia?

No BPSD is specific of any of the types of dementia, however their frequency, combination, spontaneous evolution and response to treatment may be significant characteristics for the diagnosis.[334]

Alzheimer's Disease (AD)

The presence of BPSD in AD was investigated in a prospective clinical study. The presence of one or more BPSD were found in 88% of the cases,338 whilst they appeared in 60% of the sample in a population based study. 20% presented one single symptom; affective symptoms prevailed in 28% and the prevailing symptoms in 13% were psychotic.[381]	Cohort study, 2++
Apathy is the most frequent BPSD in AD, increasing with its progression and correlated with the progression of cognitive impairment and the loss of functionality. It is correlated with executive dysfunction and disturbances in the frontal lobe. It may or may not coincide with depression.[371,374,372]	Cohort study, 2++
Depression is present in 38-49.6% of people with AD. It may, on its own, cause cognitive impairment similar to that of the initial stage of AD. The differential diagnosis between the two may be difficult.[338,371,374,372]	Cohort study, 2++
Anxiety is very frequent in people with mild AD; it is observed in 32-71% of the cases. It can often (27-57%) be accompanied by anxiety and irritability.[375,371,374,372]	Cohort study, 2++
Psychosis in AD includes delusions and hallucinations that are correlated with agitation, aggressiveness and apathy. Visual hallucinations are more frequent as they coincide with alterations in visual acuity.[381]	Cohort study, 2++

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The profile of behavioural alterations varies with the progression of AD; apathy, irritability, depression and anxiety are frequent in mild stage. Delusions of persecution, jealousy, illusions, hallucinations (visual, auditory or olfactory), agitation and aberrant motor behaviours may appear in moderate AD. [371,374,38,377]	Cohort study, 2++
Disorders of the wake-sleep cycle in initial stage may differentiate AD from DLB and from FTLD (**question 10.4.4**). [378,379,380]	Cohort study, 2++

Functional neuroimaging in AD, using SPECT reinforces the role of the anterior cingulate in apathy, with a reduction of the bilateral activity in people with AD. In depression, the hypometabolism area is observed in the upper temporal lobe, anterior cinguiate and bilateral frontal lobe. In hallucinations, the decrease of the metabolism is observed in right parietal lobe, left medial temporal lobe and left prefrontal dorsolateral cortex.[334]

Frontotemporal lobar degeneration (FTLD)

BPSD in FTLD (compulsions, altered social behaviour, emotional incontinence, loss of empathy, anosognosia and disinhibition) are present in FTLD from the first stages.[382]	Cohort study, 2++
Apathy, anxiety, irritability and aberrant motor activity are almost constant in FTLD.[371,374]	Descriptive study, 3
In a cohort study that compared BPSD in 30 patients with FTLD, 75 with AD and 34 with VD, it showed that patients with FTLD showed apathy, loss of emotions and of insight, disinhibition, negligence, bulimia and preference for sweet food, wandering, stereotypies, loss of sensitivity to pain, echolalia and mutism. This series of BPSD enables it to be differentiated from AD. It is more difficult to differentiate it from VD.[383]	Cohort study, 2++
Different patterns are distinguished in FTLD. Compulsive symptoms are more frequent in semantic dementia. There are differences depending on the hemisphere affected. FTLD of the right side causes antisocial behaviour and aggressiveness. FTLD of the left side is characterised by a change in personality and values.[381]	Cohort study, 2++

Dementia with Lewy bodies (DLB) and Parkinson's Disease Dementia (PDD)

DLB and PDD share the majority of BPSD, cognitive and motor disorders, and the pharmacological response to the ACE inhibitors.

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The profile of BPSD is dominated in both by delusions and hallucinations, but there are quantitative differences between them. In DLB, delusions are observed in 57% of the cases and hallucinations in 76%, whilst in the PDD group, delusion were observed in 29% of the cases and hallucinations in 54%. Hallucinations are associated with greater severity of the dementia, major depression and less visual acuity.[381]	Cohort study, 2++
DLB and PDD are characterised by progressive cognitive impairment, motor and non-motor fluctuations, recurrent visual hallucinations and parkinsonism. Behavioural disorders of the REM phase are very typical of DLB and may precede motor or cognitive signs by several years.[382]	Cohort study, 2++

Vascular Dementia (VD)

The most typical BPSD in VD are apathy, depression and delusions.[382] Aberrant motor activity is not usually observed.[371, 374,38]	Cohort study, 2++

Summary of evidence

Alzheimer's Disease (AD)	
2++	One or more BPSD are observed in 80% of the people with AD attended in dementia units.[338] The prevalence was less in studies (60%). One single symptom existed in 20% of the cases; affective symptoms prevailed in 28% and psychotic symptoms in 13%.[38]
2++	Apathy is the most common BPSD in AD, increasing with the progression of the disease and correlating with the worsening of the cognitive impairment and functional loss. It is correlated with executive dysfunction and frontal lobe alterations.[376]
2++	Depression occurs in 38-49.6% of people with AD and it may cause cognitive impairment very similar to the initial stage of AD; the differential diagnosis may be difficult.[338,372,371,374,376]
2++	Anxiety appears in 32-71% of people with AD.[371,374,375]
2++	Psychosis in AD includes delusions and hallucinations, at the same time as agitation, aggressiveness and apathy. Visual hallucinations are more frequent if there are alterations in visual acuity.[381]
2++	The most frequent BPSD in mild AD are apathy, irritability, depression and anxiety. Delusions of persecution, jealousy, illusions, hallucinations (visual, auditory or olfactory), agitation and aberrant motor behaviours may appear in moderate AD.[371,374,38,377]
2++	Disorders of the wake-sleep cycle in initial stage may differentiate AD from DLB and from FTLD **(question 10.4.4)**.[378,379,380]

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Frontotemporal lobar degeneration (FTLD)	
2++	BPSD (compulsions, altered social behaviour, emotional incontinence, loss of empathy, anosognosia and disinhibition) are present in FTLD from the first stages.[382]
2++	Apathy was observed in all the cases of FTLD, as well as anxiety, irritability and aberrant motor activity.[371,374]
2++	BPSD in FTLD are characterised by apathy, loss of emotions and of insight, disinhibition, negligence, bulimia and preference for sweet food, wandering, stereotypies, loss of sensitivity to pain, echolalia and mutism. This series of BPSD enable it to be differentiated from AD. It is more difficult to differentiate it from VD.[383]
2++	In FTLD, there are differences depending on the hemisphere affected. If the right side is affected antisocial behaviour and aggressiveness appear, if the left side is affected changes in personality and a change in values appear.[381]
Dementia with Lewy bodies (DLB) and Parkinson's Disease Dementia (PDD)	
2++	The BPSD profile in DLB and PDD is characterised by delusions and hallucinations. In DLB, delusions were observed in 57% of the cases and hallucinations in 76%. In PDD, delusion in 29% and hallucinations in 54%. Hallucinations are associated with more severe dementia, major depression and less visual acuity.[381]
2++	DLB and PDD are characterised by progressive cognitive impairment, motor and non-motor fluctuations, recurrent visual hallucinations and parkinsonism. Behavioural disorders of the REM phase are very typical of DLB and may precede motor or cognitive sings by several years.[382]
Vascular Dementia (VD)	
2++	The most typical BPSD in VD are apathy, depression and delirium.[382]

Recommendation

B	BPSD must be detected as soon as possible, in mild dementia stages, or throughout its subsequent evolution; they must be quantified and grouped into syndromes that facilitate differential diagnosis between the different dementias.
B	It is advisable to know and recognise the BPSD that appear in AD, VD, FTLD, DLB and PDD.

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10.4.6. Which non-pharmacological measures are indicated in each BPSD in dementia?

Pharmacological management of BPSD can be accompanied by adverse effects for the patient. So it is normal in CPG to recommend the use of non-pharmacological strategies as first line therapy for BPSD when these are not very severe and start pharmacological treatment only when these strategies have failed.[42,235]

Expert opinion, 4

The non-pharmacological treatment of BPSD has not been assessed via extensive and methodological quality RCT, but by studies with a limited sample and variable design, mainly of cases and controls that include different types of dementia in different stages, not specifying the response on behavioural alterations or specifying the therapeutic effect on a specific BPSD.42,235,385,386 There are no well-designed studies either that assess the combined efficacy of pharmacological and non-pharmacological treatment.[387]

Some recommended general standards[235,388] to manage BPSD in AD include: Preventing their appearance and treating them early on, using an adequate tone of voice, maintaining visual contact, routine exercise patterns, eating and bathing, avoiding erratic wandering, maintaining the patients orientated in time, avoiding hyperstimulation, providing a safe and well-lit environment, without mirrors, with identification notes on the doors of the home, programming distraction and re-orientation activities, and providing music of the patient's liking during some activities.

SR of RCT, and observational study, 2-
Expert opinion, 4

It is especially important for relatives to receive good information and training about the BPSD to enable them to develop co-therapeutic work when managing and preventing them. It is important for them to understand that the BPSD appear as a result of brain damage, which may be transient and may improve with treatment.[42]

A MA of observational studies that assessed the efficacy of 13 different non-pharmacological intervention programmes on the delay in institutionalisation, including a total of 9,043 patients with dementia, concluded that the active engagement of caregivers was essential for the programme to be effective.[389]

MA of observational study, 2++

Non-pharmacological treatment includes behavioural interventions, reminiscence therapy, cognitive stimulation and sensory stimulation therapies (music therapy, aromatherapy, massage, phototherapy).[390]

Depression

The pharmacological measures must be accompanied by psychotherapy, eliminating risk elements from the environment and increasing supervision and hospitalisation if necessary[42] Options must be selected depending on the intensity of suicidal thinking and on the patient' family and social support.

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Behavioural intervention techniques prove to be beneficial, in general during the execution time of the therapy on some BPSD, including depression, but there are no well-designed RCT with a broad sample.[235,388]	SR of RCT and observational study, 2–
Stimulation oriented therapies such as recreation activities and other formal or informal means to maximise the patients' pleasurable activities have proven to be effective on depression in some studies of a small sample size, during the mild and moderate stages of AD[235] and in advanced stages.[388]	Observational study, 2-
One SR of RCT concluded that reality counselling therapy has not very effective on apathy and depression.[391] Reminiscence therapy is not very effective on mood and behaviour.[392]	SR of RCT, 1-

Sleep

25-50% of patients with dementia present severe sleep disorders.[393] There are many different causes: Fragmentation of physiological sleep in advanced age, excess daytime sleep, neuronal damage in the suprachiasmatic nucleus, untreated pain and presence of medical and psychiatric comorbidity.[42] Diagnostic criteria for sleep disorders associated with AD have been proposed.[394] The objectives of the treatment are to increase the patient's comfort, reduce the strain on the caregivers, reduce nocturnal wandering and avoid accidents and falls.

Non-pharmacological management of sleep disorders is based above all on establishing appropriate sleep hygiene. Some general rules are: Establish sleep routines, maintain physical and mental activity in the morning and first thing in the afternoon, limiting daytime sleep hours, avoid nicotine, caffeine, diuretics and the intake of liquids at night; taking hot milk, having a bath in warm water and dimmed night lights may also be effective.[235]	RCT, 1-
It must be taken into account that some ACE inhibitors may alter sleep, in which case they can be administered at midday. The use of low beds or with side guards may prevent falls from occurring during sleep or when getting up.[42]	Expert opinion, 4

Agitation

If it has appeared recently, possible triggering causes must firstly be identified, such as pain, urine infection, dehydration, constipation, delirium, depression and adverse effects of drugs. Other causes may be hunger, sleep, changes in caregiver or room companion, isolation or hyperstimulation. Aggression prediction activities must be identified and eliminated when possible. Sequential activities such as getting dressed or eating may cause frustration and agitation, so they must be simplified by, for example, using clothes with Velcro or preparing simple and repeated meals instead of one large meal.[42]

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One Cochrane SR[329] concluded that there is some evidence that therapeutic massages may be effective to decrease anxiety and agitation.	SR OF RCT, 1+
Another Cochrane SR detected five studies where music therapy may be beneficial for the emotional control of people with dementia, but the low methodological quality did not permit establishing conclusions.[331]	SR of RCT, 1-
Another Cochrane SR[332] did not find any evidence of efficacy of integrated multi-sensory stimulation (*snoezelen*) on behaviour, mood or social interaction in the short or long term.	SR OF RCT, 1+

Erratic wandering or vagrancy

Wandering, within a safe environment, fosters circulation and oxygenation; it is a physical exercise and an indicator of good physical health.[395] On the contrary, wandering away from the home may lead to the patient going astray, represent a risk of falls and fractures, cause strain on caregivers and may precipitate institutionalisation.[396]

The prevalence is very variable (15-60%) and it may be more frequent in advanced stages of dementia. It is difficult to calculate because often it is included with agitation and anomalous motor behaviours.[397] The aetiology is not known and it often depends on individual environmental factors, so it is difficult to establish therapeutic strategies.

Interventions aimed at preventing and reducing wandering may be classified into several groups: a) therapies with exercises and walks (walking and conversation groups, therapy with exercises, parks to walk in), b) changes in environment (subjective barriers such as mirrors, apartments grilles, door handle camouflage, etc.), safety devices (childproof locks, alarms, etc.), home environment programmes, c) behavioural modification interventions, d) occupational therapy in the form of recreational activities, and e) electronic identification techniques.

One SR that included RCT and low quality cohort studies,[397] with multi-sensory stimulation, music therapy, aromatherapy, physical activity and behavioural therapy, concluded that there is no evidence to establish recommendations on any non-pharmacological therapy to reduce or avoid erratic wandering.	SR of RCT and cohort study, 1- Observational study, 2-
Electronic location devices are very useful, especially personalised wristbands that transmit a tracking signal, coordinated with search and rescue teams. In the Project Lifesa study developed in USA (www.projectlifesaver.org) the search time in a series of 1000 cases was reduced from days or hours to an average of 30 minute and no serious injury or death occurred.	

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One Cochrane SR[398] analysed the existence of quality RCTs performed with the above-mentioned therapeutic strategies and did not find any appropriate clinical trial on non-pharmacological interventions for the prevention and treatment of wandering in the domestic environment, so no recommendation in this regard could be established.	SR of RCT, 1-

Summary of evidence

4	Some strategies to prevent and treat BPSD are to use an adequate tone of voice, maintaining visual contact, routine exercise patterns, eating and bathing, avoiding erratic wandering, maintaining the patients orientated in time, avoiding hyperstimulation, providing a safe and well-lit environment, without mirrors, with identification notes on the doors of the home, distraction and re-orientation activities, and providing music to the patient's liking.[42,235,388]
2++	The active involvement of the caregiver is essential for the efficacy of non-pharmacological intervention programmes in patients with dementia.[389]
2+	Recreational and pleasurable activities may improve depression in mild, moderate[235] and advanced[388] AD.
1-	Reality counselling therapy is not very effective on apathy and depression in dementia.[391]
1+/1-	Sleep hygiene and other measures such as drinking hot milk, having a bath with warm water and dimmed night lights improve sleep disorder.[390]
1+	Therapeutic massages may be effective on anxiety and agitation in patients with dementia.[329]
1-	Music therapy may be beneficial on the emotional control of people with dementia.[331]
1+	Integrated multi-sensory stimulation (snoezelen) is not effective on behaviour, humour or social interaction in patients with dementia.[332]
1-	There are no quality RCT on non-pharmacological interventions for the prevention and treatment of wandering in the domestic environment, so no recommendation in this regard could be established.[398]

Recommendation

✔	Starting treatment with non-pharmacological strategic measures to manage BPSD is recommended.
C	It is especially important for caregivers to receive information and training that capacitates them to prevent the appearance of BPSD and act as co-therapists when they are already present.

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C	Stimulation-oriented treatment with recreational activities and pleasurable activities have proved to be effective to cope with depression.
✔	Non-pharmacological sleep management mainly consists of establishing guidelines and good sleep hygiene.
C	There is limited evidence that therapeutic massages may be effective to treat agitation.
D	The use of electronic identification techniques on dementia patients who present erratic wandering is recommended.

10.4.7. What are the general recommendations for the pharmacological treatment of BPSD?

Two CPG[42,235] recommend starting treatment of BPSD with non-pharmacological measures and reserving pharmacological treatment for the most severe or refractory cases. There are few studies available on non-pharmacological treatments; the RCT are practically non-existent and the availability of trained professionals is scarce and insufficient respect to the needs of this population. Therefore, the pharmacological approach is imposed in the majority of the cases. For appropriate pharmacological management of BPSD, it is essential to appropriately identify the symptom to be treated, assessing its possible causes, identifying the possible precipitating factors, those that relieve them or eliminate them, and the consequences that the symptom entails for patients and their environments.

ACE inhibitors and memantine

There is evidence of moderate but greater efficacy than placebo of ACE inhibitors on BPSD. [239,240,253]	MA of RCT, 1++
The evidence about memantine is also positive, but of lesser magnitude; it is more specific for the agitation symptom.[256,258]	MA of RCT, 1++
The efficacy on individual symptoms varies from one study to another and from one drug to another. Noteworthy is the use of all ACE inhibitors, especially rivastigmine, in DLB or PDD, where the use of psychotropic drugs such as antipsychotics is especially problematic.[272,277]	RCT, 1+
The combination of ACE inhibitors and memantine also improves the BPSD, assessed using scales such as the NPI. All of this reinforces the indication of ACE inhibitors and/or memantine as treatment of dementia, both for cognitive symptoms and for non-cognitive ones.[268]	RCT, 1+

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Psychotropic drugs

The same psychotropic drugs as in primary psychiatric disorders are used. There is no quality evidence in primary psychiatric disorders to prefer one molecule over another within the same therapeutic group or for BPSD.

The RCT that compare antipsychotics have limited power, but they do not suggest differences in efficacy in the treatment of psychotic symptoms or agitation/aggressiveness. Although these medications are used for long periods in practice, there is hardly any evidence about their efficacy in periods over 8-12 weeks.

The RCT do not generally specify which symptoms improve specifically with each molecule, and when they do so, they do not always coincide from one trial to another. The majority do not distinguish the types of dementia and usually include AD, VD and mixed dementia. The degree of dementia is variable. The quality of the studies is moderate; some are well designed but the high dropout rates reduce their quality.[149]

The effects on global scales such as NPI or on psychotic symptoms in general are generally assessed. Furthermore, the majority of RCT do not assess which drugs are useful for each symptom, but rather, what effect each drug has on certain scales and some symptoms or groups of symptoms. In the technical data sheet, only risperidone is indicated for states of agitation and aggressiveness in dementia.

Summary of evidence

4	According to CPG and bearing in mind the adverse effects of the drugs, it is considered reasonable to start with the non-pharmacological management of BPSD and use drugs in severe or rebellious symptoms.[42,235]
1++	ACE inhibitors have proven to be more effective than placebo on BPSD, generally assessed by means of the change in NIP score.[239,240,253] Memantine has shown modest efficacy on agitation.[256,258]
1+	Rivastigmine has shown a moderate improvement on the NPI score in patients with DLB and PDD.[272,277]
1-	There are very few studies on treatment of BPSD with specific psychotropic drugs on patients with dementia, and they usually have a low quality.

Recommendation

D	The target symptom that must be treated as well as its possible causes or triggers must be identified.
D	The general recommendation respect to pharmacological treatment of BPSD is to start with ACE inhibitors and/or memantine and, if the response is not sufficient, add a psychotropic drug.

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✔	Bear in mind the special sensitivity of these patients to adverse effects, especially the risk of anticholinergic effects, orthostatic hypotension, falls, extrapyramidal effects, worsening of cognitive function, confusion and delirium. Start with low doses and slowly reach the minimum effective doses. Preferential use of oral route.
✔	Review the dose and the actual treatment need at regular intervals, generally every 3 months.
ACE inhibitors and/or memantine	
B	The use of ACE inhibitors and/or memantine is recommended as treatment of dementia, not only for cognitive symptoms but also for non-cognitive ones.
B	The use of rivastigmine is recommended to treat BPSD in patients with DLB or PDD.
Psychotropic drugs	
D	The use of psychotropic drugs is recommended to treat BPSD, although evidence about their efficacy in patients with dementia is generally low and the risk of adverse effects is high.

10.4.8. What is the optimal pharmacological treatment for each BPSD?

We have the basic treatment with ACE inhibitors and/or memantine for the pharmacological treatment of BPSD. If this treatment is not «enough, psychotropic drugs have to be used. Both treatments are not incompatible and are usually prescribed together if required. Given that AD, DLB and PDD have a specific treatment with ACE inhibitors and/or memantine, it is to be expected that these drugs will improve the BPSD as supported by the RCT **(question 10.2.3)**

Psychotic symptoms (delusions and hallucinations).

One SR of RCT on the treatment of delirium in AD[400] showed the benefit of risperidone (0.5-2 mg/day) and contradictory results for olanzapine. With respect to ACE inhibitors, an improvement was observed in the intensity of the delirium in one RCT with donepezil; no benefit was observed in a small open-ended study with rivastigmine or in one RCT with galantamine. Both the typical antipsychotics and the ACE inhibitors could play a role in the treatment of delirium, but the existing information is scarce and there are no comparative data between them.	SR of RCT and of open study, 1++/1+/1–
There are not enough data to establish the benefit of atypical antipsychotics on psychotic symptoms, aggressiveness or agitation when assessed separately.[25]	RCT, 1-

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Rivastigmine may improve psychotic symptoms in DLB. In one RCT[277] twice the number of patients with rivastigmine (average dose of 9.4 mg/day) showed a significant improvement in the NPI-NH with respect to placebo at 20 weeks. — RCT, 1+

There is no evidence of efficacy of antipsychotics in DLB and up to 50% of the people showed marked sensitivity.[6]

There is moderate-high evidence in patients with AD and VD regarding the efficacy of a typical antipsychotics (aripiprazole, olanzapine, quetiapine and risperidone) compared with placebo, with a small clinical benefit measured as a score of NPI or BEHAVE-AD.[25] Clozapine is useful for psychotic symptoms in PDD and DLB, and could be useful for patients with AD who are sensitive to the extrapyramidal effects of the antipsychotics.[42] — RCT, 1++/ 1+

There is no data about the use of ziprasidone in elderly people.[42]

In one Cochrane SR[401] on antipsychotics in AD, an improvement of the psychosis was observed with risperidone 1.0 mg/day respect to placebo (DM – 0.14) assessed by the BEHAVE-AD subscale in three studies and the secondary score of the NPI in another. In one study, aripiprazole (2-15 mg/day) showed a benefit compared with placebo at 10 weeks in the BPRS-PSYCHOSIS (DM-0.66), but not on the NPI psychosis subscale. — SR OF RCT, 1+

Another MA of four RCT with risperidone 1,5-2 mg/day on patients with dementia, mainly AD, showed a significant reduction of 46% on the BEHAVE-AD psychosis subscale with risperidone and 33% with placebo, accompanied by an improvement in CGI at 8-12 weeks.. The difference was only obvious in patients with severe psychosis symptoms.[337] — MA of RCT, 1++

Depression

Treatment of depression in dementia is probably similar to the population without dementia but there are no appropriate RCT for the majority of the drugs. The evidence of efficacy of antidepressants in dementia depression is weak. Studies have been carried out on patients with mild to moderate dementia, but there is only one on severe dementia. The SSRI are preferred due to the lower risk of confusion and anticholinergic effects.[5,42,152] One Cochrane SR of 2002 found few studies and with few patients that analysed drugs not commonly used in practice. No evidence was found for venlafaxine or mirtazapine in patients with dementia and depression. — SR of RCT, 1-

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Studies have been performed with citalopram, fluoxetine, sertraline, imipramine, maprotiline, clomipramine and moclobemide. Some proved to be superior with respect to placebo and others not, seemingly due to differences in the selection of patients and in the sensitivity of the scales used. Sertraline and citalopram have proved to be effective with respect to placebo. One study that did not show any effect of sertraline was carried out on patients with severe dementia where the administration of scales could hardly be assessed. One RCT with fluoxetine did not show any difference with placebo.[149]	SR of RCT, 1-
The results in tricyclics are conflictive (for example no effect of imipramine or maprotiline was found but an effect of amitriptyline and clomipramine was found) and there is limited evidence of effect on depression in dementia.[149]	RCT, 1+
Comparative studies between SSRI and tricyclics (amitriptyline vs. mianserine, imipramine vs. paroxetine, amitriptyline vs. fluoxetine and citalopram vs. mianserine) and between sertraline and venlafaxine showed similar efficacy for depression, but the SSRI were tolerated better and the tricyclics worsened the cognitive function.[42,149]	RCT, 1+
Only one small retrospective study on 31 patients, the majority with vascular dementia, supports the efficacy of ECT for depression in dementia.[42]	Case series, 3

Apathy

There is minimal evidence based on clinical cases about the usefulness of psychostimulants (d-amphetamine, methylphenidate), amantadine, bromocriptine and bupropion for severe apathy.[42]	Case series, 3

Anxiety

There are no RCT or SR about the use of benzodiazepine in BPSD.[140]	
Olanzapine (5-10 mg/day) proved to be beneficial in the treatment of anxiety in AD assessed with the NPI-NH (DM – 0.84).[401]	RCT, 1+

Erratic wandering /vagrancy

There are no RCTs on non-pharmacological interventions in erratic wandering.[398]	
One study on vagrancy in dementia showed that 1 mg risperidone was more effective than placebo.[149]	RCT, 1-

Sleep problems

There are no RCT on pharmacological treatment of insomnia specifically in patients with dementia.

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Trazodone, zolpidem or zaleplon may be useful to primarily treat insomnia, but there are little information about their efficacy. Benzodiazapines, preferably with short half-life are only recommended in the short term due to the risk of tolerance, rebound insomnia and adverse effects. If the patient also requires medication for other psychiatric symptoms, an agents can be used with sedative properties at night, but antipsychotics must not be used just to treat sleep alteration.[42]	Expert opinion, 4
One RCT did not show any benefit of 10 mg or 2.5 mg of melatonine on placebo to prolong nocturnal sleep or to reduce nocturnal activity in AD.[42]	RCT, 1+

Agitation and aggressiveness

In one Cochrane SR it was not demonstrated that haloperidol (0.25-6 mg/day) significantly improved agitation in dementia in treatments lasting for 3 to 16 weeks. Only aggressiveness was reduced in treated patients, but there was no improvement in other aspects of the agitation, global clinical impression of change, burden of the caregivers and ADL in studies that analysed them. Studies with haloperidol have shown that extrapyramidal effects already appear at lower doses than those that improve agitation.[149]	SR of RCT, 1+
In one Cochrane SR on atypical antipsychotics in AD,[401] risperidone 1 mg/day was better than placebo in improving aggressiveness according to Cohen-Mansfield Agitation Inventory (DM –1.13) in three RCT and according to the aggressiveness subscale of BEHAVE-AD in two RCT (DM -0.84 41 mg/day, DM -1.50 for 2 mg/day); olanzapine 5-10 mg/day also showed a benefit with respect to placebo for aggressiveness in the NPI-NH (DM –0.77). The response rate of risperidone 1-2 mg/day was also greater than for placebo in aggressiveness in patients with severe dementia with agitation and/or psychosis in three RCT (45-63%), although the response rate to placebo was also high (33-47%).	SR of RCT, 1++
Olanzapine showed a higher rate of response in one RCT at a dose of 5, 10 and 15 mg/day but not in another two (one at low doses and another at doses of between 1 and 7.5 mg/day).[42]	RCT, 1+
Quetiapine (100-200 mg/day) did not show any benefit in agitation in 2 RCT.[42]	RCT, 1+
In one study on acute treatment of agitation in hospitalised patients with dementia, olanzapine 2.5 and 5 mg via intramuscular way was superior than placebo, with the response rate after 2 hours of 62, 66.7 and 37.3% respectively. In one RCT that compared lorazepam vs. olanzapine via intramuscular way in the treatment of agitation there was no difference at 2 hours but lorazepam was inferior at 24 hours.[42]	RCT, 1+

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One small controlled study showed the benefit of several SSRI on agitation of FTLD. One RCT of paroxetine in FTLD did not show any improvement and worsened cognition. One RCT of citalopram vs. perphenezine on agitation and psychosis showed the benefit of citalopram in agitation and aggressiveness; citalopram presented less adverse effects.[42]	RCT, 1+/1-
There was no improvement with respect to placebo in agitation in the only RCT with trazodone in AD. A small RCT of trazodone in FTLD did show a benefit over placebo. One small RCT of trazodone vs. haloperidol showed a reduction of agitation when this was accompanied by depressive symptoms in patients with dementia. Trazodone and some SSRI could be appropriate for patients with mild agitation without psychosis or for those that do not tolerate antipsychotics.[42]	RCT, 1-
Donepezil 10 mg/day for 12-52 weeks showed benefits on agitation and aggressiveness with respect to placebo. There are not enough data for galantamine and memantine. The addition of memantine to treatment with donepezil also showed less agitation in one study.[5]	RCT, 1+
Carbamazepine showed a modest benefit for agitation, with good tolerance at low doses and in a short treatment in two RCT, whilst valproate showed no efficacy in four RCT.[42]	RCT, 1+
There is no consistent evidence that antipsychotics improve undesired behaviour other than aggressiveness,[5401] and this is usually at the expense of sedation, increased weight, extrapyramidal signs and falls.	SR and MA of RCT, 1++
There is no evidence that the efficacy of typical and atypical antipsychotics is different.[140]	RCT, 1+
There are no RCTs for lamotrigine, gabapentine or topiramate.	

Inappropriate sexual behaviours

There are no RCT of drugs to treat inappropriate sexual behaviours in dementia. Data of uncontrolled studies or case series suggest the efficacy of antidepressants, antipsychotics, mood stabilisers, hormonal agents, cimetidine and pindolol. [403]	Descriptive studies, 3

Other BPSD

No improvement of emotional incontinence or compulsive behaviours has been observed with SSRI in FTLD.[5]	Descriptive studies, 3

There are no studies that assess the effect of any treatment specifically on false recognitions, personality alterations or eating disorders.

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Summary of evidence

ACE inhibitors or memantine	
1++	The specific treatment with ACE inhibitors or memantine may non-specifically improve some of the BPSD in patients with dementia when this is indicated.[239,240,253,256,400]
1-	Neither rivastigmine nor galantamine showed an improvement of delirium in AD.[400]
1+	Rivastigmine may improve psychotic symptoms in DLB.[277]
Antipsychotics	
1-	The efficacy of antipsychotics is similar among all of them in comparative low-power and short duration studies.[42,399,400]
1+	To treat delirium in AD, an improvement has been observed with risperidone and donepezil.[400,401,337]
1+	Atypical antipsychotics (aripiprazole, olanzapine, quetiapine and risperidone) have shown a slight benefit with respect to placebo in the treatment of psychotic symptoms in patients with AD and VD.[25,42]
Antidepressants	
1++	Sertraline and citalopram have proven to be effective respect to placebo in the treatment of depression in patients with mild and moderate dementia in small studies.[42] Fluoxetine was not effective.[149]
1++	Effectiveness is similar between antidepressants in comparative studies, but the SSRI are better tolerated and the tricyclics worsen cognitive function.[42,149]
Apathy	
3	Psychostimulants ((d-amphetamine, methylphenidate), amantadine, bromocriptine or bupropion may be useful for severe apathy in dementia patients.[42]
Anxiety	
1+	Olanzapine 5-10 mg/day reduces anxiety (-0.84 points on the NPI-NH scale) in patients with AD.[401]
Erratic wandering	
1-	Risperidone 1 mg showed greater efficacy than placebo on vagrancy in patients with dementia.[149]
Sleep problems	
4	Trazodone, zolpidem or zaleplon, or short half-life benzodiazepines may be useful for insomnia in the short term.[42]
1+	Melatonine is not effective to prolong nocturnal sleep or to reduce nocturnal activity in AD.[42]

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Agitation and aggressiveness	
1++	Haloperidol 0.25-6 mg/day improves aggressiveness in patients with dementia, but not other aspects of the agitation, global clinical impression of change, burden of the caregivers and ADL.[402]
1++	Risperidone 1 mg/day and olanzapine 5-10 mg/day improve aggressiveness in patients with AD. [401]
1+	Olanzapine and quetiapine has not proved to be beneficial in agitation in patients with AD.[42]
1+	In hospitalised patients with dementia and agitation, olanzapine and lorazepam via intramuscular route have shown twice the response rate of placebo after 2 hours.[42]
1+	Some SSRI, such as citalopram or trazodone have shown an improvement of agitation in FTLD. Paroxetine did not show any improvement and cognition got worse.[42]
1–	Trazodone did not show an improvement of agitation in patients with AD without associated depression.[42]
1+	Donepezil 10 mg/day for 12-52 weeks showed benefits on agitation and aggressiveness with respect to placebo in patients with AD.[25]
1+	Carbamazepine has shown a modest benefit for agitation in patients with dementia.[42]
1+	Valproate has not proven to be effective for agitation in patients with dementia.[42]
1++	There is no consistent evidence that antipsychotics improve undesired behaviour other than aggressiveness, and this is usually at the expense of sedation, increased weight, extrapyramidal signs and falls.[5]
Inappropriate sexual behaviours	
3	To treat inappropriate sexual behaviours in dementia, there are data of possible efficacy of antidepressants, antipsychotics, mood stabilisers, hormonal agents, cimetidine and pindolol. [403]
Emotional incontinence and compulsive behaviours	
3	Emotional incontinence and compulsive behaviours in FTLD have improved with SSRI in some cases.[5]

Recommendation

ACE inhibitors or memantine	
B	The use of these drugs in patients on whom the use of ACE inhibitors or memantine is indicated, is recommended for the initial pharmacological treatment of BPSD.
B	Donepezil may be used in patients with AD and psychotic symptoms. Rivastigmine may be used to treat psychosis in DLB.
✔	If the ACE inhibitors and/or memantine are not effective on the BPSD, the most adequate psychotropic drugs will be used for each type of symptom, considering their adverse effects.

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Antipsychotics	
A	Risperidone may be used in patients with AD and psychotic symptoms.
D	Atypical anti-psychotics may be used in patients with AD or VD and psychotic symptoms.
Antidepressants	
B	Antidepressants, preferably sertraline and citalopram may be used in patients with dementia and depression. Tricyclic antidepressants are not recommended due to their adverse effects, despite their similar effectiveness.
Apathy	
D	Psychostimulants, amantadine, bromocriptine or bupropion may be used in patients with dementia and severe apathy.
Anxiety	
-	There is not enough evidence to make recommendations about the treatment of anxiety in dementia.
Erratic wandering	
D	Risperidone may be effective in erratic wandering in AD.
Sleep problems	
D	Benzodiazepines, trazodone or hypnotics may be used to treat sleep disorders in dementia. Melatonine is not recommended.
Agitation and aggressiveness	
B	The use of neuroleptics is recommended to treat agitation and aggressiveness. The evidence is greater for risperidone than for other drugs.
D	In the case of intolerance to antipsychotics, donepezil (if indicated), SSRI or carbamazepine may be used to treat agitation and aggressiveness.
Inappropriate sexual behaviours	
D	Antidepressants, antipsychotics, mood stabilisers, hormonal agents, cimetidine or pindolol may be used to treat inappropriate sexual behaviours.

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10.4.9. What adverse effects and contraindications do drugs used to control BPSD have?

Antipsychotics

The use of antipsychotics is associated with the following adverse effects: Increase in mortality, stroke, sedation, confusion, drowsiness, parkinsonism, dystonia, tardive dyskinesia, akathisia, malignant neuroleptic syndrome, hyperlipidemia, hyperglycaemia, weight increase, orthostatic hypotension, arrhythmias, ECG alterations, anticholinergic effects and cognition worsening.[5,42,404]	RCT, 1+
In one Cochrane RS on haloperidol in dementia, greater frequency of adverse reactions was observed such as extrapyramidal symptoms, drowsiness and fatigue, compared with the controls.[402]	SR of RCT, 1+
Haloperidol induces undesired extrapyramidal effects, which already appear at lower doses than those required to reduce agitation.[149] The extrapyramidal effects and drowsiness limit their use.[140]	RCT, 1+
In one MA of RCT[405] the most frequent adverse effects with atypical antipsychotics (aripiprazole, olanzapine, quetiapine or risperidone) compared with placebo were drowsiness (OR = 2.84) and urinary infections (OR = 1.28). Extrapyramidal symptoms (OR = 1.51), movement disorders (OR = 3.42) and peripheral oedema (OR = 1.99) were the most frequent with risperidone and olanzapine. A relevant increase of lesions, falls or syncope was not detected.	MA of RCT, 1+/1-
In a small and low quality study faster cognitive impairment was seen in dementia patients treated with antipsychotics.[149]	Observational study 2-
Also in a MA of RCT with atypical antipsychotics in dementia, patients treated with aripiprazole, olanzapine, quetiapine or risperidone worsened more with respect to cognitive scores than those treated with placebo.[405]	MA of RCT, 1+/1-
Patients treated with risperidone duplicate the risk of extrapyramidal symptoms compared with placebo (more with 2 mg/day than with 1 mg/day), according to different MA of RCT (12% vs. 6% in one of them). [404,401,337] in the short-term, no differences are detected in the impact of extrapyramidal effects for risperidone and olanzapine compared with a placebo.[399]	MA of RCT, 1++
Drowsiness is 5-8 times more frequent and movement disorders 7.5-11 times more frequent with olanzapine than with placebo in one RCT. In two MA of RCT, drowsiness was more frequent in patients treated with risperidone or olanzapine than with placebo (18% vs. 8% in one of them).[404,337]	RCT, MA of RCT, 1+/1++

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The dropout rates were similar among dementia patients treated with haloperidol and controls in a Cochrane review,[402] and also among those treated with atypical antipsychotics and the controls in one MA,[405] which suggests that adverse effects were tolerated thanks to a better control of the agitation.	SR and MA, 1++
There is little information about the long-term safety of atypical antipsychotics in the elderly with dementia.[399]	SR of RCT and observational study, 1+/2++
Clozapine is associated with agranulocytosis that may be mortal, so the leukocyte count must be monitored.[42]	Observational study, 2
If typical antipsychotics via intramuscular route are used, the appearance of acute dystonias and other extrapyramidal effects must be controlled.[25]	Expert opinion, 4
The use of atypical antipsychotics has been associated with an increase in the risk of stroke and mortality in patients with dementia.[5,42,135,149] The risk with typical antipsychotics may be similar according to a large retrospective review,406 above all at the start of treatment and with high doses.	Cohort study, 2+
The risk of stroke with antipsychotics has not been clearly established. In a joint analysis of 11 RCT[407] 2.2% of those treated with olanzapine and risperidone compared with 0.8% of those treated with placebo in the RCT had a stroke (RR = 2.7). In a MA on atypical antipsychotics for dementia, an increase in risk of stroke was detected (OR = 2.13), especially with risperidone.[405] The cause of this association is not clear and large observational studies have not confirmed an increase in the risk of stroke compared with typical antipsychotics or untreated patients.[152,149]	MA of RCT, 1+ Cohort study, 2+
An increase in mortality has also been observed in patients treated with risperidone, quetiapine and olanzapine respect to placebo (4% vs. 3.1%, 5.51% vs. 3.2%, 3.5% vs. 1.5% respectively). In a MA of 15 RCT, there were 3.5% of deaths with atypical antipsychotics compared with 2.3% with placebo, OR = 1.54.405 In two studies that included patients treated with haloperidol, the magnitude of the risk was similar. According to data from RCT, with risperidone, the risk of death during treatment and up to 30 days after its suppression, was slightly greater than that of placebo (4% vs. 3.1%) but with no statistical significance and with no relation with the dose. The adverse effects most associated with death in risperidone were pneumonia, cardiac insufficiency, cardiac arrest and cerebrovascular disease.[408]	RCT, MA of RCT, 1+

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As occurs with the risk of stroke, observational studies do not support these differences, as some suggest a somewhat greater mortality with the typical ones than with the atypical ones or else there are no differences with those not treated.[152,406]	Cohort study, 2+
In patients with DLB, observational studies suggest that up to 50% may have marked sensitivity to antipsychotics, leading to extrapyramidal reactions, confusion, tremors, autonomic instability, falls and 2-3 times greater mortality.[25,5,129,404]	Observational study, 2++
Benzodiazepines	
The adverse effects of the benzodiazepines include: Sedation, worsening of cognition, confusion, delirium, worsening of the memory, paradoxical disinhibition, increase in the risk of falls, worsening of respiratory disorders, tolerance and dependence. Sleep apnoea is a relative contraindication for the use of benzodiazepines. [42,235]	RCT, 1+
Long-lasting benzodiazepines produce more cognitive alterations in the elderly. There is more evidence for diazepam than for flurazepam or nitrazepam.	RCT, 1+
Antidepressants	
Anticholinergics may worsen confusion and psychosis, and they must be avoided in dementia. SSRI produce less confusion than tricyclic antidepressants.[5]	RCT, 1+
Anticholinergics are contraindicated in patients with cardiovascular diseases, prostatism or urinary bladder diseases. They may worsen cognition, produce confusion and delirium. Orthostatic hypotension may be caused by medications or worsened by them and consequently, patients with dementia have a greater propensity to falls and fractures.[42]	RCT, 1+
The SSRI produce less anticholinergic effects than classical antidepressants, although they may produce other limiting adverse effects (gastrointestinal, weight loss, sleep alterations, hyponatraemia). They have been associated with falls and fractures due to a different action mechanism to that of the tricyclics.[152]	RCT, 1+

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Amitriptyline has been clearly associated with cognitive alterations due to its anticholinergic activity, both in elderly people and in depressed patients. Other tricyclics such as imipramine, lofepramine and maprotiline seem to have less impact on the cognitive function. Mirtazapine and mianserine also seemed to produce these adverse effects whilst they have not been observed for SSRI. The improvement in depression symptoms may conceal the worsening of cognition.[149]

RCT, 1+

Antiepileptic drugs

All the anticonvulsants may produce dose-dependent cognitive alterations. Phenobarbital produces more alterations than carbamazepine, phenytoin or valproate.[149]

RCT, 1+

ACE inhibitors (question 10.2.5).

Summary of evidence

Antipsychotics	
1+	Antipsychotics may produce an increase in mortality, stroke, sedation, confusion, drowsiness, parkinsonism, dystonia, tardive dyskinesia, akathisia, neuroleptic malignant neuroleptic, hyperlipidemia, hyperglycaemia, weight increase, orthostatic hypotension, arrhythmias, ECG alterations, anticholinergic effects and cognition worsening.[5,42,404]
1++	Haloperidol produces extrapyramidal symptoms, drowsiness and fatigue more often in patients with dementia than in controls.[402]
1++	Atypical antipsychotics (aripiprazole, olanzapine, quetiapine or risperidone) produce greater drowsiness (OR = 2.84) and urinary infections (OR = 1.28) in patients with dementia than in controls.[405]
1++	Risperidone and olanzapine produce more extrapyramidal symptoms (OR = 1.51), movement disorders (OR = 3.42) and peripheral oedema (OR = 1.99), in patients with dementia than in controls, but not more lesions, falls or syncope.[405]
1++	Patients with dementia treated with aripiprazole, olanzapine, quetiapine or risperidone worsened more in cognitive scores than those treated with placebo in the RCT.[405]
1++	Risperidone doubles the risk of extrapyramidal symptoms compared with placebo in patients with dementia.[404,401,337]
1+	Drowsiness is more frequent and movement disorders are more frequent with risperidone or olanzapine than with placebo.[297,404,337]
1++	The dropout rates among patients with dementia treated with haloperidol or atypical antipsychotics were similar to the controls.[402,405]

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1+	Clozapine is associated with agranulocytosis which may be mortal.[42]
1++/ 2+	The use of atypical antipsychotics (risperidone, olanzapine) has been associated with a slight increase in risk of stroke and mortality in patients with dementia. On the other hand, observational studies do not support the fact that there are differences between atypical, typical and placebo.[129,407,405,152,149,408,406]
2++	50% of patients with DLB may have marked sensitivity to antipsychotics, extrapyramidal reactions, confusion, tremors, autonomic instability, falls and an increase in mortality.[25,5,129,404]
Benzodiazepenes	
1+	Benzodiazepines may produce sedation, worsening of cognition, confusion, delirium, worsening of the memory, paradoxical disinhibition, increase in the risk of falls, worsening of respiratory disorders, tolerance and dependence.[42,235]
1+	Long-lasting benzodiazepines such as diazepam produce more cognitive alterations in the elderly.[149]
Antidepressants	
1+	Anticholinergics may worsen confusion and psychosis in patients with dementia. The SSRI produce less confusion than tricyclics.[5]
1+	Anticholinergics are contraindicated in patients with cardiovascular diseases, prostatism or urinary bladder diseases.[42]
1+	The SSRI may produce adverse gastrointestinal effects, weight loss, sleep alterations or hyponatraemia, and they have been associated with falls and fractures.[152]
1+	Amitriptyline has been associated with cognitive alterations. Other tricyclics such as mirtazapine and mianserin have less impact on the cognitive function. SSRI have not been associated with cognitive alterations.[5,42,152,149]
Antiepileptic drugs	
1+	Anticonvulsants may produce cognitive alterations. Phenobarbital produces more alterations than carbamazepine, phenytoin or valproate.[149]

Recommendation

A	Antipsychotics must be used with caution in patients with dementia, due to the risk of adverse reactions, always considering the risks of treating compared with the risks of not treating.
B	Antipsychotics are contraindicated in DLB due to the high risk of adverse effects.
C	Treatments with benzodiazepines must be short-term due to the adverse effects.

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10.4.10 How effective is it to combine pharmacological and non-pharmacological treatment to treat behavioural and psychological symptoms in mild, moderate and severe dementia?

There is little evidence about the efficacy of combined treatment (pharmacological and non-pharmacological) to manage behavioural and psychological symptoms of dementia.

One RCT with 150 patients with mild or moderate AD that compared the efficacy of treatment with donepezil with treatment with donepezil plus cognitive stimulation, for 6 months, did not show any significant differences.[25]	RCT, 1+
Studies performed on patients affected by severe AD, with depression or psychosis, recommended the joint use of pharmacological and non-pharmacological treatments, not specifying what they based themselves upon to make this recommendation [152].	RCT, 1-
One SR of RCT[149] recommends, as a strategy to treat BPSD, to associate non-pharmacological and pharmacological measures, not describing the studies used to make the recommendation.	RCT, 1-

Summary of evidence

1+	One RCT with 152 patients with mild or moderate AD to assess the efficacy of cognitive stimulation and ACE inhibitors, compared with ACE inhibitors in monotherapy, did not show any significant differences.[25]
1-	One SR of RCT recommends associating non-pharmacological measures with pharmacological ones to treat BPSD.[149]

Recommendation

✔	The association of non-pharmacological and pharmacological measures is recommended to treat behavioural and psychological symptoms of dementia.

10.4.11 Which are the most effective recommendations to avoid BPSD in patients with dementia?

The etiopathogeny of the BPSD is varied and affects many different factors: A predisposing genetic factor, a biological factor derived from specific degenerative changes that occur in specific areas of the brain, the presence of concomitant diseases, an inadequate environmental surrounding, and the different caring styles of the caregiver may have a significant influence on the appearance and variability of the BPSD.[409]

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We can act upon these latter factors, by detecting and treating the concomitant diseases and providing optimal environmental conditions that do not generate the appearance of BPSD.[398]

There is a specific intervention group in areas:

- **Structured activities:** The inclusion of physical activity, walks and recreational activities reduce the appearance of agitation behaviours.[410]
- **Behavioural therapy:** By reinforcement techniques of relaxed behaviours and control of stimuli.
- **Environmental modifications:** Consisting in reducing unnecessary stimulation, maintaining safety, autonomy and independence. A natural surrounding and light therapy may reduce the frequency of appearance of agitated behaviour.
- **Social contact:** This consists of creating strategies to improve the frequency and quality of social interactions among people affected by dementia.
- **Sensory stimulation and relaxation:** Manual massage, therapeutic contact and isolated sensory stimulation activities, or combined ones, may induce relaxation and reduce the prevalence of behavioural symptoms and agitation.[329,331,332]

In one SR[411,25] of seven RCT, which assessed therapeutic touch massage, as a non-pharmacological alternative to reduce anxiety, agitated behaviour and depression, only two satisfied minimal methodological criteria. These studies assessed two specific applications: Manual massage for the immediate reduction of agitated behaviour and the addition of therapeutic touch to verbal stimulus, to normalise nutritional intake. The results indicated that manual therapeutic touch massages may be useful as alternatives in behavioural and emotional treatment.

RCT, 1-

We have no scientific evidence to be able to draw conclusions and recommendations on the effect of these interventions.

Summary of evidence

4	Many different factors affect the etiopathogeny of BPSD (genetics, type of dementia, concomitant diseases, environmental surrounding, lifestyles).[409] We can act upon the comorbidity and on the environment,[398] and carry out specific structured interventions,[410,410] behavioural therapy;[387] environmental modifications; social contact; sensory stimulation and relaxation.[329,331,332]
-1	One SR[411,25] of seven RCT, which assessed therapeutic touch massage showed that they can be useful to reduce anxiety, agitated behaviour and depression.

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Recommendation

✔	A meticulous assessment is recommended if BPSD appear, to rule out concomitant pathology and achieve optimal environmental surroundings.
✔	Sensory stimulation, behavioural therapy, structured activities and social contact may be used to reduce the incidence of BPSD, although there is no scientific evidence to support this.

10.4.12 How must BPSD, which are difficult to monitor in outpatients, be treated?

Any person with dementia may, at some moment in the evolution of the disease, present BPSD that do not go away easily with verbal contention, non-pharmacological manoeuvres or with psychotropic drugs. **(question 10.4.8).**

These symptoms cause critical situations that are difficult to control in outpatients and often require the coordinated action of the PCT and of the SDCT. If they are not controlled properly, they must be referred for admission to the emergency service of the hospital or to specific units.[412]

In situations of refractory crises, admission into a hospital may be useful to diagnose possible comorbidities, optimise the pharmacological treatment of the symptom and guarantee the safety of the patients and of their environment[413,25] **(questions 13.5.1-13.5.4).**	Expert opinion, 4

Summary of evidence

4	In situations where the crises do not go away when treated in outpatients, admission into hospital is necessary to be able to diagnose possible comorbidities, optimise the pharmacological treatment of the symptom and guarantee the safety of the patients and of their environment[413,25]

Recommendation

D	If the behaviour crises do not respond to the normal pharmacological measures in the home/residence, admission into hospital or into specific units is advised to diagnose the symptoms and aetiology, treat comorbidities, optimise the treatment of BPSD and guarantee the safety of the patient and of his environment.

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10.4.13. What attitudes must caregivers satisfy to deal with patients with BPSD?

There is no scientific evidence respect to the qualities that caregivers must satisfy to deal with patients with BPSD.[5,409] The available information sources today are basically manuals and monographs aimed at caregivers of patients with dementia.

To respond to this question we must take a series of aspects into account: The different personality profiles of caregivers, the level of relationship and involvement in the care tasks, the voluntary acceptance or imposition of the function of caring, differences in age and sex of the caregivers and if the caregiver is one single member or they receive support (family, professionals). To prepare recommendations that may help caregivers manage BPSD, it is also important to evaluate the following aspects:

- The previous relationship of the caregiver with the patient: Type of relationship and its quality.
- Level of involvement of the caregiver in the care of patient: Direct care, emotional support and organisation of care.
- Degree of voluntariness in the care relationship.
- Stress that is generated during the relationship between the patient and the caregiver.
- Degree of knowledge and understanding of the disease by the caregiver.
- Degree of strain and help received from other relatives and from other support sources (Association of families, institutional help, etc).
- Expectations of the caregiver about the intervention of the physician and health personnel in general.
- Ideas of the caregiver about the future of the patient: Institutionalisation, probability of imminent death and denial of the deficiencies.

Faced with the appearance of BPSD, the caregiver's attitude must be one of:

- Acceptance of the progressive nature of the disease, and the lack of "curative" treatment at the present time.
- Understand that many of the BPSD do not have a specific treatment and that we can use limited efficacy therapeutic measures.
- Have a patient and tolerant attitude.
- Inform the caregiver that the patient's attitudes, beliefs and anomalous behaviour are symptoms of the actual disease. as is the case of memory deficiency or other cognitive deficiencies.
- Understand that the solution of the BPSD does not depend on them being explained to the patient nor on his or her willpower to solve them.
- Observe the context in which the BPSD appear, as well as the predisposing, triggering factors and manoeuvres or interventions that reduce or eliminate them.
- Request help from other members of the family, institutions and associations so as not to undertake the role of caregiver alone.
- Request professional aid if symptoms or signs of strain or claudication appear in the task of caring.[409,5]

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Recommendation

✔	It is advisable to inform and train caregivers of dementia patient in strategies to address and manage the BPSD so that it is possible to adopt and promote an appropriate attitude towards patients and prevent strain and claudication of the caregivers.

10.5. Alternative treatments of dementias

Questions to be answered

10.5. Are there any plant-based medications or food supplements that have proved to be useful in the treatment of dementia?

10.5. Are there any plant-based medications or food supplements that have proved to be useful in the treatment of dementia?

Vitamin E

One Cochrane SR that found one high-quality RCT concluded that there is not enough evidence about the efficacy of vitamin E in the treatment of Alzheimer's disease.[414] — RCT, 1++

One MA of RCT with an extensive number of individuals concluded that large vitamin E supplements (400 UI/day) could increase mortality.[415] — MA, 1++

The CPG of the EFNS (2007)5 and the Canadian CPG (CCDTD)(2006)[416] concluded in their recommendations that there was not enough evidence about the risk-benefit profile to recommend the treatment of AD with vitamin E.

Vitamin B_1, B_6, B_{12} and folic acid

The CPG[152] and one SR of RCT[149] do not recommend the use of B_1, B_6, B_{12} vitamin or folic acid supplements to treat cognitive impairment, as their efficacy has not been demonstrated except for those cases where there is a clear vitamin deficiency. — SR of RCT, 1++

Copper supplements

One RCT that assessed the efficacy of administering copper supplements to patients with AD did not show beneficial effects on cognition of treated individuals compared with the placebo group.[417] — RCT, 1+

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Ginkgo biloba

The CPG of the AAN, based on a RCT, concluded that treatment with ginkgo biloba was safe although it affirmed that it lacked quality evidence about its efficacy.[304]	RCT, 1-
A review of published case series suggested a possible association between treatment with ginkgo biloba and brain haemorrhage, with an increase of the haemorrhage time in some patients.[418]	Descriptive study, 3
The CPG of the EFNS (2007),[5] based on three low-quality RCT considered that there is not enough evidence to recommend the use of ginkgo biloba in the treatment of AD or VD. The Canadian CPG (CCCDTD)(2006) considered that there was not enough evidence to make a recommendation about the use of gingko biloba.[416]	RCT, 1-
A Cochrane SR (2009)[419] included 36 RCT that assessed the effect of ginkgo biloba at different doses on cognitive impairment (of different aetiologies and different severity) of which only nine RCT were controlled for a period of more than 6 months. Three of the four most recent studies did not show efficacy with respect to placebo, whilst only one showed efficacy of the treatment. The conclusions of this SR were that the use of ginkgo biloba seems to be safe within a short-medium term research context. No major incidents about side effects compared with placebo have been reported, although evidence about the clinical benefits of ginkgo biloba in individuals with cognitive impairment in general or AD in particular, is inconsistent.	SR of RCT, 1+

Lecithin

A Cochrane SR concluded that there is not enough evidence to recommend the use of lecithin in the treatment of AD, vascular dementia or mixed dementia.[420]	SR of RCT, 1+

Alpha-lipoic acid

One Cochrane SR (2009) concludes that failing a RCT that assesses the effect of alpha-lipoic acid in patients with dementia, its use cannot be recommended to treat AD or dementia in general.[421]	SR of RCT, 1+

Omega-3 fatty acids

One RCT that included a small number of participants did not objectify the efficacy of the use of Omega-3 fatty acids to treat AD.[422]	RCT, 1-

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Ginseng

A recent SR (2009) that included two RCT that assessed the efficacy of ginseng *(Panax ginseng)* in AD, concluded that although both studies showed a positive effect on cognitive variables, they had relevant methodological defects that made it difficult to interpret these results.[423]

SR of RCT, 1+

Yokukansan (TJ-54)

A RCT that included patients with AD, DLB or mixed dementia did not prove the efficacy of the treatment of cognitive symptoms with yokukansan (TJ-54). [424]

RCT, 1+

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Summary of evidence

Vitamin E	
1+	Vitamin E supplements have not proven to be effective in the treatment of AD and they could increase mortality.[5,416]
Vitamin B_1, B_6, B_{12} and folic acid	
1++	The use of vitamin B_1, B_6, B_{12} or folic acid supplements is not effective in patients with cognitive impairment that do not present a clear deficiency of these elements.[152,149]
Copper supplements	
1+	The use of copper supplements is not effective to treat patients with Alzheimer's disease.[417]
Ginkgo biloba	
1+	The evidence on the effectiveness of ginkgo biloba in the treatment of AD or VD is inconsistent.[304,418,5,416,149,419]
Lecithin, alpha-lipoic acid, omega-3 fatty acids, ginseng or yokukansan (TJ-54)	
1+	There is no quality evidence about the efficacy of the use of lecithin, alpha-lipoic acid,[421] omega-3 fatty acids[422] ginseng[423] or yokukansan (TJ-54)[424] in the treatment of cognitive symptoms of AD, although the analysis of available studies suggests that these are not effective in this treatment

Recommendation

Vitamin E	
B	Vitamin E supplements are not recommended in the treatment of AD.

Vitamin B_1, B_6, B_{12} and folic acid	
A	The use of vitamin B_1, B_6, B_{12} or folic acid supplements is not recommended in patients with cognitive impairment that do not present a clear deficiency of these elements.
Copper supplements	
B	The use of copper supplements is not recommended to treat patients with AD.
Ginkgo biloba	
B	There is not enough evidence in literature about the efficacy of ginkgo biloba to recommend its use in the treatment of AD or VD.
Lecithin, alpha-lipoic acid, omega-3 fatty acids, ginseng or yokukansan (TJ-54)	
C	Existing evidence does not permit recommending the use of lecithin, alpha-lipoic acid, omega-3 fatty acids, ginseng or yokukansan (TJ-54) in the treatment of cognitive symptoms of AD.

10.6. Assessment of the treatment of dementias

Questions to be answered

10.6. How must the response to the treatment of dementia be assessed in clinical practice?

10.6. How must the response to the treatment of dementia be assessed in clinical practice?

There are no studies that establish the parameters that must be monitored in the evaluation of the therapeutic response and control of patients with dementia. However, given that the patients present cognitive, functional, motor, behavioural and global alterations throughout the disease, clinical experts suggest carrying out a longitudinal evaluation of all of them.[25,5]

Given that the care of patients with dementia may have negative repercussions on the caregiver's health, this must also be taken into account in the control of the process, assessing the degree of strain **(Section 11).**

Expert opinion, 4

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

The NICE (2007)[25] CPG recommends the use of the MMSE to monitor the global cognitive function. This is the most commonly used short global cognitive test to longitudinally evaluate the cognitive function of patients with dementia and their response to therapy in both a research context and in clinical practice, and it has shown good inter-observer reliability and test-retest validity

Observational study, 2+

There are several versions of the MMSE in use in Spain. standardised version,[142] Lobo143, or Mini-Cog Test (MCT) versions.[144]

There is no consensus about which magnitude of change in the MMSE must be used to consider that a patient responds or does not respond to treatment. The NICE (2007)[25] CPG underlines that a specific treatment must be considered as effective and, therefore, must be maintained, when the patient shows an improvement or at least no impairment in the score of the MMSE 2-4 months after having reached the maintenance dose. Other authors consider that a patient responds to the medication when an impairment of less than 2 points occurs within 6 months or of less than 3 points in the MMSE in 12 months.[425]

Expert opinion, 4

For patients in moderately advanced or advanced dementia stages, there is a version of the MMSE, the "Severe MMSE", which permits carrying out a cognitive control of these patients with MMSE scores of less than 9 points and that presents a good correlation with global dementia scales.[426]

Observational study, 2+

With respect to the other aspects (behavioural, functional, motor disorders or strain on the caregiver), each one of these may be assessed in a qualitative or semi-quantitative manner through a directed history or quantified through scales, tests or specifically designed questionnaires for this purpose, as has been dealt with in each one of the relative sections **(sections 8, 10.4 and 11).**

There are no studies that compare the usefulness of both methodologies in the monitoring of patients with dementia, although published CPG[25,5] specifically recommend the use of quantitative instruments, as they consider that these would enable changes to be detected at an earlier stage. However, there is no consensus about which specific instruments are more useful to assess each one of the aspects longitudinally or about what degree of alteration in each of these must represent a modification in the management or in the therapy of patients with dementia, although the quantitative assessment would permit establishing intra- and inter-individual comparisons.

Expert opinion, 4

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

Summary of evidence

2+	Patients with dementia present cognitive, functional, motor, behavioural changes during its evolution. Caregivers also present changes in the degree of strain throughout the disease.
4	The use of tests, scales or standardised questionnaires is useful to quantify the therapeutic response and the appearance of complications in patients with dementia.[25,5]
2+	The MMSE, of which there are several Spanish versions,[142,143,144] is useful to evaluate the response to treatment in patients with dementia;[426,425,25] it is the most commonly used test in clinical practice for this purpose.

Recommendation

D	The periodic assessment of cognitive, functional, motor and behavioural aspects is recommended, as well as of the degree of strain on the caregiver in the monitoring of patients with dementia.
D	The use of tests, scales or questionnaires is recommended to quantify the therapeutic response and the appearance of complications in patients with dementia.
✔	The choice of a test, scale or questionnaire will be based on the physician's experience and on its applicability in the context.
C	The use of the MMSE is recommended to assess the response to dementia treatment in clinical practice.

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11. Caregivers of patients with dementia

Questions to be answered

11.1. What is understood by primary caregiver of a patient with dementia? 11.2. Are the characteristics of caregivers the same for people with different types of dementia?
11.3. What repercussions does caring for a person with dementia have on the caregiver?
11.4. What scales are useful to assess caregiver burden?
11.5. Are there effective interventions to prevent caregiver burden?
11.6. Are there effective interventions to deal with caregiver burden?
11.7. What are mutual aid groups (MAG)?
11.8. What benefits are obtained from participating in MAG?
11.9. In what cases is psychological treatment of the caregiver necessary?
11.10. What are associations of families of people affected by dementia and what role do they play in a comprehensive approach to dementia?
11.11. What must the relationship between the associations and the public social and health network be like?

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11.1. What is understood by primary caregiver of a patient with dementia?

The caregiver has been defined as "the person who helps or cares for another person affected by any type of disability, handicap or invalidity that makes it difficult or prevents them from carry out their life activities or their social relations in a normal manner". [427,25,428]	Expert opinion, 4
Primary caregivers of people with dementia assume the primary care tasks and responsibilities, without receiving any economic payment for their work, and they are accepted as such by the rest of the members of the family.[427] Their commitment is significant and long-lasting.	
In the majority of the cases they are direct family members or very close friends. Normally, they are wives or daughters aged between 45 and 70 years old, who live with the patient, or who spend a considerable amount of their time with them.[25,429,430]	Observational study, 2++

Often, the caregivers attend to the patient alone, without there being any network of secondary caregivers to support them. The majority of their work is carried out in the home and their tasks include accompanying patient in transport, going shopping, doing the household chores, preparing meals, and helping them in their basic activities of daily living such as getting dressed, eating, moving and sphincter control.[431] — Descriptive study, 3-

Professional caregivers, with or without specific training, are those people who directly care for the person affected by dementia, and receive an economic compensation for their work.[432]

Over the last few years, due to many different factors such as the change in family structure, incorporation of women into the working markets and the need to reduce expenses caused by caring for people with dementia, a progressive increase of professional caregivers without specific training has been observed. The percentage reaches 8.7% of caregivers in Spain. They are usually people of both sexes, immigrants, the majority originating from Latin America and aged between 26 and 50 years old. They are often married people who live with their companions, with unfinished university studies in their country and with Christian religion.[433] — Observational study, 2++

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Summary of evidence

4	Caregivers are people who help or care for other people affected by any type of disability, handicap or invalidity that makes it difficult or prevents them from carrying out their living activities or their social relations in a normal manner.[427,25] the primary caregiver assumes the main tasks and responsibilities of caring, not receiving any economic payment, and this role is accepted by the rest of the members of the family.[427]
2++	They are direct family members or friends. Wives or daughters aged between 45 and 70 years old. They live with the patient or spend a lot of time with them.[25,429,430,431]
2++	Professional caregivers, with or without specific training, are those who carry out the care work directly, receiving an economic compensation for their work.[432] Over the last few years a progressive increase of professional caregivers has been observed, with no specific training, young immigrants, Latin Americans, Christian, with unfinished university studies.[433]

11.2. Are the characteristics of caregivers the same for people with different types of dementia?

People with dementia may present different clinical manifestations and different evolution, which may pose difficulties and specific needs.[430,25] Furthermore, personal, family and contextual circumstances of the caregivers may pose differential elements in the care of patients.	Expert opinion, 4
Current research is aimed at discriminating these differential aspects: Gender, relationship, economic-cultural status, etc. With respect to gender, women suffer a greater level of burden, generally because they assume the care in a much more intense manner. With respect to relationship, caregiving children seem to have a greater level of burden than husbands or wives, due to the difficulty in making the different occupational and family responsibilities compatible.[434,435,436]	Observational study, 2++
The problems posed by Alzheimer's disease (AD) are related above all to cognitive losses, to which we can add, to a greater or lesser degree, BPSD, even from the mild-moderate stage of the disease. Basic functionality losses, including sphincter control and mobility alterations will only appear in advanced stages. As the disease progresses, the burden supported by the caregivers increases.[6,44]	Observational study, 2++
Frontotemporal lobar dementia (FTLD) usually appears in younger people, in whom the BPSD are relevant from the start and have an early effect on the family, occupational and social environment. The primary caregivers in these cases are either the spouse, who still usually and needs to work, and must make their task of caring compatible with other unavoidable obligations such as looking after their children, often in school age. In other cases, they are the parents, of advanced ages and with difficulties in their caring capacity.[6,52]	Observational study, 2++
In dementia with Lewy bodies (DLB) and in Parkinson's Disease Dementia (PDD), the work of the primary caregiver is complicated due to the actual characteristics of the disease. These patients are difficult to understand, accept and manage the motor, cognitive, behavioural fluctuations, parkinsonism, autonomous-sphincter disorders, frequent falls, REM sleep behaviour alterations, hallucinations and delusions with paranoid ideation.[6,47]	Observational study, 2++

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In vascular dementia (VD), focal alterations may be present from the onset or appear early on. Cognitive impairments may have a subcortical, cortical or mixed variable origin, and BPSD are not infrequent. The fact that in this type of dementia, communication between patients and caregiver is possible until very advanced stages, enables the emotional contact between both to be more feasible.[6,46]	Observational study, 2++

Summary of evidence

4	Every person with dementia and their centre of coexistence have different characteristics and needs, which require individualised care.[4,20,25]
2++	Female caregivers usually have a greater burden in the task of caring. Caregiving children have a greater burden than husbands or wives.[434,435,436]
2++	AD, in the mild-moderate phase, poses problems related to cognitive deficiency, and to a lesser extent with BPSD. Basic functionality losses, including sphincter control and mobility alterations are added in advanced stages.[6,44]
2++	FTLD usually occurs in younger people and presents relevant BPSD from the onset. The primary caregivers are their young companions with many different obligations to make compatible (work, family).[6,45]
2++	In DLB and in Parkinson's Disease Dementia (PDD), patients are difficult to manage due to their motor, cognitive, behavioural fluctuations, parkinsonism, autonomic-sphincter disorders, frequent falls, REM sleep behaviour alterations, hallucinations and delusions with paranoid ideation.[6,47]
2++	VD is associated with early focal signs, variable cognitive impairment (subcortical, cortical or mixed) and frequent BPSD. Communication is preserved until very advanced stages.[6,46]
4	There is no specific caregiver for each type of dementia. Every person with dementia and their environments are a different reality; however, each type of dementia has its own individual characteristics that may have an influence on the burden that the caregiver is going to suffer, and on the needs generated.

Recommendation

C	During the care of every person with dementia, their individual characteristics and the actual characteristics of the disease must be evaluated to be able to evaluate and prevent the burden and needs of the caregiver, and act consequently to optimise their support network.

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11.3. What repercussions does the care of a person with dementia have on the caregiver?

Dementia generates concern, uncertainty and fear in the family. It causes changes in roles occupied by each one of its members, which may represent important modifications in their lives. The role of caregiver evolves with time; it starts with assimilating the diagnosis, supervising and helping in the instrumental activities of daily living (IADL), progressive tolerance faced with the behaviour disorders and attention to the basic activities of daily living (BADL). The physical and psychological burden that the primary caregiver has to support will increase with the evolution of the disease. Their tasks will increase, they must assume new responsibilities, and they will lose their freedom and independence to continue carrying out their own activities, which may finally represent a change in their life project. This situation endangers their physical and emotional health, above all if they are fragile or elderly people. When the stress is continuous, and especially if there is no adequate support network, the possibility of psychological, functional and social complications appearing increases.[437,436]

Descriptive study, 3

The caregiver burden is defined as the extent to which physical and emotional health, social life or the financial situation of the caregiver, are negatively affected as a result of caring for the patient. The term "caregiver burden" refers to the psychological and physical consequences, as well as changes derived from the care because of the dementia.[438]

For different reasons, although usually due to an emotional bond with the patient, caregivers assume a greater burden than they are able to support, not taking into account their real capacities and their own state of health. The strain that entails the risk of claudication depends on a lot of factors such as the type and severity of the symptoms, the duration of the dementia, the caregiver's personal characteristics and the support received from health resources and from the family environment.

Often, when the caregivers are sons or daughters, and they live with the patient and assume other family responsibilities, they will accumulate feelings of blame and disorders will appear such as anxiety, depression, feeling of loneliness and isolation. This strain decreases if the patient is admitted into a nursing home. However, when the caregiver is the companion, these symptoms intensify at the moment of institutionalisation. The morbidity and mortality of the caregivers increase significantly in all these situations of stress and burden.[437,436]

Descriptive study, 3

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Summary of evidence

3	Dementia generates concern, uncertainty and fear in the family and causes changes in roles among its members. The caregiver's tasks change throughout the process, and the physical and psychological burden increases progressively, free time decreases and health problems may appear, above all if there is no suitable support network.[437,436]
3	The caregiver burden is understood as all those negative consequences on their physical and emotional health, social life or financial situation, derived from the task of caring.438 The children are those who undergo a greater burden in the care, if they live with the patient and assume other family responsibilities.[437,436] They often accumulate feelings of blame, and disorders appear such as anxiety, depression, difficulty in expressing feelings, and the feeling of loneliness and isolation increases. Morbidity and mortality significantly increase.[437,436]

Recommendation

D	Dementia is a dynamic process which commits and compels the caregiver more. It is recommendable to meticulously evaluate the burden supported by the primary caregiver and the support he / she receives in their task of caring. If the burden is too much, it is advisable to establish the appropriate measures to prevent this from affecting his or her physical and psychological health, thus giving rise to the risk of claudication.

11.4. What scales are useful to assess caregiver burden?

The Zarit scale is the most commonly mentioned in the studies and clinical practice guidelines. It is a self-administered questionnaire, with subjective frequency measurements on 22 items. The test is very consistent and has a high test-retest concordance. It has been adapted and validated in its Spanish version with a score of each item from 1 to 5 (evaluating the frequency of each case of "never" to "almost always").

Observational study, 2++

Some authors have carried out a factor analysis of this scale, grouping the items into different factors: social burden, psychological stress, feelings of blame, emotional pressure, and dependence relationship.[438,439,440] There are abridged versions that may be equally useful.[441]

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Many of the studies that assess the degree of caregiver burden also use other scales designed to assess the consequences of the burden, evaluating anxiety, depression or quality of life related to health. In the case of anxiety, an appropriate scale is the Beck Anxiety Inventory,[442] in depression, the GDS scale,394 and for physical and mental health, the SF-36 or the SF-12.[443,444]

Observational study, 2++

Summary of evidence

2++	The Zarit scale is a self-administered questionnaire that is used to evaluate the caregiver burden. It has 22 items grouped into sections on social burden, psychological stress, and feelings of blame, emotional pressure and dependence relationship. This scale is very consistent and has a high test-retest concordance.[438,439,440] There are also short versions that may be equally useful.[441]
2++	There are different scales to evaluate the consequences of caregiver burden; the Beck Anxiety Inventory to evaluate anxiety,[442] the GDS scale, for depression,[394] and the SF-36 or the SF-12 for physical and mental health.[444,443]

Recommendation

C	The use of the Zarit scale (long and short versions) is recommended to quantify the caregiver burden.
✔	The use of specific adapted and validated instruments is recommended to assess other aspects they may be affected by the caregiver burden.

11.5. Are there effective interventions to prevent caregiver burden?

There are studies that assess the factors that have an influence on the burden perceived by the caregiver (e.g. Financial repercussions, behavioural disorders, bad social acceptance, previous psychological history, caregiver of presenile onset patient, age of the caregiver and duration of care) that might identify caregivers with a greater risk of suffering unfavourable effects due to caring for a patient. The objective would be to focalise the support strategies on them and trying to change modifiable elements.[445]

Descriptive study, 3

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Caregivers who are better informed about the disease seem to have less depression, but similar levels of stress and perception of their own health than those who are worse informed, so offering caregivers complete information about the disease, possible complications, its management and available resources, both clinical as well as social and legal, could prevent the stress. However, some of the studies analysed warn that this information in very early stages of the disease could also increase the level of anticipatory anxiety of the caregiver.[25] — Descriptive study, 3

The NICE guideline recommends establishing regular assessment and care programmes for the caregivers, which will include group or individual psychoeducation, support groups, telephone or online support, educational programmes on the disease, problem-solving and available resources, and inclusion of other members of the family apart from the primary caregiver, at meetings of the therapeutic team. These support interventions could be effective both at a strain prevention and treatment level.[25] — Expert opinion, 4

Clinical experience suggests that completing the clinical assessment with data of the patients' and caregivers' families and social context, has a preventive purpose, in so far that it is going to enable us, from the onset of the process, to identify the social needs that may arise in the care of a person with dementia and in their immediate social environment. Detection of these needs, which has a direct effect on the strain of the caregiver, will permit the implementation of the most suitable available measures.

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Summary of evidence

3	There are factors that affect caregiver burden; the assessment of these factors permits identifying risk caregivers: a) the existence of previous psychological pathology, b) age of the caregiver, c) young dementia, d) behavioural disorders, e) bad social acceptance, f) duration of the care, g) little support in task of caring and h) economic repercussion.[445]
3	Caregivers who are better informed about the disease seem to have less depression.[25]
4	Support interventions for the caregiver are effective to prevent and treat their excessive burden. These are programmes with regular assessments and activities. The actions they develop include group or individual psychoeducation, support groups, telephone or online contact, involvement of the family, educational programs, problem-solving and provision of available resources.[25]

Recommendation

D	A basal evaluation of caregiver of a person with dementia is recommendable in order to identify the factors that affect the burden of caring, the difficulties that might arise in the course of the disease and the degree of burden that the caregiver already has at the time of the diagnosis.
D	The caregiver should be informed well and progressively about the disease and its possible complications, offering him or her available social resources, as well as the formal or informal support systems to prevent strain.

11.6. Are there effective interventions to deal with caregiver burden?

Reviews about support experiences with caregivers provide different perspectives.

In one SR, nine of 11 studies showed that interventions with caregivers are beneficial. The combination of educational support, emotional support and resources was more effective than the treatment of just one of these aspects.[446]	Observational study, 2++
Another SR on RCT of 15 articles with an experimental group and control group indicated that interventions regarding caregivers had significant although moderate effects on strain (40%), anxiety (50%) and depression (90%). Various coincident with other authors in that strain is the most difficult variable to modify, as it is a stressful element that may be maintained throughout the time the care lasts.[447]	RCT, 1++
Another SR on 44 studies showed little evidence of the effectiveness of support/information interventions with caregivers of people with dementia.[448]	SR descriptive study, 3
Another SR on observational studies showed that therapeutic interventions with caregivers of people with dementia had a moderate effect on anxiety, depression or strain. There are differences in opinion between the perception of the researchers and that of the families who evaluate it as being very positive.[449,450,451]	Observational study, 2++
Better results were obtained with individualised interventions carried out at the caregivers' homes, as they adapted better to their specific circumstances.[452,453,454]	Observational study, 2+

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Dementia is a disease of the family, in the sense that it involves patients and their closest environment (family and friends). The support and attention given to the family by the professionals of the different health and social levels, associations of families of people with Alzheimer type dementia and other related dementias (AFA), and above all by the actual family, as the closest resource, is essential both to cope with the disease and adapt to the process, and to distribute responsibilities. The burden is minimised and supported better if there is internal and external support, and if the different people involved can enjoy time to care for themselves and to continue improving in their task of caring.

The best treatment for strain is its prevention and this is achieved and exercised through information, education, professional support, a solid family and social network, and by obtaining resources. Recognising that dementia is changing process, with new burdens and needs throughout time, with new challenges to solve, and that the losses usually appear in a hierarchic and predictable manner, make it easier to design personalised strategies. Every caregiving family has its own dynamics with factors that have a positive or negative influence and on which action can be taken.

All the measures that facilitate the task of caring are understood as support for caregivers, they make the task more tolerable, they favour the maintenance of free time to develop their own needs and activities, and enable them to rest.

The caregiver's position and attitude with respect to the different problems linked to dementia is heterogeneous and variable. Caregivers can accept, refuse, participate and get involved in the care of the family member. The task of caring is difficult, it causes tiredness and in 30% of the cases, it can cause secondary psychological alterations, and a large number of them are at risk of claudication There are signs that enable us to detect the risk of claudication and that help us take action soon to prevent or reduce the consequences to a minimum.

Caregivers must be offered solutions and help to respond to their needs and strain. When caregivers refuse aid and are not aware of the problem and risk, it is advisable to inform them again or do so in the network that cares for them, to guarantee the most appropriate approach in each case. There is evidence that caregivers will need training at some time to improve their care skills and, on the other hand, have sufficient capacity to cope with the situation. Social resources, educational and emotional support, would sum up the key aspects in help to caregivers[435].	Observational study, 2+
The aspects that must be contemplated in the comprehensive support to caregivers, to care, prevent and treat strain, avoid claudication and re-establish a state of well-being, quality of life and satisfaction of the actual caregivers, include:[193]	Expert opinion, 4

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- **Establishing a welcome programme for people with dementia** and their caregivers, by professionals from the primary care team (PCT), with the collaboration of the AFA and of the specialised dementia care (SDC). Contact with the AFA is important in order to bring community resources closer to families.
- **Personalised information sessions for each family unit**. The information offered must be clear and adapted to the recipients and it must include clinical information about the treatments, prognosis and existing resources. These sessions must be given by professionals from the PCT. The attendance of relatives is advisable after dementia is diagnosed. Information about the disease and its updates should be repeated or reinforced, depending on the needs of the family group, and it must be done in a regular manner.
- **Theoretic and practical training aimed at family caregivers** to prepare for daily problems and to act appropriately to cope with the difficulties that are going to arise, due to the loss of cognitive skills, appearance of behavioural disorders and alteration of the functional capacity.
- **Counselling**: Economic, legal, on health and social resources. The AFA are a good source of counselling.
- **Emotional support to caregivers and to families**, individual or group; in this type of support, we can find therapeutic aid groups (TAG) and mutual aid groups (MAG).
- **Adaptation of resources**: Detection of needs, help in formalities, explained the circuits, evaluate compliance with needs and expectations. Identify the most appropriate resource: Social workers, day hospitals, day centres, night care centres, respite admission, care of crises.
- **Pharmacological treatment of the caregiver**, if necessary, which will help solve insomnia, anxiety, depression, and other concomitant pathologies that may appear (example: Control of vascular risk factors, treatment of osteoarticular pain, etc.
- **Accompaniment at end-of-life stage**, co-participating in palliative care (PC) strategy and in grief care.

Mixed strategies, which combine different support measures, are the most effective. The team of professionals caring for these families must evaluate on a regular basis if the interventions have been adequate, if their objectives have been achieved, and if the situation should be reconsidered, designing new strategies, programmes or revising the old ones.

One of the aspects that must continuously be reinforced is the proximity family support network. Good information, from the onset, to all members of the family involved, is the basic pillar of this network. A continuous attempt must be made for this network to enjoy good physical, psychological, emotional health and communication.

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Summary of evidence

2++	Caregivers must be offered solutions and help to respond to their needs and strain. Caregiver support interventions are beneficial, above all the combination of educational, emotional support and resources.[446,455]
1++/ 2++	Their benefits, slight or moderate, are significant on the burden, anxiety and dep ression.[447,449,450,451,448]Families usually have a very positive opinion of educational and emotional support interventions.[449].
2+	Interventions held in the home or in a personalised manner are the most beneficial.[452,453,454]
4	The following aspects must be contemplated in the comprehensive support to the caregiver: welcome programme, information sessions, theoretical and practical training, economic and legal counselling; adequate resources; individual or group emotional support; treatment of the caregiver and accompaniment throughout the entire process.[193]

Recommendation

B	To improve the care of caregivers of people with dementia and reduce their burden in the task of caring, as well as anxiety and depression, a programme that combines educational support, emotional support and the provision of resources may be beneficial.
B	Interventions carried out in the caregiver's own home and in a personalised manner are recommendable.
D	Comprehensive care of the caregiver must contemplate many different actions: Welcome programme, information sessions, theoretical and practical training, advisory services, emotional support, adaptation of resources, pharmacological treatment if required and accompaniment throughout the entire process.

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11.7. What are mutual aid groups (MAG)?

At the first International Conference for Health Promotion in Ottawa in 1986, the bases were established to boost community participation in the care of its health and the creation of social networks to favour the social participation of the different groups within the community. The WHO supported this proposal with the creation of a European Centre of Mutual Aid Groups (MAG) in Leuven (Belgium).[456]

In general terms, we can define the MAGs as movements that are characterised by the existence of quality, horizontal, symmetric and generalised reciprocity among their members. Comprised of people who share the same health problem or social situation, in this case of caregivers of people affected by dementia, united on a voluntary basis.[455]

The MAGs take advantage of the human being's natural need to share, seek contact and trust in other people faced with a situation of joy, sadness, disease, danger or anxiety. Mutual aid is, therefore, an exchange, giving and receiving between two or more people, with positive results for their own health and with an impact on the social welfare of the community.[457]

The MAGs are comprised of a group of people whose aim is to mutually help each other to achieve a certain objective. In general, they are comprised of people who share the same problem, who find themselves in the same situation. The membership is free, with no supervision from any professional.

The MAGs place emphasis on personal interaction and the individual assumption of responsibilities by its members. Meetings are informal and are programmed depending on the needs of the group. In some cases professional counselling is accepted, although only as a consultant figure.[455]

Some of the functions of the MAG are: a) to provide and exchange information (exchange of experiences and knowledge among its members); b) offer emotional support among the members (empathise and verify that other people are in the same or similar situation); c) provide services; d) organise social activities and defend interests, and e) lobby with the institutions.[455]

Professional support can have different functions within the group: Launch the group, disseminate its existence, develop it, be a consultant, assume responsibilities within it and offer help so that the group can be independent. However, the relative position of the professional should avoid the professionalisation of the members of the group, as well as the possible dependence on experts. An optimal intervention must consider the promotion of the group members' own skills by way of increasing their self-perceived competence.[458,459]	Expert opinion, 4

With respect to the types of MAGs, we can find the model proposed by:[460]

- Type I: Self-care groups focused on diseases
- Type II: Groups focused on positive lifestyles.
- Type III: Mutual aid groups focused on coping with stress
- Type IV: Lobby groups, focused on social action

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Summary of evidence

4	The mutual aid groups (MAG) for caregivers of people with dementia, are comprised of people who freely share their problems of caring, which enables them to exchange information and experiences, and give each other emotional support. Group work is beneficial for the health of each one of them and for the welfare of the rest of the group. The MAG satisfies common needs, it helps overcome problems, it achieves social and personal changes.[459,458,455]
4	If there is a professional in the MAG, his or her function is to favour and foster the skills of the other members of the group.[459,458]

Recommendation

D	There should be a professional in the MAGs to favour and foster the skills of the group members.

11.8. What benefits are obtained from participating in MAG?

Forming part of a MAG permits:[456,457] Expert opinion, 4

- Finding information and sharing experiences.
- Increasing knowledge about people in dependent situations.
- Access to information about the resources of the administrations.
- Share, with normality, painful experiences, doubts and fears.
- Find ways of having free time.
- Improve the knowledge of oneself and manage the day-to-day problems.
- Find understanding from other people who are in the same situation.
- Create a meeting place to coincide with people in a similar situation.
- Make friends with people who understand and accept us.
- Offer emotional support.
- Reduce the feeling of isolation and loneliness.
- Increase one's self belief and confidence.
- Offer services and resources.
- Raise awareness of the public opinion, organising conferences, congresses, etc.

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A study carried out on 70 MAGs of caregivers of people with Alzheimer's disease, through a survey sent to participants, showed that the group provided them with benefits in aspects related to education, socialisation, skills in managing symptoms and in accepting the diagnosis.[461]	Descriptive study, 3
Notwithstanding these potential benefits, the evidence observed in literature did not show significant results in a reduction of aspects such as anxiety or depression. The different methodologies, the size of the groups, the ethical problem of using a control group, comorbidity between different pathologies in the caregiver, the multidimensional nature of the care, the number of intervention groups used, as well as the assessment instruments used, could be some of the reasons for the scarce evidence in the data found.[462]	Descriptive study, 3
Despite the possible benefits commented about the MAGs, focused basically on the positive effects of sharing experiences and overcoming isolation, it must be pointed out that there is also another type of group, where the presence of professionals is normal: The therapeutic aid groups (TAG) or the so-called educational and emotional support groups (EESG). The interventions in this type of group usually have more ambitious objectives: Provide care skills and strategies, relieve the strain, reduce anxiety and depression, either with brief structured programmes or with extensive continuity in the group support.[463,464,465]	Descriptive study, 3
However, there are more and more studies that point out the mistake of dealing with the caregivers of Alzheimer patients as homogeneous group. The interventions will be more effective the more individualised they are; in any case they must be designed bearing in mind some differential variables: Level of strain, gender and relationship, as the content will vary when these different situations are taken into account.[466]	Descriptive study, 3

Summary of evidence

3/4	There are many benefits provided by the MAG to the caregivers. It gives them all kinds of information, they share experiences with normality, they compile opinions and suggestions, they improve self-knowledge, they learn how to manage conflicts better, they are accepted and understood, they establish friendship bonds and reduce isolation, and they increase their security and confidence. There are studies that demonstrate that caregivers benefit each other subjectively.[456,457,461]
3	The therapeutic aid groups (TAG) or educational and emotional support groups (EESG), aimed at specialised professionals, provide the group members with strategies and skills to improve the care function, relieve their burden and reduce their anxiety and depression.[464,463]
3	Effectiveness is improved if the interventions in TAG (therapeutic aid groups) are adapted to the strain, gender and relationship of its members.[466]

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Recommendation

D	It is advisable and desirable for the caregivers of people with dementia to participate in MAGs, as they provide many different benefits, which will enable them to cope better with the care work and improve their personal situation.
D	Participation in TAGs or EESG to improve the strategies to cope with dementia is recommendable, relieving the burden and improving the level of anxiety and depression that might affect the caregiver.
D	Professionals that run the TAG or EESG must personalise their interventions to be more efficient.

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11.9. In what cases is psychological treatment of the caregiver necessary?

An assessment of this type of intervention is included n the NICE guideline,[25] Descriptive and it concludes that psychotherapy, especially cognitive-behavioural study, psychotherapy has a beneficial effect on the levels of 3 depression and anxiety, strain and well-being of the caregiver, although in some of these aspects the magnitude of the effect was small and variable between the studies, whilst the combined interventions (psychoeducation, training in managing symptoms, support groups, etc. presented a magnitude of a greater effect.

Descriptive study, 3

There are no studies that compare the effectiveness of the therapy in different types of caregivers, but as the effective psychotherapy was more obvious in depression and anxiety symptoms, it can be concluded that this is probably more effective when applied to caregivers whose levels of anxiety and depression are within or close to pathological levels.[25]

On a practical level, in our medium, caregivers are not normally patients of the professional who visits the patient with dementia, or the professional is not a specialist in mental health, so if signs of strain are seen in the caregiver he cannot make out a prescription but rather recommend a specific evaluation through their primary health care physician; specialists in mental health are responsible for carrying out the clinical evaluation and for establishing the most adequate therapy in each case.[193]

Summary of evidence

3	If the caregiver of a person with dementia presents anxiety and/or depression he or she can benefit from cognitive-behavioural psychotherapy, which will help reduce the intensity of the systems, the strain and improve global well-being.[25]
3	Therapeutic interventions that combine psychoeducation, training in managing systems and support groups are more effective to improve the clinical manifestations of the caregivers.[25]
4	Caregivers who present anxiety and/or depression benefit from the assessment and treatment offered by the primary care team and/or specialised care.[193]

Recommendation

✔	It is recommended for those caregivers who express a significant degree of stress and/or depression to be referred to their primary care physician and/or mental health specialists for their assessment and treatment.
C	Psychotherapy, especially cognitive-behavioural therapy would be recommended to treat stress or depression due to strain of the caregiver when he or she presents clinically relevant symptomatology.

11.10. What are associations of families of people affected by dementia and what role do they play in a comprehensive approach to dementia?

Associationism of families and people affected by a chronic neurological problem, including dementia, is relatively recent. The Association of Families of Patients with Alzheimer's Disease of Barcelona (AFAB) was the first to be created in Spain in 1987.

Over the last 20 years many different associations have been created all over the Spanish territory. Today there is scarcely no large town that does not have a support group for relatives affected by dementia. Later on, they grouped together into a confederation, the Spanish Con federation of Associations of Families of Alzheimer's Disease (CEAFA).[467]

The main objective of the associations of families of Alzheimer's disease and/or other dementias is to improve the quality of life of the patient and of the families affected. Other objectives include:[467] — Expert opinion, 4

- Promoting the need for a correct diagnosis.
- Counselling towards the comprehensive care of the patient

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- Helping families support the psychological impact represented by the disease.
- Giving advice and informing about health, psychological, legal, economic or social assistance questions related to dementia.
- Help in fostering scientific research.
- Informing and raising awareness of society.
- Representing the interests of patients and their families before the administration and other institutions.

The AFA play an essential role in the comprehensive approach of dementia throughout the entire process; they start their specific work with the family affected, at the time of the diagnosis and throughout the entire life of the patient. The AFA accumulate the experience of families that have lived with people affected by dementia for years. They act as a support group of people who are able to give information based on experience and provide many different solutions to specific problems of day-to-day life.[467] — Expert opinion, 4

Despite the existence of the AFA and the consensus about their efficiency and effectiveness, less than 30% of the families affected ever get in contact with the relative AFA to get information or any other type of resources. There are many different reasons, including the lack of information about their existence, the refusal of the patient and/or family to do so for reasons of confidentiality, culture, education or due to rejection on considering it to be marginal and/or with a risk of being stigmatised.[467] — Descriptive study, 3

The approach and joint work of the healthcare teams (primary, specialised or social health resources) and the AFA is recommendable. It is advisable for the health teams to inform of the existence of this resource. A closer approximation between the two organisations would be desirable to achieve a more complete and quality care; however no express indication of the advisability of this approximation is found in literature. There are no evidence-based publications that guarantee the benefits provided by the contact and participation in the associations' activities, but there is consensus among experts about recommending this resource, with high satisfaction levels among users.[468] — Expert opinion, 4

A resource provided by the association are the TAG or EESG managed by professionals, where families with mild and moderate dementia can socialise and learning, exchange experiences and feelings, and receive psychological and emotional support. In a review based on 8 support groups, participants positively informed about the educational aspects, the socialisation and improvement of the coping capacity.[461] — Descriptive study, 3

Other contributions of the AFA are summed up in **Table 4.**[193]

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Table 4. Activities carried out by t he associations of families of people affected by dementia

Concept	Activities
Information	• Dissemination and diffusion of knowledge about dementia • Activities of the world Alzheimer's Day • General advice • Conferences, courses, seminars • Congresses, symposium, conferences • Publications, journals, books, videos • Online information
Training	• Training of family caregivers • Training of professional caregivers • Training of volunteers • Monographic workshops on different topics
Support to the patient and/or family	• Psychological assistance to both caregiver and patient • Mediation of family conflicts: • Mutual aid groups (MAG) • Psychological and emotional support groups • Pleasure-recreational activities programme • Therapeutic holidays • Weekend rest programme • Helpline • Volunteer programme • Sporting activities • Provision of technical aid • Evaluation and counselling in resources • Legal advice
Provision of services	• Health control • Psycho-stimulation programmes • Polyvalent stimulation programmes • Memory workshops • Day Centres • Technical aid • Home aid • Evaluation and adaptation of the environment • Music therapy • Miscellaneous workshops: Laughter therapy

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Summary of evidence

4	The main objective of all of them is to improve the quality of life of the patient and of the families affected. They are interested in promoting a correct diagnosis, counselling towards comprehensive care, helping families support the psychological impact represented by the disease; giving advice and informing about medical, psychological, legal, economic and social questions; stimulate scientific research; raise the awareness of society, and represent their interests before the Administration and other institutions.[467]
4	The AFA play an essential role in the comprehensive approach of dementia; they act specifically with the family affected, at the time of the diagnosis and throughout the entire life of the patient, and they are able to provide experience and many different solutions to the specific day-to-day problems.[467]
3	The AFA are an underutilised resource, as only a percentage of less than 30% of the caregivers of people with dementia get into contact with them.[467]
4	The approach and coordination between the different healthcare levels (PC, SC, SHC) and the AFA is useful for the caregivers to improve their knowledge and manage the disease, receive emotional support, relieve their burden and increase their quality-of-life.[468]
3	The MAG, TAG and/or EESG are all resources of the AFA that benefit caregivers, improving information, socialisation and coping capacity.[461]

Recommendation

D	Health practitioners and social services professionals who care for people with dementia and their families should comment on the existence of the AFAs and the benefits that they can obtain from them, and insist on their experience in living with people with dementia.
D	To achieve optimisation in the approach and management of dementia throughout the entire process, from diagnosis until after death, the existence of good coordination between the different healthcare levels and the AFAs is recommendable.

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11.11. What must the relationship between the associations and the health and social public network be like?

The public administration, at autonomous community level and at State level, evaluate the essential role of the AFA in the direct care of families affected by Alzheimer's disease and other dementia. It expresses this through communications supporting their work, and gives them explicit support through subsidies to programmes that they develop. This collaboration is expressed in different areas such as dissemination, home care or cognitive intervention workshops.[193,467]	Expert opinion, 4
A lot still has to be done, in this recommendable symbiosis, as the primary care teams (PCT), specialised dementia care teams (SDCT) and social services professionals do not always place emphasis on the important contribution of the AFA in the care of patients and of their families.[193,467]	Expert opinion, 4
The AFA are experts in the knowledge provided by coexisting for years with dementia in its different stages and having qualified professionals who are able to give a good evaluation of the case, provide information and advice, applying non-pharmacological treatment measures and emotional support.[467]	Expert opinion, 4
The AFA have a very positive effect on the lives of people with dementia and their families. They facilitate the work of the public administrations (health and social services). They help lighten the workload of the primary care centres, of the specialised units and they provide families with their own resources. The public health care network must recognise this role of the AFA and provide specialised, complementary and quality aid.[467]	Expert opinion, 4

The relationship between the tertiary sector and the Public Administration must not be limited to giving subsidies, but it must extend to the joint execution of care programmes for those affected by dementia and establishing collaboration agreements. An example of this common interest is the promotion of specialised training courses that the AFA organise for family and professional caregivers who work or live with people affected by the disease.

The underlying benefit of this mutual work between public administration and the AFA is the beneficial impact on the quality of life of people with dementia and of their relatives. It also permits redistributing the workloads of the network and partly releasing it from the weight of the dementia, and it recognises and visualises the work carried out for years by the actual associations.[467]	Expert opinion, 4

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There are a series of aspects that must be taken into consideration in the dynamic and changing process of care of dementia:

- The social services and health network must include information and referral of families to the AFA in its protocols.
- Recognise that the AFA are adequate institutions where specialised and quality training can be received in coping with dementia.
- The EESG and the TAG developed in the AFA are a good resource for caregivers which will enable them to cope with the disease.
- The AFA can create classical specific workshops or use the new technologies (connect-Alzheimer, touch screens).
- It is advisable to have day hospitals and day centres that satisfy the approval criteria established to satisfy their function adequately and with quality indicators.
- Increase the endowment of resources, if necessary, so that the AFA can continue to develop their activities in a complementary manner to the activities offered by the health and social services, with efficiency, security and effectiveness criteria.
- Improve the care of patients with dementia and of their families at the end-of-life stage of the disease.

Summary of evidence

4	The public administrations of the autonomous community and of the State positively value the role of the AFA.[193,467]
4	The symbiosis in the healthcare and social network with the AFA is not optimal, as the caregivers of people with dementia are not systematically informed about the existence and contribution of the AFA.[193,467]
4	The AFA are experts in living with dementia and have qualified professionals for a comprehensive approach.[467]
4	The AFA provide the health and social services system with quality, complementary and specialised bonus.[193,467]
4	There are many benefits of the collaboration between public administration and the AFA: better quality-of-life of the people with dementia and their families; redistribution of workloads in the healthcare network, and visualisation and recognition of the work carried out by the actual associations.[193,467]

Recommendation

D	There must be a close relationship between the tertiary sector and the Public Administration with continuous dialogue, thus favouring the exchange of knowledge both on the needs and collaboration proposals (programmes, subsidies, agreements, etc.).

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D	It is recommendable to continue improving the relationship between the Public Administration and the AFAs to improve the quality of life of the people affected by dementia and their families, by drafting referral protocols, recognising the role of the AFAs in the training of caregivers and professionals; fostering the creation of TAG and/or EESG and therapeutic programmes (DH, DC, rehabilitation workshops) and aid for the development of complementary activities.

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12. Early onset or pre-senile dementia

Questions to be answered

12.1. What is understood by early onset or pre-senile dementia?
12.2. What are the most frequent causes of early onset or pre-senile dementia?
12.3. Do patients with early onset dementia have different clinical manifestations to patients with later onset?
12.4. Must the diagnostic process in people with early onset dementia be different to the process of a patient who is more than 65 years old when the disease starts?
12.5. Is the pharmacological treatment of a person with early onset dementia different to that of a person with late onset dementia?
12.6. Is the non-pharmacological treatment prescribed to a person with early onset dementia different to that of a person with late onset dementia?
12.7. Are there differences in impact and psychological, social, family, occupational and economic repercussion between a group of people diagnosed with early onset dementia and a group of people with late onset dementia?
12.8. What health and social-health resources do people with early onset dementia require?

12.1. What is understood by early onset or pre-senile dementia?

It is considered, by convention, that dementia has presenile or early onset when the symptoms start before the age of 65.[25] Some authors[469] operatively differentiate, among patients with early onset dementia, those with onset under the age of 45 (young onset dementia).

12.2. What are the most frequent causes of early onset or pre-senile dementia?

AD is the most frequent cause of presenile or early onset neurodegenerative dementia (43-58%), followed by FTLD.[11,25,470,471,469] The most frequent causes among secondary early onset dementia are vascular, post-traumatic and alcohol. In individuals whose symptoms appear before the age of 45, AD is not very frequent and FTLD is the most frequent degenerative dementia; self-immune and metabolic aetiologies represent almost one third of the cases and in up to one fifth of the cases, the cause of dementia cannot be objectified despite extensive studies.[471]

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12.3. Do patients with early onset dementia have different clinical manifestations to patients with later onset?

As a whole, patients with early onset dementia present a higher percentage of BPSD than patients with late onset dementia and a lower degree of cognitive and functional impairment at the time of the diagnosis.[470] However, as the clinical manifestations are determined by the type of dementia, part of these group differences may possibly be attributed to the different relative frequency of each type of dementia among individuals of early and late onset, rather than the onset age per se. Patients with early onset dementia present a greater risk of death than patients with late onset dementia, compared with control individuals (43.3 compared with 3.4).[472]

When we analyse the main neurodegenerative aetiologies, patients with early onset AD, compared with those with late onset, as a group, present more severe language disorders, difficulties in carrying out tasks that require sustained attention and BPSD in initial stages of the disease.[473] Atypical forms of presentation of AD, such as posterior cortical atrophy or corticobasal syndrome are also more frequent in cases of presenile onset. An early onset age of AD is also associated with a greater frequency of myclonus during the course of the disease.[473] These clinical differences are also reflected in comparative structural neuroimaging studies, that show a greater neocortical affectation in initial stages in early onset cases.[474,475] On the other hand, there are contradictory studies about whether the evolution of early onset AD is or is not more aggressive than late onset disease.[476,470]

With respect to FTLD, one study did not detect differences between the symptoms of patients with early onset and late onset,[477] although another study[478] objectified a greater degree of apathy and amnesic and visuospatial problems in patients with late onset with respect to patients with early onset.

12.4. Must the diagnostic process in people with early onset dementia be different to the process of a patient who is more than 65 years old when the disease starts?

The diagnostic process of dementia should not be affected by the age of the individual, as the most broadly used definitions of this syndrome, DSM-IV16,17 and ICD-1018, do not include age as a criterion (Section 8). However, patients with early onset dementia in our medium, suffer a greater average delay in diagnosis (37 months) than patients with senile onset dementia (29 months),[470] attributed both to the delay in the initial medical consultation and to the delay in referrals to specialised units and to the difficulty in making a correct diagnosis in this age group.

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To objectify cognitive deficiency, the majority of the cognitive impairment, memory and dementia screen tests in Spanish are not validated in individuals under the age of 60, so they are not valid in this age group, and appropriate neuropsychological test batteries, available in specialised units, usually have to be resorted to.[6]	Expert opinion, 4
With respect to the aetiological study of dementia syndrome, the CPG reviewed[25,479,129] do not include differences in the basic diagnostic process depending on age. The distribution of frequencies in dementia aetiology changes with age groups. In early onset dementia, the aetiological possibilities extend to causes that could be considered rare in older age groups. On the other hand, even in AD, the clinical form of presentation may differ from that presented by patients with late onset AD, so the degree of experience of the assessment team must be greater to evaluate patients of this age. Thus, the diagnosis test battery is often more extensive and complex in early onset individuals.	Expert opinion, 4
No specific protocols have been assessed and published of aetiological diagnosis in early onset dementia, although Sampson and collaborators[471] have proposed an approach to the diagnosis, suggesting a list of routine tests for all patients, including a complete cognitive study, structural neuroimage, complete blood analysis with levels of vitamin B_{12}, folic acid, thyroid hormone, luetic serology and basic immunology, electroencephalographic and electrocardiographic study, and a list of specific tests depending on the clinical characteristics and onset age of the symptoms. In some cases, these specific studies may include genetic studies **(section 7).**	Expert opinion, 4

Summary of evidence

4	The majority of the cognitive impairment, memory and dementia screen tests in Spanish are not validated in individuals under the age of 60, so they are usually not valid in this age group.[6]
4	The causes of early onset dementia include aetiologies that have little impact on older age groups, and frequent atypical presentations of dementia.[471]

Recommendation

D	The use of neuropsychological test batteries validated for this age group is recommended in the assessment and characterisation of cognitive impairment in people with pre-senile dementia.

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D	The aetiological study of a patient with early onset dementia should also include the study of low incident causes in later age groups and atypical presentations of frequent dementias.
✔	It is recommendable for patients with early onset dementia to be assessed by professionals with experience in this age group and at centres that have the appropriate supplementary tests to carry out this study.

12.5. Is the pharmacological treatment of a person with early onset dementia different to that of a person with late onset dementia?

Four drugs, approved by the Spanish Medicine Agency (AGEMED) for the specific treatment of AD (donepezil, rivastigmine, galantamine and memantine) are currently used with no age restriction. However, no RCT have been specifically carried out on this population group. No *post hoc* studies have been carried out either on this population group in MA of RCT, which assessed the effectiveness of ACE inhibitors or memantine in patients with Alzheimer's disease, probably due to a lack of sample to carry out an appropriate statistical study, given that the average age was 74 in the former and 76.2 in the latter. Therefore, there is no clinical evidence to support or rule out the fact that the onset age of AD is a decisive factor in pharmacological response. There are no studies that assess the specific response to drugs in individuals with early onset of other types of dementia.

Technical data sheet

Summary of evidence

-	There are no specific studies on the effectiveness of drugs in the treatment of patients with early onset dementia.[263,480]

Recommendation

✔	Although there is no scientific evidence in presenile dementia, it is advisable to follow the same therapeutic guidelines used for older people.

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12.6. Is the non-pharmacological treatment prescribed to a person with early onset dementia different to that of a person with late onset dementia?

Patients with early onset dementia have not been included in many of the studies that assess the effectiveness of non-pharmacological therapies, although the proportion of them is marginal and they are not analysed differentially. Therefore, no evidence has been found in favour of or against the non-pharmacological treatment, prescribed to patients with dementia, having to be different depending on the age of the individual **(Section 10.3).**

However, when non-pharmacological therapy has to be planned for pre-senile onset individuals, it must be taken into account that young patients with dementia are a minority and the proportion of non-Alzheimer's dementia in the group of patients with young dementia is higher. Consequently, it is difficult to integrate them into standard programmes, especially in mild or moderate dementia stages, due to the fact that group interventions carried out normally focused on older patients and with typical AD symptoms.

Summary of evidence

-	There are no studies that specifically evaluate the effectiveness of non-pharmacological therapies on patients with early onset dementia.

Recommendation

✔	It is advisable for people with presenile dementia to carry out the same non-pharmacological therapies that have proved to be effective in people over the age of 65.
✔	If we wish to favour their adherence to individual or group non-pharmacological therapeutic programmes, these must be adapted to the specific needs of the person with early onset dementia.

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12.7. Are there differences in impact and psychological, social, family, occupational and economic repercussion between a group of people diagnosed with early onset dementia and a group of people with late onset dementia?

Firstly, on a psychological level, the perception of loss of independence is greater in these individuals as they are forced to drop out of activities that are normal for their age, such as work, driving cars, managing financial affairs, travelling independently etc. Furthermore, having to stop work, apart from the actual economic loss that this may represent, as well as the loss of independence, may have a negative impact on patient' self-esteem and their actual perception of patient.[473] All of this is accompanied by the difficulties of the medium to understand and adapt to the individual's new situation, which often produces social isolation and withdrawal.

Case and control study. Cohort study, 2-

On a family level, during the stage prior to the diagnosis, the family relations may have deteriorated as a result of an erroneous interpretation of the symptoms, especially when the behavioural disorders are relevant. Once diagnosed, in the majority (82%) of the cases, it is an informal caregiver who takes responsibility for providing the patient with the necessary health care, normally the spouse who like the patients, belongs to an occupationally active population and also have responsibilities with respect to young children.[473] For the these spouses, the project of a couple or of a family is broken, and they must assume the responsibilities acquired on their own, added to the care of the person with dementia.

Studies carried out show that informal caregivers of patients with early onset of dementia present a greater level of strain than the caregivers of patients with late onset dementia, and the majority (66%) perceive that their emotional state is bad or very bad, and they present anxiety and/or depression symptoms. The female sex, the presence of disrupting behavioural symptoms and the bad marital relationship prior to the onset of dementia have been co-related to a greater level of strain of the caregiver in these cases.[481]

Case and control study. Cohort study, 2-

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On an occupational level, individuals with early onset dementia, unlike those with late onset dementia, are normally occupationally active, which generates an added problem in these cases. After the diagnosis of dementia, patients usually stop their occupational activity. In our medium, after a period of leave, patients have access to a disability pension (normally with a degree of “total disability"). However, even in the initial stages when the cognitive impairment does not clearly interfere with the individuals’ activity and they wish to continue maintaining a certain amount of occupational activity, the labour environment is not likely to favour the continuity of their active lives, offering them an activity that adapts better to their new cognitive situation. On the other hand, during the last years of active life, a low occupational performance is often referred to, which may have resulted from a lack of promotion or even dismissal or bad economic management, with losses at a company or family level, which may even have legal consequences.[481]

Expert opinion, 4

At a global economic level, there are no studies in our medium that quantify the economic cost of a patient with early onset dementia. In one study carried out in the United Kingdom in the 1990s, the direct cost of a year's care of presenile patient was similar to the cost of a patient in senile age.[473] The majority of this cost was attributable to institutionalisation costs. Indirect costs such as morbidity, mortality, informal care and loss of income due to interruption of occupational activity were not included in this study, so the real total annual costs are expected to be greater in patients with early onset dementia than in those with later onset.

Summary of evidence

2-	The perception of loss of independence is greater in people with early onset dementia than in those with late onset dementia due to the abandonment of normal activities, such as: Work, driving cars, managing financial affairs, travelling, etc. The loss of work may have a negative impact on their self-esteem. Social isolation and withdrawal often occur as a reaction.[473]
2-	Relevant behavioural symptoms may change family relationships. Their caregivers are usually young, active and with other responsibilities and many of their life projects have to be interrupted.[473] They have a greater level of strain than caregivers of patients with late onset dementia, and the majority of the cases perceive their emotional state as bad or very bad, and they present anxiety and/or depression symptoms. Being a woman, the presence of relevant behavioural symptoms and the bad previous marital relationship is correlated to greater strain.[481]

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4	Young people diagnosed with dementia usually stop their occupational activity and after a period of leave have access to a disability pension. In initial stages, although individual may wish to continue working, their occupational environment does not usually favour continuity, adapting their work to their capacity. Decreases in occupational performance are often verified prior to the diagnosis of dementia.[481]
4	The direct cost of caring for a person with early onset dementia is similar to the cost of caring for a person with senile dementia.[473] The majority of this cost was attributable to institutionalisation costs.

In short, if dementia causes psychological, social, family and economic difficulties at any age both for the patients suffering from it and for the environment, the impact is more negative in the case of patients with early onset dementia in areas such as the perception of loss of independence, social isolation, strain of the caregiver or loss of income.[473,481]

12.8. What health and social-health resources do people with early onset dementia require?

At a social health level, there are no specific studies in this sense in our medium, but resources such as day hospitals, centres where non-pharmacological therapies are carried out, home care, medium-stay centres, long-stay centres, nursing homes or support groups seem to be adequate resources so long as they are specifically focused on caring for patients with early onset dementia,[473] but they are still scarce in our medium. On the other hand, the existing services for patients with late onset dementia are either not available for individuals with early onset dementia or are not considered appropriate. Patients with early onset dementia, apart from presenting differential clinical characteristics, especially due to the greater prevalence of behavioural disorders that are difficult to manage, present generational differences with different cultural habits, lifestyles and family dynamics than those of patients with late onset dementia. Likewise, the families' expectations and their needs for care and support differ to a great extent.	Expert opinion, 4
In a study conducted in Ireland, only 40% of patients with early onset dementia had access to some type of social support service.[473]	Cohort study, 2-

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On the other hand, in a study conducted in the United Kingdom, access to home social support services was observed to be scarce in this group of patients compared with older patients and that, on the contrary, up to 29% of patients with early onset dementia lived in residential centres or long stay care homes.[481]	Cohort study, 2-	

Summary of evidence

-	There are no studies that determine which social health resources are the most suitable for individuals with early onset dementia and their families. On the other hand, only a minority of patients with early onset dementia have access to social health resources in countries of our environment.[473,481]

Recommendation

✔	It is recommendable for patients with early onset dementia to have access to social-health and health resources that focus specifically on their care.

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13. Ethics and legal aspects of dementias

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Questions to be answered:

Abuse of people with dementia.

13.1.1. What is understood by abuse of people with dementia?
13.1.2. How frequent is abuse in dementia and what are the risk factors?
13.1.3. What intervention strategies exist to detect a case of abuse?
13.1.4. What must professionals do when a case of abuse is detected?
13.1.5. What social resources exist to address abuse?

Advance directives

13.2.1. When must the possibility of drafting advance directive documents, living wills and/or granting powers of attorney be suggested to people with dementia?

Evaluation of competences

13.3.1. Are there instruments that have been strictly designed to assess the competence of patients with dementia?
13.3.2. How are the specific competences assessed: driving licence, firearms licence and participation in clinical trials?
13.3.3. Which are the indications to start the legal incapacitation process of a patient with dementia?

Aspects relating to the patient's legal protection

13.4.1. What does legal incapacitation consist of?
13.4.2. What type of legal protection exists for a patient with dementia?
13.4.3. What is guardianship?

Restraint of the patient

13.5.1. What are the indications for pharmacological and/or psychological restraint of a patient with dementia?
13.5.2. What are the indications for physical restraint of a patient with dementia?
13.5.3. What are the ethical and legal aspects of restraint?
13.5.4. What are the indications for involuntary admission and what process must be followed?

Abuse of people with dementia

13.1.1. What is understood by abuse of people with dementia?

The concern of society for the abuse of older people with dementia is an emerging topic.[482,483] There is no universal definition of abuse of people with dementia. Cultural differences must be taken into account, as there are different interpretations of the same events. — Expert opinion, 4

In the Almeria Declaration (1996) abuse would be any act or omission suffered by a person aged 65 or more, which violates their physical, psychic, sexual or economic integrity, or else the principle of autonomy or one of their essential rights regardless of the intentionality or of the medium where it occurs (family, community and institutions).[484]

According to the Toronto Declaration (2002), elder abuse is a single or repeated act, or lack of appropriate action, which causes harm or stress to an older person, and which occurs in any relationship where there are expectations of trust.[485]

Detecting abuse is often difficult due to the social isolation suffered by these people, their refusal or inability to communicate it, the limited awareness of the professionals and the discrimination that this group usually suffers.

Abuse can occur anywhere, either in the home (domestic or family violence), or in institutions by professionals or other residents. There is abuse by act or omission.[486,487,484,488] — Descriptive study, 3-

Depending on the characteristics, the abuse can be:

- **Physical**: Bodily harm, pain or physical impairment, produced by non-accidental violence.
- **Sexual:** Gestures, insinuations, exhibitionism, etc. or sexual contact of any type, due to non-consented consummation or intention.
- **Psychological:** Cause anxiety, shame, and feeling of indignity, fear, stress, insults, mockery, intimidation, humiliation, infantilisation, indifference, isolation and lack of respect.
- **Economic:** Illegal or inadequate use of funds, properties or resources, falsification of signatures signing documents with intimidation, inappropriate use of guardianship, occupation of the home.

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- **Neglect:** Lack of attention to basic health, food, clothing, personal hygiene and housing needs.
- **Abandonment:** By the caregiver.
- **Violation of rights:** To privacy or intimacy or belongings, to decide, to receive visits, to mix with friends, involuntary admission, to remain in their homes.

Abuse causes unnecessary suffering, injuries, pain, loss or violation of human rights, and there a decrease in quality of life.[489]	Descriptive study, 3
Abuse of people with dementia is a personal, family, intergenerational and health problem, as well as one of justice and human rights. Alerting about abuse, knowing of its prevalence, its consequences for the person affected and the aggressor, permits establishing prevention strategies, change of attitudes and seeking solutions.[490]	Expert opinion, 4

Summary of evidence

4	There is an emerging concern by society for the abuse of the elderly or people with dementia.[482,483]
4	Elder abuse is defined as a single or repeated act, or lack of appropriate action, which causes harm or stress to an older person, and which occurs in any relationship where there are expectations of trust,[485] or any act or omission suffered by people aged 65 or over, which violates their physical, psychic, sexual or economic integrity, or else the principle of autonomy or an essential rights, regardless of the intentionality or of the medium where it occurs, which may be family, community or institution.[484]
4	Detecting abuse is often difficult in elderly people or people affected by dementia due to the social isolation they suffer, their refusal or inability to communicate it, the limited awareness of the professionals and the discrimination that this group usually suffers.[484]
3	Abuse can occur anywhere: Domestic violence or in the institutional area. It can be by act or omission. Depending on the characteristics, it can be: Physical, sexual, psychological, economic, neglect, abandonment and violation of rights.[484,488,486,487]
3	Abuse causes unnecessary suffering, injuries, pain, loss or violation of human rights, and a decrease in quality of life.[489]
4	Abuse of people with dementia is a personal, family, intergenerational and health problem, as well as one of justice and human rights. Alerting about abuse, knowing of its prevalence, its consequences for the person affected and the aggressor, permits establishing prevention strategies, change of attitudes and seeking solutions.[490]

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Recommendation

D	It is necessary for health practitioners, the social services and society in general to be concerned and become aware of the abuse that many elderly people suffer, whether they are affected or not by dementia. It is a personal, family, intergenerational, health problem, as well as one of justice and human rights. Its detection permits establishing prevention strategies, changes in attitude and the promotion of solutions.

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13.1.2. How frequent is abuse in dementia and what are the risk factors?

Frequency of abuse in dementia

Elder abuse is estimated at 6% according to the WHO.[485] According to the International Network for the Prevention of Elder Abuse (INPEA), domestic abuse is estimated at 5% and institutional abuse at 10%.[491]	Descriptive study, 3
According to one study, less than 0.02% of people diagnosed with abuse are admitted into hospital, with a 2:1 proportion of women and men; the average stay is longer, the cost is higher and the destination, on discharge, is to nursing homes.[492]	Descriptive study, 3
A survey, carried out on 2,111 people in the United Kingdom (2006)[493] and another on 5,111 people in the USA (2010)[494]. showed the existence of abuse in 2.6 and 10%, respectively. Depending on causes, the abuse was due to neglect (1-5.1%), economic abuse (0.6-5.2%), psychological (0.4-4.6%), physical (0.4-1.6%) or sexual (0.2-0.6%). In another study, the global percentage of abuse reached 6% and prevailed in women, and varied depending on the social economic position and on the state of health.[23]	Descriptive study, 3
One SR of 21 studies on abuse with 5,325 professionals that assessed the capacity to detect it and to declare it, showed an under-evaluation of their prevalence, as only 25% knew of the existence of an elder abuse guideline, 33.7% had detected one case in the last year and only 50% of the cases detected were declared.	SR of descriptive study, 3
In people with dementia, the average abuse incidence is 25% (12-52%), the majority is psychological and 5% is physical. It may be a one-off act, but in 34% of the cases it is repetitive. [487,492,490]A survey by the Alzheimer's Association of Florida (USA) on 254 caregivers, verify the existence of verbal aggression in 60.1% of the people with dementia,[495] which is indicative of the fact that abuse continues to be underestimated.	Descriptive study, 3

Abuse may cause depression, reduction of self-esteem, alteration of immunity as well as premature death in the person targeted by it.[496]	Descriptive study, 3
Family dynamics also changes and if the situation is not solved soon, the quality of life of the other members may get worse.[495]	Descriptive study, 3

Risk factors of abuse in dementia

The risk of abuse is usually multifactorial (personal, family, social and cultural factors). Some depend on the patient, others on the aggressor or on the circumstances that surround the situation of abuse.[497]	Descriptive study, 3
The vulnerability and fragility of the person affected may favour the appearance of abuse, the same as with social isolation, unfavourable economic conditions and a climate of hostility in the home.[498]	Descriptive study, 3
Many of the women attended in mental health services, in PC or in emergency services, suffer domestic violence. There are no specific data of women affected by dementia.[499,500,501,391]	Descriptive study, 3
Caring for a person with dementia without external help throughout the entire illness is a factor that may predispose to abuse, above all if the caregiver has not been adequately trained and/or is under extreme strain due to having to attend to other sick relatives. This risk increases if there is a background of violence, psychiatric disorders of the caregiver, strain and low self-esteem, economic difficulties, inadequate housing and too many responsibilities.[502,503]	Descriptive study, 3
People with dementia who are more likely to receive abuse are those people with BPSD where there is a prevalence of hostility, aggressiveness, provocative attitudes, and who also require assistance for ADL, without there being an adequate social support network.[502]	Descriptive study, 3
The person responsible for the abuse is usually a family member who acts as a caregiver, with symptoms of anxiety, depression and excessive stress derived from the burden of caring, aggravated by the characteristics of the person cared for, who is extremely dependent and with BPSD.[503]	Descriptive study, 3

Summary of evidence

Frequency of abuse in dementia	
3	6% of the elderly suffer abuse,[485] 5% domestic abuse and 10% institutional abuse.[491]

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3	Surveys in the United Kingdom (2006)[493] and in the USA (2010)[494] showed abuse in 2.6% and 10% of the sample, respectively. The causes were: neglect (1-5.1%), economic abuse (0.6-5.2%), psychological (0.4-4.6%), physical (0.4-1.6%) or sexual (0.2-0.6%).
3	In hospital, less than 0.02% of the admissions are diagnosed with abuse, a greater proportion of women, longer average stay, high cost and destination on discharge to nursing homes.[492]
3	Health practitioners underestimate the prevalence of abuse, in the majority of the cases they are not aware of elder abuse guidelines, they detect few cases and they do not always declare them.
3	In people with dementia, abuse occurs in 25% of the cases, the majority is psychological and 5% is physical. It may be one-off or repetitive. Verbal aggression is very frequent.[495,487,492,490]
3	Abuse can cause depression, reduction of self-esteem and alteration of immunity and an increase in mortality.[496]
3	Family dynamics change with abuse, and the quality of life of its members gets worse.[495]
Risk factors of abuse in dementia	
3	The risk of abuse is multifactorial, combining personal, family, social and cultural elements. They can be associated with the person affected, the person responsible for the abuse or the circumstances surrounding it.[497]
3	The vulnerability and fragility of the person affected, social isolation, unfavourable economic conditions and a climate of hostility in the home may favour the appearance of abuse.[498]
3	Many of the women attended in mental health services, in PC or in emergency services, suffer domestic violence. There are no specific data of women affected by dementia.[499,500,501,391]
3	Prolonged care without having external aid or support may favour abuse, especially if the caregiver has not been trained, is stressed, has a background of violence, low self-esteem, psychiatric disorders and too many responsibilities, economic difficulties and inadequate housing.[502,503]
3	Very dependent people with dementia with BPSD (aggressiveness and provocative attitudes), are more likely to receive abuse, especially if there is no adequate social support network.[502]
3	The profile of an abuser is usually a family caregiver, with symptoms of anxiety, depression and excessive physical and emotional stress, who must care for an extremely dependent and hostile patient.[503]

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Recommendation

D	Health and social services professionals must be trained and made aware to detect, declare, prevent and treat problems derived from the abuse of people with dementia.
D	It is important to identify the type of abuse (action or omission), and determine its characteristics (psychological, physical, sexual, economic).
D	If abuse is suspected, the person must be questioned in private and with delicacy, given their fragility, bearing in mind their state of mind and fear of the consequences that discovery of abuse may entail, in their environment.
D	For a complete diagnosis of abuse, it is advisable to evaluate the risk factors, those that depend on the patient, on the abusing caregiver and the circumstances that surround it.
D	The possibility of the existence of abuse must be suspected, if the person with dementia is hostile, aggressive, provocative, dependent for ADL and there is a lack of an appropriate support network.
D	Caregivers must be suspected as abusers if we observe symptoms of anxiety, depression, strain in the task of caring, low cultural level and when the patient they are looking after is very dependent for ADL and/or presents BPSD.

13.1.3. What intervention strategies exist to detect a case of abuse?

Many countries have action protocols if abuse is suspected and if there are alarm signals that might point towards this possibility. There are scales to detect abuse and the abused person, but few of them translated and validated into Spanish.

To diagnose abuse in people affected by dementia, the risk values and the alarm signals must be evaluated. A clinical record and a complete physical, neurological, cognitive, behavioural and functional examination must be used.[504]	Descriptive study, 3
In mild-moderate dementia, clinical interviews help obtain information about the care the patient receives from the caregiver and from the closest environment (family and social). In advanced stages, patients are unable to express their desires and emotions due to the actual disease.	Expert opinion, 4

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Communication with the person affected must always be attempted in conditions of tranquillity, comfort, intimacy, guaranteeing confidentiality and using clear and simple language, fostering trust and facilitating the verbalisation of problems and attitudes, as well as feelings and emotions derived from them.

It is advisable to interrogate the patient alone and with the caregiver, and observe all those signs and symptoms that will give us clues to the detection of abuse; among them, concern, fear, passivity, facial expression, anxiety, depression, etc., placing direct emphasis on risk factors.

Physical examinations must be extremely meticulous, looking for injuries or bruises; evaluating the state of the skin and the presence of malnutrition with no cause that justifies it.

There are standardised scales to detect abuse in people with dementia: Elder Abuse Suspicion Index (EASI) is brief (2 minutes) and has proven its utility with 0.47% sensitivity and 0.75% specificity in a sample of 953 people.[505] the Indicators of Abuse (IOA) is an instrument with 22 items that discriminates between abuse and non-abuse.[506,507]	Observational study, 2++
The Caregiver Abuse Screen (CASE) is an instrument that enables us to suspect abuse. It is a sensitive and specific instrument that can be used as a screen, but it must be complemented with a more accurate evaluation.[508]	Observational study 2++

Table 5. Suspect possible abuse if any of the following circumstances exist[488,502,503]

- Inconsistent explanations with respect to injuries
- Delay in requesting care
- Repeated visits to the emergency services and to hospitals
- Administration of drugs without medical indication
- Lack of response to adequate treatment
- Bad evolution of the injuries
- Malnutrition and dehydration due to non-clarified causes.
- Repeated unexpected falls
- Contradictory information about the facts from patient and abuser
- Detection of fear, concern or passivity in the patient
- Symptoms of depression and anxiety in patient and caregiver
- Refusal by the caregiver for the patient to be interviewed alone

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Summary of evidence

3	If abuse is suspected, a clinical record and a complete and meticulous physical, neurological, cognitive, behavioural and functional examination must be carried out.[504]
4	People with dementia in mild to moderate stage may be able to give information; if there are fluctuations we must seek the most appropriate and reliable moment to obtain it. In advanced stages, this will only be possible if we take advantage of the moments of lucidity.[504]
4	Detecting abuse requires expertise on behalf of the professional and be surrounded by an adequate environment. The information obtained from patients must be compared with the information from reliable relatives/caregivers.[504]
4	A meticulous clinical examination permits detecting signs that suggest abuse: Ulcers, wounds, bruises, signs of malnutrition and dehydration.[504]
3	Identifying alert signals and suspicion of abuse permits setting up correction measures as soon as possible.[504]
2++	It is advisable to systematically ask about aspects related to abuse and use standardised scales to detect them.[505,506,507,508]

Recommendation

D	If the person has mild to moderate dementia, we must get them to give us information about their physical and psychic state of health through fluent and true communication. In initial stages, this can be relatively easy to obtain; in fluctuating dementia, the most appropriate and reliable moment must be sought; in advanced stages, it will be possible to obtain information at moments of lucidity.
D	A meticulous and thorough clinical examination is recommendable to detect signs that lead us to suspect the possibility of abuse, evaluating physical, psychological and behavioural aspects.
D	It is advisable to be mindful of the possibility of abuse, as this facilitates its detection and permits protection, prevention and correction measures.
B	We must systematically interrogate about aspects related to the abuse of any elderly person, with or without dementia, and use standardised scales to detect it.
B	We must assess the caregiver of a person with dementia to detect a possible person responsible for abuse. Scales can be used to detect it.

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13.1.4. What must professionals do when a case of abuse is detected?

Health and social services professionals must be trained to prevent, detect, care for, protect, declare and recuperate a person with dementia suffering from abuse.[488]	Expert opinion, 4
The fundamental rights of the person with dementia to dignity, participation, autonomy and self-determination must be preserved, if possible. People suffering abuse must be informed, respecting their right to confidentiality, in order to cover their basic needs, and to preserve their social relationships.	Expert opinion, 4
If the person is in an advanced stage of dementia preventing them from having autonomy and self-determination, and there is a certain suspicion of abuse, the health professionals must activate the judicial resources, both because this is a way of defending a victim of abuse and if the health personnel have the administrative category of civil servant because communicating any situation that might be an offence and which they know about due to their position, is a legal obligation. Judicial resources will be activated depending on the specific circumstances of the case, namely; - If there are physical injuries, a judicial report of injuries will be drafted. - If there are no physical injuries at that time and/or acute contingencies, the Public Prosecutor can be informed of the case in order to adopt the measures established by the legislation	Applicable legislation

Summary of evidence

4	Health and social services professionals must be trained to prevent, detect, care for, protect, declare and recuperate a person with dementia suffering from abuse.[488]
4	The fundamental rights of the person with dementia suffering from abuse to dignity, participation, autonomy and self-determination must be preserved.[488]
4	People receiving abuse must be informed, respecting their right to confidentiality, in order to cover their basic needs, and to preserve their social relationships.[488]
Applicable legislation	If abuse is definitely suspected, the health and social services professionals have the ethical and legal obligation to protect the victim, so they must activate the judicial resources. If there are physical injuries, they will draw up a judicial report of injuries; if there are no injuries, they will inform the Public Prosecutor of the case in order to adopt the measures established by law.[509]

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Recommendation

D	Health and social services professionals must be trained to prevent, detect, care for, protect, declare and recuperate a person with dementia suffering from abuse.
✔	The fundamental rights of the person to dignity, participation, autonomy and self-determination must be preserved.
✔	People suffering abuse must be informed, respecting their right to confidentiality, in order to cover their basic needs, and right to preserve their social relationships.
✔	If there is probable suspicion of abuse, the health personnel must activate the judicial resources that permit the defence of the victim of abuse. If there are physical injuries, a judicial report of injuries will be drafted. If there are no injuries or other acute contingencies, the Public Prosecutor will be informed.

13.1.5. What social resources exist to address abuse?

Once the abuse has been detected and diagnosed, action strategies must be put into motion with the victim and the aggressor, and monitor the problem. The action of the professional who detected the case must be coordinated with the social worker and specialised services.

The data corresponding to the patient, the type of abuse, the measures or interventions applied must recorded in the clinical record.

To present and correct the abuse, we have a series of social health interventions and strategies:[510]

Expert opinion, 4

- Avoid social isolation: Through home care services; day centres; guardianship by the social services.
- Optimise and organise the patient's care, providing means and simplifying the treatment.
- Adapt the house to the limitations of the person with dementia.
- Institutionalise the patient if the family cannot guarantee their care.

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To improve the conditions of the abusing person, when this is the caregiver or relative, and present and correct the abuse:[488] • The stress of the family or of the caregiver must be reduced: Sharing the task of caring, moving house, support groups, guaranteeing rest periods for the caregiver. • If the caregiver suffers a psychiatric problem, consumes alcohol or drugs, or suffers some type of gaming problem, an attempt must be made to get to know their emotional state, provide support and treatments for the psychiatric or drug abuse problems if these exist. • Evaluate the capacity of the family to guarantee the care.	Expert opinion, 4

Summary of evidence

4	There are strategies, interventions and social resources for the person who receives abuse: Avoid social isolation, facilitate and simplify the patient's care, adapt the home and institutionalise if necessary.[510]
4	There are strategies, interventions and social resources to improve the situation of the caregiver or relative who abuses: Sharing the work of caring, moving house, support groups, rest for the caregiver, medical or psychological treatment if necessary.[510]

Recommendation

D	When abuse is detected and diagnosed, it is recommendable to launch strategies that permit improving the situation of the victim and of the aggressor. The actions of the different professionals must be coordinated, recording all the data of the abuse in the clinical record.
D	To prevent and treat abuse, avoiding social isolation, optimising the patient's care, adapting their home and institutionalising them if the family cannot guarantee their care, are recommended.
D	It is advisable to attend to the abuser, who is often a stressed or sick relative, or with an excessive burden. The burden can be reduced by sharing the task of caring, removing the patient from the family environment, participating in support groups, guaranteeing rest and offering medical treatment if required.

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Advance directives

13.2.1. When must the possibility of drafting advance directive documents (ADD), living wills and/or granting powers of attorney be suggested to people with dementia?

People with dementia lose their autonomy and capacity to take decisions. In the initial stages of dementia, patients, if they wish, should be able to freely express their preferences about medical treatment, tube feeding, artificial life support, etc. In moderate or severe stages, they lose this capacity and consequently the decision-making must be assumed by others. Health and social services professionals, and their relatives must try to discover their wishes and respect their medical, legal and financial preferences.[511,512,513]	Expert opinion, 4
The Spanish legislation in force and, more specifically basic Law 41/2002, 14 November, on the autonomy of patients and their rights and obligations with regard to clinical information and documentation, in its article 11 ("Previous instructions") pertaining to Chapter V (" Respect for the patient's autonomy") establishes that "by means of the advanced care document, an elderly person, able and free, expresses his or her wishes in advance, in order for these to be fulfilled in the event that such situations should arise whereby he or she is not able to express them personally, regarding their health care and treatment or, in the event of death, about the destination of his or her body or the organs therein. The executor of the document may also appoint a representative to act, if the case arises, as his or her interlocutor with the physician or health team to procure compliance with the prior instructions".[514] The prior instructions document or ADD may be formalised in a public document (before notary) or be private. The advance directive document, also called living will, must be considered as an expression of freedom of choice that must be respected and fostered. The legal system does not establish any time or specific moment to draw up the ADD document. This is an exercise of right that is recommended to be carried out in adult age and being of sound mind.	Applicable legislation

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In the case of a person who is diagnosed with dementia, the recommendation to draw up the ADD should accompany the diagnosis. That is, that both acts should be consecutive in time and as soon as possible after the diagnosis in order to be able to guarantee maximum possible integrity.

Expert opinion, 4
Applicable legislation

Although it is true that the diagnosis will not always coincide with the onset of dementia when this is mild, the health practitioner in contact with the sick person may also consider if the recommendation is equally appropriate.

Under these terms, whenever these people come to the health sector, professionals must advise them to have their degree and level of dependence and/or disability and their resources evaluated, so they must refer them to the relative social services. With this measure, it is guaranteed that the intervention of the professional contributes to bringing the affected people and their families nearer to the healthcare and/or protection measures included in Law 39/2006, 14 December, on Promotion of Personal Autonomy and Care of dependent people.

The Law does not specify the content of the ADD document, which may contain all those indications the person executing it considers of interest. Those aspects of the prior instructions documents that are not permitted by Law or are expressly forbidden, will not be taken into consideration. This will not represent the loss of validity of the other indications contained therein and that are not contrary to law.

The ADD document must be registered in each autonomous community, normally at the Regional Ministry of Health, and it must be added to the patient's clinical record. It would be advisable for it to be incorporated by computer links into the health card. The prior instructions document may be freely revoked at any moment in time, leaving record in writing.

Expert opinion, 4
Applicable legislation

The National Registry of prior instructions documents or ADD created by the Ministry of Health and Consumer Affairs ensures the effectiveness in the entire national territory of the ADD/prior instructions documents expressed by patients and formalised pursuant to the legislation.[515]

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Summary of evidence

4	People with dementia lose their autonomy and capacity to take decisions. Health and social services professionals, and their relatives must try to discover their wishes and respect their medical, legal and financial preferences.[511,512,513]
Applicable legislation	Basic Law 41/2002, 14 November, on patients' autonomy and on their rights and obligations with regard to clinical information and documentation, indicates that the prior instructions document or advance directive (ADD) includes the advanced will of a person of full legal age, able and free, for their desires to be fulfilled at a moment in time when they are not able to express them personally, about the care and treatment they must receive. It also serves to appoint a valid representative who may decide on his or her behalf in each health circumstance and, in the event of death, about the destination of their organs. This ADD or living will may be formalised in a public or private document.[514]
4	The legal system does not establish any specific moment of time to draw up the ADD; it is advisable to do so in adult age and in being of sound mind. In respect of people with dementia, this must be attempted as soon as possible after the diagnosis to guarantee their cognitive integrity to the utmost.[193]
4	Health professionals must recommend the ADD to their patients, and especially if they detect emerging cognitive impairment.[516]
4	All those indications considered of interest by the person executing it, can be noted down in the ADD. Those aspects that are not permitted by Law or are expressly forbidden, will not be taken into consideration. This will not represent the loss of validity of the other indications contained therein and that are not contrary to law. These AD documents may be freely revoked at any moment in time, leaving record in writing.[193]
Applicable legislation	There is a National Registry of Prior instructions document or ADD of the Ministry of Health and Consumer Affairs and registry in the autonomous communities.[515] For it to be easier to know the ADD of a person, this must be incorporated into their clinical record, and it would be advisable to do so by computer link to their health card.

Recommendation

D	Health and social services professionals, and relatives must try to discover the ADD of the sick person to be able to comply with his or her wishes and respect his or her medical, legal and financial preferences.

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D	It is important to continue informing and raising the awareness of the population at large as well as of the health and social services professionals, about the need for able and free adult people to exercise their rights to draw up an ADD containing their wishes regarding the care and treatment they accept to receive, as well as the appointment of a valid representative that can decide on their behalf in each health circumstance, and after death, about the destination of their organs.
D	It is advisable to draw up the ADD in adult age and being of sound mind. In respect of people with dementia, this must be attempted as soon as possible to guarantee their cognitive integrity to the utmost.
D	Health professionals must recommend the ADD to their patients, and insist upon it especially if they detect emerging cognitive impairment.
D	It is recommendable for the ADD to include everything that is important for the person, bearing in mind that another person, on whom they delegate, will have to decide in their name, following their own indications.
D	To make it easier for a person to have access to the ADD, the ADD must be registered in the autonomous community and at the National Registry Office for advance directives or ADD of the Ministry of Health and Consumer Affairs, and it must be attached to the clinical record and to the health card.

Evaluation of competences

13.3.1. Are there instruments that have been strictly designed to assess the competence of patients with dementia?

The legal need arises in people suffering from dementia to evaluate their capacity for self-determination, to decide about their property, ability to drive vehicles, use firearms or participate in clinical trials.[517]	Expert opinion, 4
There are no universally accepted CPG to assess the competence of patients with dementia.[518,519,520,521] In Spain we have the Sitges Document, in two versions, the 2005 version[522] and the revision of 2009[206], drawn up using the Delphi techniques as a consensus methodology.	Expert opinion, 4

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Five topics are developed in the Sitges Document: 1) capacity and self-management; 2) decision-making in the personal field and regarding assets; 3) neurological conditions required to take decisions; 4) examination of neurological conditions, and 5) correlation between the neurological state and the capacity to take decisions. A decision capacity assessment instrument has been drawn up in the Sitges Document, using a graphic and comprehensible table, indicating all the neurological and cognitive aspects that must intervene in the decision making. Each function is assessed and quantified using the necessary tests and examinations; the maximum permissible alterations are established to be able to recognise the capacity or incapacity to take decisions on personal aspects and/or aspects related to assets. The Sitges Document (2009)[206] is a document aimed at raising the awareness of social agents on the exquisite and fair treatment that people with dementia deserve, whatever their condition. It contributes to improving the quality of the medical act relating to the care of these patients and their families, and to preventing these people, who are no longer in a situation to decide, from being able to be exploited by third parties.

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Summary of evidence

4	As the dementia progresses, the clinical, social and legal need arises to evaluate the capacity of these people for self-determination, to decide about their assets, and other responsibilities, such as drive vehicles, use firearms or participate in clinical trials.[517]
4	There are no universally accepted CPG to assess the competence of patients with dementia.[518,519,520,521] In Spain we have the Sitges Document (2005)[522] and its updated version of 2009,[206] drawn up by consensus methodology.
4	The Sitges Document (2009)[206] refers to capacity and self-management; taking decisions that affect their person and their assets; the neurological conditions required to take decisions, and it provides a decision capacity assessment instrument, through a graphic and comprehensible table, indicating all the neurological and cognitive aspects that intervene in decision-making. Each function is assessed and quantified. Maximum alterations are established that permit recognising decision incapacity, bearing in mind personal aspects as well as those related to assets.

Recommendation

D	The utmost efforts should be made to maintain the autonomy of people affected by dementia, respecting their decision-making capacity, whenever possible, even at the end of their lives.

D	It is recommendable for health and social services professionals, as well as the legal institutions that attend to them, to use a common language and share knowledge.
D	The decision capacity of any person affected by dementia should be assessed, using the assessment instrument of the Sitges 2009 document.
D	It is advisable to involve the patient, if possible, in decisions made about the treatment. The patient's desire must prevail; however, differences in opinion between patient and caregiver must be evaluated.
D	Total or partial incapacitation must be used as a legal resource to protect the person with dementia.
D	When carrying out a comprehensive and multidisciplinary assessment of a person with dementia, the evaluation of their decision-making capacity must be included, as well as if there is appropriate legal protection or not.

13.3.2 How are the specific competences assessed: driving licence, firearms licence and participation in clinical trials?

Driving licence

Driving vehicles is a complicated activity that requires the coordinated functioning of multiple cognitive functions. Driving provides autonomy and independence, freedom and mobility. The decision to drive must bear in mind, on the one hand, the individual freedom, and on the other hand, the safety of the actual patient and public safety for third parties. The driving capacity is affected in dementia and as a result the risk of accidents increases.[517]	Expert opinion, 4
Although driving can already be affected in MCI and in the first stages of dementia, these people may still maintain their driving capacity. As dementia progresses, the risk of accidents significantly increases.[523] The dementia diagnosis, therefore, does not mean stopping driving. The decision will be made based on the severity or on a demonstration of incompetence in their ability to drive.	Expert opinion, 4

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To obtain a driving licence, a medical certificate of the person's psychophysical capacity must be provided, issued by an authorised driver examination centre according to Royal Decree 1277/2003, 10 October. In article 15 of the new Regulation of 2010, it establishes that the results of the psychophysical examination will be included in a report that will be issued on an official form, specifying if the person may be affected by cognitive impairment. There is no definition on how the capacity must be assessed.[525]

Applicable legislation

The assessing process comprises a clinical record and an examination carried out by a general practitioner, an ophthalmologist and a psychologist. The results may be ordinary fit (no deficiency and/or pathological processes that represent a risk for driving); extraordinary fit (this includes people with pathological processes and/or deficiencies accepted as causes of risk to maintain an adequate road safety level); not fit (people with disorders that are incompatible with driving temporarily or that may have a permanent nature). Reliable and validated methods and scales are used. The psychological evaluation includes mental disorders, behaviour and cognitive disorders.

People with mild dementia should not drive, as they do not pass the test that determines this ability when evaluated with the entire ASDE Drivetest driving battery (which is the one used at the Examination Centres in Spain).[523]

Cohort study, 2++

Patients with MCI should be studied comprehensively to determine their competences as only about 50% pass these tests.[523]

The neuropsychological tests that correlate with these competences and that can help detect people with a driving risk are Kohs Block test, word learning test, logical memory, delayed memory and TMT-A.[523]

In MCI and in the initial stages of dementia, it is difficult to identify which people should stop driving. Both the compulsory and optional examinations and tests established must be carried out, if we wish to detect people with mild-moderate risk. A practical interactive driving exam based on road skills can give additional information. The British Psychological Society considers that there is no test battery that can be recommended.[526] One SR of the cognitive tests used (including the clock test or the Trail Test, recommended by the American Medical Association),[527] concludes that they are sufficient in clinical practice to determine if a more extensive neuropsychological assessment is necessary.

Cohort study, 2++

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A driving limitation must be proposed when alterations are detected in attention, orientation, executive functions or in visuospatial perception.[517]	Descriptive study, 3
The physician must warn the patients and family about the advisability of stopping driving. If there is a reasonable risk, which endangers third parties, if the patient or family refuses to accept it, the competent authority must be informed.	Expert opinion, 4
Although people with dementia pass the assessment tests, and they are given a licence, new assessments should be repeated within a short period of time, every 6-12 months. It is important to inform the patients and family that the driving capacity is going to be turned down. This will enable them to plan the appropriate moment to stop driving in time and the most adequate alternative to maintain their freedom and autonomy.[517]	Descriptive study, 3

Firearms pe rmit

There is little information in CPG that define the capacity to manage firearms in people with dementia. If there are behavioural disorders with false interpretations and alteration of the perception of reality, with violent and aggressive responses, the possibility of handling a firearm is a risk to themselves and to third parties. It is important for the caregiving family and the professionals to evaluate the circumstances and establish the most adequate protection measures. To obtain the firearms permit a medical certificate of psychophysical fitness must be provided. There is no specific medical report model or an assessment of their physical, cognitive or behavioural capacity.[140,25]	Expert opinion, 4

Participation in clinical trials/research

Research is regulated by scientific and ethical principles. Clinical, genetic research, the donation of brains and trials with new drugs are all important in dementia. Over the last few years, codes, documents and declarations have appeared that have established ethical principles that must be fulfilled to participate in experiments. The contents of documents, codes and declarations have been updated and improved since Nuremberg in 1949, until Helsinki in 2002.	Expert opinion, 4

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Participating in research is an opportunity that benefits patients and their families. People wishing to participate must be informed in depth and in detail about the objectives of the study, its possible benefits and safety. The content of this information must make it easy to understand. Candidates must be able to understand and ask questions to clear up their doubts before signing their consent. Researchers must bear in mind their decision-making capacity. When patients are not capacitated, it will be the family or legally authorised person who must take the decision.

Law 29/2006, 26 July, in its article 60, section 4, offers guarantees in the rational use of medication and demands the free and informed consent of the person participating in the trial.[528]

Applicable legislation

Good Clinical Practices must be implemented in research studies. A series of conditions must be fulfilled to carry out clinical trials: a) correct methodology and competent team; b) acceptable risk-benefit ratio; c) independent supervision; d) fair load distribution, random distribution, with equal probability of efficacy and safety in all groups; e) informed consent and confidentiality; f) an insurance that guarantees the risks are covered, and g) appropriate payment.

In biomedical research, the professionals who intervene must know about the convention relating to human rights and biomedicine (Oviedo convention) and the Helsinki declaration[529] as well as the international ethical guidelines (Council for International Organizations of Medical Sciences, CIOMS) (Genoa)[530].

Expert opinion, 4

Summary of evidence

Driving licence and dementia	
4	People with MCI and mild dementia may have driving problems that increase the risk of accidents and endanger their own safety and that of third parties.[517,523]
4	Driving vehicles provides autonomy and independence, freedom and mobility to people with MCI or mild dementia, too. This autonomy must be respected, but the evaluation of their capacity enables the professional to advise if it is necessary or not to stop driving for safety reasons.[525,517]
2+	A full psychological evaluation at drivers' examination centres, systematically using compulsory and optional tests, permits the detection of people with cognitive impairment in mild dementia and determines their risk of suffering accidents.[526,517]

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2++	People with mild dementia should not drive as they do not pass the tests that determine this ability when evaluated with the entire ASDE Dritest driving battery (which is the one used at the Examination Centres in Spain). Patients with MCI should be studied comprehensively to determine their competence as only about 50% pass these tests. The neuropsychological tests that correlate with these competences and that can help detect people with a driving risk are Kohs Block test, word learning test, logical memory, delayed memory and TMT-A.[523]
3	Alterations of attention, orientation, executive functions or visuospatial perception limit the driving capacity.[517]
4	When a significant risk for driving is acknowledged in a person with dementia who has been suitably assessed, their physician is under the obligation to inform the person affected and the caregiving family.[526,517]
3	The severity of the cognitive deficiencies progress in people with dementia and with it their driving capacity can decrease in months. A revision of their capacity at shorter intervals than normal, between 6 and 12 months, permits detecting the problem and avoids risks of accidents.[517]
Firearms permit and dementia	
4	People with dementia, especially if they present agitation, aggressiveness, violence, delirium and hallucinations, may use firearms inappropriately and thus cause danger for themselves or for others.[140,25]
Research and dementia	
4	The participation of people with dementia in research studies is well regulated. There are documents, codes and declarations that protect their rights. Their participation must be free. Before taking decisions and signing consent to participate, they must receive understandable, extensive and detailed information.[528]
4	Any research study today requires that the research team is aware of the latest versions of the Good Clinical Practice Guidelines.
4	The importance of the clinical trials, due to the possible benefit, risk and cost, always requires the research team to fulfil a series of conditions: a) correct methodology and competent research team; b) acceptable risk-benefit ratio; c) independent supervision; d) fair load distribution, random distribution, with equal probability of efficacy and safety in all groups; e) informed consent and confidentiality; f) safety guarantees, and g) appropriate payment.[529,530]
4	There are conventions and ethical guidelines to preserve the human rights of people who participate in biomedicine studies (Oviedo, Helsinki, Geneva).[529,530]

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Recommendation

Driving licence and dementia	
D	The ability of people with dementia to drive a vehicle should be assessed, even during the initial stages, as an increase in the risk of suffering accidents has been proven.
D	A full psychological evaluation should always be carried out at drivers' examination centres to detect people with cognitive impairment in mild dementia.
D	Health professionals must inform patients with dementia and their families about the risk that continuing to drive may entail.
D	If a person with mild dementia continues to hold a licence, their ability to drive must be reviewed every 6 to 12 months, or earlier if necessary, to evaluate their risk.
D	A driving limitation must be proposed when alterations are detected in attention, orientation, executive functions or in visuospatial perception.
Firearms permit and dementia	
D	It is advisable to keep firearms or elements that might be dangerous to them or to third parties, away from people with dementia, above all if there are behavioural disorders.
Research and dementia	
D	People with dementia and their relatives must be informed of the possibility of participating in clinical trials.
D	People participating in research studies must receive extensive, detailed and understandable information, and they must sign an informed consent.
D	Good Clinical Practice Guidelines must be implemented in research studies.
D	The RCT should satisfy a series of conditions: a) correct methodology and competent research team; b) acceptable risk-benefit ratio; c) independent supervision; d) fair load distribution, random distribution, with equal probability of efficacy and safety in all groups; e) informed consent and confidentiality; f) safety guarantees, and g) appropriate payment.
D	Professionals taking part in research studies must know about the agreements relating to human rights and biomedicine as well as the standards established by international ethical guidelines.

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13.3.3. Which are the indications to start the legal incapacitation process of a patient with dementia?

The decision capacity is decreased in dementia. This poses specific problems that family and society must solve. In AD, FTLD, DLB and PDD, both at the onset and throughout its evolution, they lose awareness of the disease, and the cognitive and behavioural impairment entails taking inappropriate decisions that may harm them and/or other people.[522]	Descriptive study, 3
Few people, even today, have expressed their advance directives, or have decided to protect themselves, through decision-making powers. They may, with time, also change their way of viewing things and their decisions. Their right to autonomy and to beneficence must be respected, ensuring safety of means and treatment.	
In DLB, PDD and VD, their capacity may vary with fluctuations. There can also be intermittent periods of lucidity in other dementia.[522]	Descriptive study, 3
The decision-making capacity must be analysed with great care, carrying out a complete evaluation of the cognitive skills that intervene in the decision-making.[206]	Expert opinion, 4
If there are high risk situations, the control and protection measures must be stepped up, proceeding to start the incapacitation process. The incapacitation process must be started: a) if there is dementia; b) if the symptoms are persistent; c) it prevents self-management (ability to solve one's own matters, ability to attend to basic needs and reach objectives or fulfil desires).[531]	Expert opinion, 4
Based on the respect for free decisions taken by an adult if they do not harm the rights of others and are legal,531 one of the most important problems in daily clinical practice is that they do not leave a record of their advance directives and the professionals and their families have to decide.[532]	Expert opinion, 4
Self-management has an external dimension: Related to legal acts that have to do with third parties; and an internal dimensional: relative to one's own acts, such as self-care. Something to always be taken into account is the fact that the main objective of the legal incapacitation process is to defend people who, due to their pathology, have become disabled to a greater or lesser degree, for their self-management, and therefore in a clear situation of personal and social risk.	Expert opinion, 4

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The evaluation of the loss of self-management must be carried out in agreement with different criteria, which affect different fields and professions, so the indication to start the legal incapacitation process must be the result of a multidisciplinary evaluation.

These criteria are: Diagnostic, clinical, dependence, social, use of services and evolution.

Diagnostic criterion (at least one is a necessary and essential condition):

- Stable, severe psychiatric diagnosis with more than two years' evolution.
- Mental retardation or borderline intelligence.
- Other diagnoses related to non-reversible important cognitive deficiencies.

Clinical criterion (at least two criteria must be fulfilled):

- Instrumentally assessed persistent cognitive deficiency.
- Markedly affected judgement of reality, not including acute
- situations.
- Lack of awareness of disease or of the deficiency and/or non-adherence to the treatment.
- Impulsiveness and risk behaviour derived or closely related to the disease or to the deficiency.

Physical and/or mental dependence criterion (one of the two is a necessary condition):

- The person examined requires constant supervision.
- Lack of objectified autonomy (scales, GAF).

Social criterion (at least two),

- Social and economic precariousness.
- Loneliness, isolation and lack of social support network.
- Inadequate use of money: Putting their assets or own future at risk.
- Family claudication or lack of reference family.
- Evidence or reasonable suspicion of manipulation by third parties or that somebody is taking decisions for them.
- In hospitalised people: Involuntarily admitted into a centre for more than 2 years and discharge not predictable. The person is hospitalised without any awareness and has no reference family bond.
- Different resources and work plans have been applied and the objective has not been achieved, and the person is dissociated from the social and health services network.
- Need for forward thinking.
- Person who has an assistant for a long time.
- Any other cause of risk of social marginalisation.

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Criterion of use of services:

- Frequent hospitalisations over the last year (normally involuntary).
- The patient does not accept outpatient treatments, although this has been attempted on several occasions.
- The patient does not accept rehabilitation although they need it..
- Evolution criterion:
- Prognosis towards stability of the impairment or towards a greater degree of impairment.
- High frequency of relapses related to not following the prescriptions.

Summary of evidence

3	The decision capacity is decreased in dementia. Even at the onset of AD, FTLD, DLB, PDD and VD, and throughout their evolution, the awareness of the disease may decrease: Cognitive and behavioural impairment entail inadequate decision making which may harm them and/or other people. This poses specific problems that family and society must solve.[522]
3	In DLB, PDD and VD, the decision capacity may vary with fluctuations. There can also be intermittent periods of lucidity in other dementia.[522]
4	The capacity to take decisions is difficult to assess at times. A meticulous and comprehensive analysis of the cognitive functions permits defining their decision capacity degree.[206]
4	The incapacitation process must be started: a) if there is dementia; b) if the symptoms are persistent; c) it prevents self-management (ability to solve one's own matters, ability to attend to basic needs and reach objectives or fulfil desires).[531]
4	One of the most important ethical and legal problems in daily clinical practice with people affected by dementia is the lack of a record of advanced directives.[532]
4	The main objective of the legal incapacitation process is to defend people who, due to their pathology, have become disabled to some extent to manage for themselves, and therefore in a clear situation of personal and social risk. The evaluation of the loss of self-management must be carried out in agreement with different criteria (diagnostic, clinical, degree of dependence, social aspects, use of services and evolution of the process), which affect different fields and professions, so the indication to start the legal incapacitation process must be the result of a multidisciplinary evaluation.

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Recommendation

D	It is very important to respect the autonomy and freedom of the people at the time of the diagnosis and throughout the entire evolution process, bearing in mind that, despite the existence of advance directives, people, with age, due to circumstances and/or due to the actual disease process, may change their way of seeing things, and thus change their decisions.
D	Beginning the incapacitation process must be recommended when the dementia progresses and the cognitive and/or behavioural impairment determines taking inadequate decisions that might harm the person affected by dementia and their environment.
D	The incapacitation process must be the result of a multidisciplinary evaluation, and must contemplate many different aspects such as: Diagnostic, clinical manifestations, degree of dependence, social aspects, use of services, and evolution of the process.

Aspects relating to the patient's legal protection

13.4.1. What does legal incapacitation consist of?

Applicable legislation

Civil capacity encompasses two concepts, namely:

A) Legal capacity or legal personality: This is the aptitude that any person, because they are holders of rights and obligations, and which is characterised by: all people possess it in themselves (art. 29 Civil Code), it is acquired with birth (art. 30 Civil Code), and it ends with death (art. 32 Civil Code), it is the same throughout life and cannot be modified.

B) Capacity to act: This is the aptitude of the person to exercise their rights and obligations, and which is characterised by: It is not possessed by all people in themselves; it is acquired when coming of age (18 years) (art. 315 Civil Code), it is not the same throughout life and it can be modified.

Depending on the degree of loss of capacity to act, two types of disability are differentiated:

A) Total incapacity: The person is not able to take any kind of decision that refers to the attention and care of any person, or to carry out any legal business or acts related to the administration and disposal of their assets, legal rights and interests and those related to assets of any kind.

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The person who has to take all the decisions that are withdrawn by ruling from the incapable person is the guardian and what they exercise is called guardianship **(question 13.4.3).**

B) Partial incapacity: The person is incapable only or exclusively for acts related to assets (administration of assets) or related to other areas such as care of their health (e.g. monitoring and control of medical treatments that the person is following to treat the disease; access to medical information; giving consent, etc.) or the promotion of social integration (e.g. request access to social services, represent the incapacitated person in administrative acts, etc), indicated by the ruling.

The person who has to take the decisions that are withdrawn by ruling from the incapable person is the conservator and what they exercise is conservatorship **(question 13.4.3).**

In article 199, the Civil Code indicates: "Nobody can be declared incapable unless by judicial ruling by virtue of the causes established by law". Therefore, the necessary condition to declare a person incapable requires the existence of the judicial ruling in this sense.

Likewise, article 200, of the Civil Code indicates: "Causes of incapacitation are persistent, physical or psychic diseases or impairments that prevent a person from managing on their own".

Therefore, the legal requirements that must exist to declare a person incapable are: Suffer a disease (a process in progress that alters and impairs health) or deficiency (dysfunction, limitation or impediment that is definitely established); persistent nature of the disease or deficiency which cannot be cured and whose limiting effects cannot be mitigated in a controlled and constant manner.

These effects will have an impact on the person's capacity, making them generally incapable self-management.

The incapacitation process is comprised of different steps that are established in article 756 and following of the Code of Civil Procedure (LEC) and which, chronologically, are:

Applicable legislation

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1) Onset: People who can start the process (presentation of the demand) (a.757 LEC): Alleged incapable person, spouse or person who is in a comparable situation, descendants, ascendants or siblings. The Public Prosecutor will start the process in the following cases: If the above do not exist or have not requested it, after having being informed by a person who is aware of the situation (neighbours, private doctor, any family member…), after having been informed by a public servant who, because of their job, is aware of this (physician, etc.) and who, due to their administrative category (civil servants) is under the obligation to do so; in the case of minors: Only the person with parental authority or guardianship.

2) If the Public Prosecutor's office acts jointly and severally, it will carry out different steps: Interview with the people for are aware of the existence of the alleged incapable person, forensic medical examination of the alleged incapable person, request for reports from institutions believed appropriate (social services, primary care centres, etc).

3) Decision by the Public Prosecutor about whether or not to present a demand (decision against which it is not possible to bring any appeal).

4) Personal interview (hearing) between the judge and the alleged incapable person and relatives believed appropriate. They will be asked both about the state of the alleged incapable person and about which of them would be willing to assume the guardianship; and all those who the judge believes appropriate as witnesses.

5) Medical-forensic decision about the alleged incapable person.

6) Intervention by the Public Prosecutor: a) As plaintiff when it starts the process: researching the situation of the alleged incapable person to prevent them from being left unprotected as a result of the declaration of incapacity, plus the appointment of a judicial defender for the alleged incapable person; b) as defendant when it does NOT start the process: To prevent people from being declared incapable when they are not.

7) Judicial declaration (RULING) respect to: Whether the person is incapable, establishing the type of incapacity (what they can or cannot do), establishing the protection system for the incapable person.

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Summary of evidence

Applicable legislation	The declaration of incapacitation or modification of the capacity to act recognises that a certain person, as a result of the disease they suffer, has no capacity (total incapacitation) or has partially limited capacity (partial incapacitation) (Law 1/2009 m. Civil Registration Law).[533] This declaration can be requested, through a demand, by the actual person, the spouse or partner, descendants, ascendants, siblings and the Public Prosecutor (Law 41/2003, 18 November, article 757 of the Code of Civil Procedure).[534] It will be opposed by the Public Prosecutor or a lawyer after an examination by the judge and by the forensic doctor and a hearing with closest family members. The judge will pronounce a ruling in favour or against the modification of the capacity and will appoint a guardian if necessary.

Recommendation

According to applicable legislation	To request the incapacitation or modification of the capacity to act, the procedure laid down by the Spanish Procedural and Civil Registration Law must be followed, whereby, based on a demand, the case is studied, opposed and the judge gives judgement.

13.4.2. What type of legal protection exists for a patient with dementia?

During the first stages of dementia, in order to plan the future of the person affected and predicting the possibility of being judicially incapacitated, and providing that the person still preserves his or her capacity to take decisions, any of the three legal figures below may be chosen: Self-guardianship, special power and advance directive document **(question 13.2.1)**

Applicable legislation

Self-guardianship: regulated in article 223 of the Civil Code, it permits any person, with sufficient capacity to act, in anticipation of being declared incapable, to appoint the person they wish as their guardian, as well as adopt any provision referring to their personal care or the administration of their assets, identifying any person who should not be appointed, under any circumstances. The "self-guardianship" must be formalised in deed executed before notary, which will send a copy of it to the Civil Registry where the person is registered.

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In the event that this person were declared incapable, the judge who agrees to the incapacitation will request the Civil Registry to send him a copy of the deed on self-guardianship drawn up, in order to bear in mind the provisions of the person that executed it. The provisions contained within the self-guardianship deed binds the judge, unless the benefit of the person should demand otherwise. In this case, the judge must issue a reasoned decision.

Applicable legislation

Special power or preventive power: The current drafting of article 1732 of the Civil Code foresees the possibility of conferring powers in favour of a third person, via the execution of a power, establishing that this can continue to be used at the time when ensuing incapacitation should concur in the person granting the power. This type of power is called special power or preventive power.[536]

The same article foresees that the power, if it is not special or preventive, will no longer be effective if the person who has granted it, incurs incapacitation. To this end, there is no need for there to be any change in capacity: just by proving that the person has lost his or her sound mind, the power would not longer be valid. For that reason, any person who knows or believes that he or she is going to lose his decision-making capacity, may grant a special power for another person, conferring upon this person the powers to act on their behalf, being able to represent them even in the event that incapacitation is incurred. The importance of this assignment and its consequences (someone may act on behalf and in the interest of a certain person when this person is not able to understand the scope of the acts carried out on his or her behalf nor be able to revoke the special power granted at the time) require that a special power should only be granted in favour of someone in whom the person explicitly trusts. «Finally, and as in all notary documents, a special power may only be signed if the person is fully able to understand and wishes to execute it.

Summary of evidence

Applicable legislation	When people affected by dementia still preserves their capacity to take decisions, foreseeing the subsequent evolution towards a situation of incapacity, they may protect themselves legally with three options: Self-guardianship: Appoint a guardian as well as adopt any provision referring to their personal care or the administration of their assets, identifying any person who should not, under any circumstances, be appointed.[535]

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	Special power or preventive power: conferring powers in favour of a third person, via the execution of a power, establishing that this can continue to be used at the time when ensuing incapacitation should concur in the person granting the power.[536] Advance directives **(question 13.2.1)**

Recommendation

✔	People with mild cognitive impairment and mild dementia should be advised to protect themselves through self-guardianship, or giving special power or writing the advance directive document.
✔	Any person with dementia who still has sufficient capacity to act, should appoint a guardian, foreseeing the possibility of being declared incapable. As well as adopt any provision referring to their personal care or the administration of their assets, identifying any person who should not be appointed, under any circumstances.

13.4.3. What is guardianship?

Applicable legislation

Guardianship is the true protection mechanism of a person who has lost their capacity for self-management (modification of the capacity would be the means), as it is through the guardian that the person obtains the complement of self-management that the disease has reduced or annulled. In Law 13/1983, 24 October, of the Civil Code these terms are defined and the procedures, rights and obligations of all the players are specified.[537,538,539,540]

Guardianship means caring, attending, covering both the personal aspect and also the aspect related to the administration of assets that the person owns. Guardianship is a responsibility that is subject to different control measures, such as the drawing up of an initial inventory, annual accountability, the need to obtain prior authorisation for certain acts of economic importance and the presentation of the final statement of accounts when it ends.

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Both physical persons and legal non-profit persons may be guardians, including among their objectives or purposes, the protection of people whose capacity has been modified. It is preferable to appoint the person or entity named by the actual person in the self-guardianship, rather than the spouse, parents, descendants, ascendants or siblings appointed by the judge. The judge may, exceptionally, based on reasoned decision, alter the order mentioned or rule out the people indicated, if this is deemed to benefit the person.

Other guardianship figures are conservatorship, asset administration and judicial defence.[537,538,539,540]

Conservatorship would be guardianship with a reduced scope, which is usually assigned in cases of partial modification of capacity. The conservator must attend to the person under conservatorship to carry out those acts determined by the ruling. This is a person who accompanies, counsels or assists, but who under no circumstances can substitute the will of the person, as they do not hold their representation.

The asset administrator is usually appointed when the assets of the person are so great that, to attend to them adequately, it is advisable to differentiate personal care from the administration of property.

The judicial defender may be appointed to cope with urgent situations if the guardian has still not been named or when important differences arise between guardian and the ward.

Summary of evidence

Applicable legislation 4	Guardianship means caring, attending, covering both the personal side and also the administration of the assets that the person owns:[537,538,539,540] Guardianship is a responsibility that is subject to different control measures, (drawing up an initial inventory, annual accountability, the need to obtain prior authorisation for acts of economic importance and the presentation of the final statement of accounts). Both physical persons and legal non-profit persons may be guardians whose objectives include the protection of people whose capacity has been modified. Curatorship is a guardianship of reduced scope for cases of partial modification of capacity, when the function assigned is to accompany, counsel or assist, but who under no circumstances can substitute the will of the person, as they do not hold their representation. Asset Administrator is the person named to administer the assets of the person with reduced decision capacity.

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	Judicial defender appointed to cope with urgent situations if a tutor has still not been named or when important differences arise between guardian and the ward.

Recommendation

✔	People with dementia who have lost their self-management capacity, should have a legal representative or guardian to protect them, and substitute them.
✔	People with dementia with reduced decision capacity should name a representative who shall care for their conservatorship, accompanying them, advising them and helping them take decisions.
✔	People with dementia with reduced decision capacity should name an administrator for their estate to administer their assets if these were considerable.
✔	A judicial defender of the person with dementia must be named, to cope with urgent situations if a tutor has not been named or when important differences arise between guardian and the ward.

Restraint of the patient

13.5.1. What are the indications for pharmacological and/or psychological restraint of a patient with dementia?

States of psychomotor agitation and aggressive behaviour are relatively frequent behavioural disorders in people with dementia in moderate to advanced stage, whatever the aetiology of the process.[369,374] They are characterised by a significant or inappropriate increase of the motor activity, accompanied by alterations in the emotional sphere which may become violent and dangerous, causing harm to the person affected or to other people and to the physical environment around them.[541,542]

Observational study, 2++

Aggressiveness, vagrancy or false interpretations of reality may appear from time to time and be unpredictable, or be persistent. Patients may flee from stimuli they interpret as harmful, or on the contrary they may confront them with belligerent actions and attitudes. Other times, situations that entail a risk of them harming themselves or falling down, arise as a result of inadequate activities that they carry out due to a lack of knowledge of their own possibilities.

Descriptive study, 3

Expert opinion, 4

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To prevent these expressions of aggressiveness or recklessness, the triggering factors can be corrected, modifying the patient's environment, fostering psychosocial skills and optimising resources **(Table 6)**. [541,542]

If agitation arises, systematised and hierarchical interventions must be carried out, starting with verbal dissuasion measures, and modifications in the environment **(question 10.4.6.).** If these are not sufficient they must be accompanied by the use of psychotropic drugs **(questions 10.4.7 and 10.4.8)** and only extraordinarily should mechanical restraint (MR) measures or physical restriction be used **(question 13.5.2).** The limitation or control of movement and of their behaviour aims to protect the patients, providing safety for both themselves and for their environment **(Table 7).**[140,541,542]

RCT
1++/ 1+
Observational study
2++

Table 6. Dementia: prevention of aggressive and reckless behaviour[541,542]

Correct the triggering factors: • Relieve any type of pain. • Correct sensory deficit: Auditory and visual. • Evaluate and correct alterations of the nutritional state. • Control current medication and its possible side effects, • Adequately treat comorbidity (infections, etc). • Improve gait, equilibrium and posture with physiotherapy. • Improve functionality in ADL.
Modify the environment: • Use adequate furniture (adapted chairs, etc). • Adequately use the brakes on beds and on wheelchairs. • Improve lighting and access to bells. • Step up safety measures. • Remove the sidebars, adapting the height of the bed. • Remove unnecessary utensils. • Place nonslip strips (baths, at the foot of the bed, etc). • Facilitate conditions of comfort and intimacy.
Foster psychosocial skills: • Control, reduce or eliminate provocative stimuli. • Carry out cognitive and sensory stimulation programmes. • Foster social activities., walks. • Provide company, therapeutic treatment, active listening. • Favour reality counselling.
Optimise resources: • Increase control and surveillance. • Support the caregiving family

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Table 7. Dementia: Treatment of psychomotor agitation[541,542]

Verbal restraint: • Listen carefully and actively: As the person needs to speak and express his emotions. • Calm the person down: Offering help, protecting him from himself, from the disease and from the hostile environment (real or imagined). With a professional and non-paternalistic attitude. • Approach with empathy: For the patient to realise that the professional is concerned with his welfare, showing interest and understanding. • Reinforce his feeling of reality: Responding to questions, analysing options, offering aid. • Not shouting, speaking slowly, showing interest in what he says. • Not intimidating, preventing him from feeling trapped, penned in, humiliated.
Pharmacological treatment: (questions 10.4.7 and 10.4.8). • Atypical antipsychotics – Quetipaine at a dose of 25-300, gradual start at 25 mg. – Risperidone, solution, tablets and mouth dispersible tablets). Initial dose of 0.5-1 mg, gradual start, increase 0.25 mg/day, maximum 1.5 mg/day – Olanzapine (tablets and fast absorption tablets), a dose of 2.5-5 mg • Typical antipsychotics: – Inject. haloperidol 1 vial of 5 mg. I5 mg. IM. • Benzodiazepine type sedatives: – Lorazepam 1 mg oral. – Diazepam 5-10 mg orally, sublingual or rectal. – Midazolam 1-15 mg, im, iv.

Summary of evidence

2++	Psychomotor agitation, aggressive, violent or dangerous behaviour may appear quite frequently in moderate or severe dementia, and it may cause harm to the person affected or to other people, or to the physical environment.[541,542,369,374]
3/4	To prevent aggressiveness or recklessness in people with dementia, action can be taken on the triggering factors, modifying the environment, fostering psychosocial skills and optimising resources.[541,542]
2++	The treatment that has to be followed in the event of psychomotor agitation/ aggressiveness in people with dementia, must be started with verbal persuasion measures, modifications in the environment, and if these are not sufficient, drugs and only, extraordinarily, mechanical restraint measures can be used.[140,541,542]
1++/ 1+	Atypical antipsychotic drugs (quetiapine, risperidone, olanzapine) are the first line pharmacological treatment of psychomotor agitation and aggressiveness in people affected by dementia. **(Questions 10.4.7 and 10.4.8).**

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Recommendation

B	It is recommendable to prevent and detect psychomotor agitation and aggressiveness of people with dementia at an early stage and treat it. The measures to be followed may be pharmacological or non-pharmacological, using mechanical restraint if required.
A	The use of atypical antipsychotic drugs is recommendable as first line pharmacological treatment of psychomotor agitation and aggressiveness of people affected by dementia.

13.5.2. What are the indications for physical restraint of a patient with dementia?

Mechanical restraint (MR) must be used in people with dementia who present considerable psychomotor agitation, which is not controlled with verbal and/or pharmacological measures, and providing this does not entail a danger of injury or damage to the actual patient or his surroundings. Pursue physical restriction or control by means of any mechanism, material or equipment, tied to the body or very close to it, that the patient cannot control or easily remove and which prevents him from moving freely and/or having normal access to his own body.[543,541,542]	Descriptive study, 3 Expert opinion, 4
It is a therapeutic measure, used exceptionally, which must only be applied under medical prescription, if other restraint methods are not applicable or have failed. The objective is to protect the actual patient and in turn, other people, objects or facilities around them. With this measure no greater harm must be caused than the harm aimed to be avoided.[543,541,542]	Descriptive study, 3 Expert opinion, 4
MR is usually used in moderate and advanced stages of dementia in people who are hospitalised or who live in nursing homes. It is a measure which, in our country, is used with a frequency of 40%, and in other countries the frequency is less: Australia (27%), France (17%), Italy (17%), USA (16%) or Sweden (15%).544 It is advisable for the MR to be maintained for a short period of time (hours, some days); however, it is usually prolonged up to weeks (average of 86.5 days).[544]	Observational study, 2+
MR is advised in people with dementia and agitation to achieve certain objectives:[545,546,543] To prevent injury to the actual patient. To prevent injuries to other people around them.	Observational study, 2+

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To avoid interferences in the treatment (routes, tubes, etc.)

To avoid material harm in the patient's environment.

To avoid escapes and prevent falls.

To help maintain the correct position of the body.

To achieve the centre's organisational objectives.

To maintain a comfortable social environment.

MR is used a lot on people with dementia who live in homes for the elderly. Its justification is doubtful in some cases. MR can become complicated, it represents a loss of autonomy, it alters their dignity, it affects their self-esteem and it may entail physical and psychological consequences.[543] — Observational study, 2+

MR must not be carried out[543] if:

- It is not indicated by the responsible health professional.
- There are alternative methods with similar effectiveness.
- The physician indicates that it should not be applied.
- It is prescribed as punishment or a show of force.
- It is applied to replace surveillance, convenience or comfort for the health and/or social staff, or residents of the centre.
- The state of health and comorbidities are not known.

It is indicated due to a lack of staff (health care places/staff ratio).

MR can be achieved by using a series of fastening elements approved in agreement with the legislation in force, and in perfect conditions. They can secure them to the chair or to the bed, or they can be protective bars, mittens or full pyjamas with zip to prevent manipulations.[541,546] — Descriptive study, 3; Expert opinion, 4

The decision to use MR must be prescribed by the responsible physician or doctor on duty. It is advisable for the decision to be shared with other members of the team. The nursing or medical staff is authorised, in emergency situations, to start the procedure. The decision must be signed by the physician, included in the medical record, and informed and accepted by the family.[541,543] — Descriptive study, 3; Expert opinion, 4

Four or five well-trained, coordinated, meticulous people are necessary for the MR, who will secure arms and legs and head, acting calmly and firmly, safely and with respect.[547,542,541] — Descriptive study, 3

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MR requires certain conditions, which are: a) padding and inspecting the fastenings each shift, verifying the state of the skin and/or possible injuries; b) when possible, maintain communication and contact when applying the care; c) frequently observe the patient and remove all dangerous objects from around him;d) prevention of pressure ulcers; e) use of technical aid (mattresses, local protections, silicone cushions, etc.); f) carry out necessary postural changes, mobilisation; g) provide periods of mobility and/or exercise, at least 10 minute every 2 hours; h) regulate and control the room temperature; i) help in personal hygiene, cleaning, drying, care of skin creases/folds, good skin hydration; j) offer liquid food, ensure adequate hydration; k) care to physiological needs; l) provide privacy.[547,542,541]	Descriptive study, 3 Expert opinion, 4
Additional measures must be taken to permit respect for the person's dignity and preserve their privacy. It is essential to involve the family in the care, as this favours comfort, accompaniment, proximity control, shortening of the procedure and reduction of the complications. The room must be quiet, well lit, well ventilated, guaranteeing easy contact with the personnel controlling the patient.[543]	Descriptive study, 3 Expert opinion, 4
Monitoring the person submitted to MR must avoid, detect and deal with complications. Medical evaluation must be guaranteed during the first hour. All remarks must be written down on the medical record. The risk of thromboembolism will be prevented, administering low molecular weight heparin (clexane, fraxiparine) at a dose of 0.4 mL/day, subcutaneous route.[547,542,541]	Observational study, 2+ Descriptive study, 3 Expert opinion, 4
The nurse will observe patient every 15 minutes, monitoring their vital signs, adapting diets, controlling liquid intake, urine output, and minimum personal hygiene care, postural changes, and erosions to the contact areas between the fastening straps and skin every 4-8 hours. During the first days of CR, there must be close supervision to detect any complications and changes early on. The training, qualification and attitude of the staff caring for the MR is very important.[547,542,541]	Descriptive study, 3 Expert opinion, 4
The MR must be brought to an end when there is a certainty of having suitably controlled the situation and this will be done progressively.[547,542,541]	Descriptive study, 3 Expert opinion, 4

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The risks or complications of mechanical restraint are included in **Table 8.**[547,542,541,543]	Observational study, 2+

Table 8. Mechanical restraint: Risks and complications[547,542,541,543]

Direct injuries: Nervous compression: Plexus, nerves Skin lesions: Ulcers, lacerations and haematomas Peripheral ischaemia Dislocation and fractures Pain Asphyxia on getting caught up with the fastenings Sudden death after a prolonged period of agitation and struggling
Indirect effects: Worsening of cognitive, social and functional Impairment, isolation, depression, increase of the state of confusion Loss of mobility, stability, equilibrium and gait. Increase of susceptibility to falls. Muscular atrophy Eating problems • Dehydration • Faecal impaction • Respiratory insufficiency • Thromboembolism • Faecal and/or urinary incontinence. • Multiple infections

Summary of evidence

3/4	Mechanical or physical restraint (MR) is used to control agitation/aggressiveness in people with dementia in moderate or severe stage, when there is a danger for the patient and for the environment, and these symptoms cannot be controlled with other restraint means (verbal or pharmacological). Fastening materials are used which prevent them from moving freely; they must be approved in agreement with the legislation in force, and in perfect state of preservation.[541,546,543] Safety and comfort measures must be stepped up. 4 or 5 trained, coordinated, meticulous people are necessary, who will secure arms and legs and head, acting calmly and firmly, safely and with respect.[547,542,541] The dignity and privacy of the person must be respected at all times. The family must be involved in the care and observation of the patients subject to MR. The room must be quiet, well lit, ventilated and safe.[548]
3/4	MR is a therapeutic protection measure, of exceptional use, which must only be applied under medical prescription. The benefits must exceed the risks of the measure.[543,541,542]

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2+	It is used frequently in Spain: 40% of people with moderate or severe dementia who present psychomotor agitation in hospitals or nursing homes.[544]
3/4	The decision about MR must be prescribed by the responsible physician or doctor on duty, signed, described in the medical record, informed and accepted by the family and shared with the other members of the team.[541,543]
2+	The objectives of the MR are: a) to prevent the patient from injuring himself and harming the environment; b) to avoid interferences in the treatment; c) to avoid escapes and prevent falls; d) to help maintain the correct position of the body; e) organisational objectives of the centre; f) comfortable social environment.[545,546,549]
2+	MR must not be used if it is not indicated.[543]
2+	It is advisable for MR to be maintained for a few hours or days; however it is usually prolonged for weeks (average of 86.5 days).[544]
2+/3/4	During the monitoring of CR, complications must be avoided, detected and dealt with. Medical evaluation and observation must be a constant feature during the first hour, taking note of all the changes. All remarks must be written down in the medical record. The nurse will carry out an extensive control every 15 minutes during the first hour, which will be spaced out later on.[547,542,541]
3/4	The MR will end when there is certainty of having managed to control the situation correctly. This will be done progressively.[547,542,541]
2+	There is a risk of multiple direct and indirect complications in people submitted to MR **(Table 8).** [547,542,541,543]

Recommendation

D	When it has not been possible to control a person with dementia with pronounced psychomotor agitation using verbal and/or pharmacological measures, and they continue to be dangerous or at risk of causing harm to themselves or to others, mechanical restraint (MR) must be proposed.
D	Approved fastening elements must be used in the MR, in agreement with the legislation in force, and they must be in perfect conditions to be effective and safe.
D	To achieve adequate and safe MR, a coordinated team is required, comprised of 4 or 5 well-trained people, who secure the patient properly, taking care not to harm him or her, and acting calmly and serenely, but firmly and surely. Throughout the entire treatment of MR, all those measures aimed at preventing direct or indirect complications must be maximised, guaranteeing the patient's comfort, privacy and respect. The MR measure will be stopped as soon as possible, and progressively, when the symptoms are under control.

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D	MR is a therapeutic physical restriction measure that must only be applied under medical prescription. It must only be used if other restraint methods are not applicable or have failed. Their objective is to protect the actual patient and other people, objects or surrounding environment. It cannot cause greater harm than the harm aimed to be avoided.
D	Excessive use of MR should be avoided in people with dementia, only using it when it is really justified, either due to the intensity of the symptoms and the possibility of them harming themselves or others. It must be as brief as possible to preserve the dignity and freedom of the person and reduce the risk of complications.
D	It is advisable for the MR to be a shared decision, agreed upon by the other members of the interdisciplinary team. The parentage details, the type and date of application of the measure, the reason for the restriction, the care guideline to follow, the periodicity of the controls, as well as the information given to the patient and to the family, as well as the informed consent, must be described in the clinical record, and signed by the physician.
C	The MR must be used in the following cases: to prevent injuries to the patients and to other people around them; to avoid interferences in the treatment (route, probes, etc.) and material damage to the patient's surroundings; to avoid escapes and prevent falls and maintain the correct position of the body; to achieve the centre's organisational objectives and maintain a comfortable social environment.
C	The contraindications of the MR must be respected and it must not be carried out if not explicitly indicated by the health professional responsible, or if, on the contrary, there are medical orders not to apply it. It must not be used, either, if there are equally effective alternative measures or procedures that have not been tried. They must never be used as punishment or as a show of force, or as a substitute for surveillance, or for the exclusive convenience or comfort of the professionals caring for them.
C	It is advisable for the MR to be maintained for a short space of time (hours, days). With monitoring in order to guarantee adequate observation, to avoid risks and complications. When appropriate control has been achieved, it must gradually be brought to an end.

13.5.3. What are the ethical and legal aspects of restraint?

The ethical aspects of restraints focus on a series of points: Beneficence: The decision to apply a restraints purports to protect, in the most adequate manner, the person with dementia and his environment.	Expert opinion, 4

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Non-maleficence: Applying the restraints with good care practice, respecting indications and contraindications, and using the best, most effective and safest procedure, with a control and monitoring plan that permits reaching the objective with the minimum risk of producing physical or psychological harm.

Autonomy: The procedure interferes with the freedom of movement of the person and the management of their body. It represents a loss of free decision and choice.

Justice: The decision to use a restraint must be in keeping with the behavioural disorder and the consequences that are to be avoided.

With respect to the legal aspects of the restraint, the following coercive measures in psychiatry can be specified:

- Involuntary internment
- Therapeutic isolation
- Therapeutic immobilisation
- Forced medical treatment

To start with, it must be pointed out that, with the exception of the case of involuntary internment **(question 13.5.4)**, in the Spanish legislation there is no regulation about these coercive measures, thus understanding that they form part of the therapeutic arsenal available to the practitioner, who will apply them according to clinical criterion and at a moment in the evolution that he deems appropriate, and whose possible application is, in one case, known and specifically agreed to by the patient when he is voluntarily admitted into hospital and, in another case, authorised by the judge when the patient is hospitalised in an involuntary manner.

Applicable legislation. Expert opinion, 4

Having established the above, noteworthy is the fact that, focusing on involuntary internment, during the course of it and during the application of the treatments, situations may arise that entail the limitation of other basic rights, as occurs with mechanical restraints, especially costly treatments, imposition of limitation of communications, etc. Thus, the question arises about whether a limited judicial control is sufficient to determine the origin of the internment or if this must be extended to the actual development of the treatment, as a guarantee of the patient's fundamental rights.

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In this sense, it is worth repeating that article 5 of the European Convention for the Protection of Human Rights and Fundamental Freedoms (Oviedo Convention, CEDH)[550] and the jurisprudence of the European Court of Human Rights (ECHR)[551] liken internment to detention and that, when its origin lies in a criminal process, detainees, prisoners and convicts possess a whole series of rights and obligations established in the Spanish Constitution, the Criminal Procedure Law, Criminal Code and LOGP (General Organic Law on Prisons), in such a way that if they come to harm, they can implore the relative legal guardianship.

Based on these considerations, there are more than a few –O'Callaghan Muñoz, Peces, Morate, García García, Aznar López, Bardají Gómez– who sustain, to a greater or lesser extent, the following:

1. The need for the judicial control of treatment when measures are applied that entail an extra restriction of the patient's fundamental rights, for example, mechanical restraints, isolation rooms, electroconvulsive treatments, psychosurgery, etc.
2. The approval of these practices for all centres, in order to identify the cases when it would be fitting to adopt these restrictions and integrate them into the so-called lex artis. Thus, this would also prevent it from being left to the free will of the management of the establishment or of the nursing staff.
3. The compulsory nature of a judicial review in inspections of the internment.
4. The appointments of a judicial defender for prolonged internment, pursuant to article 758.2 of the Law of Civil Procedure.

Thus, entering into a more detailed analysis of some of the conflictive cases mentioned above, we see:

Isolation rooms and mechanical restraints. As we have seen above, the former consist of confining a person, on their own, in a closed room, used for this purpose, for a limited period of time, to prevent the patient from being able to inflict serious harm on themselves or to third parties, including other patients or staff of the centre. The latter are defined as the use of physical or mechanical procedures aimed at limiting the movements of all or part of the body, in order to control their physical activity and protect them from injuries that they may cause to themselves or to others.

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The Parliamentary Assembly of the Council of Europe on psychiatry and human rights of 12 April 1994[552] indicates that mechanical restraint measures will not be used and that isolation will be applied very restrictively. In any case, the Ruling of the European Court of Human Rights pronounced in the case HERCZEGFALVY affirms that the use of coercive means form parts of the treatment, although the authors mentioned above state that this is only legally feasible when it is a question of controlling the patient's hetero-aggressive outburst, pharmacological treatments have no effect, they are adopted by prescription and under the control of the psychiatry specialist, and the dignity of the person is respected at all times. It would not be legal to resort to them, under any circumstance, to solve problems of lack of staff - which was the reason for the sentence by the ECHR in the matter referred to.

Right to be informed, both of the medical and legal aspects, when their mental state permits this. This means that they will be informed about both the medical and legal resources and means available to them to cope with their situation. In this sense, the general assembly of the World Association of Psychiatry held in Madrid on 25 August 1996 declared, on stating that the patient must be accepted as a common law partner in the therapeutic process.

Right to privacy: This is recognised in article 10.3 of the General Law on Health.[163] The aforementioned Parliamentary Assembly of the Council of Europe on psychiatry and human rights, 12 April 1994,[552] expresses that accommodation in large size rooms must be avoided.

Adequate treatment: The jurisprudential doctrine of the Supreme Court is consistent in the sense that the doctor-patient relationship only imposes on the former an obligation regarding activity and resources and not results, aimed at providing all the care required according to the state of science. In those cases where, following prolonged internment, an improvement does not occur and the Administration does not provide an adequate device in a reasonable length of time, some of the authors mentioned sustain that the transfer of the patient to an adequate centre must be ordered.

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Based on the above considerations, some authors propose -the aforementioned and Silvia Ventura- that legislative reforms should be carried out in order to describe the regulation of involuntary internment is in such aspects as the application of especially aggressive treatment, rights to privacy, and to the communication and effectiveness of the advance directive. What does seem obvious, at least from a current judicial perspective, is that there are no mechanisms that permit establishing a jurisdictional control of the development of psychiatric treatment, beyond the cases of medical responsibility, if negligent action or omission, a real danger and an adequate causal relationship between them concur. But, it is an action of redress and not of control.

Finally, and given its especial importance in the psycho-geriatric population, mention must be made of article 4 of Spanish Law 39/2006, 14 December, on the Promotion of Personal Autonomy and Care for dependent persons[516], whereby it establishes that dependent people will enjoy all the rights established in the applicable legislation, and especially the following:

- To enjoy basic freedoms and human rights, with full respect for their dignity and privacy.
- To receive, in understandable and accessible terms, full and ongoing information related to their situation of dependence.
- To be informed about whether the procedures applied to them can be used in agreement with a teaching or research project, in which case the prior express written authorisation from the dependent person or the person representing them is necessary.
- For confidentiality to be respected in the compilation and processing of their data pursuant to Spanish Organic Law 15/1999, 13 December (RCL 1999, 3058) on Personal Data Protection.[553]
- To decide, when they have sufficient capacity to act, about the guardianship of their person and their assets, in the event that they lose their self-management capacity.
- To freely decide about admission into a home. - To the full exercise of their jurisdictional rights in the case of involuntary internment, guaranteeing a contradictory process.

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Article 8 of Basic Law 41/2002, 14 November, regulating the patient's autonomy and rights and obligations with respect to clinical information and documentation, deals with informed consent for all types of procedures, including restraints, which in this case is protective but represents risks and negative effects on health. The patient must be duly informed, if possible, and failing this, the legal representative or person responsible de facto for the person affected. Written consent must be requested from family and/or representatives, and if possible also from the patient.	Applicable legislation
There are a series of principles of the United Nations[514] in favour of older person and among them those affected by dementia. In point 9.1 it says that all patients are entitled to be treated as least restrictively as possible and to receive the least restrictive and altering treatment that corresponds to their health needs and the need to protect the physical safety of third parties.[554] In point 11.1 it declares that no patient will be submitted to physical restrictions, or only when this is the only means available to prevent immediate or imminent harm to the patient or to third parties. These practices will not be prolonged more than the time strictly necessary to reach this objective. This measure must be noted down in the medical record, (reason, nature and duration). A qualified person must regularly supervise the person in restraint. The legal representatives and/or closest relatives must be informed.	Applicable legislation Expert opinion, 4

Summary of evidence

2+	Mechanical restraint (MR) has its indications, contraindications, limitations, risks and complications in people with moderate or severe dementia **(question 13.5.2).**[140]
4	Ethical aspects about restraint: Beneficence: protect, in the most adequate manner, the person with dementia and his environment. Non-maleficence: Do so using good practices, respecting indications, contraindications and using the best procedure, effectively and safely. Autonomy: interferes with the freedom of movement of the person and the management of their body. Justice: It must be in keeping with the behavioural disorder and the consequences that are to be avoided.

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	Legal aspects about restraint: a) involuntary internment; b) therapeutic isolation; c) therapeutic immobilisation, and d) forced medical treatment.
Applicable legislation	Legislation only exists in Spain on involuntary internment **(question 13.5.4.)** Coercive measures form part of the therapeutic arsenal, they must be applied according to clinical criterion, at the right time, prior authorisation or consent from the patient or from the judge if the admission is involuntary. Spanish and European legislation compare internment with detention, with rights and obligations of the holders (in this case, the patients). (Spanish Constitution, Criminal Procedure law, Criminal Code and LOGP): Expert opinion: 1) need for judicial control when treatment measures are applied that entail a restriction of the patient's fundamental rights; 2) approval of such practices for all centres; 3) compulsory nature of the judicial examination in inspections of the internment, and 4) appointment of the judicial defender for very prolonged interments (article 758.2 of the Civil Procedural Law) Aspects with legal implication: Isolation rooms and mechanical restraints, right to be informed, right to privacy and adequate treatment. Article 4 of Spanish Law 39/2006, 14 December, on the Promotion of Personal Autonomy and Care for dependent persons[516], whereby it establishes that dependent people will enjoy all the rights established in the applicable legislation, and especially the following: Enjoy basic freedoms and human rights, with full respect for their dignity and privacy. Receive, in understandable and accessible terms, full and ongoing information related to their dependent situation. Be informed about whether the procedures applied to them can be used in agreement with the teaching or research project, in which case the prior express written authorisation from the dependent person or the person representing them is necessary. Respect confidentiality in the compilation and processing of their data pursuant to Spanish Organic Law 15/1999, 13 December (RCL 1999, 3058) on Personal Data Protection.[553] Decide, when they have sufficient capacity to act, about the guardianship of their person and their assets in the event that they lose their capacity to manage for themselves. Freely decide about admission into a home. Full exercise of their jurisdictional rights in the case of involuntary internment, guaranteeing a contradictory process.

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Applicable legislation	Informed consent (Law 41/2002, article, 14 November):[514] The patient must be duly informed, if possible, and failing this, the legal representative or person responsible de facto of the person affected. Written consent must be requested from family and/or representatives, and if possible also from the patient.
Applicable legislation/ 4	Any patient will have the right to be treated as least restrictively as possible and to receive the least restrictive and altering treatment that corresponds to them for their health needs and the need to protect the physical safety of third parties (Principle 9.1 of United Nations).[554] No patient will be submitted to physical restrictions are only when this is the only means available to prevent immediate or imminent harm to the patient or to third parties. These practices will not be prolonged more than the time strictly required to reach this objective (principle 11.1 of United Nations).[554] This measure must be noted down in the clinical record (reason, nature and duration). A qualified person must regularly supervise the person in restraint. The legal representatives and/or closest relatives must be informed.

Recommendation

D	As restraint measures affect people's freedom of movement, and their free of decision, and they are also not free from complications, before starting to apply them, the legal regulations that govern them must be carefully and strictly observed and enforced. The action must contemplate the principles of beneficence, non-maleficence and justice, and respecting the right to personal autonomy.

13.5.4. What are the indications for involuntary admission and what process must be followed?

People with moderate or advanced dementia, Alzheimer's or other related dementias may present behavioural disorders such as aggressiveness, states of agitation, delusions, aberrant motor activity and disinhibition, which if severe, may become dangerous for the actual patient and/or for the people around them. If they cannot be controlled with non-pharmacological or pharmacological measures by oral route, they will require more decisive measures, and will require admission to control the crisis and at the same time give the family a rest and provide them with the possibility of reorganising themselves again. If admission is possible, it should be carried out in units that are specialised in this type of alteration.[543]

The crises, or behavioural decompensations, may be caused by different reasons, including systemic processes, worsening of sensory alterations or the actual evolution of the disease. Programmed or urgent, voluntary or involuntary admission must be used to clear up the aetiology of the process, establish the most adequate treatment strategy. It may be even require verbal, pharmacological and physical restraint manoeuvres.[556,545]

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The admission indications for crisis control are:[543]

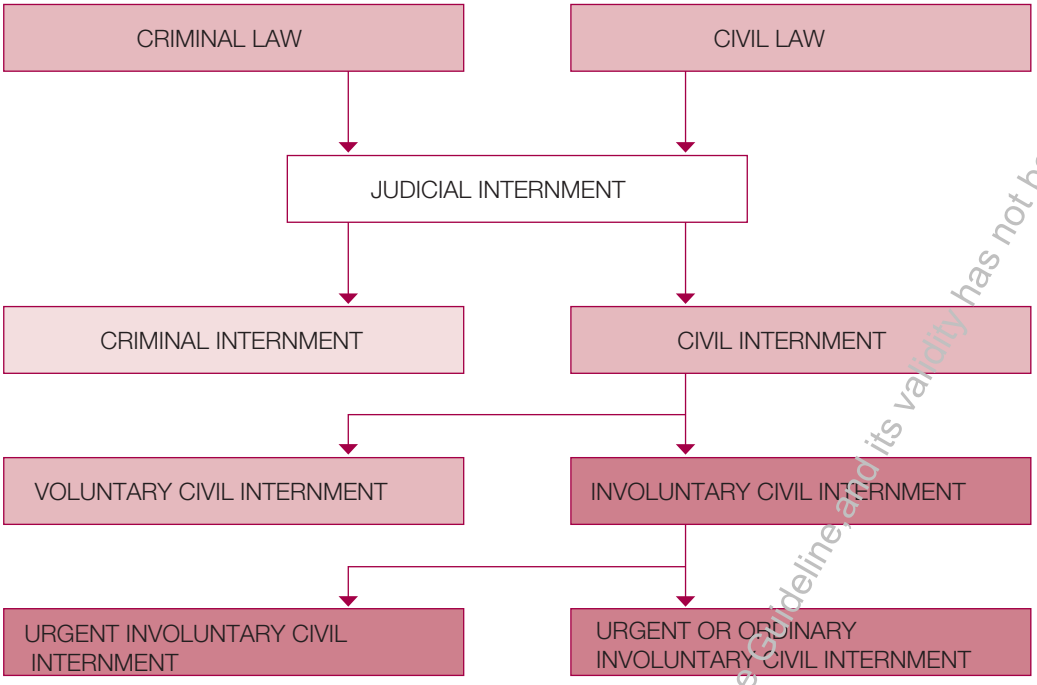
- Situations or behaviours that threaten the physical integrity of the person affected, or of other people of their family/social environment.
- Psychomotor agitation that is not controlled with first level therapeutic procedures: Verbal restraints, modification of the environment, oral sedation pharmacological measures.
- Need for isolation from the environment to try to decrease or eliminate the stimuli that generate the behavioural decompensation and/or the state of agitation.
- Optimise the treatments, when safe parenteral treatment is required and specialised personnel.

People with dementia, from moderate to advanced, are not usually able to decide on their admission. Sometimes they vehemently refuse or oppose it. The family may be overwhelmed by the clinical situation and be close to claudication.

The clinical situation set out above may, following a therapeutic criterion, be tributary of the admission of the patient into a health institution in order to control their symptoms and their evolution better. It is an admission that is specifically characterised because it is carried out in respect of patients who, due to their own pathology, are not able to decide for themselves about the therapeutic proposal which, according to clinical criterion, is made by the practitioner, regardless of the fact that the patient are submitted to parental authority or to guardianship. The existence in these clinical situations of two circumstances that have special legal relevance, such as, on the one hand, the situation of defencelessness of the actual patients (derived from their pathology) and, on the other hand, the restriction of individual freedom represented by the therapeutic internment measure, led to the enforcement of a legal regulation in civil law (legal field that encompasses all physician-patient relationships and which differentiates it from the criminal internment, which occurs in other circumstances and is governed by other criteria). This legal regulation is established today in article 763 of Law 1/2000, 7 January, on Civil Procedure (LEC).[557] Special mention must be made of the sensitivity of the Office of the Public Prosecutor towards the special characteristics of the psychogeriatric population and their health care, and, more specifically, their admission into Geriatric Centres, and which led, in 1990, to the issuance of Instruction 3/1990 of the Office of the Public Prosecutor, which especially mentions the admission of people into psychogeriatric homes,[558] and which recalls the obligation for informed consent from the patient for admission into a health centre. This consent is set out as an expression of free and conscious will, referring to the aforementioned article 763 of the LEC, when these circumstances are not present in the patient.[557]

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Figure 13.1. Types of internment



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This article 763 of the LEC differentiates two types of involuntary civil internment, according to an emergency criterion, namely: Urgent involuntary civil internment and non-urgent or ordinary involuntary civil internment, respectively **(Figure 13.1).**

Urgent involuntary civil internment: This is internment which, due to the patient's clinical situation, must be carried out immediately. The following legal requirements must be fulfilled:

- Communication of the internment by the person responsible for the centre where it takes place, to the court corresponding to the place where the centre is located as soon as possible, and in any case within 24 hours.
- Judicial ratification within 72 hours at the latest from the moment the court is informed of the internment and after having been carried out by the responsible judge:
  - Examination by them of the person to be interned.
  - Listen to the decision of a practitioner appointed by him (in practice and in the majority of the cases this is the forensic medical examiner).
  - Listen to Public Prosecutor's Office and any other person whose appearance is deemed advisable or is requested by the person affected by the measure.
  - Practice any other test deemed relevant for the case.
  - In all the actions, the person affected by the hospitalisation measure may have their own representation and defence. If this is not the case, the person will be defended by the Public Prosecutor, providing that this is not the party promoting the procedure.
- Evolution: Obligation of the doctors attending to the interned person to periodically inform the court, and every six months at the latest (unless the court, depending on the nature of the disorder that gave rise to the internment, indicates that this should be done in a shorter period of time).

about the need to maintain the measure, without prejudice of other reports that the court may require when it deems this relevant. After receiving the aforementioned reports, the court, after carrying out, where fitting, the actions it deems essential, will resolve on what has to be done about the continuation or not of the internment.

- Discharge: When the doctors attending to the interned person consider that it is not necessary to maintain the internment, they will discharge the patient, immediately informing the same court that was notified when the internment began.

Thus, urgent involuntary civil internment is defined as **(Table 9).**

- It is considered as a therapeutic measure that is governed by clinical criteria.
- The legal requirements set out above must be fulfilled: Notification to the court, plus subsequent judicial ratification plus regular information obligation.
- It will be carried out in the most adequate type of centre according to the characteristics of the individual's age and mental pathology.
- Its duration in time will depend on the doctor's criterion.
- There are two possibilities of evolution, and the responsible court must be notified of them: Discharge by order of a doctors or the internment becomes voluntary, respectively.
- It is recommendable to inform the responsible courts of any possible contingencies that might occur during the internment (e.g. escapes, etc).
- It may be revoked by the judge, if after practising the legally established diligences within a period of 72 hours after admission, its need is no longer observed

Non-urgent or ordinary involuntary civil internment: This is internment which, due to the patient's clinical situation, must not be carried out immediately.

In this case, and unlike urgent internment, as there is no clinical situation that requires immediate internment, the judicial authorisation will be prior to the admission and therefore it will not be a ratification of a doctor's decision. This authorisation will also fulfil the requirement for the judge to examine the patient, hearing the decision of a doctor appointed by him (in practice and in the majority of the cases this is the forensic medical examiner), Public Prosecutor and any other person whose appearance the judge deems advisable or is requested by the person affected by the measure.

Likewise, on the one hand, the compulsory nature of regularly informing the court, and every six months at the most (unless the court, in agreement with the nature of that cause the internment, indicates a shorter period of time) on the need to sustain the measure, is maintained regardless of any other reports that the court may request when it deems this relevant and, on the other hand, to inform of the discharge of the patient when the doctors attending to the interned person clinically deem this appropriate.

Thus, non-urgent or ordinary involuntary civil internment has the same characteristics as urgent internment, except for **(Tables 9 and 10).**

- The judicial authorisation (which fulfils the same requirements regarding procedure as the urgent one) is prior to the admission of the patient in the centre.
- It may be revoked by the centre if the centre believes that the criteria established by the doctors for admission are not satisfied.

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Table 9. Urgent or involuntary civil internment

Legislation	Article 763 of the Civil Procedure Law.
Consideration	Internment is a therapeutic measure
Requirements	1) Notification to the judge where the centre is located in less than 24 hours. 2) Judicial ratification in less than 72 hours and after examination of the person affected + hearing of any person 3) Evolution report to the court every 6 months 4) Notification to the court of discharge on the physicians orders
Criteria	Clinical
Judicial decision	Judicial authorisation not prior (or after), admission Gratification
Type of centre	The most adequate for the characteristics of the individual's age and mental pathology.
Duration	According to doctor's criterion
Evolution possibilities	Discharge Change to voluntary
Special circumstances (Escapes, permits, changes of units, etc)	Not compulsory but recommendable
Revocation of the internment by the centre and/or by its doctors	Yes by the judge

Table 10. Non-urgent or ordinary involuntary civil internment

Legislation	Article 763 of the Civil Procedure Law.
Consideration	Internment is a therapeutic measure
Requirements	1) Prior judicial notification of the individual + hearing of any person deemed appropriate. 2) Evolution report to the court every 6 months 3) Notification to the court of discharge on the doctor's orders
Criteria	Clinical
Judicial decision	Judicial authorisation prior to admission from the court where the affected person
Type of centre	The most adequate for the characteristics of the individual's age and mental pathology.
Duration	According to doctor's criterion
Evolution possibilities	Discharge Change to voluntary
Special circumstances (Escapes, permits, changes of units, etc)	Not compulsory but recommendable
Revocation of the internment by the centre and/or its doctors	Yes by the centre's doctors

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Summary of evidence

4	People with moderate or advanced dementia, Alzheimer's or other related dementias may present behavioural disorders such as aggressiveness, states of agitation, delirium, aberrant motor activity and disinhibition, which is severe, may become dangerous for the actual patient and/or for the people around them. If these BPSD cannot be controlled with non-pharmacological or pharmacological measures by oral route, in outpatients (primary or specialised care) they will require more decisive measures, which will require admission to control the crisis, to give the family a rest and the possibility of reorganising themselves again. Admission should be carried out in units specialised for this type of alteration.[543]
4	The crises or behavioural decompensations may be caused by systemic processes, worsening of sensory alterations or the actual evolution of the disease. Programmed or urgent, voluntary or involuntary admission must be used to clear up the aetiology of the process, establish the most adequate treatment strategy. Verbal, pharmacological and physical restraint manoeuvres may even be required.[556,545]
3	The admission indications for crisis control are:[543] • Situations or behaviours that are threatening for the physical integrity of the person affected, or for other people of their family/social environment. • Psychomotor agitation that is not controlled with first level therapeutic procedures: • Need for isolation from the environment to try to decrease or eliminate the stimuli that generate the behavioural decompensation and/or the state of agitation. • Optimise the treatments, when safe parenteral treatment is required and specialised personnel.
Applicable legislation	If involuntary internment is urgently required, for a person with dementia and severe BPSD, it will be the physician attending to that person who shall take the decision. In this case, the person responsible at the centre must inform the competent court as soon as possible.
4	Admissions in order to control crisis situations must be as short as possible, guaranteeing, at the time of discharge, that the symptoms have been controlled, that the environment and the receiving family are adequate, the caregiver's burden has been reduced and support measures for them to continue with their care work have been established.[543, 556,545]
Applicable legislation	The legal regulation that protects people who are involuntarily submitted to admission into hospital must be respected. The opinion and consent of the family will be required as well as the judicial authorisation before carrying out the admission. The reasons must be suitably justified, ensuring their beneficence and respect for the dignity and freedom of the person affected.

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	People with moderate to advanced dementia are defenceless with respect to their own pathology. Instruction 3/1990 of the Public Prosecutor, which makes special mention of the admission of people into psychogeriatric homes, **recalls the obligation for informed consent by patients;** however, they are usually able to decide on their admission. Voluntary admission represents a restriction of individual freedom, it is legally regulated in article 763 of **Law 1/2000, 7 January, on Civil Procedure.** This article 763 of the LEC differentiates two types of involuntary civil internment, according to an emergency criterion, namely: Urgent involuntary civil internment and **non-urgent or ordinary** involuntary civil internment, respectively,
Applicable legislation	**Urgent** involuntary civil internment: **This is internment which, due to the patient's clinical situation, must be carried out immediately.** It is legislated in article 763 of the Civil Procedure Law. Internment is considered as a therapeutic measure. The following requirements must be fulfilled: 1) notification to the court where the centre is located in less than 24 hours; 2) judicial ratification in less than 72 hours and after examining the person affected, plus hearing of any other person; 3) evolution report to the court every six months; 4) notification to the court of discharge ordered by a physician. The criteria are clinical. The judicial decision gives authorisation not prior to the admission, which is later ratified. The internment centre must be the most adequate for the characteristics of the individual's age and mental pathology. The duration will be based on the doctors' criterion. The internment may be revoked by the judge.
Applicable legislation	**Non-urgent or ordinary** involuntary civil internment: **This is internment which, due to the patient's clinical situation, must not be carried out immediately.** It is legislated in article 763 of the Civil Procedure Law. Internment is considered as a therapeutic measure. The requirements are: 1) prior judicial examination of the individual plus hearing of any person deemed appropriate; 2) evolution report to the court every six months; 3) notification to the judge of discharge on doctors' orders. The criteria are clinical. Judicial authorisation is required prior to admission from the court where the affected person resides. The centre must be the most adequate for the characteristics of the individual's age and mental pathology. The duration will be based on the doctors' criterion. The revocation of the internment is carried out by the doctors of the centre.

Recommendation

C	People with dementia with severe behavioural disorders that entail a risk for the actual patient and/or for the people around them, and which are not adequately controlled in outpatients (primary and specialised care), should be admitted to control the crisis and enable the family to rest. Admission into these centres should satisfy the dual objective of diagnosis and treatment.

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D	Admissions in order to control crisis situations must be as short as possible, guaranteeing, at the time of discharge, that the symptoms have been controlled, that the environment and the receiving family are adequate, the caregiver's burden has been reduced and support measures for them to continue with their care work have been established.
According to applicable legislation	The legal regulation that protects people who are involuntarily submitted to admission into hospital must be respected. The opinion and consent of the family will be required as well as the judicial authorisation before carrying out the admission. The reasons must be suitably justified, ensuring their beneficence and respect for the dignity and freedom of the person affected.
D	If involuntary internment is urgently required, for a person with dementia and severe behavioural disorders, it will be the physician attending to that person who shall take the decision. In this case, the person responsible at the centre must inform the competent court as soon as possible.

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14. Care of people with advanced dementia and at end-of-life stage

Questions to be answered

14.1. Which criteria define an advanced and terminal situation with prognosis of limited life in patients with dementia?

14.2. Is it possible to determine, in people with advanced dementia at end-of-life stage, if their survival is going to be less than 6 months?

14.3. When must palliative care be started on people with dementia?

14.4. Which are the most suitable health resources to care for people with dementia at end-of-life stage?

14.5. How are the clinical manifestations and the needs of people with dementia and their caregivers identified and managed in the advanced and terminal stage of the disease?

14.6. How can worsening due to the natural evolution of the illness be differentiated from worsening caused by a potentially reversible concomitant process?

14.7. What are the objectives of caring for people with dementia in terminal phase?

14.8. What extraordinary or greater measures should be questioned in the care of people with advanced dementia?

14.9. What therapeutic intermediate measures should be questioned in the care of people with advanced dementia?

14.10. What information and aid must be provided to the families of people with terminal dementia?

14.11. What legal regulations and ethical principles exist relating to communication with people with advanced dementia or with their families at the end-of-life stage?

14.12. In what cases is a post-mortem pathoneurological study recommended?

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14.1. Which criteria define an advanced and terminal situation with prognosis of limited life in patients with dementia?

Advanced stage of dementia corresponds to stages 6 and 7 of the GDS,[559] FAST[560] scales and with stage 3 of the CDR.[561]	Descriptive study, 3

Although the scales have been designed for AD, they can be applied to VD and to other degenerative dementia.

In these stages of the disease, patients have great difficulty carrying out BADL (getting dressed, having a bath, washing and keeping control of the sphincter). There is a hierarchical order of functional loss in the GDS and FAST scales, which sub-classifies the stages of dementia, adding more severity in each one of them. In stage 7, ability to walk, remain seated, hold their head upright, smile, and communicate through verbal language and gestures is altered.[559,560]

The terminal stage of dementia is difficult to identify as it is a progressive and chronic degenerative process. It could be defined by the following characteristics:[562,563,564,565,566,567]

Descriptive study, 3

1. Severe cognitive impairment (score of under 6 on the MMSE or cognitive impairment that prevents its execution).
2. Loss of the reasonable possibility of benefiting from specific pharmacological treatment.
3. Stage GDS 7 (severe disability for BADL, unable to speak or does not make sense when communicating).
4. Multiple comorbidity with severe, multifactorial and changing symptoms (aspiration pneumonia, dyspnoea, infections of the upper urine tract, sepsis, pressure ulcers, pain, serious eating disorder).
5. Serious difficulty to intake food, either due to dysphagia or rejection, with a weight loss or more than 10% in the previous 6 months and serum albumin of less than 2.5 mg/dl.
6. Unable to carry out any voluntary activity with a certain purpose. Unable to recognise the caregivers.
7. Great emotional impact on the patient, family and professional team caring for them, related partly to the proximity of death.
8. Relatively short vital prognosis, depending on the age and comorbidity (it varies between a few months and 2 years, although it may be greater).
9. Subsidiary palliative measure person.

Although the survival time or life prognosis has traditionally been used as a basic element in defining terminal disease, recently the concept of "advanced and terminal situation of chronic evolution disease with limited life prognosis" (SEAT)[568] has been developed. This term can be applied to advanced dementia.[565,566,569]

Expert opinion, 4

These patients generate a great demand for attention and the main objective is to promote the comfort and quality of life of the patient and of the family, based on controlling symptoms, providing emotional support and good communication.

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A screen method has recently been decribed that permits identifying patient, with or without dementia, in SEAT state. The assessment must be carried out by a traditional multidisciplinary team and the GSF (Gold Standards Framework) is used as an instrument **(Table 11)**.[570,566,569]	Observational study, 2++

Table 11. Gold Standards Framework Criteria.[57]

1. A question: Would you be surprised if this patient were to die within the next year?
2. Expectations or demand for limitation of the therapeutic effort or palliative measures (patient, relatives or members of the professional team)
3. General clinical criteria: a. Existence of comorbidity. b. Limitation of functional state. c. Fast and sustained deterioration attributable to dementia (reject potentially reversible intercurrent processes) d. Clinical and analytical signs of malnutrition (10% weight loss over the last six months, serum albumin under 2.5 mg/dl
4. Additional parameters (above all in fragile elderly, with pluripathology and dependence): a. Resources consumption (more than three urgent admissions in the previous 3 months) b. Repeated opportunistic infections (more than three in the previous 3 months) c. Decubitus ulcers resistant to traditional treatment (more than 3 months' evolution)
5. Other elements to consider: a. Frequent situations that require ethical-clinical decisions (nutrition, hydration, resources, institutionalisation, etc.) and planning of advanced care
6. Frequent crisis of needs, which appear in a more or less predictable manner, which require management of the case as a work method

Summary of evidence

3	Advanced stage of dementia corresponds to stages 6 and 7 of the GDS and FAST scales and to stage 3 of the CDR.[559,560,561]
4	The term SEAT is useful to define the "advanced and terminal evolution situation and with limited life prognosis of a chronic disease", as is the case of dementia.[571]
2++	The identification of people with SEAT is carried out by assessment made by a traditional multidisciplinary team using the GSF screen instrument.[570]
2++	The main objective of the assessment using the GSF scale is to identify patients in SEAT situation (quick and worsening, functional state, comorbidity, nutritional state). Determination of the knowledge and expectations of the patient, family and of the professionals about the immediacy of death, opinion about palliative measures and limitation of the therapeutic effort, and of other additional parameters such as opportunistic infections, decubitus ulcers and superimposed crisis situation.[570]

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3	Some characteristics of advanced dementia in terminal stage are: cognitive impairment (MMSE < 6), no expectations of benefit with the specific pharmacological treatment, GDS-FAST of 7, severe malnutrition (weight loss > 10% in previous 6 months, serum albumin of < 2.5 mg/dl), need for palliative measures and great impact on caregiving family.[572,573,562,563,564,574]

Recommendation

D	The term SEAT can be used in advanced degenerative dementia in terminal phase, which corresponds to stage GDS 7.
B	Evaluate the stage of SEAT using the Gold Standards Framework (GSF) instrument. The GSF is recommendable to find out the expectations of the caregivers regarding the death of the patient, the need to establish palliative measures, the limitation of the therapeutic effort, and about the consumption of resources, complications and crisis situations.
C	Advanced dementia must be considered as terminal dementia if cognitive impairment is severe and there is severe dependence for the BADL, there is no possibility of therapeutic benefit with the specific treatment, there is multiple comorbidity and a suitable nutritional status cannot be maintained.

14.2. Is it possible to determine, in people with advanced dementia at end-of-life stage, if their survival is going to be less than 6 months?

The prediction of survival in advanced and terminal dementia is a complicated but useful process to be able to establish the therapeutic strategy and therapeutic effort limits and to suitably inform the families.

The majority of scales to determine survival in terminal patients have been developed to be applied to patients with cancer.

Lacking simple and validated scales to predict survival in patients with dementia, some variables can be used that usually predict life expectancy of less than 6 months, such as: Severe cognitive impairments GDS-FAST 7c-7d, severe disability with D on the Katz index or worse, deficient nutritional state with a weight loss of > 10% during the previous 6 months and serum albumin of < 2.5 mg/dl, recurrent infections and decubitus ulcers.[575,576,577]	Observational study, 2++

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Other data that predict a bad vital prognosis are: The presence of motor disorders, apathy, hallucinations, male sex, over 85 years of age and background of diabetes and cardiovascular disease.[578,579,577,580,581]	Observational study, 2++
The most frequent causes of death in this period are pneumonia, other infectious processes and malnutrition.[572,582]	Observational study, 2++

People with terminal dementia are included within the group of pathologies where patients must not be submitted to inadequate interventions, but must receive palliative measures that improve their comfort, decrease suffering and do not unnecessarily prolong life.[575,583,584]

Summary of evidence

2++	The variables that best predict survival of less than 6 months in people with terminal dementia are: Katz index of D or worse, GDS-FAST stage 7c-7d, deficient nutritional state (weight loss of > 10% during the previous 6 months and serum albumin of < 2.5 mg/dl), recurrent infections and presence of decubitus ulcers.[575,576,577]
2++	Other signs of bad vital prognosis in advanced dementia are: presence of motor disorders, apathy, visual hallucinations, male sex, over 85 years of age and background of diabetes and cardiovascular disease.[578,579,577,580,581]
2++	The most frequent causes of death in terminal dementia are pneumonia, other infectious processes and malnutrition.[572,582]

Recommendation

B	To establish a life prognosis of less than 6 months in a person with advanced dementia, parameters with predictive power must be identified, such as degree of cognitive impairment, degree of functional disability, presence of malnutrition and presence of systemic complications and comorbidity.

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14.3. When must palliative care be started on people with dementia?

The World Health Organisation (WHO) defines palliative care (PC) as "the approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual". They are non-curative, active, ordinary measures, based on scientific evidence and well-proven experiences, which pursue the comfort of the person affected and of the family environment, covering the needs that are generated and with the main objective of improving their quality of life.[572]

PC must be applied to all terminal and chronic diseases of clinical practice, including people with dementia.[585,572,25,517,575,583]	Expert opinion, 4
PC must be introduced as soon as possible when the first unsolved needs or problems arise, and to prevent the appearance of undesirable predictable problems. It must be maintained and intensified throughout the entire process; it is most needed in advanced stages when patients no longer respond to specific treatment and all interventions become palliative ones. Curative and palliative measures coincide in time. The proportion and transit towards exclusively PC management is gradual and personalised.[585,517,586,564]	Descriptive study, 3
PC in dementia must relieve physical and psychological suffering, provide the best possible quality of life and consider death as a natural process. It does not consist of accelerating or delaying the death process and must integrate psychosocial and spiritual aspects, supporting family and friends during the disease and throughout the grief process.[587,571,575]	
The need to receive PC is encoded according to the ICD as a secondary diagnosis, after the base disease, with the supplementary classification codes of factors that have an influence on state of health and on the contact with the necessary services (ICD-9: V66.7; ICD-10: Z51.5).[573]	Expert opinion, 4
All health and social services professionals caring for people with dementia must be prepared, theoretically and practically, to offer PC. There are specialised PC teams comprised of physicians, nurses, psychologists and social workers.	Expert opinion, 4

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Summary of evidence

4	There is a universal agreement to use PC in the management of people with dementia.[585,572,25,517,575,583]
3/4	The aim of PC is to relieve physical and psychological suffering, promote quality of life and consider death as a natural process. Psychosocial and spiritual aspects must be integrated, giving support to relatives throughout the entire process. They must be introduced after the diagnosis and be intensified throughout the evolution[587,571,575,585,517,586,564]
4	Health and social services professionals caring for people with dementia must be prepared to offer PC.

Recommendation

D	Palliative care (PC) must be implemented in the management of people with dementia, and this must be introduced early on after carrying out the diagnosis and it must be prolonged and increased as the disease progresses.
D	The aim of PC is to relieve physical and psychological suffering, provide quality of life and consider death as a natural process. Psychosocial and spiritual aspects must be integrated, giving support to relatives.
D	Health and social service professionals must be prepared to offer PC to people affected by dementia.

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14.4. Which are the most suitable health resources to care for people with dementia at end-of-life stage?

PC in people with advanced dementia can be offered in the different health services and areas, both at home and in hospital or in social health centres, with or without specific palliative care units.[573,575,517]	Expert opinion, 4
This care must be provided to all patients who need it and when they need it, quality care must be guaranteed and there must be coordination between the different healthcare levels for the process to be seamless.[573,588,589,575]	Expert opinion, 4

The National Palliative Care Strategic Plan establishes an organised system to guarantee coordination between the different social health resources, promoting integrated actions. The Plan establishes that there must be healthcare continuity of the PC throughout the entire illness, once the care has been established, promoting the training of professional teams that care for these patients.[573]

Expert opinion, 4

The organisational model proposed contemplates:

Basic PC level (primary, general or palliative approach): This refers to the care that must be provided to all people and by all health professionals. The specific needs must be assessed and responded to, as well as knowing when patients must be referred to other services.

Specific PC level (secondary, specialised or advanced): This contemplates more complex interventions that require specialised procedures or techniques, or that require performing additional diagnostic tests or specific treatment that require a hospital environment to control them.

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Summary of evidence

4	All people are entitled to receive PC when they need it, at any of the healthcare levels. The use of PC is probably beneficial. [573,588,589,575]
4	Healthcare continuity must be maintained when receiving palliative type measures.[573,588,589,575]
4	Coordination between the different healthcare levels in PC is desirable when caring for people in advanced and terminal stage of dementia, including the specific PC units when more complex needs have to be attended to.[573]

Recommendation

D	All people with advanced dementia must be provided with PC, whatever the healthcare level that is being applied.
D	Healthcare continuity must be maintained in PC when there is a change in the healthcare level of the person with advanced dementia.
D	Health organisations should foster training of all professionals to provide basic PC.

D	Health organisations must guarantee accessibility to specialised PC when necessary.
D	Coordination between the different services and healthcare areas must be guaranteed, as well as continuity of palliative care.

14.5. How are the clinical manifestations and the needs of people with dementia and their caregivers identified and managed in the advanced and terminal phase of the disease?

To identify and quantify the needs of people with advanced dementia in terminal stage and the needs of their caregivers, it is necessary to carry out an comprehensive, global and multidisciplinary initial evaluation, bearing in mind all the aspects that converge in this stage of the disease. The assessment system must be homogeneous and easy to apply, with validated and reliable, simple, fast, objective and standardised scales. A periodic control of all the variables must be carried out.[590,591]

Expert opinion, 4

In general, the evidence about patients in terminal stage who receive PC comes from studies performed on cancer patients; research on non-oncological diseases must be improved.575 The National Palliative Care Strategic Plan[573] acknowledges the creation of specific PC programmes for invalidating and progressive degenerative neurological diseases, such as cerebrovascular disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis and dementia, as an improvement that must be carried out. Especially important is the need to have specific PC programmes in advanced and terminal dementia; this research area still has to be developed as dementia is one of the most important causes of death in elderly patients.[592]

In this question, some aspects about management in PC that may be important in patients with dementia will be commented on, such as the management of some BPSD (delirium, depression and anxiety), dysphasia and nutrition and hydration alterations, pain, fever and decubitus ulcers. Psychosocial type aspects, information to families and attention to spiritual aspects during the final days and grief will also be commented on.

The authors have been inspired mainly by the CPG on Palliative Cures of the National Plan for the National Health System (2008)[575] (http://www.guiasalud.es/GPC/GPC_428_ Paliativos_ Osteba_compl.pdf), where it is possible to find comprehensive information about managing complications that appear in advanced and terminal stages of chronic diseases and that will not be commented on here (asthenia, anorexia, dyspnoea, coughing, mouth infections, nausea and vomits, diarrhoea, constipation, intestinal obstruction, ascites, hiccups, pruritus, haemorrhage, convulsions, metabolic disorders, etc.).

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Delirium

Delirium in patients with advanced and terminal dementia (GDS 6-7) is very difficult to diagnose, as their verbal communication ability is varied and reduced or non-existent, and the sudden onset of psychomotor agitation may be their only clinical expressiveness.[575]

In patients with some sort of verbal communication, delirium may be identified via the Confusion Assessment Method (CAM), a validated and easy-to-use instrument, which assesses four items: Acute onset, fluctuating course, lack of attention and disorganised thinking.[593,594]	Expert opinion, 4
When managing delirium the first thing to do is to identify the triggering or precipitating cause which is often multifactorial (pain, drugs, fever, dehydration), and correct it.[575,595]	Expert opinion, 4
If the agitation persists, pharmacological treatment may be used. There are no RCT on the effectiveness of pharmacological treatment of delirium in terminal cancer patients or on non-cancer patients due to ethical reasons,[575] with the exception of a small randomised double-blind RCT with no placebo group in patients with AIDS at the end-of-life stage when haloperidol and chlorpromazine but not lorazepam, proved to be effective for delirium taken orally or by intramuscular route, and with good tolerability for haloperidol.[596]	Descriptive study, 3 SR of RCT, 1+
In clinical practice, benzodiazepines are also used, apart from haloperidol, in cases of delirium with great agitation (midazolam, lorazepam, clonazepam and diazepam), based on expert opinion and short series studies on patients.[564,575]	Descriptive study, 3 Expert opinion, 4
When there is no response to haloperidol, this is not tolerated or it is contraindicated, atypical antipsychotics can be used. We must remember that in the case of PDD and DLB, atypical antipsychotics may cause a serious extrapyramidal reaction (K-series).[6]	Descriptive study, 3 Expert opinion, 4

Depression and anxiety

The epidemiology of depression in patients with advanced neurodegenerative diseases is practically unknown.[575] Depression and anxiety may be perceived in patients with advanced dementia who preserve some introspection capacity and are able to communicate (GDS-FAST 6) and who are in a situation of terminal stage of life, due to a concomitant process,

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Depression in this stage is often underdiagnosed or confused with apathy, so it may deprive patients from treatment that would improve their quality of life. The possibility of hypoactive delirium must also be taken into account in the differential diagnosis. The clinical observation, the information provided by relatives, and if possible, the use of specific scales, help make the diagnosis.[575]	Descriptive studies, 3 Expert opinion, 4
In order to treat depression, its triggering factors must be identified, applying non-pharmacological support interventions and using tricyclic antidepressants and SSRI, although their effectiveness has not been specifically determined in this stage of dementia.[575]	SR of RCT, 1+
Psychostimulants such as dextroamphetamine, methylphenidate modafinil and pemoline may have a fast response and are well-tolerated. They can be useful above all when a fast onset of the antidepressant effect is required, or in cases with short life expectancy. Its effectiveness has only been demonstrated in cancer patients.[575]	Expert opinion, 4

Dysphagia. Malnutrition and dehydration

Dysphasia is frequent in advanced dementia; it appears independently from the aetiology and usually gets worse with the progression of the disease. It appears earlier on in VD and in dementia accompanied by motor symptoms. Apart from the actual dysphasia that causes direct damage to the neurological structures that control swallowing, the possibility of the oral intake difficulty being due to swallowing-chewing apraxia must also be taken into account or if it is a question of rejecting the food.

There is little evidence about the management of dysphagia in PC. The treatment requires personalised evaluation to determine its cause and, if possible solve it.[575]	Expert opinion, 4
General measures can be used aimed at favouring swallowing such as correct hydration, a soft diet adapted to the patient's preferences or the use of thickeners in liquid dysphasia. Postures that facilitate swallowing according to advice given by the speech therapist are also effective.[25,597,598]	Expert opinion, 4 Descriptive study, 3
An improvement with SSRI has been described in some patients who rejected the oral intake of food.[196]	Descriptive study, 3 Expert opinion, 4

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Dysphasia in advanced dementia is often complicated with hydration and nutrition problems, and it is a frequent cause of aspiration pneumonia, the most important cause of death in these patients.[572]	Observational study, 2++
Dehydration may be expressed by thirst, dryness of the mouth and state of confusion. Whenever possible rehydration will be carried out by oral route. If it is essential to provide liquids via parenteral route, the advantages and disadvantages must be assessed in this specific case, appropriately informing relatives so that they can take part in the decision. Hospital admission is usually required for parenteral hydration, so this must be taken into account.[517,575]	Expert opinion, 4
The effectiveness of endovenous and subcutaneous route (hypodermoclysis) is comparable, but hypodermoclysis is more comfortable and presents fewer complications. Subcutaneous route permits the continuous administration of electrolytes and saline solutions 24 hours, at a daily rate of 40-60 mL/hour and a nightly rate of 80 mL/h or intermittent bolus of 500 mL/h, 2-3 times a day.[575]	Observational study, 2+ + Descriptive study, 3
It must be taken into account that the hydration symptoms may persist despite an adequate replacement therapy, probably because the cause of the dehydration is, in many cases, polyfactorial.[517]	Descriptive study, 3
The use of extraordinary measures to maintain nutrition and hydration when the patient stops eating by mouth, such as the placement of a nasogastric probe (NGP) or permanent percutaneous gastrostoma (PPG), is one of the most difficult decisions to be taken by professionals and relatives.[196,599,600] Before taking any decision, the advance directive document, if any, or the so-called replacement opinion (what the patient would have chosen according to his history of values) should be taken into account. The relatives should be informed about the real effectiveness of these techniques and about their complications.	Expert opinion, 4
One Cochrane SR that included seven controlled observational studies, not finding any RCT, concluded that enteral nutrition by NGP or PPG in people with advanced dementia does not prevent aspiration pneumonia, does not improve the nutritional parameters, does not reduce the decubitus ulcers, does not improve infectious complications, does not improve the functional state or comfort or survival.[600] On the other hand, NGP and PPG are not free from complications (micro-aspirations, pneumonia, gastrointestinal alteration and local problems).	SR of prospective study, 2++
These techniques should only be used when the person preserves unacceptable BMI, there is no severe comorbidity associated with the dementia, and the opinion of professionals and caregivers is also favourable.	Expert opinion, 4

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Pain

Pain is present in many people with dementia but it is often not identified and consequently not treated adequately. It is normal for patients with cognitive impairment to receive less analgesics than patients with integral cognitive state.[601,602]	Observational study, 2+
The presence of pain must always be suspected, investigated as routine and it must not be forgotten that it may only be expressed as an alteration of behaviour.[603,598,603,604]	Expert opinion, 4
To evaluate pain in advanced dementia, behaviour scales, interviews with the caregivers or scales that have been specifically designed such as the PACSLAC (Pain Assessment Checklist for Seniors with Limited Ability to Communicate) and the DOLOPLUS-2 can be used.[605] These scales are not validated in Spanish. They are based on observing the patient's behaviour in a short period of time and on the response to the application of care such as cures, mobilisations, etc.	Expert opinion, 4
There are no RCT that support which is the best treatment of pain in advanced and terminal stage of dementia; however the use of the analgesic ladder of the WHO is advisable, where three levels of action are contemplated: A first rung with non-opioid analgesics, a second with weak opioids and finally the administration of powerful opioids. Apart from classical analgesics, adjuvant drugs can also be used (tricyclic antidepressants, SSRI, anticomitial drugs, benzodiazepines, etc), although their use is based on expert opinion.[606,605,575]	Expert opinion, 4
There are also some non-pharmacological measures (massages, aromatherapy, transcutaneous electrical nerve stimulation) that can reduce pain.[607]	Observational study, 2+

Fever

An intercurrent infection may be suspected in cases of fever in advanced dementia. The most frequent are pneumonia and infection of the urinary tract. Pneumonia is a frequent cause of admission into acute treatment hospital and the main cause of mortality in these people.[608,572]	Observational study, 2+
There is controversy about the use of antibiotics, as they do not seem to reduce mortality respect to patients treated exclusively with palliative measures such as antipyretics and analgesics.[609,610]	RCT, 1++ Observational study, 2++

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Hospital admission is not indicated, either, to treat it.[610,611]	Observational study, 2++
However, under certain circumstances, the use of antibiotics may benefit the patient, reducing discomfort caused by infected bronchial secretions.[612,613]	Observational study, 2++

Pressure ulcers

Skin problems are frequent in this stage of dementia, especially the appearance of decubitus lesions or pressure ulcers (PU). The origin is polyfactorial, including the characteristics of the actual skin (fragility, sensitivity) and systemic problems (nutrition, cardiovascular state, etc).[375]	Expert opinion, 4
To prevent the appearance of PUs, there must be frequent position changes, maintaining the best possible state of nutrition, and adequate hydration and hygiene of the skin. The use of mechanical protections, pillows or special contact surfaces[610,614,615], and the application of hyper-oxygenated fatty acids.[616]	Observational study, 2+

Psycho-emotional and psychosocial needs of people with advanced dementia and in end-of-life stage

The psychosocial needs of people in advanced stage of dementia and end-of-life may be difficult to identify, as there are serious communication difficulties. Observing the reactions of the person and knowledge of previous characteristics may help us in this task. We can never forget that the person being studied may be aware of their problem and suffer psychologically because of this, and in these cases the professional support and support from their families may help them.	Expert opinion, 4
The assessment of the psychosocial aspects should be extensive, considering aspects related to the moment in life, the meaning and impact of the disease, coping style, impact on the perception of oneself, relationships with family and friends, sources of stress (economic difficulties, family problems, etc), spiritual resources, economic circumstances, doctor-patient relationship and social resources network. (Social health centres, social workers, etc).	Expert opinion, 4

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Identifying and evaluating the psycho-emotional and psychosocial needs of people with advanced dementia and in end-of-life stage

Spiritual needs can be deduced from the behaviour or be specified by the actual person affected, if possible, or by families and/or friends. Spirituality is a dimension that combines attitudes, beliefs, feelings and practices that go beyond what is strictly rational and material.[617] When evaluating any person, this need must be taken into account. Basic communication techniques must be used, such as open-ended questions, active listening and silences, in order to obtain information. The patient's spiritual needs may vary throughout time.[618]

Spirituality has an impact on the general welfare of patients in PC and on their quality of life.[619]	Observational study, 2+ Descriptive study, 3
There is no evidence to determine how spiritual care must be provided. Listening to the patients' experiences is recommended as well as any questions that might arise; affirm their humanity; protect their dignity, self-esteem and identity; and guarantee that spiritual support is offered as an integral part of their care. Spiritual support can be offered by relatives, friends, faith-based groups, priests or other spiritual advisors, and health or social services professionals.[575]	Expert opinion, 4

Psychosocial support to the family and social needs

The needs and wishes of relatives providing care for people with advanced dementia and in end-of-life stage are: Have home aid, psychological support, informal support, support groups, information, training, economic aid, respite services and help for tiredness, anxiety and isolation. The priority needs among these, correspond to information and to support.[620,621]	Observational study, 2+ Descriptive study, 3 Qualitative study

Care of people with dementia and their families during the final days of their lives

The care during the final days of their lives must be exquisite, meticulous and caring. The suffering of both patient and family must be understood, offering them the best possible care and support. These are moments that leave deep marks, and if they do not feel comfortable or they feel that they are being neglected, negative feelings are going to be created that are difficult to erase.[622]	Expert opinion, 4

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It is important to attend to the special demands that arise in these moments of extreme fragility.[623,624]

Physical care:

- Revise the medication and suspend all treatments that are not essential.
- Make sure that the medication that may be necessary is available and prepare alternatives to oral route (subcutaneous or rectal).
- Suspend all unnecessary interventions and tests (analytical, checking vital signs, etc).
- Maintain the observation to control the symptoms as best possible.

Psychological aspects:

- Explore the patient's fears and wishes whenever possible. This is practically impossible in the majority of people with dementia in terminal stage.
- Allow patient to express their sadness and anxiety.
- Calm them down with respect to symptoms and ensure them that they will be offered all possible means to relieve their suffering.
- Evaluate religious and spiritual needs

Social or family aspects:

- Make sure that the family is aware of the state of imminent death of the patient.
- Use a clear language, without ambiguities: do not take for granted the knowledge of the dying process.
- Consider all the reasons for doubt and concern that might arise: Tiredness, fear of responsibilities, fear of not realising that death is imminent, feelings of blame due to moments of distraction or rest.
- Whenever possible provide a quiet atmosphere where patient can spend their final days.

The factors that affect decision-making about death vary depending on the patient's needs, the resources available and the preferences expressed earlier on by the patient or the wishes of their families.	Expert opinion, 4

Needs related to death: Grief and losses

Human grief is a natural reaction to loss, especially the loss of a loved one. It is a totally personal and non-transferable experience, and it is an extremely stressful life event.[625,626]

The majority of people get over their loss and effectively cope with grief -normal grief-, and some even get stronger in adversity -resilience-; but sometimes circumstances make the process especially difficult -risk grief- and sometimes it becomes complicated-complicated grief.[627,628]

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The personality, personal history, experiences related to previous losses or the moments in life of the person are all decisive factors in the way they express their grief and in its subsequent evolution. There are people who are more susceptible to suffering health problems associated with grief and adapting to the loss.[629,630]

The evaluation of risk grief must be carried out on the primary caregiver, on relatives and closest friends; it must take into account: The characteristics of the disease, the care in end-of-life stage, the nature of the death, the characteristics of the griever and interpersonal relations.[575,629]	Observational study, 2+ Descriptive study, 3
Professional interventions (psychological advice, psychodynamic counselling therapies and cognitive-behavioural techniques) in normal grief are not effective and they may even be harmful; in risk grief they can achieve a slight improvement, and in complicated grief they are usually effective.[628,630,631,632]	RCT 1+ Observational study, 2+

Summary of evidence

Delirium	
4	The diagnosis of delirium in patients with dementia in GDS 6-7 stage is very difficult due to the patient's problems with verbal communication and gestures, but it may be suspected in the case of sudden onset intense agitation.[575]
4	The CAM scale can be used to assess dementia in patients who preserve some sort of effective verbal communication.[593,594]
4	The treatment of delirium in PC must start by identifying the cause (fever, pain, dehydration, drugs) and by its correction.[575,595]
1+	Haloperidol has proved to be effective and well tolerated in the management of delirium in patients with AIDS in terminal stages.[575,596] Chlorpromazine has also proved effective, with less tolerability.
3/4	Benzodiazepines (midazolam, lorazepam, clonazepam and diazepam), can be used in delirium with marked agitation and based on short series of cases.[564,575]
3/4	When there is no response or good tolerability to haloperidol, atypical antipsychotics can be used. In the case of PDD and DLB there is a risk of adverse extrapyramidal reactions.
Depression and anxiety	
3/4	The clinical observation, the information provided by relatives, and some specific scales, are useful for the diagnosis.[575]
4	SSRI and tricyclic antidepressants (based on RCT) are effective.[575]
4	They are entitled to be suitably informed, respecting their right to confidentiality, covering their basic needs, and preserving their social relationships

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4	When abuse is highly suspected, there is an ethical and legal obligation to protect the victim, activating legal resources. If there are physical injuries, a judicial report of injuries must be drawn up; if this is not the case, the Public Prosecutor will be notified to adopt the measures established by law.
Dysphagia, malnutrition and dehydration	
4	There is little evidence about the management of dysphagia in advanced dementia and final stage. The treatment requires personalised evaluation to identify the cause and treat it.[575]
4	The diet must be adapted to the characteristics of the dysphagia. This must generally be soft and adapted to the person's tastes. Thickeners must be used if it is liquid dysphasia
2++	The use of NGP or PPG to maintain the intake and hydration in a person with advanced dementia is not supported by the evaluation of risk/benefit.[600]
3	Providing liquids does not always improve dehydration symptoms, as it is often multifactorial.[517,575]
4	The decision to hydrate via parenteral route in the end-of-life stage must always be agreed upon with the relatives, evaluating the need for hospital admission.[196,599,600]
2++/3	The effectiveness of endovenous route and hypodermoclysis to provide liquids and treat dehydration is similar.[575]
2++/3	Hypodermoclysis provides suitable hydration in an easy and safe manner for 24 hours a day.[575]
Pain	
2+	Pain is frequent in advanced dementia but it may go unnoticed and as a result un treated.[601,602]
4	Clinical observation, the opinions of the caregivers and specifically designed scales (PACSLAC and DOLOPLUS-2) must be used to evaluate pain in advanced dementia.[605]
4	The use of the WHO analgesic ladder is recommended to treat advanced and terminal dementia. Adjuvant drugs can be added to relieve and reduce adverse effects of classical analgesics.[606,605,575]
2+	Some non-pharmacological measures such as massages, aromatherapy and transcutaneous electrical nerve stimulation can also reduce pain.[607]
Fever	
2++	Pneumonia is a frequent complication in people with advanced dementia and the main cause of mortality.[608,572]
1++/ 2++	Antibiotics do not reduce mortality from pneumonia in people with advanced dementia, and they are a frequent cause of admission into acute treatment hospitals.[609,610]

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2++	Patients with severe dementia do not benefit from being admitted into hospital to treat pneumonia.[610,611]
2++	Antibiotics may reduce discomfort caused by infected bronchial secretions in patients with advanced dementia.[612,613]
Pressure ulcers	
4	PU are frequent in this stage. Many different factors intervene: Local or systemic cause.
2+	The prevention of PUs entails the association of different measures: Postural changes, local protection elements and the maintenance of a good nutritional and hydration state as well as skin hygiene.[610,614,615,616]
Psycho-emotional and psychosocial needs of people with advanced dementia and in end-of-life stage	
4	There are many different factors to evaluate in the psychological field and emot ions in people affected by advanced dementia and at end-of-life stage.
4	It is difficult to identify the psychological and emotional needs of people with advanced dementia and at end-of-life stage, due to the problems involved in acknowledging their actual illness and with verbal communication and gestures
4	The assessment of the psychosocial aspects must be extensive and contemplate many different factors:
Identifying and evaluating the psycho-emotional and psychosocial needs of people with advanced dementia and at end-of-life stage	
2+/3	Spirituality has an impact on the general welfare of people and on their quality of life.[619]
4	Spiritual support to people with dementia must not necessarily be offered by health professionals or by those responsible for religious services. The method to be followed in spiritual care is based on active listening.[575]
Psychosocial support to the family Evaluate the family and social needs	
2+/3 qualitative study	Relatives providing care for people with advanced dementia and at end-of-life stage have many needs. The priority needs are information and psychological support.[620,621]
2+/3/ qualitative study	There is no single intervention model for relatives of people with advanced dementia and at end-of-life stage, which is guaranteed with sufficient scientific evidence.[620,621]
Care of people with dementia and their families during the final days of their lives	
4	The care during the final days of the end-of-life stage must be extremely exquisite, meticulous and caring.[622]

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4	It is important to attend to the special demands that arise in these moments of extreme fragility (physical care, psychological, family and social aspects).[623,624]
4	The factors that affect decision-making about death vary depending on the patient's needs, the resources available and the preferences expressed by the patient or relatives.
Needs related to death: Grief and losses	
2++/3/4	The majority of people get over the loss of a loved one and effectively cope with grief. However, there are people who are more susceptible to suffering complicated grief and have problems in adapting to the loss.[627,628]
2+/3	The characteristics of the disease, the care received at the end-of-life stage, the nature of the death, the characteristics of the griever, and of the deceased, and interpersonal relations have an influence on risk grief.[575,629]
1+/2+	Psychological advice, psychodynamic counselling therapies and cognitive-behavioural techniques in normal grief are not effective and they may even be harmful; in risk grief they can achieve a slight improvement, and in complicated grief they are usually effective.[628,630,631,632]

Recommendation

Delirium	
D	Initial management of delirium must include the identification and treatment of the triggering causes, as well as appropriate information for relatives and caregivers, and an evaluation of the need to use pharmacological treatment.
B	Haloperidol is the drug of choice for treating delirium in patients in terminal phase.
C	Benzodiazepines are effective in the management of delirium with marked agitation.
D	The use of haloperidol and atypical antipsychotics must be avoided in patients with PDD and DLB, due to the risk of extrapyramidal reactions.
Depression and anxiety	
D	In people with advanced dementia at end-of-life stage due to a concomitant process, the diagnosis of depression must be based on the clinical observation, the information provided by relatives and, if possible, the use of specific scales.
B	If necessary, antidepressant drugs, such as SSRI and tricyclics may be used, bearing in mind the possibility of central anticholinergic effects.
D	Psychostimulants such as methylphenidate, dextroamphetamine, modafilin and pemoline may have a fast response and are well-tolerated.

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Dysphagia, malnutrition and dehydration	
D	Treatment of dysphagia requires individualised assessment of each case in order to identify and if possible, treat the cause.
D	The diet must be adapted to the clinical characteristics of the dysphagia. In the case of liquid dysphagia, thickeners may be effective. A soft diet that adapts as much as possible to the patient's tastes is recommended. If the patient collaborates, the adoption of postures that facilitate swallowing with the supervision of the speech therapist is effective.
D	Whenever possible, liquids must be administered orally.
D	The parenteral administration of liquids during the end-of-life phase must be carried out weighing up the advantages and disadvantages, and always after discussing it with relatives.
B	The use of a nasogastric probe or permanent percutaneous gastrostomy must be assessed individually and with caution in patients with advanced dementia, as there is evidence of a bad relationship between benefit and risk.
Pain	
C	The presence of pain must always be suspected in advanced dementia. This must be assessed through the patient's behaviour, the observation of relatives and the appropriate scales such as PACSLAC and DOLOPLUS.
D	The use of the WHO analgesic ladder guideline is recommended for the pharmacological treatment of pain in advanced dementia, and, if necessary, adding adjuvants.
Fever	
B	It is recommendable not to treat pneumonia with antibiotics in a person with advanced dementia as it does not entail a benefit.
B	Hospital admission is not recommendable to treat pneumonia in a person with advanced dementia.
B	Treatment with antibiotics is recommendable in people with advanced dementia who have breathing difficulties due to super-infection of bronchial secretions.
Pressure ulcers	
C	To prevent the appearance of pressure ulcers, there must be frequent changes in posture, using mechanical protections and maintaining a good state of nutrition, hydration and hygiene of the skin.
Psycho-emotional and psychosocial needs of people with advanced dementia and in end-of-life stage	
D	The psychosocial well-being of patients with life-threatening chronic diseases must be evaluated on a regular basis.

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D	The psychosocial assessment of patients in PC should include the following fields: Aspects related to the moment in life, the meaning and impact of the disease, coping style, impact on the perception of oneself, relationships, sources of stress, spiritual resources, economic circumstances, doctor-patient relationship and social resources network.
D	Health and social services professionals attending to them should offer them basic emotional support.
D	People with significant levels of psychological suffering should receive specialised psychological help.
Identifying and evaluating the psycho-emotional and psychosocial needs of people with advanced dementia and in end-of-life stage	
D	The team attending to people with dementia must bear in mind their beliefs and spiritual needs.
D	In the absence of appropriate evidence about what is the best way to provide spiritual support, offering this support as an integral part of the care is recommended, whatever the care context, and with an approach based on the principles of effective communication.
D	It is important to consider cultural differences with respect to spirituality, but this does not justify a lack of attention to these aspects in people who belong to different cultural or religious groups to our own.
Psychosocial support to the family. Evaluate the family and social needs	
C	Caregivers must be offered the possibility of expressing their needs for support and information.
D	Identifying the most vulnerable or depressed caregivers is recommended in order to offer them intensive psychosocial support or specialised services.
Care of people with dementia and their families during the final days of their lives	
D	Appropriate care during the final days of their lives should include: • Informing the family and caregivers of the situation of approaching death and, in general, provide the necessary information that adapts to their needs. • Explain and agree to the care plan with the patient, and whenever possible, with their families. • Evaluate the medication the patient takes, suspending non-essential drugs, after explaining the reasons for this. • Treat symptoms that produce suffering. The necessary drugs must be available if the patient is at home. • Interrupting unnecessary or futile interventions or tests, according to the patient's desires. • Evaluate psychological, religious and spiritual needs of the patient, family and caregivers.

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	• Provide care in a quiet atmosphere, respecting privacy and facilitating proximity with family and friends. • Provide the channels and resources necessary both for hospitalisation and for home care.
Needs related to death: Grief and losses	
B	Referral of patients with complicated grief to specialised services (psychology, psychiatry, etc.) is recommended for them to receive specific and structured care.
B	Regular monitoring is recommended in risk grief, with emotional support, individually evaluating the need for specific and structured psychotherapies.
B	Formal or structured interventions are not recommended in normal grief.
D	In normal grief, providing information about the grief and about the available resources is recommended, as well as basic emotional support.
D	Professionals caring for patients at the end-of-life stage as well as their relatives, should have access to elementary training in grief, which will enable them to provide basic care to the grievers, understand and explore their needs, evaluate the risk factors, detect people with complicated grief and refer them to specialised service.

14.6. How can worsening due to the natural evolution of the illness be differentiated from worsening caused by a potentially reversible concomitant process?

People affected by dementia present a variable clinical course but a relatively predictable prognosis. Dementia passes through different stages, with well-defined characteristics and duration in AD, and more difficult to specify in other type of dementia such as DLB where the fluctuating course is even a diagnostic criterion. In very advanced stages, the different types of dementia tend to become more homogeneous in their symptoms and functional disability.

If the deterioration course is too fast and unpredicted sudden changes appear in functional capacity, a concomitant process must be suspected, which has an influence on the clinical expression of dementia. In these cases it is essential to differentiate what corresponds to the natural history of dementia from what is a potentially reversible worsening due to comorbidity or an effect related to drugs.[573]

Expert opinion, 4

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Professionals must investigate the causes of the crisis and decide on the most appropriate measures to correct it and guarantee the comfort and quality of life of the person affected.	Expert opinion, 4
When this worsening appears, whatever the cause, there are a series of factors that must be evaluated when taking a therapeutic decision. The limitation of the therapeutic strategy is an important aspect to decide if the dementia has reached a very advanced stage: FAST of over 7c in AD; when the Barthel index is 0; if the progression is very fast from the onset; if the infections are serious, repeated and with no relevant benefit with the treatment; if the dysphagia is problematic, with malnutrition and/or dehydration, and if there are refractory pressure ulcers.	

Summary of evidence

4	If the deterioration course is too fast and unpredictable sudden changes appear in functional capacity, a concomitant process must be suspected, which has an influence on the clinical expression of dementia.[575]
4	In advanced dementia, considerable worsening may mean that a limitation of the therapeutic strategy has to be established following a multidisciplinary assessment of the case.

Recommendation

D	In a person with advanced dementia, the existence of a concomitant process must be suspected if the progression suddenly speeds up and above all if there are unpredictable changes.
D	When considerable worsening appears, regardless of the cause, a series of factors must be evaluated that may affect the therapeutic decision, always bearing in mind the values of the person and of the family.
D	It is recommendable to evaluate the possibility of therapeutic limitation if the dementia has reached a very advanced stage: FAST of over 7c in AD; when the Barthel index is 0; if the progression is very fast from the onset; if the infections are serious, repeated and with no relevant benefit with the treatment; if the dysphagia is problematic, with malnutrition and/or dehydration, and if there are refractory pressure ulcers.

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14.7. What are the objectives of caring for people with dementia in terminal phase?

The objective of applying palliative measures in the care of people with dementia in terminal phase is to provide comfort, eliminate reasons for suffering and improve the quality of life as far as possible, using non-aggressive measures. These measures may be applied at home, and other times and exceptionally they may require admission into hospital to treat complications.[25,517,573]	Expert opinion, 4

Summary of evidence

4	The application of palliative measures in the care of people with advanced and terminal dementia can be carried out at home or in hospital. Their objectives are to provide comfort, eliminate suffering and improve the quality of life.[25,517,573]

Recommendation

D	Whatever the location, it is recommendable for patients with advanced or terminal dementia to receive palliative measures to improve their comfort, suffering and quality of life, insofar as this is possible.

14.8. What extraordinary or greater measures should be questioned in the care of people with advanced dementia?

In advanced dementia and in terminal phase of life, extraordinary therapeutic measures that are not very beneficial and may cause discomfort and adverse effects must be avoided.

The higher ranking measures considered are, cardiopulmonary resuscitation in the case of various cardiac arrest, artificial respiration in asphyxia or dialysis in the case of kidney failure, as they do not reduce mortality or modify survival in this stage of dementia.[633,634]	Observational study, 2++

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Cardiopulmonary resuscitation carried out outside the hospital is not effective and in the hospital it is not very effective either in this group of people, as the result obtained is three times worse than in people with intact cognition. In light of these results, its execution is not advisable as the efforts required are excessive when compared with the benefits; thus in severe dementia there is no moral imperative to use it.	Observational study, 2++

Summary of evidence

2++	In advanced dementia, if there is cardiac arrest, artificial respiration in asphyxia or dialysis in the case of kidney failure, do not reduce mortality or modify survival in this stage of dementia.[633,634]
2++	CPR in advanced dementia carried out outside hospitals is not effective. In hospital, it is three times less effective than in people with intact cognition.[635,636]

Recommendation

B	Cardiopulmonary resuscitation is not indicated in people with advanced dementia, as it is an extraordinary therapeutic measure that does not provide any significant benefit.
B	Neither artificial respiration nor dialysis are recommendable, either, in advanced dementia, because they provide no benefit.

14.9. What therapeutic intermediate measures should be questioned in the care of people with advanced dementia?

In advanced dementia and at end-of-life stage, intermediate range therapeutic measures should not be carried out; however, this must be considered as a controversial topic and often the decision is difficult.[638]

Intravenous infusions to correct dehydration, the administration of antibiotics in the case of infection, artificial feeding by NGP or PPG due to dysphasia or rejection of food, hospitalisation as a health resource and the performance of unnecessary diagnostic tests, are considered to be included within this group[639,640,584] **(question 14.5, section on dysphagia, malnutrition and dehydration).**	Observational study, 2++/2+

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However, some of these measures may exceptionally be effective to relieve suffering or be the only alternative available. If this is the case, we will recommend internment in a health centre when care cannot be provided in the home or nursing home.[641]	Observational study, 2+

Summary of evidence

2++/ 2+	In advanced dementia and at end-of-life stage, the evaluation of the effectiveness and safety advises against the use of intermediate range therapeutic measures (intravenous infusions, administration of antibiotics, artificial feeding, hospitalisation and execution of unnecessary diagnostic tests).[639,640,584]
2+	There are exceptional situations when intermediate range measures may be effective to relieve suffering or are the only available alternative.[641]

Recommendation

B	At the end-of-life phase of patients with advanced dementia, the use of intermediate range therapeutic measures (intravenous infusions, administration of antibiotics, artificial feeding, hospitalisation and execution of unnecessary diagnostic tests) is not recommended.
C	The use of intermediate range therapeutic measures should only be considered on those occasions when they can reduce suffering or they are the only available resource.

14.10. What information and aid must be provided to the families of people with terminal dementia?

In advanced stages of dementia and in the terminal phase of life, patients have already completely lost their capacity to understand and decide. Families need more information and support to continue assuming there task of caring and take decisions. Good communication may improve the involvement of relatives and have an influence on their capacity to adapt.[642]	Descriptive study, 3

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In this end stage a lot of care must be taken when giving bad news and improvisation is not acceptable. Some studies performed in PC context highlight the importance of the decision-making in the end of life stage being shared, and for the relationship between the health professionals and caregivers to be established in horizontal and participatory conditions.[643,644]	Descriptive study, 3 Expert opinion, 4

Summary of evidence

3	Families need more information and support to continue assuming the caring task, take decisions, adapt and get more involved.[642]
3/4	At this end stage of dementia a lot of care must be taken, not improvising when giving bad news.[643,644]
4	In many aspects, information is useful for the caregiver of a person with advanced dementia, both if it is given at information sessions and through audiovisual material.

Recommendation

D	It is recommendable to give information and support to caregivers of people with advanced dementia for them to continue assuming their work as caregivers, take decisions, adapt and engage more.
D	Informing and communicating bad news to the caregivers of people with dementia at the end-of-life stage requires adequate preparation of the professionals.

14.11. What legal regulations and ethical principles exist relating to communication with people with advanced dementia or with their families at the end-of-life stage?

Access to the truth is the right of all people, as everyone is entitled to decide, with support and with due counselling, about such important aspects as health/disease or life/death.[643]	Expert opinion, 4

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Sincere communication is an ethical imperative that entails respect for the wishes and values of the patients,[642] it permits the organisation of care according to priorities and preferences, and facilitates decision-making. Special circumstances arise in people with advanced dementia, as they have lost their ability to understand and decide, and it will be their families that must be informed and assume decisions. The information must be true, understandable, adequate, and it must contemplate the purpose and nature of each intervention, with the advantages and risks or consequences.	Expert opinion, 4

Summary of evidence

4	People with advanced dementia have lost their ability to understand and decide, and it will be their families that must be informed and assume decisions.[643,642]
4	The information must be true, understandable, adequate, and it must contemplate the purpose and nature of each intervention, with the advantages and risks or consequences.[643,642]

Recommendation

D	The participation of patients and caregivers in decision-making at the end-of-life stage must be fostered.
D	If patients are not able to decide at this end-of-life stage, the advance directives expressed by them or their wishes included in the clinical record, or else the opinion of their legal representative and/or closest family, must be contemplated.
D	Informing the team of the decisions adopted at this end-of-life stage is recommended, recording the process in the clinical record.
D	If there are doubts during the decision-making process, consulting other expert professionals (other professionals, healthcare ethics committee, etc.) should be consulted.

14.12. In what cases is a post-mortem pathoneurological study recommended?

There are no publications that address the topic specifically. Given that for the majority of subtypes of dementia, the definite diagnosis requires a neuropathological study, it is normal practice in our media to foster this in those cases where a firm diagnosis in life has not been possible.

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Epidemiological surveillance systems recommend carrying out a post-mortem neuropathological study due to public health reasons when a prion disease or other diseases of compulsory declaration are suspected and which were not properly diagnosed in life.	Expert opinion, 4
On the other hand, there are several neurological tissue banks in the national territory whose objective is to promote the study of neurological diseases through the collection, processing and storage of neuropathological tissue originating both from healthy donors and from people affected by different neurological diseases, and provide them on a non-profit basis to independent researchers. The assignment of post-mortem neuropathological tissue to these banks is channelled through the donation by the actual individual or through his or her legal representatives following protocols.[646]	Expert opinion, 4

Summary of evidence

4	It is useful to carry out a pathological study of the brain in those cases where it has not been possible to reach a firm diagnosis in life.
4	When a prion disease is suspected, for public health reasons, it is compulsory for this to be declared, and confirmation of the diagnosis is always recommended by an anatomopathological study.[645]
4	The study of neurological tissues in patients who have suffered dementia is useful in research into these diseases.[646]

Recommendation

D	It is recommended for the medical team attending to the patient at this end-of-life phase to request the post-mortem neuropathological study to confirm the diagnosis (above all in those cases where there is not an accurate diagnosis, or if a prion disease is suspected or any other disease of compulsory declaration) and foster the investigation.

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15. Diffusion, training and research in care of people with dementia

Questions to be answered:

Dissemination

15.1. How must the topic of dementia be dealt with in the media in order to suitably inform the public, and which are the most appropriate media?

Training

15.2. What undergraduate dementia training must be given to health sciences and social services professionals?
15.3. What dementia training must be given in healthcare branches of vocational training?
15.4. What post-graduate dementia training must health professionals in general receive?
15.5. What post-graduate dementia training must health professionals engaged in the specific care of people with dementia receive?

Research

15.6. How important is research in the field of dementia?
15.7. What role must the different healthcare levels play in research on dementia?

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Diffusion

15.1. How must the topic of dementias be dealt with in the media in order to suitably inform the public, and which are the most appropriate media?

In modern society, the general population and the health and social services professionals must be aware of the major social and health realities that affect them, such as normal ageing and pathological ageing, mainly when this is characterised by cognitive function impairment.	Expert opinion, 4

The great prevalence of dementia means that this is practically a universal experience and that a large number of families live, for many years, with the people affected, or that they are aware of the problem indirectly through friends, neighbours, work colleagues, etc. The dissemination of knowledge on dementia through the media must be done adequately and in a way that is understandable for the different groups that make up society.[647]Currently the media references about people affected by dementia are routine,648 therefore the subject must be dealt with normally and with the necessary sensitivity to prevent dramatising or stigmatising people who suffer the problem, always with due respect to the privacy and dignity of the person affected and of their environment.

All media are adequate to disseminate information about dementia. However, journalistic treatment in certain television or film formats, (reports, documentaries, news, films) that include cases about people affected, either fictitious or real, may have a very high impact on the population and be able to transmit values such as dignity and respect towards the affected people. Especially important is the diffusion about the disease when those affected are socially important people.[193] Expert opinion, 4

One important aspect that the media must consider is their responsibility about disseminating certain technological and therapeutic advances that might awake false expectations in the population.[647] It would be recommendable for the different media to have specialised informants about health matters who can advise them on the real scope of these scientific advances, contacting professional organisations that are competent in the subject, such as scientific societies, groups of professionals, associations of families, etc.[648]

Summary of evidence

4	The media must deal with the topic of dementia with normality, in a rigorous, respectful, sensitive and understandable manner.[647,648]
4	All media may be adequate to disseminate information about dementia. They should have specialised informants in health-related matters, to give advice about the real scope of scientific advances, and not awake false expectations in the population.[193,647,648]

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Recommendation

✔	Information about dementia through the media must be based on ethical principles and good practice.
✔	The existence of specialised journalism in health issues is recommendable. The media, the competent professional associations and family associations must collaborate in fostering good information about dementia.

Training

15.2. What undergraduate dementia training must be given to health sciences and social services professionals?

The great prevalence and incidence of the disease and its impact at personal, family, professional and social level, justifies the general training received by all the health practitioners (physicians, nurses, psychologists, social workers, physiotherapists, occupational therapists, speech therapists, etc,) about the care of people with dementia, during their basic studies. Today, the training received at universities by the majority of them is insufficient.[649,650,651,650,652,653,654,655]	Expert opinion, 4

Summary of evidence

4	Insufficient training is provided, in general, today, at the health sciences and social services faculties on such a frequent and impacting process as is dementia.[649]

Recommendation

✔	It is recommendable for health sciences university students to receive general dementia training, in aspects such as epidemiology, pathophysiology, clinical manifestations, diagnosis techniques, pharmacological and non-pharmacological treatment, on the needs of the patients and relatives, and resources available, as well as on associated ethical and legal aspects.

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15.3. What dementia training must be given in health branches of vocational training?

In general, there is a lack of appropriate training in dementia in the health branches of vocational training. Many of these professionals work very closely with patients and families, and they must respond adequately to needs and demands, and therefore they must receive general basic training, both theoretical and practical, on the effects of dementia related to cognitive aspects, BADL, BPSD and the appearance of physical disability, among other aspects.

Vocational training must foster the development of positive attitudes of respect and tolerance, which must be added to the theoretical and practical knowledge. The health personnel must carry out continuous ecological stimulation aimed at being able to maintain people's capacities and thus delay the decline of the person affected. It is also advisable to know what social-health and social resources exist, as this will enable them to be better informants.

These include, most importantly, auxiliary nurses, geriatrics auxiliary nurses, social-health care (education for health, basic care, treatment administration, etc.), dietetics and nutrition technicians (prepare and supervise diets), pharmacy assistants (technical support in complying with treatments), or emergency medical and transport technicians (containment in crisis situations), etc.

Expert opinion, 4

Summary of evidence

4	There is a lack of appropriate training in the health branches of vocational training when preparing students in such an important topic as dementia.

Recommendation

✔	Health vocational training must guarantee the acquisition of theoretical and practical knowledge, as well as positive attitudes of respect and tolerance, to appropriately manage dementia.
✔	VT health personnel must be prepared to carry out continuous ecological stimulation aimed at maintaining the capacities of the individual affected by dementia at a maximum level, delaying the decline of the person affected and to give information about the management and resources in dementia.

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15.4. What post-graduate dementia training must health professionals in general receive?

Some experts have expressed that there is a lack of appropriate dementia training among PCT and that, therefore, it is essential to insist on the need for an interdisciplinary and longitudinal approach to the process of dementia.[656]	Cross-sectional study, 3
The PC professionals, as well as many of the professionals from the hospital area, frequently attend elderly people, among whom dementia is prevalent. All of them must increase the basic training received with adequate post-graduate training, which must be periodically updated, and which must include ethical and legal aspects, to (right to die with dignity, last wishes documents, etc.) and care in advanced and terminal stages of the disease.	Expert opinion, 4
There are different medical, surgical specialities, or those that provide complementary inputs, contributing specifically to the diagnosis and treatment of people with dementia. According to the model of the Ministry of Health and Consumer Affairs of Spain, the subject matters referring to mild cognitive impairment and dementia,[657,658,659,660] mental health, geriatric nursing and community nursing[661] should be extended in the curricula of the different medical specialities.	Training plan

Summary of evidence

3	There is a lack of appropriate training dementia of PCT professionals.[656]
3/4	Health and social services professionals, whatever the healthcare level, are in repeated contact with people and families affected by dementia. There are continuous scientific advances in this field. Quality care requires up-to-date knowledge.[656]

Recommendation

✔	All health and social services professionals must update their knowledge to be competent in the comprehensive management of dementia. Dementia must be addressed in an interdisciplinary fashion, providing care seamlessly from the moment it is detected until the end of life.

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15.5. What post-graduate dementia training must health professionals engaged in the specific care of people with dementia receive?

Post-graduate training, that is the training that all professionals must acquire after their basic training, is understood here as lifelong training and also as a guarantee for society of that its professionals are constantly updating their knowledge.

Lifelong training becomes especially important at a time when the changes in social values and the sustainability of the system are geared towards responsible self-care, where patients' 'values and preferences become especially important.[662]

Expert opinion, 4

In Spain, neurology, geriatrics and psychiatry are the medical specialities that usually attend to people with dementia, at the specialised health care level. Contents related to dementia are contemplated extensively in their speciality curricula, placing emphasis, in each one of them, on those aspects that concern them.[657,658, 659 660]

Training plans

Neuropsychologists are professionals who have been trained to accurately assess cognitive functions; to this end they use psychometric tests that enable them to interpret and control the evolution of the process. They must also be capacitated to design and apply cognitive intervention therapeutic programmes. There is no national policy of consensus regarding the training programme for neuropsychology specialists. However, there are many different programmes that place emphasis on this topic, and which are the ones that accredit the professionals who are carrying out this job today in the different SCTD.[663,664,665,666]

Expert opinion, 4

Nursing staff who are specialised in the care of people with dementia play a relevant role throughout the entire process: They accompany patients and their families, they encourage them with their advice and they carry out actions in order to maintain maximum autonomy of the person, paying special attention to the appearance of alarm signals of claudication or strain of the family, and, during the final stretch of life, making sure they are comfortable and trying to reduce suffering.[667,668,669,670,671,672]

In nursing speciality training, the topic of dementia is addressed in the training plans of mental health, geriatric nursing and community nursing specialities.[673,674,675]

Training plans

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Social workers from specialised units must be especially prepared to correctly interpret any modifications in the family dynamics related to dementia and its continuous changes. These professionals, like the rest of the interdisciplinary team, must take part in discussing each case, in the team work and contact all the other health and social professionals at PC level, other social health resources and the associations of families.[676,677]	Training plans
The specific post-graduate dementia training for other health professionals who work with people with dementia, is not sufficiently developed either, although there are proposals to improve it, as is the case of physiotherapy[678] or occupational therapy.[679] Throughout the training, health and social services professionals must have been made aware of the repercussion of the disease on the caregivers and families, about the essential role that the associations of families play, and about the need for a multidisciplinary and interdisciplinary approach.	Training plans

Summary of evidence

Training plans	In Spain, neurology, geriatrics and psychiatry are the medical specialities that usually attend to people with dementia. Other specialities also collaborate in the diagnostic assessment and in the treatment.
Training plans	The National Teaching Commissions of the medical specialities of neurology, geriatrics and psychiatry, have drawn up a theoretical and practical programme related to dementia, which includes specific preparation for its diagnosis and treatment, as well as information on health and social resources, ethical and legal aspects.[657,658,659,660]
Training plans	Neuropsychology, nursing, social work, physiotherapists, occupational therapists and speech therapists, who are specifically trained to be competent in managing people with dementia, are required on the basic multidisciplinary team.[662,663,669,679]

Recommendation

✔	All health and social services professionals integrated into the specialised care of people with dementia must receive specific training that will cover aspects related to the diagnosis and treatment, needs and resources available, ethical and legal aspects, and the need for it to be managed in an interdisciplinary manner.

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Research

15.6. How important is research in the field of dementia?

Dementia affects millions of people and their families. The majority of the cases are due to neurodegenerative diseases; AD is the most prevalent. We still do not have any curative or preventive treatments to avoid its devastating consequences. All of this justifies the great effort that must be made in research, to adequately solve this.[193]

Dementia action plan Catalonia

Progress must continue to be made in diagnostic techniques, biological markers, neuro-imaging studies, et cetera.), which permit establishing a safe diagnosis or predicting which asymptomatic people or with MCI will develop dementia.

Research on dementia must be carried out with a multidisciplinary, interdisciplinary, global and multidimensional approach, contemplating basic, clinical and epidemiological aspects, new diagnosis techniques, treatment optimisation, cost efficiency and also psychological and social aspects.

Research must be promoted and favoured by the Public administrations, the government bodies of the State and of the autonomous communities, and it must be coordinated with all other countries. Dementia is a universal problem. Exchanging knowledge and know-how, the speed and facilities provided by the media, enable us to advance in research, making the most of the synergies among the different teams.

National scientific research plan 7th European Framework Programme

The research lines and priorities must be framed within continuity and harmonisation projects, although they may vary depending on the context and strategies established in each territory and in each country. In general, research in dementia today should adapt to the lines indicated, at the Spanish level, in the National R&D&I Plan 2008-2010[680] and at a European level by the 7th R&D framework Programme.[681]

Summary of evidence

4	It is necessary to continue researching into the knowledge of diseases that accompany dementia.[682,193]

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4	It is necessary to continue researching into the knowledge of diseases that accompany dementia.[682,193]
National scientific research plan 7th European Framework Programme	The research lines and priorities must favour continuity, harmonisation and they may vary depending on the context and strategies established in each territory and in each country. Research in dementia should adapt to the National R&D&I Plan 2008-2010[680] and at a European level to the 7th R&D framework Programme of the European Union.[681]

Recommendation

✔	The collaboration of everyone involved (health and social services professionals, patients and relatives) is important to make a joint effort in the study and research in dementia.
✔	Research in dementia must be promoted and fostered from the public administrations, the governing bodies of the State and of the autonomous communities; it must be coordinated with other countries and it must favour the exchange of knowledge between the different teams that work in the same research line in dementia.

15.7. What role must the different healthcare levels play in research on dementia?

PCT is the grassroots of our SNS and it is the health care level that is closest to the population. Its contribution to research in dementia may provide information about epidemiology, concomitant pathologies, risk factors, drug consumption, etc. Cognitive, behavioural or functional impairment are detected in PCT at the very earliest stages, which is a key factor to control the process and with respect to all the circumstances that surround it (changes, resource management, support to the family, etc.), assessment of the quality of life, advanced stages of the disease, etc. Likewise, the PCT teams may collaborate in obtaining biological samples and donations to the NTB.[193,683]	Dementia action plan. Catalonia. Expert opinion, 4

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The SDC is the ideal framework to promote research on diagnosis, new pharmacological and non-pharmacological treatments, as well as to assess and conduct studies on factors that condition the response to different therapies, etc.[193]	Dementia action plan Catalonia
The SDC must promote the transfer of basic research to clinical research, through data or human biological sample banks and vice versa, collaborating with the basic research teams.[683]	Expert opinion, 4
The social health network, due to its characteristics, is the ideal framework to perform research on the needs of patients with dementia and their families; on pharmacological and non-pharmacological treatments, on the solution of crises provoked by severe behavioural alterations or disorders that are difficult management, quality of life studies and palliative care, etc.[193]	Dementia action plan Catalonia
One aspect to be taken into consideration is the need for training in research methodology at all healthcare levels and for all disciplines that intervene in the process.[683]	Expert opinion, 4

Summary of evidence

Dementia action plan Catalonia	PCT may provide relevant information on the epidemiology of dementia, early detection, use and adherence to treatments, management and control; it can also collaborate in obtaining biological samples and donations to the NTB.[193]
Dementia action plan Catalonia	SDC professionals must carry out research into the diagnostic validity, new techniques, clinical criteria, pharmacological and non-pharmacological treatments, etc., in collaboration with basic researchers.[193]
Dementia action plan Catalonia	The social health network may provide information to carry out research on dementia, regarding pharmacological and non-pharmacological treatments, the needs of patients and families, the management of severe behavioural disorders, care at end of life, etc.[193]
4	There is a need for training in research methodology at all healthcare levels and for all disciplines that intervene in the process22496}.

Recommendation

✔	It is recommendable for the three healthcare levels: PCT, SDCT and the social-health network to participate in research on dementia; to this end, training in research methodology is required.

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16. Dissemination and implementation

CPGs are useful to improve the healthcare and results in patients. The great challenge today is to achieve the adherence of professionals. An implementation strategy, aimed at overcoming the existing barriers in the setting where it is going to be applied, is therefore essential.

The CPG is comprised of three versions for health professionals: full, abridged and quick. The first two have information for patients. All the versions of the CPG are published in online version and can be accessed on the GuiaSalud and AIAQS websites. The abridged version and quick guideline are also published on hard support. The abridged version contains a CD-ROM with the full version of the guideline.

Dissemination and implementation strategy

For this CPG to reach the health professionals of the SNS, it will be disseminated through the GuíaSalud Catalogue (www.guiasalud.es). Also on the AIAQS website (www.aatrm.net).

Once the national dissemination plan has ended within the general framework of GuiaSalud, the guideline development group, together with the AIAQS, will perform those diffusion activities they consider appropriate.

Measuring the adherence or implementation of the CPG recommendations by monitoring and/or audita can improve its use. The AGREE instrument manual stresses the importance of preparing indicators; item 21 on the applicability dimension deals with this aspect.13 Consequently, a CPG must offer a list of clear and quantifiable quality indicators or criteria, which are derived from the key recommendations included in the guideline. The most well-known classification of indicators, and used in this guideline is the Donabedian classification,[684] which groups them into: Structure, process and results. To know and evaluate compliance with the recommendations considered to be most important, the assessment of some process variables and most important clinical results is proposed.

Indicator proposals

Table 12 contains a description of the 37 indicators proposed by the guideline development group, classified according to the clinical area, type of indicator, dimension of the quality they address and the healthcare level where they may be applied (primary care, specialised care and social-health care). It is important to bear in mind that the indicators are a proposal inspired by those drawn up by the Catalan Health Department (2006)[685] and they are only an estimate. As they are quantitative measures, if obtained on a regular basis, they will permit the analysis of the evolution in time (monitoring).

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Table 12. Indicators proposed

Area	Type of indicator	Name of indicator	Quality dimension	Healthcare Level*
Prevention	Process	Percentage of patients aged 65 and over with an adequate control of the vascular risk factors (HBP, DM, hypercholeterolaemia)	Adaptation	1/2
Diagnosis	Process	Percentage of patients under the age of 65 with MCI or dementia with genetic study	Diagnostic Effectiveness	2
Diagnosis	Process	Number of patients diagnosed with MCI and classified into subtypes	Diagnostic Effectiveness	1/2/3
Diagnosis	Process	Number of patients with aetiological clinical diagnosis of dementia and specifications of the stage	Diagnostic Effectiveness	1/2/3
Diagnosis	Process	Number of patients with diagnosis of dementia and determination of vitamin B_{12}	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients with diagnosis of dementia on whom a thyroid function study (TSH) has been carried out	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients with diagnosis of dementia with diagnostic neuroimaging test and classification of significant findings	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients with CSF study for diagnosis and classification of significant findings	Diagnostic Effectiveness	2
Diagnosis	Process	Number of patients with APOE determination and classification	Diagnostic Effectivene	2
Diagnosis	Process	Time elapsed between the first signs of the cognitive or behavioural process, and its detection by primary care	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients diagnosed with MCI with confirmatory neuropsychological study	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients diagnosed with mild dementia with neuropsychological study	Diagnostic Effectiveness	1/2

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Table 12. Indicators proposed (continued)

Area	Type of indicator	Name of indicator	Quality dimension	Healthcare Level*
Diagnosis	Process	Number of patients that satisfy diagnostic criteria for Alzheimer's disease (possible/probable)	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients that satisfy diagnostic criteria for dementia with Lewy bodies (possible/probable)	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients that satisfy diagnostic criteria for Parkinson's disease dementia (possible/probable)	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients that satisfy diagnostic criteria for frontotemporal lobar dementia (possible/probable)	Diagnostic Effectiveness	1/2
Diagnosis	Process	Number of patients that satisfy diagnostic criteria for vascular dementia (possible/probable)	Diagnostic Effectiveness	1/2
Pharmacological treatment	Process	Number of patients diagnosed with mild or moderate Alzheimer's disease who receive specific pharmacological treatment with ACE inhibitors	Therapeutic effectiveness	1/2
Pharmacological treatment	Process	Number of patients diagnosed with mild or moderate dementia with Lewy bodies who receive specific pharmacological treatment with ACE inhibitors	Therapeutic effectiveness	1/2
Pharmacological treatment	Process	Number of patients diagnosed with mild or moderate Parkinson's disease dementia who receive specific pharmacological treatment with ACE inhibitors	Therapeutic effectiveness	1/2
Pharmacological treatment	Process	Number of patients with diagnosis of moderate or advanced Alzheimer's disease, who receive specific pharmacological treatment with memantine	Therapeutic effectiveness	1/2
Pharmacological treatment	Process	Number of patients diagnosed with moderate or advanced dementia with Lewy bodies who receive specific pharmacological treatment with memantine	Therapeutic effectiveness	1/2

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Table 12. Indicators proposed (continued)

Area	Type of indicator	Name of indicator	Quality dimension	Healthcare Level*
Pharmacological treatment	Process	Number of patients treated with ACE inhibitors whose treatment has to be withdrawn due to adverse effects	Therapeutic effectiveness	1/2
Pharmacological treatment	Process	Number of patients treated with memantine whose treatment has to be withdrawn due to adverse effects	Therapeutic effectiveness	1/2
Non-pharmacological treatment	Process	Number of patients with MCI included in cognitive intervention programmes	Therapeutic effectiveness	1/2/3
Non-pharmacological treatment	Process	Number of patients with mild dementia included in cognitive intervention programmes	Therapeutic effectiveness	1/2/3
Control	Process	Number of families who have participated in information sessions on the disease after diagnosis	Adaptation	1/2
Control	Process	Number of patients/families diagnosed with dementia who have received information about the AFA	Adaptation	1/2
Control	Process	Number of people/families referred to the AFA		1/2
Control	Process	Annual assessment by families of patients with dementia of the degree of satisfaction with: • Information received • Professional support • Adaptation of health resources • Adaptation of social resources	Adaptation	1/2
Control	Process	Number of caregivers with assessment of risk of claudication	Adaptation	1/2

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Table 12. Indicators proposed (continued)

Area	Type of indicator	Name of indicator	Quality dimension	Healthcare Level*
Control	Process	Existence of protocols on processes that may affect a person with dementia: • Advance directives • Legal protection • Restraint • Abuse	Adaptation	1/2
Control	Process	Number of patients with dementia controls in PCT, who have presented a crisis situation during the last year	Adaptation	1
Control	Process	Time interval between the request for visit by PC and written reply from the specialised dementia unit	Adaptation	1/2/3
Control	Process	Number of reports issued by the specialised dementia unit specifying: • Diagnosis and stage • Neuropsychological evaluation • Evaluation of BPSD • Social evaluation • Therapeutic strategy • Control patterns	Adaptation	2
Control	Process	Number of patients with dementia who receive palliative care	Adaptation	1/2/3

*1: Primary Care; 2: Specialised care; 3: Social-Health Care.

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Appendices

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Appendix 1. Clinical material

Appendix 1.1. DSM –IV-TR criteria for the diagnosis of dementia (translated from APA, 2000)[16]

A. Presence of multiple cognitive deficits manifested by:

(1) Memory impairment (impaired ability to learn new information or recall previously learned information), and

(2) One (or more) of the following cognitive disturbances:

(a) Aphasia (language impairment)

(b) Apraxia (loss of ability to execute motor activities despite an intact motor function)

(c) Agnosia (loss of ability to recognise or identify objects despite an intact sensory function)

(d) Deficiency in executive functions (e.g., planning, organisation, sequencing, abstraction)

B. The cognitive deficits of criteria (1) and (2) cause a significant disturbance in social and occupational functioning and represent a significant impairment with respect to the previous level.

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Appendix 1.2. ICD-10 criteria for the diagnosis of dementia, adapted and summed up from the WHO, 1992[18]

G1. Evidence of the following two:

(1) Memory impairment
(2) Impairment in other cognitive abilities with respect to the previous function level: Reasoning, planning, organisation and general processing or information.

G2. Preserved awareness of the environment during a period of time long enough to clearly demonstrate G1. When there are superimposed episodes of delirium, the diagnosis of dementia should be deferred.

G3. Impairment in emotional control or motivation, or a change in social behaviour, manifest as at least one of the following:

(1) emotional incontinence
(2) Irritability
(3) apathy
(4) Coarsening of social behaviour.

G4. For a confident clinical diagnosis, G1 should have been present for at least six months.

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Appendix 1.3. Criteria for the diagnosis of dementia by the consultancy group of the neurology behaviour and dementia group of the SEN guideline, 2002,[19] - abridged

I. Alterations of at least two of the following cognitive areas:

a. Attention/concentration
b. Language
c. Gnosia
d. Memory
e. Motor control
f. Visual-spatial functions
g. Executive functions
h. Behaviour

II. These alterations must be:

a. Acquired, with impairment of the patient's previous capacities, confirmed through a reliable informant or via successive assessments.
b. Objectified in neuropsychological examination.
c. Persistent for weeks or months, and verified in the patient with normal consciousness level.

III. The intensity of these alterations is sufficient so as to interfere in the individual's normal activities, including occupational and social activities.

IV. The alterations are not accompanied by any disturbance of consciousness until terminal stages, although intercurrent transient disturbances may occur.

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Appendix 1.4. Classification of the dementia is adapted from the SEN guideline, 2009[6,35]

1. Degenerative dementias

1.a. Degenerative diseases where dementia is one of the main manifestations

Alzheimer's Disease
Dementia with Lewy bodies
Frontotemporal lobar degeneration
Prion dementia
Other infrequent dementia

1.b. Degenerative diseases where dementia may form part of the symptoms

Huntington's chorea
Corticobasal degeneration
Progressive supranuclear palsy
Parkinson's disease
Motor neuron disease

2. Classification of vascular dementia

2.a. Ischaemia multi-infarct dementia

Strategic infarct dementia
Lacunar state
Subcortical arteriosclerotic leuko-encephalopathy (Binswanger's disease) Inherited angiopathies
Hypertensive and arteriosclerotic angiopathy
Vasculitis

2.b. Hypoxic ischaemia

Diffuse anoxic-ischaemic or restricted encephalopathy due to selective vulnerability. Incomplete infarction of white matter
Borderline area infarction

2.c. Haemorrhagic

Chronic subdural haemotoma.
Subarachnoid haemorrhage.
Cerebral haematoma.
Amyloid angiopathy

2.d. Combined

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3. Secondary dementia

Due to alteration of the CSF dynamic
Associated with neoplasia
With infectious origin
With endocrine-metabolic origin, deficient or toxic.
Due to demyelinating disease
Due to vasculitis and collagenosis
Due to trauma
Due to psychiatric disease
Others

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Appendix 1.5. DSM-IV-TR criteria for AD summed up from Spanish Version, published by Masson, 2005[17]

A.– The development of multiple cognitive deficits manifested by:

A.1.– Memory impairment (impaired ability to learn new information or recall previously learned information), and

A.2.– One or more of the following cognitive disturbances: a.- Aphasia; b.- Apraxia; c.- Agnosia; d.- Disturbance in executive functioning.

B.– The above disturbances represent a decline from previous level of functioning and cause significant difficulties in social or occupational functioning.

C.– The course is characterised by gradual onset and continuing cognitive decline.

D.– The cognitive deficits in criteria A.1 and A.2 are not due to any of the following:

D.1.– Other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural haematoma, normal-pressure hydrocephalus, brain tumour).

D.2.– Systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B_{12} or folic acid deficiency, neurosyphilis, HIV infection).

D.3.– Substance-induced conditions.

E.– The deficits do not occur exclusively during the course of a delirium.

F.– The disturbance is not better accounted for by any other psychiatric disorder that might justify the manifestations, such as major depression or schizophrenia.

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Appendix 1.6. NINCDS/ADRDA Criteria for AD[131], translated in the SEN guideline, 2009[6,44]

Probable AD

- Dementia syndrome established by specific questionnaire and confirmed by a neuropsychological test.
- Deficits in two or more areas of cognition.
- Progressive worsening of memory and other cognitive functions.
- No disturbance of consciousness.
- Onset between the ages of 40 and 90.
- Absence of systemic diseases or other brain diseases that could explain the symptoms in the patient.

Dementia is defined as a decline of memory and of other cognitive functions respect to the state of the patient prior to the onset of the disease.

The data that support the diagnosis, excluding other causes, include a progressive deterioration of specific functions such as language (aphasia), motor skills (apraxia) and of perception (agnosia), impaired activities of daily living and behavioural disorders, family history of a similar disease, above all if documented neuropathologically, normality in routine studies of CSF, and specific changes in the EEG, cerebral atrophy data on CT which increase if verified serially.

Other data consistent with the diagnosis of probable AD, after exclusion of other causes, either are:

- Plateaux in clinical course.
- Associated symptoms, such as depression, insomnia, incontinence, delusions, hallucinations, catastrophic verbal, emotional or physical outbursts, sexual disorders, weight loss, increased muscular tone, myoclonus or gait disorder, especially in the late stage, and epileptic crises in advanced disease.
- Cranium CT normal for patient's age.

The diagnosis is less probable if symptoms start in an acute manner, if there are focal neurological findings or if there are epileptic crises or gait disturbances in the early stage of the disease.

Possible AD

The diagnosis of possible AD is based upon the following:

- Dementia syndrome with no apparent cause, although there are variations in the onset, in the presentation or the clinical course with respect to typical AD.
- If there is another brain disorder or another systemic process sufficient to produce dementia, but not considered to be the cause of dementia.

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- If the patient has gradually progressive severe cognitive deficit in the absence of other symptoms.

Certain AD

The patient must have satisfied in life the diagnostic criteria of probable AD and there must be pathological confirm treat data obtained via brain biopsy or necropsy.

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Appendix 1.7. Research criteria for AD proposed by Dubois et al., 2007[133]

Probable AD: A + one or more supporting feature B, C, D or E

Core diagnostic criteria

A. Presence of an early and significant episodic memory impairment that includes the following features:

1. Gradual and progressive change in memory function reported by patients or informants over more than 6 months.
2. Objective evidence of significantly impaired episodic memory on neuropsychological assessment: generally consisting of a deferred recall deficit that does not significantly improve or does not normalise with cueing or recognition testing, after effective encoding of information has been previously assessed.
3. Episodic memory impairment may be isolated or associated with other cognitive changes at the onset of AD or as it advances.

Supporting features

B. Presence of medial temporal lobe atrophy:

- Volume loss of hippocampus, entorhinal cortex and amygdale evidence on MRI with qualitative ratings using visual scoring or quantitative volumetry of regions of interest (references to well-characterised population with age norms).

C. Abnormal cerebrospinal fluid biomarkers:

- Low amyolid β1-42 concentrations, increased total tau or increased phospho-tau concentrations or combinations of the three.
- Other well-validated markers to be discovered in the future.

D. Specific pattern on functional neuroimaging with PET:

- Reduced glucose metabolism in bilateral temporal parietal regions.
- Other well-validated ligands, including those that foreseeably will emerge such as Pittsburgh B or FDDNP

E. Proven AD autosomal dominant mutation within the immediate family.

Exclusion criteria

History

- Abrupt onset
- Early appearance of the following symptoms: Gait disorders, convulsions, behavioural disorders.
- Clinical features.
- Focal signs such as hemiparesis, sensory loss or campimetric deficits.

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- Early extrapyramidal signs.
- Other diseases of sufficient intensity so as to explain memory deficits and associated symptoms.
- Non-Alzheimer's dementia.
- Major depression.
- Cerebrovascular disease.
- Toxic and metabolic disorders that might require specific examinations
- FLAIR or T2 signal changes in MRI in medial temporal lobe consistent with infectious or vascular lesions.

Criteria for definite AD

AD is considered definite if the following are present:

- Clinical and histopathological evidence (cerebral biopsy or autopsy) of the disease, according to NIA-Reagan criteria for the post-mortem diagnosis of AD. Both must be present.
- Both clinical and genetic evidence (mutation in chromosomes 1, 14 or 21) of AD. Both must be present.

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Appendix 1.8. Revised criteria for the clinical diagnosis of DLB (translated from McKeith et al., 2005)[40]

1. Central features

- Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function.
- Prominent or persistent memory impairment may not necessarily occur in the early stages, but it is usually evident with progression.
- Deficits on tests of attention and frontal-subcortical skills and visuospatial ability may be especially prominent.

2. Core features (two are sufficient to diagnose probable DLB, one for possible DLB)

- Fluctuating cognition with pronounced variations in attention and alertness.
- Recurrence of visual hallucinations which are typically well formed and detailed.
- Spontaneous motor features of parkinsonism.

3. Suggestive features (if there are one or more in the presence of one or more core features, a diagnosis of probable DLB can be made. In the absence of core features, one or more permits the diagnosis of possible DLB. Probable DLB cannot be diagnosed just with suggestive features)

- REM sleep behaviour disorder.
- Severe neuroleptic sensitivity.
- Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging.

4. Supportive features (these are usually present, but diagnosis specificity has not been shown)

- Repeated falls and syncope.
- Transient and unexplained loss of consciousness
- Important autonomic dysfunction (e.g., orthostatic hypotension, urine incontinence).
- Hallucinations in other modalities
- Systematised delusions
- Depression
- Relative preservation of medial temporal structures in CAT or neurological MRI.
- Generalised hypoperfusion in SPECT or perfusion scan with reduced occipital activity
- Hypo-uptake in SPECT of myocardium with MIBG
- Prominent slow wave activity in EEG with temporal transient sharp waves.

5. The diagnosis of DLB is less likely:

- In the presence of cerebrovascular disease, evident as focal neurological signs or in neuroimaging.

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- In the presence of another systemic or neurological disease sufficient to partly or totally account for the clinical picture.
- If the parkinsonism only appears for the first time in an advanced dementia stage.

6. Temporal sequence of symptoms

DLB should be diagnosed when dementia occurs before or currently with parkinsonism (if it is present). The term *Parkinson disease with dementia* should be used to describe dementia that occurs in the context of well-established Parkinson's disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as *Lewy body disease are often helpful*. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended. Adopting other periods would simply confuse the compilation of data and comparison between studies. In other research contexts that include clinical pathological studies and clinical trials, both phenotypes can be considered together under categories such as *Lewy body disease* or *alpha synucleinopathy*.

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Appendix 1.9. Diagnostic criteria and features for dementia associated with Parkinson's disease, translation and adaptation of Emre et al., 2007[41] taken from the SEN CPG, 2009[6,48]

I. Central or core features

Diagnosis of Parkinson's disease according to Queen Square Brain Bank criteria or others accepted in Spain. A dementia syndrome with insidious onset and slow progression, developing within the context of established PD, diagnosed by case history, clinical and mental examination, defined as:

- Impairment in more than one cognitive domain.
- Decline from premorbid level.
- Intensity of deficits sufficient to impair daily living (social, occupational or personal care) regardless of the impairment ascribable to autonomic or motor symptoms.

II. Associated clinical features

Cognitive features:

- Impairment in attention. Impairment in spontaneous and focused attention. Poor performance in attentional tasks; performance may fluctuate during the day and from day to day.
- Impaired executive functions. Impairment in tasks requiring initiation, planning, concept formation, rule finding, set shifting or set maintenance. - Impaired mental speed (bradyphrenia).
- Impaired visuospatial functions. Impairment in tasks requiring visuospatial orientation, perception or construction.
- Impaired memory. Impairment of free recall memory or of recent events or in tasks requiring learning new material, memory usually improves with cueing. Better recognition than free recall.
- Core language functions preserved for a long time. Word finding difficulty or impaired comprehension of complex sentences may be present

Behavioural features:

- Apathy: Decreased spontaneity; loss of motivation and interest.
- Changes in personality and mood, including depressive features and anxiety.
- Mostly visual hallucinations, usually complex, with visions of people, animals
- Usually paranoid delusions, such as infidelity or phantom boarder (unwelcome guest living in the home).
- Excessive daytime sleepiness.

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III. Features which do not exclude Parkinson's Disease Dementia, but make the diagnosis uncertain

- Coexistence of any other abnormality which may by itself cause cognitive impairment, but judged not to be the cause of dementia (e.g., presence of relevant vascular disease in imaging).
- Time interval between the development of motor and cognitive symptoms not known.

IV. Features suggesting other conditions or diseases as cause of mental impairment, which make it impossible to reliably diagnose Parkinson's Disease Dementia

- Cognitive or behavioural symptoms appearing solely in the context of other conditions, such as:
  - Acute confusion syndrome due to:
    - Systemic diseases or abnormalities
    - Drug intoxication
  - Major depression according to DSM-IV classification.
- Features compatible with NINDS-AIREN criteria for probable vascular dementia.

Probable Parkinson's disease dementia

A. Central or core features: Both must be present.
B. Associated clinical features:

- Typical profile of cognitive deficits, including impairment of at least two or more of four cognitive domains (impaired attention that may fluctuate, impaired executive functions, impaired visuospatial functions and impaired free recall memory that generally improves with clueing).
- The presence of at least one behavioural symptom (apathy, depressive or anxious mood, hallucinations, delusions, excessive daytime sleepiness) support the diagnosis of probable Parkinson's disease dementia. The absence of behavioural symptoms however does not exclude the diagnosis.

C. None of the features of group III.
D. None of the features of group IV.

Possible Parkinson's disease dementia

A. Central or core features: Both must be present.
B. Associated clinical features:

- Atypical cognitive impairment profile in one or more domains, such as prominent or receptive type aphasia (fluent), or pure storage failure amnesia (amnesia that does not improve with clueing or with recognition tasks) with reserved attention.
- Behavioural symptoms may or may not be present.

C. One or more features of group III.
D. No feature from group IV.

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Appendix 1.10. Criteria for the clinical diagnosis of FTLD, semantic dementia and progressive non-fluent aphasia[51] translated by the SEN guideline, 2009,[6,52]

Criteria for the clinical diagnosis of frontotemporal dementia

I. Central criteria:

A. Insidious onset and gradual progression
B. Early deterioration of social behaviour and interpersonal relations.
C. Early impairment of quantitative self-regulation capacity of personal behaviour
D. Early superficiality and emotional indifference
E. Early anosognosia

II. Manifestations that support the diagnosis:

A. Onset before the age of 65
B. Family unit of dementia or history of a similar disorder within the immediate family.
C. Behavioural disorder

1. Deterioration in personal care and hygiene
2. Lack of flexibility and mental rigidity
3. Distract ability and lack of persistence
4. Hyperorality and dietary changes.
5. Stereotyped and perseverative behaviour
6. Utilisation behaviour

D. Speech and language impairment

1. Alteration in expressive facet:
   - Loss of spontaneity and language concreteness
   - Laboured speech
2. Stereotyped language
3. Echolalia
4. Perseverance
5. Late mutism

E. Physical signs

1. Reflection of cortical disinhibition
2. Urine incontinence
3. Akinesia, rigidity, tremors
4. Low and labile blood pressure
5. Bulbar palsy, muscular atrophy and weakness, fasciculation (neuron motor disor**der)**

F. Additional tests

1. Neuropsychological examination: Intense alteration during examination of the frontal functions, in the absence of considerable memory, language and spatial perception disorder.

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2. Normal electroencephalogram in stages with obvious dementia
3. Brain neuroimaging tests (structural and/or functional): Abnormality of frontal and/or anterior temporal region

III. Aspects that exclude the diagnosis:

A. Clinical aspects

1. Sudden onset, acute intercurrent deterioration episodes
2. Previous head trauma close to the onset of the manifestations
3. Intense memory disorder during the initial stages of dementia
4. Spatial disorientation
5. Logoclonia and rapid loss of chain of thought
6. Myoclonia
7. Corticospinal type weakness
8. Cerebellar ataxia
9. Choreoathetosis

B. Additional tests

1. Predominantly postrolandic location alterations in structural or functional neuroimaging tests, or multifocal brain lesions in computed tomography or magnetic resonance
2. Results in laboratory tests indicative of brain affectation of an inflammatory or metabolic alteration, such as for example multiple sclerosis, syphilis, AIDS or herpetic encephalitis.

Criteria for the clinical diagnosis of semantic dementia

The semantic disorder (difficulty to understand the meaning of words and/or identify objects) is the most outstanding alteration at the onset and during the entire disease. Other cognitive functions, including autobiographic memory, remain intact or relatively preserved.

I. CENTRAL DIAGNOSTIC ASPECTS

A. Insidious onset and gradual progression
B. Language disorder characterised by:

1. Fluent spontaneous speech but progressively poor in content
2. Loss of meaning of words, evidenced by an alteration in the capacity to name and to understand
3. Semantic paraphasia

and/or

C. Perception disorder characterised by:

1. Prosopagnosia: alteration of recognition of the identity of known faces and/or
2. Associative agnosia: alteration of recognition of the identity of objects

D. Copy of drawing and tests of element association based on perception data remain normal

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E. Normal repetition of isolated words
F. Normal reading and writing to dictation (of words that are read and written according to standard language rules)

II. ASPECTS THAT SUPPORT THE DIAGNOSIS

A. Aspects that support the diagnosis of frontotemporal degeneration
   1. Onset before the age of 65
   2. History of similar disorder in immediate family
   3. Motor neurone disease (in a minority of patients), with bulbar palsy, muscular weakness and wasting and fasciculations.

B. Speech and language
   1. Logorrhoea
   2. Idiosyncratic use of words
   3. Absence of phonemic paraphasia
   4. Dyslexia and superficial dysgraphia (in irregular words of non-Spanish language whose pronunciation does not correspond to that of its syllables)
   5. Arithmetic calculation not changed

C. Behaviour
   1. Loss of interest and empathy (effective syntony) with other people
   2. Decrease of interest in surroundings
   3. Miserliness or greed

D. Physical signs
   1. Absence or late appearance of cortical disinhibition reflexes
   2. Akinesia, hypertonia, tremors

E Additional tests
   1. Neuropsychology
      a. Intensive semantic impairment, evidenced by deficiencies in the understanding of words and in naming and/or recognising objects and faces
      b. Phonology and syntaxes, elementary perceptive processing, spatial skills and episodic memory preserved
   2. Normal electroencephalogram.
   3. Brain neuroimaging (structural and/or functional): Abnormality (symmetric or are symmetric) that prevails in the anterior temporal region

III. ASPECTS THAT EXCLUDE THE DIAGNOSIS

A. From the case history and examination
   1. Sudden onset and ictal events
   2. Head trauma close to the onset of the manifestations
   3. Intense early amnesia
   4. Spatial disorientation

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5. Propulsive or accelerated speech, logoclonia, with losses in the thinking course
6. Myoclonia
7. Corticospinal weakness
8. Cerebellar ataxia
9. Choreoathetosis

B. Additional tests

1. Brain neuroimaging
   a. Structural or functional deficiency prevails in the retrorolandic region.
   b. Multifocal lesions in computed tomography or magnetic resonance
2. Analytical laboratory tests discover signs of brain affectation due to inflammatory or infectious processes such as multiple sclerosis, syphilis, AIDS or herpetic encephalitis.

Criteria for the clinical diagnosis of progressive non-fluent aphasia

Initially and throughout the evolution, the most prominent feature is difficulty with expressive language, all other cognitive functions remaining relatively unimpaired or normal.

I. CENTRAL DIAGNOSTIC ASPECTS

A. Insidious onset and gradual progression
B. Spontaneous non-fluent speech and at least one of the following alterations: Agrammatism, phenomic paraphasia, anomia.

II. ASPECTS THAT SUPPORT THE DIAGNOSIS

A. Aspects support the diagnosis of frontotemporal degeneration

1. Onset before the age of 65
2. History of similar disorder in immediate family
3. Motor neuron disease (in a minority of patients), with bulbar palsy, muscular weakness and wasting and fasciculations.

B. Speech and language

1. Stuttering or oral apraxia
2. Alteration in repeating ability
3. Alexia, agraphia
4. Understanding of normal words in initial stages
5. Mutism in advanced stage

C. Behaviour

1. Appropriate social behaviour in initial stages
2. Behavioural alteration similar to those observed in frontotemporal dementia, in advanced stages

D. Physical signs: late appearance of contralateral cortical disinhibition reflexes, akinesia, rigidity and tremors

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E. Additional tests

a. Neuropsychology: Non-fluent aphasia, in absence of intense amnesia and spatial perception disorder
b. Normal electroencephalogram Or slight are symmetric slowing down
c. Brain neuroimaging (structural and/or functional): Asymmetric abnormality that prevails in the dominant hemisphere, generally the left)

III. ASPECTS THAT EXCLUDE THE DIAGNOSIS

A. From the case history and examination

1. Sudden onset and ictal events
2. Head trauma close to the onset of the manifestations
3. Intense early amnesia
4. Spatial disorientation
5. Propulsive or accelerated speech, logoclonia, with losses in the thinking course
6. Myoclonia
7. Corticospinal weakness
8. Cerebellar ataxia
9. Choreoathetosis

B. Additional tests

1. Brain neuroimaging

   a. Structural or functional deficiency prevails in the retrorolandic region.
   b. Multifocal lesions in computerised tomography or magnetic resonance

2. Analytical laboratory tests discover signs of brain affectation due to inflammatory or infectious processes such as multiple sclerosis, syphilis, AIDS or herpetic encephalitis.

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Appendix 1.11. NINDS-AIREN Criteria for vascular dementia, adaptation and translation taken from the SEN CPG, 2009[6,46]

I. Compulsory criteria for the diagnosis of **probable vascular dementia**:

1. Dementia: decline from a previous level of memory and two or more cognitive functions (orientation, attention, language, visuospatial function, executive functions, motor control, and praxis), severe enough to interfere with activities of daily living (regardless of how physical deficiencies interfere). Patients are excluded with disturbance of consciousness, acute confusional syndrome, psychosis, severe aphasia or major sensorimotor impairment that prevents the adequate objectification of neuropsychological alterations. Also excluded are patients with systemic disorders or other brain diseases (such as Alzheimer' disease) that in and of themselves could account for the cognitive deficits.

2. Cerebrovascular disease, defined by the presence of focal signs consistent with prior stroke, with or without history of prior stroke, and evidence of vascular lesion in neuroimaging tests – CT or MRI—(multiple large vessel infarct or single strategically placed infarct to produce cognitive deficit – angular gyrus, thalamus, basal forebrain, PCA or ACA territories -, or multiple basal ganglia and subcortical or periventricular white matter lesions, or combinations thereof).

3. Relationship between sections 1 and 2 above, inferred by the presence of one or jore of the following:

– Onset of dementia within 3 month following a stroke
– Abrupt deterioration in cognitive function
– Fluctuating or stepwise progression of cognitive deficits.

II. Feature consistent with probable vascular dementia:

a. Early presence of gait disturbance.
b. History of unsteadiness and frequent falls
c. Early appearance of increase of urinary frequency, urgency and other bladder control disorder not explained by urological disease.
d. Pseudobulbar palsy
e. Personality and mood change, abulia, depression, emotional incontinence, and other subcortical defcits including psychomotor retardation and abnormal executive function.

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III. Features that make the diagnosis of vascular dementia uncertain or unlikely:

a. Early onset of memory deficit and progressive worsening of memory and other cognitive function, in the absence of corresponding focal lesions on brain imaging.
b. Absence of focal neurological signs, other than cognitive disturbance
c. Absence of cerebrovascular lesions in CT or MRI.

IV. Criteria for **possible vascular dementia**:

Dementia (according to I.1), with focal neurological signs, in patients in whom brain imaging studies to confirm CVD are missing, or in those that do not show a clear temporal relationship between dementia and stroke; also in patient with evidence of cerebrovascular disease, with subtle onset or course different to that expected (prolonged plateaux or improvements).

V. Criteria for **definite vascular dementia**:

a. Clinical criteria for probable vascular dementia
b. Histopathological evidence of cerebrovascular disease obtained from biopsy or autopsy
c. Absence of neurofibrillary tangle and neuritic plaque exceeding those expected for age
d. Absence of other clinical or pathological disorder capable of explaining dementia

VI. Classification of vascular dementia for research purposes:

– Cortical vascular dementia
– Subcortical vascular dementia
– Binswanger's disease
– Thalamic dementia:

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Appendix 1.12. Hachinski ischaemia scale to distinguish between VD and AD[59]

Abrupt onset	2
Stepwise deterioration	1
Fluctuating course	2
Nocturnal confusion	1
Preservation of personality:	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
High Blood Pressure	1
History of stroke	2
Signs of atheroclerosis	1
Focal neurological sign	2
Focal neurological symptoms	2

A score of 4 or less supports an Alzheimer's type dementia, and a score of 7 or more supports a diagnosis of multi-infarct dementia.

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Appendix 1.13. SEN criteria for mild cognitive impairment (2009)[6,65]

Disturbance in one or more of the following cognitive areas (or domains): Attention/executive functions:

- Language
- Memory
- Visuopatial area

This disturbance must be:

- Acquired
- Reported by the actual patient or by a reliable informant
- Evolution of months or years
- Objectified in neuropsychological examination (performance < 1 or 1.5 DE respect to the group of the same age and study level)

The cognitive disturbance interferes minimally or does not interfere with normal activities

There is no disorder of consciousness level, acute confusion state, focal neurobehavioural syndrome or dementia

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Appendix 1.14. Global Deterioration Scale (GDS) and Functional Assessment Staging (FAST), correspondence in AD, adapted from the translation into Spanish by the behaviour and dementia study neurology study group (SEN guideline, 2002)[19]

GDS Stage	FAST stage and clinical diagnosis	Characteristics
GDS 1. No cognitive disturbance	1. Normal adult	No difficulty either subjectively or objectively
GDS 2. Very mild cognitive deficit	2. Normal aged adult	Complaints of memory loss. No deficit is objectified in clinical examination. Full knowledge and evaluation of symptoms.
GDS 3. Mild cognitive deficit	3. Incipient AD	First clear-cut deficits Manifestations in one or more of these areas: • Getting lost in an unfamiliar location • Evidence of poor working performance • Incipient difficulty to remember people's names • After reading, retains little material • Forgets location, loses or misplaces valuable objects • Little ability to remember new people they have met • Decreased organisation capacity. Objective evidence of memory deficit only observed with an intensive interview.
GDS 4. Moderate cognitive deficit	4. Mild AD	Decreased ability to perform complex tasks. Clear-cut deficit on careful clinical interview: • Decreased knowledge of current and recent events • Patients may exhibit some deficit in remembering personal history • Obvious concentration difficulty on serial subtractions.

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		• Decreased capacity to travel, handle finances, etc. Frequently, there are no defects in: • Orientation in time and person. • Recognition of familiar people and faces. • Capacity to travel to familiar places. Denial is dominant defence mechanism
GDS 5. Moderately severe cognitive deficit	5. Moderate AD	The patient cannot survive for a long time without some assistance help. Requires help to choose clothing. Is unable to remember important aspects of daily life (address, telephone, relatives' names). Certain disorientation in time and space is frequent. Difficulty to count down from 40 by 4s, or from 20 by 2s. They generally know their own name and their spouse's and children' names.
GDS 6. Severe cognitive deficit	6. Moderate-severe AD	Improperly put on clothing without assistance or prompting. They sometimes forget the name of their spouse on whom they are dependent to survive. They retain some data from the past. Time and space disorientation Difficulty to count by 10s both backward and forward. They remember their name and differentiate family from strangers. Diurnal rhythm frequently disturbed. Personality and emotional change occur (delusions, obsessive symptoms, anxiety, agitation or aggressiveness and cognitive abulia).
	6a	Improperly put on clothing without assistance or prompting
	6b	Unable to bath themselves correctly
	6c	Unable to use the toilet
	6d	Urine incontinence
	6e	Faecal incontinence
GDS 7. Very severe cognitive deficit	7. Severe AD	Progressive loss of all verbal and motor skills. Neurological signs are often seen

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	7a	Unable to say more than half a dozen words
	7b	Only able to say one single intelligible
	7c	Unable to walk without assistance
	7d	Cannot sit up without assistance
	7e	Loss of ability to smile
	7f	Loss of ability to hold up head independently

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Appendix 2. Information for patients

What is dementia?

The World Health Organisation defines dementia as a "syndrome due to a disease of the brain, usually of a chronic or progressive nature, in which various disturbances of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement. Consciousness is not clouded. Impairments of cognitive function are accompanied by deterioration in emotional control, behaviour or motivation".

These losses are greater than in normal ageing and with sufficient entity to affect the daily activities that the person used to carry out.

If the cognitive problems start after the age of 65, it is considered that the dementia is late onset or senile. If it starts under the age of 65, it is considered that the dementia is early onset or presenile.

Is dementia frequent?

It affects 5% of people over the age of 65 and increases with age, until it affects 20% of people over the age of 80. The most frequent dementia is Alzheimer's disease, which represents 70% of the total of dementias. Other dementias that occur less frequently, are:: Vascular, dementia with Lewy bodies, frontotemporal degeneration and secondary dementias.

What are the symptoms of dementia?

The symptoms are mainly cognitive (memory, language, calculation skills and decision-making, etc), but behaviour disorders may also appear (indifference, depression, irritability, aggressiveness, improper behaviour, delusions, hallucinations,) functional disturbance (repercussion of work, on social and family life, loss of autonomy for hygiene and dressing), sleep, eating disorders or urinary incontinence.

What is the natural course of dementia?

With the exception of dementia due to a cause that can be treated, as is the case of secondary dementias, the course of the disease is unavoidably progressive. With time, patients lose independence, they are unable to care for themselves, get dressed, go to the toilet, eat or wash themselves and behavioural disturbances may also appear. The disease evolves in a way that there may be periods of stability and periods of fast deterioration.

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What are the risks factors of dementias?

Some factors slightly increase the risk of suffering dementia. The most outstanding are age, depression, nicotine addiction, exposure to pesticides or low schooling level. For inherited cases, if any immediate relatives are affected, that is considered a risk.

On the other hand, physical exercise, intellectual activity and the moderate consumption of alcohol could act as beneficial factors.

How is dementia diagnosed?

The diagnosis must be carried out by a physician based on the symptoms shown by the patient and what they are told by the informant. There must be a reliable informant, as, due to the nature of the disease, patients will not be able to inform well and will not be aware of all their symptoms.

Some tests help rule out other diseases that may simulate dementia or distinguish between different types of dementia.

Which tests must be performed to diagnose dementia?

The systematic tests that must be carried out to diagnose dementia are:

- Blood analysis.
- Cognitive tests: They permit establishing the patient's degree of deterioration, distinguishing between dementias, mild cognitive impairment, depression and normality.
- Radiological tests (head scan or magnetic resonance).

In complex cases with uncertain diagnosis, other more complex tests may be required, which are normally carried out in specialised centres.

Is dementia inherited?

The majority of the cases of dementia are not inherited, although if there is a history in the family this may slightly increase the risk of suffering it in the future. Only a very small percentage of cases of dementia (one or two cases out of every thousand) is caused by alterations in the genes. These cases are inherited and are transmitted from parents to children with 50% probability of each child suffering from it.

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When must genetic studies be performed on patients with dementia?

Genetic studies must only be performed in cases of early onset Alzheimer's (< 65 years) with immediate family affected; in cases of frontotemporal lobar degeneration with immediate family affected or in cases of prion diseases, provided that the person affected or their relatives want to.

In these cases, it is recommended for the patient and family to be referred to specialised centres in genetic counselling.

What treatments exist for dementias?

Some secondary dementias have specific treatment depending on the cause (surgery for hydrocephalia or tumours, corrections of endocrine and metabolic disorders, etc).

But the great majority of dementias are degenerative and currently there is no treatment that might curb its natural progression; however, there are some drugs that have proved to be effective in Alzheimer's disease, (donepezil, galantamine, rivastigmine, memantine) and some of them also in other degenerative diseases.

Other pharmacological treatments may be necessary at times to treat behavioural disorders (insomnia, delusions, hallucinations, aggressiveness, etc.).

Non-pharmacological treatments, especially cognitive intervention programmes may also provide benefits in some aspects, although the magnitude of this effect is moderate.

Other treatments, such as hormones, anti-inflammatorie, piracetam, propentofylline, nimodipine, selegiline, hydergine, idebenone, citicoline, ginkgo biloba, vitamins E or B, supplements of copper, ginseng, lecithin, omega-3 fatty acids, yok or the use of traditional medicine or medicinal herbs, vitamins, acupuncture, yokukansan have not shown a beneficial effect in available studies.

What role does the caregiver occupy in the care of people with dementia?

Dementia is a disease that has a great impact on the patient's close environment, so the figure of caregiver is extremely important.

The care of a patient with dementia requires great dedication and it may sometimes involve leaving work, having less personal freedom, need for economic resources, etc. for the person carrying out this work. All of these aspects may produce anxiety, depression, stress and changes in the caregiver's health and they must be considered by the health team.

There are currently social resources that are managed through social work professionals, or community resources, mainly associations of families, that can provide help to care for patients at home or to plan and evaluate the use of external services (external caregiver, day centre, nursing home, law of dependence, etc).

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May the care of people with dementia have ethical and/or legal implications for their family or caregivers?

In the event of a case of dementia in the family, some ethical and legal aspects must be considered. The drafting of advance directives or living will, when people still preserve their capacity, must be questions to be taken into account. Also, aspects such as the evaluation of the capacity to drive vehicles or own firearms requires reconsideration. At other times, it is necessary to start a legal incapacitation process, or else take financial decisions, etc, for which it is advisable to receive legal advice.

How can we contribute to research in dementia?

Given that the causes of the majority of the different types of dementia are unknown, research is essential to advance in the understanding of these diseases and in the development of future treatments. To be able to do this, the collaboration of as many patients as possible is necessary, who may contribute in many different ways. These include:

- Participating in studies of new drugs (clinical trials).
- Participating in non-pharmacological research studies. For example, just by way of blood extraction, it is possible to obtain a sample of DNA, which may help in numerous studies.
- Donating the brain: This permits, in the case of death, confirming the diagnosis and having a biological sample of great value for research.

What is Alzheimer's disease?

It is a neurodegenerative disease and the most frequent type of dementia, especially, although not exclusively, in the older population. The process usually starts with loss of memory and inability to retain new information. Patients repeat the same things and do not recognise their faults. Other faculties are then affected, (speech, reasoning, orientation, etc). In parallel, patients are going to lose autonomy; thus, in a first stage, people require supervision for complex activities. As the disease progresses, they will require direct assistance for the most basic activities of daily living.

Furthermore, the majority of patients may present neuropsychiatric symptoms, such as indifference, loss of control of emotions, depression or changes in appetite. As the disease progresses, hallucinations, delusions, agitation and aimless movements, such as erratic wandering, may appear.

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What is the cause of Alzheimer's disease?

The cause of Alzheimer's disease is unknown today. However, it is known that there are abnormal deposits of proteins (beta-amyloid and hyperphosephorylated tau) in the brain of patients with Alzheimer's, which alter the neuronal functioning, which leads to the death of the neurons affected. The lesions initially concentrate in regions of the brain that are essential for memory and progressively spread through the cerebral cortex, affecting areas that control other functions.

There are cases, not many, when the disease is inherited and may affect patients under the age of 60, in whom genetic mutations that cause the disease have been found.

What is vascular dementia?

This is a type of dementia produced by the lack of blood irrigation in important areas for normal cognitive functioning. Vascular dementia is the second most frequent dementia after Alzheimer's disease, and represents 12% of dementias. It is normal for both types of dementia to co-exist, interacting together and often it is impossible to distinguish the extent to which each one contributes to the patient's clinical picture.

Are there different types of vascular dementia?

There are several types of vascular dementia, including:

- Multi-infarct dementia: Due to repeated infarctions of the large arteries in the brain cortex area. It is a sudden onset dementia with stepwise progression.
- Dementia due to single strategic infarct, that is, which produces one single lesion but in an area of the brain that is important for cognition.
- Subcortical vascular or small vessel dementia: Accumulation of infarcts or vascular lesions of the deep white matter of the brain due to disease of the small vessels. Normally it is caused by arteriosclerosis. Dementia caused in this case is progressive and there is usually slowness, gait disturbance and incontinence.
- Mixed dementia: This is a combination of several types of dementia. The most normal is the combination of Alzheimer's disease and vascular disease.
- Dementia due to haemorrhagic lesions.

What is the natural course of vascular dementia?

Generally, whether it is stepwise or continuous, the evolution is similar to the other types of dementia, that is, a tendency towards progressive deterioration.

However, due to its variability, the evolution of vascular dementia is not very predictable. Certain stability is often observed for longer or shorter periods of time, although a new vascular event may cause a sudden decline of the cognitive function.

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How is vascular dementia diagnosed?

The diagnostic criteria are based on the presence of dementia, on a history of stroke, focal neurological signs and vascular lesions in neuroimaging. There must also be a correlation between the degree of vascular affectation and the clinical and neuropsychological data.

What treatment exists for vascular dementia?

Although infarcts are not reversible, the vascular risk factors must be treated (diabetes, high blood pressure, high cholesterol, etc) to reduce the risk of new lesions. Some drugs used to treat Alzheimer's disease may be used, although the clinical benefit is small.

What is frontotemporal lobar degeneration or frontotemporal dementia?

Frontotemporal lobar degeneration is a rare neurodegenerative disease, but in patients under the age of 65 it is the second cause of degenerative dementia. Atrophy of the frontal and/or temporal lobes and of subcortical structures is observed in the brain, with abnormal protein deposits.

There are different clinical and neuropathological variants, but the frontal variant is the most frequent and represents more than half of the cases. In the frontal variant cases or frontotemporal dementia, behavioural changes are the most prevalent at the start. In other cases, so-called semantic dementia and non-fluent progressive aphasia, their ability to express themselves and/or understand are initially the prevailing disorders. Memory disorders, although they may appear, are not so important in the initial stages as in Alzheimer's disease.

What are the symptoms of frontotemporal lobar degeneration?

The early manifestations are behavioral disorders (disinhibition, violation of social norms, abandonment of personal care, lack of empathy, etc.) and/or of language, (loss of meaning of words or difficulties to express themselves and/or articulate words) and less memory affectation. In advanced stages, all the cognitive functions are affected and motor complications also appear in some patients, either with similar symptoms to Parkinson's disease (parkinsonism) or with similar symptoms to amyotrophic lateral sclerosis (associated motoneuron disease). The patients' symptoms and additional tests differentiate frontotemporal lobar degeneration from Alzheimer's disease in the majority of the cases, although in others the clinical evolution of both may be very similar, and there are cases when a certain diagnosis may only be established in the post-mortem study.

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What is the natural course of frontotemporal lobar degeneration?

Just like all other neurodegenerative diseases, the evolution of this dementia is progressive in a similar way to Alzheimer's disease and the cognitive deterioration worsens and finally becomes global. However, it must be pointed out that the disease is very heterogeneous and its clinical course varies a great deal in different patients.

How is frontotemporal dementia diagnosed?

The diagnosis is carried out based on clinical criteria, due to the presence of certain symptoms and with the support of radiological tests and ruling out other processes. If there is a family background of the same disease, it may be a genetic case. In those cases, a genetic study may be performed if the patient and/or family are interested.

What treatment exists for frontotemporal lobar degeneration?

As in all other neurodegenerative diseases, there is no curative treatment. The drugs used to treat Alzheimer's disease do not offer any benefit in frontotemporal lobe degeneration, and at times they make produce side effects.

What is dementia with Lewy bodies?

This is a neurodegenerative disease that produces typical lesions (Lewy bodies and neurites) in different regions of the nervous system.

What are the symptoms of dementia with Lewy bodies?

Other typical symptoms appear, apart from the dementia:

- Motor symptoms similar to those of Parkinson's disease: Tremors, rigidity, slowness, inexpressive face, small step gait with blockage, accelerations and hunched posture or lack of equilibrium.
- Fluctuations of consciousness level, where the patient is more sleepy or not very reactive, for hours or days, or is attentive and with a clearer mind.
- Visual hallucinations, with visions of people or animals, that appear spontaneously and not only as a result of the medication.
- Other symptoms: Abnormal functioning of the autonomous nervous system, which may produce low blood pressure when they get up, urine incontinence or erectile dysfunction, agitated dreams or intolerance to the drugs used to treat the agitation, aggressiveness and hallucinations and delusions.

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Is Dementia with Lewy bodies frequent?

Dementia with Lewy bodies is less frequent than Alzheimer's disease, but it is the third most frequent after the latter and vascular dementia. It represents approximately 8% of all dementias.

What is Parkinson’s disease dementia?

This is dementia that appears in patients who previously had had Parkinson's disease. In people affected by the disease, it is normal to find small cognitive deficits, mainly mental slowness, memory problems and lack of attention, but some patients end up developing considerable cognitive impairment, which may develop into dementia.

The brain lesions caused are similar to those of dementia with Lewy bodies.

Is Parkinson's disease dementia frequent?

Parkinson's disease dementia is very frequent in patients affected by this disease and it may affect up to 80% of them after eight years with the disease.

What is its natural course?

Like all neurodegenerative diseases, the evolution is progressive. The motor and cognitive symptoms worsen with the passing of time, as well as the patient's degree of dependence. Furthermore, the need to increase the number of drugs and the dose usually causes more side effects.

What is the cause of dementia with Lewy bodies and Parkinson’s disease dementia?

As in the majority of degenerative diseases, there is no known cause. A minority of the cases of Parkinson's disease have been associated with genetic mutations and families have been found where some members have Parkinson's disease and others have dementia with Lewy bodies, so genetics could play an important role, although in the majority of the cases, there is no past history in the family or genetic alterations.

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How is dementia with Lewy bodies diagnosed?

The diagnosis is clinical and is based on the presence of dementia, hallucinations parkinsonism, (slow movements, muscular rigidity, lack of stability, etc.), ruling out other diseases that may justify the symptoms. As in all dementias, the normal tests are blood analysis and neuroimaging tests, (scan or resonance) to rule out other diseases. If in doubt between Alzheimer's disease and dementia with Lewy bodies, especially when there is no clear parkinsonism, more complex neuroimaging tests must be carried out.

How is Parkinson's disease dementia diagnosed?

Parkinson's disease dementia is diagnosed when a patient already has a diagnosed Parkinson's disease via appropriate criteria, and presents cognitive impairment of sufficient magnitude to be considered dementia. The fact that this impairment is not due to other diseases must be ruled out. Cognitive impairments may be difficult to evaluate when the patient is a very affected by Parkinson symptoms.

What treatment exists for dementia with Lewy bodies and Parkinson's disease dementia?

As with Alzheimer's disease, these are degenerative dementias and currently there is no treatment that can curb its natural progression. Some of the drugs used in Alzheimer's disease may also slightly improve the cognitive, psychiatric (hallucinations) and functional symptoms in some patients.

Treatment of Parkinson symptoms presents a considerable limitation in the use of drugs, as anti-Parkinson drugs may produce or worsen the psychotic symptoms, such as delirium and hallucinations, whilst the other medications used to treat the symptoms may worsen the Parkinson symptoms.

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Appendix 3. Glossary

Abuse: This refers to either a single or repeated act, or lack of appropriate measures, which occurs within any relationship where there are expectations of trust that causes harm or anguish in the elderly person.

ACE inhibitors: These are drugs whose action mechanism is the competitive and reversible inhibition of the cholinesterase enzyme (donepezil and galantine). Rivastigmine also inhibits the butyrylcholinesterase enzyme at a peripheral level.

Acute pain: Of sudden onset and short duration.

ADAS-Cog: This is the cognitive part of the Alzheimer's Disease Assessment Scale, which includes 11 individual tests: Spoken language ability (from 0 to 5), spoken language comprehension (from 0 to 5), ability to remember test instructions (from 0 to 5), word-finding difficulty (from 0 to 5), commands (from 0 to 5), naming objects (from 0 to 5), constructive praxis (from 0 to 5), ideational praxis (from 0 to 5), orientation (from 0 to 8), word recall (from 0 to 10), and word recognition (from 0 to 12). The score varies between 0 and 67; the high score indicates greatest impairment.

ADCS-ADL: alzheimer's disease Cooperative Study - Activities of Daily Living. This was specifically designed to assess the functional ability over a wide severity range in patients with Alzheimer's disease. The 19-item ADCS-ADEsev19 has 54 points. The 23-item ADCS-ADL23 has 78 points.

Advance directive document (ADD): Prior instructions document, which may include indications that must be taken into account, in the medical area, when the time comes when one cannot express one's will, as well as appoint a representative who will become a valid interlocutor with the physician or medical team. It may be formalised in public document before notary or it may be private.

Advanced Activities of Daily Living (AADL): These are a series of especially complex and elaborate activities to control the physical medium and the social environment that allow individuals to develop a social role, maintain good mental health and good quality of life. They include: Work, gardening, DIY, hobbies, travelling, social participation, sports, etc.

Advanced dementia: Stage of dementia, whatever its aetiology, characterised by great difficulty to carry out basic activities of daily living, (getting dressed, having a bath and washing and use of the toilet). With a hierarchical loss of functions that sub-classifies it into degrees of more severity. Mobility reduction and sphincter disturbances are common in the most advanced stage.

Agnosia: Recognition impairment that is due to sensory disorders or global cognitive deficits, with prior knowledge of the object to be recognised.

Agony: State that precedes death in those diseases where life gradually fades away. It may last for hours or a few days and is characterised by the appearance of general physical impairment, which may be quickly progressive, showing an increase in weakness, prostration and decrease of alertness, with a consequent increase in hours in bed, decreasing intake and alteration of vital signs, progressive tendency to low blood pressure, tachycardia and oliguria, with perception of imminent death by the patient, family and team of health professionals.

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Alzheimer's disease: It is a degenerative type clinical-pathological entity that evolves progressively, which is clinically characterised by cognitive impairment and dementia and neuropathologically by the presence of neurofibrillary tangles and neuritic plaques. It is the most frequent type of dementia, representing up to 70% of the dementia cases. In the majority of cases, the presentation is sporadic, but there are cases associated with known autosomal dominant transmission mutations.

Anorexia: This is an eating disorder, which is characterised by a lack of normal appetite; it may be due to physiological causes, and which disappears when the cause disappears or else to psychological causes.

Aphasia: Loss of ability to produce and/or understand language. Language impairment due to brain lesion.

APOE: Glycoprotein involved in the transport of cholesterol and other lipids through the cell membranes in the brain. It occurs mainly in the glial cells and seems to be involved in cell growth and neuron regeneration.

Apolipoprotein E (ApoE): Glycoprotein involved in the transport of cholesterol and other lipids through the cell membranes in the brain. It occurs mainly in the glial cells and seems to be involved in cell growth and neuron regeneration. The ApoE Gene has three polymorphisms: ε3 (the most frequent, present in 75% of the population), ε4 and ε2.

Apraxia: Disturbance of gesture (motor action with purpose) which is not explained by elementary motor disorders (paresia, dystonia, tremors, etc) and with full knowledge of the action that is carried out.

Asthenia: Tiredness following minimal effort, decrease of functional capacity, weakness defined as an advanced feeling of inability to start any activity, decrease of the capacity of concentration, memory disturbance and emotional incontinence.

Barthel Index: It assesses 10 activities of daily living (ADL): Feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfers, walking on level surface, going up and down stairs. It is scored from 0 to 100 (90 for patients limited to wheelchair). The scores are not the same for each activity. Bladder and bowels must be evaluated with respect to the previous week. The global results are grouped together in four categories of dependence, in agreement with the score obtained: Independent (86 to 100), light dependence (60 to 85), moderate dependence (40 to 55), severe dependence (20 to 35), total dependence (0 to 19).

Basic Activities of Daily Living (BADL): These are a series of primary activities for people, aimed at their self-care and mobility, which provide them with elementary autonomy and independence, enabling them to live without requiring continuous assistance from others; they include activities such as: Eating, sphincter control, using the toilet, getting dressed, getting washed, moving about, walking, etc

Before-after study: Study whereby the same group of people is assessed before and after an intervention or treatment.

Behavioural and psychological symptoms: These are symptoms of disturbed perception, thought, content, mood and behaviour that might appear in people with dementia, forming part of the expression of the disease.

Bias: This is an error that appears in the results of the study due to factors that depend on the collection, analysis, interpretation, publication or review of the data, and which might lead to incorrect conclusions or are systematically different to the truth about the objectives of a research.

Blind study: A study where some of those involved do not know which person is receiving one treatment or another, or placebo. The treatment is hidden to prevent the results of the research

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being "influenced" by the placebo effect or by the bias of the observer. To correctly evaluate the blinding, it is necessary to know who in the study has been blinded (patients, researchers, health professionals, results and/or statistic awarders).

Cachesia: Picture of malnutrition and weight loss that may be associated with asthenia.

Caregiver: A person that provides unselfish and voluntary support to people affected, who either live with the patient or else devote part of their time (over 20 hours a week) to caring for the patients.

Case and control study: This is an observational epidemiological study, where the individuals are selected depending on whether they have (cases) or do not have (control) a certain disease, or in general a certain effect. Once the individuals have been selected for each group, it is studied whether they were exposed or not to a characteristic of interest, and the proportion of those exposed in the case group is compared with the proportion of the control group.

Categorical scales: Qualitative descriptors are used, and the patient selects which is the most appropriate. Their advantage is the easy understanding thus favouring completion even in advanced stages of the disease. Its disadvantage is the limitation of the response options and the individual variability in the interpretation of the categories. The scores are: 1. Nothing; 2. Little; 3. Quite a lot; 4. A lot.

CDR: Clinical dementia rating is a global evaluation scale of the degree of dementia that assesses six cognitive and functional areas: Memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care. A total score is obtained by summing up the scores in each area and a composite score, where the evaluation of the state of the memory is fostered.

Cerebrovascular or vascular dementia: This is dementia secondary to one or several vascular brain lesions, of any aetiology.

CGIC: The clinical global impression of change is a global classification of all the domains of the current disease of the patient compared with the initial value. It is a seven-point scale, which goes from 1 (much better) to 7 (much worse): 4 indicates changes. The same professional carries out the assessments at both time points with contributions from family and caregivers.

Chronic pain: Lasts for more than 1 month.

CIBIC-plus: Change impression scale based on interviews with the physician, it provides a global assessment of the function in four areas: general, cognitive, behavioural and of the activities of daily living. All participants receive 4 points at the start of the study and the subsequent assessments on a scale from 1 to 7 points are associated with the initial value where 1 is notorious improvement, and 7 is considerable worsening. The information is obtained from the caregiver and from the patient. There are different versions.

Clinical Practice Guideline: Set of systematically developed instructions, directives, statements or recommendations, whose purpose is to help professionals and patients take decisions about the most appropriate healthcare modality for specific clinical circumstances.

Clinical series: Also called case series, it is a type of study where the experience with a group of patients with a similar diagnosis, with no comparison group, is described.

Clinical Trial: Experimental study to evaluate the efficacy and safety of a treatment or intervention.

Cochrane library: Database on effectiveness produced by the Cochrane Collaboration, comprised among others, of original systematic reviews of this organisation.

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Cochrane review: Systematic Review carried out according to the Cochrane Collaboration methodology and published in the Cochrane Library.

Cohort study: This consists in monitoring one or more cohorts of individuals who present different degrees of exposure to a risk factor in whom the appearance of the illness or condition studied is measured.

Comorbidity: Presence of several added or associated diseases.

Confidence Interval: This is the interval in which the real magnitude of the effect is found (never known exactly) with a pre-established degree of safety or confidence. 95% confidence interval (or 95% confidence limits) are often spoken of. This means that within that interval the real value would be found in 95% of the cases.

Confusion factor: This is a variable that distorts the measurement of the association between another two variables to be studied. The result of the presence of a confusion variable may be the observation of an effect when it really does not exist, or the exaggeration of a real association (positive confusion) or, on the contrary, the mitigation of a real association and even a reversal of the sense of a real association (negative confusion).

Consent (*): Expression of the free and conscious will, validly expressed by a capable person, or by their authorised representative, preceded by adequate information.

Conservator: This is the person who is responsible for assisting, accompanying or advising the person under conservatorship to carry out those acts determined by a ruling. They may not, under any circumstances, replace the will of the person, as they do not represent them.

Conservatorship: It is a reduced scope guardianship which is usually assigned in cases of partial modification of capacity.

Contracture: This is defined as a 50% reduction or more of normal passive movement of the joint.

Delirium: Acute confusion state resulting from diffuse brain dysfunction. It is clinically characterised by the simultaneous disturbance of attention, perception, thought, memory, psychomotor behaviour, emotion and weak-sleep rhythm.

Delphi method: Qualitative research technique of consensus, aimed at comprehensive and dynamic explanation, and the analysis of certain phenomena with the purpose of generating ideas, sharing experiences and sensing tendencies for the future. It purports to analyse a reality, reaching agreements on the phenomena regarding which there is no conclusive information. It is especially useful when working with very subjective elements, when it is difficult to determine their intrinsic value. The method is applied by phases. The problem is formulated and a panel of trained experts is selected to contribute to the study with their knowledge and experience. The questions that will be submitted to study are determined and posed to the members of the panel. An anonymous questionnaire posed to the members of the panel in successive rounds until a consensus is reached. The study concludes with the preparation of a report containing the final results of the survey.

Dementia: It is a clinical syndrome characterised by an acquired deficiency in more than one cognitive domain, which represents a loss with respect to the previous level and which significantly reduces functional autonomy. Dementia frequently appears with behavioural and psychological symptoms (BPSD), also called behavioural and emotional symptoms or neuropsychiatric symptoms.

Dementia with Lewy bodies: Dementia with Lewy bodies is clinically characterised by the association of fluctuating cognitive impairments, parkinsonism and psychotic symptoms, and pathologically by the presence of Lewy bodies and neurite in the brain cortex.

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Donepezil: Reversible central inhibitor of acetylcholinesterase. It is indicated for the symptomatic treatment of mild and moderate AD.

Dyspnea: Subjective experience of breathing problems.

Early onset or pre-senile dementia: A picture of dementia is considered to be early onset or presenile by convention, when the first symptoms appear before the age of 65.

Edmonton Symptom Assessment System: New symptoms or reasons for discomfort are analysed using visual analogical scales: Pain, dyspnoea, nausea, depression, anxiety, well-being, drowsiness, appetite, tirednes. Each scale has a 100 mm line. On the left of the line (0) with the term "absent" reference is made to the absence of the problem in question. On the right side, with the term "worst possible" (100) the maximum intensity of the symptom is expressed. The sum of the measurements on the different lines corresponding to the different symptoms, gives a global score which would be at least 0 and a maximum score of 900. Completion of the scale in people with dementia must be carried out by the caregiver and/or relative with proven and reliable observation capacity. Despite the extensive use of this instrument in Palliative Care units, there are no validation studies.

Effectiveness: Results of a diagnostic, preventive or therapeutic intervention when applied in normal practice, in non-experimental conditions.

Efficacy: Results of a diagnostic, preventive or therapeutic intervention when applied in experimental and/or controlled conditions, for example, in a clinical trial.

Estate/assets administrator: Person named to adequately look after the estate of people who have lost their capacity for self-management and who own a considerable fortune.

Evidence: Tests. Evidence-based Medicine: Medicine based on scientific tests.

Executive functioning: Capacity to think and plan, start, sequence, supervise and stop a complex behaviour.

Formal caregiver: A person, capacitated or not, who directly looks after the person affected, receiving a salary or pecuniary benefits for their work.

Frontotemporal lobar degeneration: It is a neurodegenerative disease that is clinically characterised by prominent behaviour and/or speech alterations, and pathologically by focal atrophy of the frontal and/or temporal lobes. Although it is not very frequent, it is the second cause of dementia in people under the age of 65, after Alzheimer's disease. It does not usually predominantly affect the memory or spatial skills.

Galantamine: Reversible central inhibitor of acetylcholinesterase. It is indicated for the symptomatic treatment of mild and moderate AD.«

GDS: Global deterioration scale is a scale that assesses the deterioration stages from normality (0) to the most advanced stage of dementia (7),

Genetic analysis (*): Procedure aimed at detecting the presence, absence or variants of one or several genetic material segments, which includes indirect tests to detect gene product or a specific metabolite that is indicative above all of a certain genetic change.

Genetic counselling (*): Procedure aimed at informing people about the possible consequences for them or for their descendants of the results of a genetic analysis or screen and its advantages and risks, and where appropriate, to give them advice with respect to possible alternatives derived from the analysis. It takes place both before and after a genetic test or screen and even in absence of these.

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Guardian: Person who is responsible for the care and attention of personal aspects, as well as the administration of their assets, of a person who has lost their self- government capacity due to illness.

Guardianship: Protection mechanism for people who have lost their self-government ability, subject to different control measures, such as the drawing up of an initial inventory, annual accountability, the need to obtain prior authorisation for certain acts of economic importance and the presentation of the final statement of accounts when it ends.

Healthcare Levels: Different clinical care modalities that are provided to people depending on the type of care and the place where this care is provided.

Hyperorality: Oral or dietetic changes, binges, eating whims, excess tobacco and alcohol consumption, oral examination of objects.

Incidence: This is the number of new cases of an illness that are developed in a population during a certain period of time. It tells us the probability of a disease-free individual developing it in a certain period of time.

Informal caregiver: Person who provides unselfish and voluntary support to the person affected. In the majority of the cases they are direct family members (spouse, son/daughter, son-in-law/mother-in-law, siblings, cousins, etc.) or very close friends.

Informed consent (*): This is a formal medical procedure whose objective is to apply the patient's principle of autonomy. Three requirements must exist at least, which are: Free will: Individuals must freely decide to submit themselves to a treatment or participate in a study without there being persuasion, manipulation or coercion. Information: This must be understandable and must include the objective of the treatment or of the study, its procedure, benefits and potential risks, and the possibility of rejecting the treatment or study at any time after it starts, without this being able to harm them with respect to other treatments. Comprehension: This is the capacity that patients receiving the information have to understand.

Instrumental Activities of Daily Living (IADL): These are activities that allow people to adapt to their environment and maintain independence in the community. They depend, like the basic activities, on individuals' state of health, but other elements intervene such as affective state, cognitive performance and aspects of the social environment. They include activities such as: Telephoning, shopping, cooking, looking after the house, using transport, managing medication, handling money, etc.

Irruptive pain: Moderate or severe intensity pain that appears over a chronic pain. It may start unexpectedly or predictably, (triggered by certain manoeuvres known by the patient and/or caregiver).

Judicial defender: Person appointed to cope with urgent situations if a guardian has still not been named or when important differences arise between guardian and the protected person.

Katz Index: This is a valid method to evaluate activities of daily living. It has good inter- and intra-observer reproducibility and with acceptable predictive capacity in the examination of functional capacity. It can be used by different members of the team, performing a structured examination of the patient's capacities.

Legal guardian: Physical persons and/or legal non-profit person, whose objectives include the protection of people whose capacity to act has been modified.

Legal incapacity: Ruling that recognises that a certain person, as a result of a disease they suffer, does not have the capacity to act or that this capacity to act is partially limited.

Living will: Advance directive document.

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Mechanical restraint: This is a medical action that pursues the physical restriction or control by means of any mechanism, material or equipment, tied to the body or very close to it, that patients may control or easily remove and which prevents them, or it is designed to prevent them, from moving freely and/or having normal access to their own bodies.

Memantine: It is a non-competitive NMDA (N-methyl D-Aspartate) receptor antagonist, which is reversibly linked to these receptors, blocking the entry of calcium and reducing the concentration of glutamate

Meta-analysis: This is a statistical technique that permits integrating the results from different studies (diagnostic test studies, clinical trials, cohort studies, etc.) in one single estimator, giving greater weight to the results of the larger studies.

Mixed pain: Coexistence of several of the pain producing mechanisms in one same person.

MMSE: Mini-mental State Examination is a test used for a short assessment of cognitive skills. The test poses questions about time and spatial orientation, mnesic abilities, calculation of series and attention, memory, spoken and written language, copy of a drawing. There is a Spanish version with 35 (Lobo, 1979), 30 (Lobo, 1999) items, and the Spanish version with standardised score according to age and schooling level.

Morbidity: Disease caused.

Mutual aid groups (MAG): Groups made up of caregivers of people affected by dementia, where they receive theoretic and practical training, as well as psychological support.

Neuropathic pain: Caused by direct lesion of nervous structures, either by direct tumour invasion, consequences of the treatment, or infections in a weakened patient (herpes zoster, etc.). Patients describe it as unpleasant, burning or stinging sensation or as a sensation of numbness, tingling, tightness, pruritus or pressure.

NICE: Institution that forms part of the NHS (British National Health Service). Its role is to provide physicians, patients and the public in at large with the best available evidence, mainly in the form of clinical guidelines.«

NNT/NNH: This is a measurement of the efficiency of a treatment. It is the number of people need to be treated ("number needed to treat" [NNT]) with a specific treatment to produce or prevent an additional episode. Likewise, it is defined as the number needed to harm (NNH) to assess undesirable effects.

Normal grief: Natural, normal and expected reaction -dependent upon the social cultural environment -, faced with having to adapt to the loss of a loved one, suffered by relatives and friends before, during and after death. Grief begins a long time before death, anticipatory grief; it increases dramatically around the moment of death (hours, days) acute grief; this continues afterwards as early grief (weeks, months), intermediate grief (months, years) and late grief (years). It probably never ends, always leaving an indelible mark on the person, latent grief, which may be reactivated at any time.

NOSGER: Nurse's Observational Scale for Geriatric Patients. An observational scale completed by nurses for geriatric patients. It contains 30 behaviour items, each one placed on a 5-point scale in agreement with the appearance frequency. The scores of the items are summed up as scores of daily living, self-care activities of daily living, mood, social behaviour and disturbing behaviour.

NPI: Neuropsychiatric inventory that assesses the frequency and severity of behavioural and neuropsychiatric symptoms in patients with dementia, based on an interview with the caregiver. It contains 12 items with a total score that goes from 0 to 144.

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Numerical scale: On a line divided into 0-10 intervals, patients indicate the problem intensity. If it is not possible to indicate the line, they may verbally indicate the "number" that indicates the intensity of the problem. Score of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10.

***Odds Ratio* (OR):** This is a measurement of the efficiency of a treatment. If it is 1, the effect of the treatment is no different to the effect of the control. If the OR is greater or less than 1, the effect of the treatment is greater (or less) than the effect of the control. Take note that the effect that is being measured may be adverse (e.g. death, disability) or desirable (e.g. stop smoking).

Pain: Pain is defined by the Association for the Study of Pain (IASP) as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage".

Palliative care: Approach that improves the quality of life of patients and families who cope with problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other physical, psychosocial and spiritual problems.

Palliative care. Basic level: The aim is to assess the patients' needs at different times or in different care areas, responding to these needs and knowing when to refer patients to other services.

Palliative care. Specific level: They require specialised procedures or techniques. And their objectives are to provide care to patients with more complicated and intensive healthcare needs, perform additional diagnostic tests or very specific treatments that have to be carried out in the hospital, and attend to certain needs that do not need to be clinically complex, but are of a social or family nature.

Palliative care. Support team: They may intervene at home or in the hospital, with different patterns. They offer advice as well as specific or intermittent interventions, or they share responsibility in direct care

Palliative care. Units: These are specialised PC units, requiring hospitalisation, attended by a competent interdisciplinary team.

Parkinson's disease dementia: Parkinson's disease dementia (PDD) is dementia that appears in the context of an established Parkinson's disease, and which affects more than one cognitive domain, mainly attention and executive and visuospatial function. For the operational diagnosis of PDD, it is considered that at least 1 year must have elapsed from the onset of parkinsonism and the appearance of dementia, unlike Lewy body dementia.

Partial incapacity: Capacity to act that is partially limited.

Percentile: A value that divides a sorted set of statistical data in a way that a percent of these data is less than this value. One of the 99 points that divide the distribution into 100 parts of equal frequency.

Placebo: This is an inert intervention or substance that is used as control in clinical research. It is used to rule out cures due to unknown causes that would not be attributable to the therapy that is being researched.

Prevalence: It is the proportion of individuals of a population who present a disease or a characteristic at any time, or during a certain period of time. It tells us the likelihood of an individual from a certain population having a disease at a time or during a certain period of time.

Primary caregiver: This is a person who comes from the patient's informal support system, who devotes the majority of their time, measured in number of hours/day, to their care.

Prior instructions document: Advance directive document.

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Psycho-educational programme: This is a resource that is used to provide information and training in skills to caregivers of people with dementia, so that they can carry out a better task of caring and also care for themselves better.

Psychomotor agitation: This is a behavioural disorder that is characterised by a significant or inadequate increase of motor activity and that is accompanied by alterations of the emotional sphere.

Randomisation: Procedure whereby the selection of the sample or assignment to one treatment or another, or to placebo, is done by random mechanisms.

Randomised clinical trial: Type of clinical trial where patients are assigned randomly, by chance, to the different treatments that are compared

Relative risk (RR): The quotient between the rate of events in the treatment and control groups. Its value follows the same interpretation as the OR.

Risk factor: This is any circumstance that increases the probabilitie of a person contracting a disease.

Rivastigmine: Reversible central inhibitor of acetylcholinesterase and butyrylcholinesterase. It is indicated for the symptomatic treatment of mild and moderate AD and for the Parkinson's disease dementia.

Safeguard: This means caring, attending, covering both the personal side and also the administration of the assets that the person owns.

Self-government: This is the ability to sort out one's own matters, the ability to tend to needs, reach objectives or satisfy desires. It has two dimensions: a) external dimension: Related or not to legal acts that have to do with third parties; b) internal dimension: Relative to one's own acts, such as self-care. The first component of self-government is the capacity to act or capacity to take decisions, and the person must have sufficient theoretic intelligence to be aware of the elements of the decision and of its consequences. Willingness is also required for the decision to be effective, and material means that make it possible or do not prevent it.

Self-guardianship: Any person, with sufficient capacity to act, foreseeing the possibility of being declared incapable, appoints the person they wish as their guardian, and also adopts any provision referring to their personal care or the administration of their assets. Special power or preventive power: conferring powers in favour of a third party, who can represent them, through a written notarial document, establishing that it may continue to be used at the time in time when the person granting the power should become incapacitated.

SIGN: Scottish multidisciplinary agency that prepares evidence-based clinical practice guidelines as well as methodological documents on their design.

Somatic pain: This is produced by the stimulation of pain receptors in the deeper musculoskeletal and superficial skin structures.

Special power or preventive power: Confer powers in favour of a third person, who can represent them, through a written notarial document, establishing that it can continue to be used when the time comes that the person granting the power is incapacitated.

Statistical power: It is the capacity of a test to detect differences of a certain magnitude as statistically significant among the groups compared.

Statistically significant: In a study, if the probability of the differences in the effect found, when comparing two groups, is less than a previously defined significance level, it is said that the differences are statistically significant; that is, that it is very little probability of the differences observed between treatments or groups compared being due to chance. Normally a significance

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level of 5% is used, and they are usually presented as $p < 0.05$. However, it must be taken into account that a difference between treatments may be statistically significant, but this does not always mean that the difference found is "clinically significant" or relevant.

Strain of the caregiver: The strain of the caregiver is defined as the extent to which physical and emotional health, social life or the financial situation of the caregiver, are negatively affected as a result of caring for the patient.

Systematic review (SR): This is a review where the evidence about a topic has been systematically identified, assessed and summed up in agreement with predetermined criteria. It may or may not include the meta-analysis.

Tau protein: The tau are micro-tubular proteins that are abundant in neurons, and which are much less frequent outside the central nervous system. Their main function is to stabilise the axonal microtubules through the interaction with the tubulin.

Terminal stage of dementia: Short life prognosis, less than 2 years, characterised by severe cognitive impairment, highly pronounced incapacity and total dependence for basic activities of daily living, inability to speak and communicate; and the impossibility of benefiting from specific treatments. As well as the presence of multiple comorbidity with severe, multifactorial and changing symptoms. Severe swallowing difficulty or rejection that prevents the intake of food and liquids; weight loss of more than 10% in 6 months, and albumin levels of less than 2.5 mg/dl.

Total incapacity: Has no capacity to act.

Visceral pain: Caused by infiltration, distension or compression of organs within the thoracic or abdominal cavity.

Visual analogical scales: They have been used to measure pain, but they are also of interest in assessing other subjective symptoms. They have the advantage of not being limiting and can be monitored visually. The main disadvantage is the difficulty patients have in understanding the instructions for use, and the physical and cognitive problems for completion in advanced stages of the disease.

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Appendix 4. Abbreviations

AADL	Advanced Activities of Daily Living
AAN	American Academy of Neurology
ACE inhibitors	Acetylcholinesterase inhibitors
AChEI	Cholinesterase inhibitors
ACTH	Adrenocorticotropic hormone
AD	Alzheimer's Disease
ADAS-Cog	Alzheimer's Disease Assessment Scale - Cognitive
ADCS-ADL	AD Cooperative Study - ADL Inventory
ADCS-ADL-Sev.	Alzheimer's Disease Cooperative Study - Activities of Daily Living Scale
ADD	Advance directive document.
ADDTC	California Alzheimer's Disease Diagnostic and Treatment Centers
ADFACS	AD Functional Assessment and Change Scale
ADL	Activities of Daily Living
AES	Apathy Evaluation Scale
AFA	Association of families with Alzheimer's Disease
AIAQS:	Agència d'Informació, Avaluació i Qualitat en Salut (before Agència d'Avaluació de Tecnologia i Recerca Mèdiques, AATRM)
ALS	Amyotrophic lateral sclerosis
AMA	American Medical Association
AMT	Abbreviated Mental Test
APO-E	Apolipoprotein E
APP	Amyloid precursor protein
ASA	Acetylsalicylic acid
B-A	Beta-amyloid
BADL	Basic Activities of Daily Living
BDS	Barthel Index and Blessed Dementia Scale
BEHAVE AD	Behavioural Pathology in Alzheimer's Disease Rating Scale
BMI	Body mass index
BPRS	Brief Psiquiatric Rating Scale
BPSD	Behavioural and psychological symptoms of dementia
CAM	Confusion Assessment Method

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CAMDEX	Cambridge Mental Disorders of the Elderly Examination
CASE	Caregiver Abuse Screen
CBD	Corticobasal degeneration
CCB	Calcium channel blockers
CCDTD	Canadian Consensus Conference on the Diagnosis and Treatment of Dementia
CDR	Clinical Dementia Rating
CEAFA	Spanish Confederation of Associations of families with Alzheimer's Disease
CGIC-C	Clinical Global Impression of Change Dementia Rating
CHMP2B	Chromatin modifying protein 2B
Chol	Cholesterol
CIBIC	Clinician's Interview-Based Impression of Change
CIBIC-Plus	Clinician's Interview-Based Impression of Change
CIDS	Concord Informant Dementia Scale
CIWD	Cognitive impairment without dementia
CJD	Creutzfeldt-Jackob Disease
CLOX 1&2	Executive Llock-Drawing Task 1 and 2
CMAI	Cohen Mansfield Agitation Inventory
CPG	Clinical Practice Guideline
CPR	Cardiopulmonary resuscitation
CSDD	Cornell Scale for Depression in Dementia
CSF	Cerebrospinal fluid.
CVA	Cerebral vascular accident
DAD	Disability Assessment in Dementia
DC	Day Centre
DH	Day Hospital
DLB	Dementia with Lewy bodies
DM	Diabetes Mellitus
DRS	Dementia Rating Scale
DS	Down Syndrome
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV	Diagnostic and Statistical Manual of Mental Disorder, 5th edition,
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorder, 4th edition, Text revised
DUE	Graduate nurses

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EADC	European Alzheimer's Disease Consortium
EANA	Elder Abuse Neglect Assessment
EASI	Elder Abuse Suspicion Index
EAST	Elder Abuse Screening Test
ECAQ	Elderly Cognitive Assessment Questionnaire
EEG	Electroencephalogram
EFNS	European federation of neurological societies
E-IOA	Expanded Indicators of Abuse
ELS	End-of-life stage
EOFAD	Early-onset familial Alzheimer's disease
ESAS	Edmonton Symptom Assessment System
ESR	Erythrocyte sedimentation rate
EXIT25	Executive Interview 25
FAST	Functional Assessment Staging Tool
FDA	Food and Drug Administration
FFI	Fatal familial insomnia
FTLD	Frontotemporal lobar degeneration
G&CP	General and Community Practitioner
GAG	Glycosaminoglycan
GBS	Gottfries-Brane-Steen scale
GDS	Global deterioration Scale.
GMS-AGECAT	Geriatric Mental State
GPCOG	General Practitioner Assessment of Cognition
GSF	Gold Standard Framework
HAD	Hamilton Anxiety Depression
HBP	High Blood Pressure
HC	Home Care
HD	Huntington's Disease:
HIS	Hachinski Ischaemia Scale
HIV	Human immunodeficiency virus
HR	Hazard ratio
IADL	Instrumental activities of daily living
IADL	Instrumental Activities Daily Living
ICD-10	International Classification of Diseases (10th version) of the World Health Organisation
INPEA	International Network for the Prevention of Elder Abuse

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IOA	Indicators of Abuse
IPA	International Psychogeriatric Association
IQCODE	Information Questionnaire on Cognitive Decline in the Elderly
IU	International Units
LDLR	Low-density lipoprotein receptor
LTE	Limitation of therapeutic effort
LWB	Lewy Bodies
MAG	Mutual Aid Group
MAPT	Microtubule-associated protein tau
MCI	Mild cognitive impairment
MCT	Mini-Cog Test (Lobo)
MHIS	Modified Hachinski Ischaemic Score
MIS	Memory Impairment Screen
MMSE	Minimental State Examination
MMSE - SEV	Minimental for severe disease
MR	Mechanical restraint
MRI	Magnetic Resonance imaging
NGP	Nasogastric probe
NICE	National institute for health and clinical excellence
NINCDS/ADRDA	National Institute of Neurological, communicative disorders and Stroke-Alzheimer Disease and related Disorders Association Work Group
NINDS-AIREN	National Institute of Neurological Disorders and Stroke/ Association Internationales pour la Recherche et l'Enseignement
NMDA	N-methyl D-apartate
NOSGER	Nurses Observation Scale for Geriatric patients
NPI	NeuroPsychiatric Inventory
NPI-NH	NeuroPsychiatric Inventory-Nursing Home
NRS	Neurobehavioural Rating Scale
NSAID	Non-Steroid Anti-inflammatory Drugs
NTB	Neurological Tissue Bank
OR	Odds ratio
PC	Palliative care
PCC	Primary Care Centre
PCT	Primary Care Team
PD	Parkinson's disease

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PDD	Parkinson's disease dementia
PDS	Progressive Deterioration Scale
PENTIEN	National Strategic Plan for the integral treatment of Neurological Disease
PET	Positron emission tomography
PGRN	Progranulin-associated protein gene
PSEN	Presenilin
PSP	Progressive supranuclear palsy
PU	Pressure ulcers
RAGE	Rating of Agressive Behaviour in the Elderly
RAVLT	Rey auditory verbal learning test
RCT	Randomised clinical trial
RDRS-2	Rapid Disability Rating Scale-2
REM	Rapid Eye Movement sleep phase
RR	Relative risk
SBP	Systolic Blood Pressure
SBU	Swedish Council on Health Technology Assessment
SCT	Specialised Care Team
SCTD	Specialised Care Team in Dementia
SDCT	Specialised dementia care team
SEAT	Advanced and terminal situation of chronic disease with limited prognosis
SEMFYC	Spanish Society of Family and Community Medicine
SEN	Spanish Neurology Society
SHC	Social-Health Care.
SIB	Severe Impairment Battery
SIBL	Severe Impairment Battery Language
SLE	Systemic lupus erythematosus
SNS	Spanish National Health System
SPECT	Single-photon emission computed tomography
SPMSQ	Short Portable Mental State Questionnaire (Pfeiffer)
SR	Systematic review of scientific evidence
SSRI	Selective Serotonin Reuptake Inhibitors
T@M	Memory impairment Test
TSH	Thyroid stimulating hormone
USA	United States of America

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VADAS	Vascular Alzheimer's Disease Assessment Scale
V-ADAS-Cog	Vascular Alzheimer's Disease Assessment Scale-Cognitive
VCP	Valosin-containing protein gene
VD	Vascular Dementia
WHO	World Health Organisation

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Appendix 5. Declaration of interest

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CPG Development Group on Alzheimer's disease and other dementias

Daniel Andrés Alcolea, has received support from the Pfizer, Janssen and Novartis laboratories to attend congresses; he has also received fees from Angelini for his participation as a speaker at congresses, as well as financial support from Pfizer and Janssen to finance a collaboration in clinical studies. **Felex Bermejo Pareja** has given advice and collaborated in clinical trials, studies, symposiums or scientific monographs sponsored by the following laboratories: AstraZeneca, Bayer, Delangrange-Synthelabo, Eisai, Esteve, Ferrer Internacional, Glaxo Wellcome, Grünenthal (Andrómaco), Hoescht MR, Janssen-Cilag, Lilly, Lundbeck, Novartis, Parke Davis, Pfizer, Pierre Fabre, Servier, SKB, UCB Pharma, Uriach and Wyeth Research as well as in foundations linked to the industry or to private corporations: Mutua Madrileña Foundation and Pfizer Foundation. **Albert Lleó Bia** has received support from the Pfizer and Janssen laboratories to attend congresses, and he has also received fees from Esteve, Novartis and Janssen for his participation as a speaker in courses and conferences. **José L. Molinuevo Guix,** has received fees as a speaker, funded by Pfizer-Eisai, Novartis, Janssen-Cilag, Lundbeck, Esteve, Andrómaco, and fees from Pfizer-Eisai, Novartis, Lundbeck, Elan and Janssen-Cilag for his participation as a consultant. **Mª Teresa Abellán Vidal,** has received support from Pfizer-Eisai, Lundbeck, Esteve, Janssen, Andrómaco Pfizer, to attend congresses and conferences, as well as funding from Eisai laboratories to finance her participation in clinical trials. **Benito J. Fontecha Gómez,** has received support from the pharmaceutical industry, Novartis, to attend the SEGG Congress, as well as fees from Lundbeck as a speaker at conferences. **Sebastia Riu Subirana,** has received fees from the Official College of Pharmacists of Barcelona and from the Janssen-Cilag laboratories for his participation as a speaker at courses and conferences. **Guillermo Amer Ferrer,** has received support from Novartis, Grünenthal, Pfizer, to attend congresses and conferences, he has given advice and collaborated in clinical trials sponsored by the laboratories, Novartis, GSK, Eisai, Wyeth, participating on the Advisory Board of the General Electrics laboratories. **Jaime Kulisevsky Bojarski,** has received financial support from the laboratories, Boehringer, Novartis, Pfizer, Lundbeck, and Merck Serono to give presentations at scientific courses. **Rosa M. Rodríguez Fernández,** has participated in several research projects sponsored by the Esteve laboratories. **Rosa M. Yañez Baña** has attended congresses and has participated in research projects sponsored by the Esteve laboratories. **Antonio Turon Estrada** has received support from Novartis, Pfizer, Esteve, Andrómaco and Janssen to attend congresses and to prepare books on neurology. **Guillermo García Ribas** has received financial support to attend congresses and meetings of the Spanish Society of Neurology, International Conference on Alzheimer's Disease, Expert Meeting on Alzheimer's disease, Springfield/Geneva Conference on Alzheimer's Disease, and to participate as a speaker in the courses on Dementias in Clinical Practice, Experts in Dementias, Frontiers in Dementia, Immersion in Dementia, and course on Vascular neurology for Residents, from the laboratories, Pfizer, Lundbeck, UCB Pharma, Novartis, Grünenthal, Janssen-Cilag, Pfizer/Eisai, Esteve, Sanofi Aventis. Funding to participate in Clinical Trial research, to participate as a consultant for the laboratories, Pfizer/Eisai, Noscira, Servier, Wyeth, Janssen-Cilag. Non-economic type conflicts of interest that may be significant with respect to the authorship in writing the guideline: Employee of pharmaceutical company; Chapter of a book on Advances in Neurology and Chapter of a book on Frontiers in Dementia. Janssen-Cilag, S.A., MSD and Grünenthal Laboratories. Significant endowment of material to unit or services: Computer for consultation. Lundbeck Laboratories. **Francesc Pujadas Navinés** has received funding to attend congresses and training courses from the laboratories, Pfizer, Eisai, Novartis, Esteve, Janssen, Lundbeck, Andrómaco. Fees as speaker to deliver courses and give conferences on dementia and

Alzheimer's disease from the laboratories, Pfizer, Lundbeck and Janssen. Funding to participate in clinical trials on Alzheimer's disease and Mild Cognitive Impairment from the laboratories, Eisai, Servier, Pierre Fabre, Araclon. Significant endowment of material to unit or services: Computer material from the Lundbeck laboratories. Recruitment or financial aid to recruit personnel in the unit or services: Donations to recruit psychologists for Dementia Unit from the laboratories, Pfizer, Esteve, Novartis, Eisai. Funding for educational programmes or courses for the unit: V and VI symposium on Alzheimer's disease from the Janssen laboratories.

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Coordination

Miquel Aguilar Barberá has received support from Pfizer, Eisai, Esteve, Novartis, Lundbeck and Almirall to attend congresses and conference, he has received fees from Lundbeck, Esteve and Almirall as a speaker at symposium and financial support from Wyeth, Servier, Eisai, Pfizer and Novartis for his participation in research studies **Raquel Sánchez del Valle Díaz** has received support from the laboratories, Janssen, Pfizer-Eisai, Novartis and Esteve to attend congresses and participate in clinical trials. **Ramon Reñé Ramírez** has received financial support from the laboratories, Pfizer, Eisai, Esteve, Novartis, Lundbeck to attend conferences and congresses, support from Esteve and Pfizer to participate as a speaker in symposiums and to be able to collaborate in research studies related to dementia; he has received funding from the laboratories, Wyeth, Servier, Eisai, Pfizer and Novartis. **Pilar Quilez Ferrer** has received funding to attend meetings, courses and congresses from the laboratories, Lundbeck, GSK, Allergan, Esteve, Novartis, Boehringer lngelheim, Janssen-Cilag, Grünenthal, Eisai and Pfizer, and has received fees as a speaker at training courses and conferences from the laboratories, Allergan and Lundbeck. Carmen Caja López has received funding from the Bayer laboratories as a speaker at training courses. **Jaume Campdelacreu Fumadó, Carme Ferrando Belart**, **Maria-Dolors Estrada Sabadell** have declared absence of conflict of interest.

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Collaboration

Leticia A. Barajas Nava, Maria Estrella Barceló Colomer, Silvina Berra Ramos, Carmen Carrión Ribas, Josep Maria Elorza Ricart, Anna Ferrer Traid, Mireia Guillén Solà, Joan Mendivil Medina, Marta Millaret Senpau, Toni Parada Martínez, Maria Graciela Rodríguez Garavano, Mercè Salvat Plana, Claudia Liliana Sánchez Camargo, Vicky SerraSutton have declared absence of conflict of interest.

External Review

Manuel A. Franco has received funding to collaborate in different clinical trials and to attend congresses from Janssen-cilag, Lilly, Servier, Lundbeck, Bristol-Myers, Pfizer and Astra. **Rafael Blesa** has received fees to participate as a speaker in courses and conferences from the laboratories, Novartis, Esteve, Lundbeck, Pfizer, Andrómaco, Janssen, Almirall. He has received funding to participate in educational programmes and to carry out research in clinical trials from the Novartis laboratories, financial support to recruit personnel in the memory unit, from the laboratories, Novartis, Pfizer, Janssen and Lundbeck. **Oscar López** has participated as a consultant for the pharmaceutical companies, Pfizer-Eisai, Bristol-Myers-Squibb.

Secundino López-Pousa has received funding to attend meetings of the Spanish Society of Neurology, Spanish Society of Psychogeriatrics and Catalan Society of Neurology from the laboratories, Angelini, Novartis and Pfizer. He has received fees to participate as a speaker at the meetings of the Spanish Society of Neurology, Spanish Society of Psychogeriatrics and Catalan Society of Neurology from the laboratories, Angelini, Novartis, Pfizer, Esteve and Grünenthal. Funding to take part in clinical trials, from the laboratories, Pfizer, Roche and Eisai and financial support to fund research: Study on the Integral Monitoring of Alzheimer's disease from the laboratories, Grünenthal, Pfizer, Esteve and Novartis.

Pablo Martínez Martín has received funding to attend meetings and congresses from the laboratories, GlaxoSmithKline, Novartis, Britannia, Movement Disorder Society. He has received financial support to participate as a speaker at congresses of the laboratories, Boehringer Ingelheim, Novartis, GSK, UCB, Solvay, Britannia, Cephalon; funding to participate in a research study: Support to carry out epidemiological type studies from Novartis laboratories; Consultancy for a pharmaceutical company/other technologies: Methodological aspects for data analysis: From the GSK laboratories; financial support to fund research study: Logistics (not direct financial) aid to carry out a project (epidemiological study) UCB laboratories; financial aid to carry out the project: Université Clermont-Ferrand (France); F. Reina Sofía-AFAL; I.S. Carlos III-Ciberned. **Antoni Salvà Casanovas** has received financial aid to fund the research study: Health and Nutritional Promotion Programme for Patients with Dementia (Nutrialz Study) from thje laboratories, Nestlé Research Center, Longterm clinical evolution & RU of Alzheimer patients (Nutrialz database) from the Lundbeck laboratories. Prospective epidemiological study on the clinical evolution and cost associated with the management of Spanish basements with Moderate Alzheimer's disease, from the Lundbeck laboratories. **Pablo Martínez Lage Álvarez** has received funding to attend different meetings as well as national and international courses from the laboratories, Pfizer-Eisai, Novartis, Janssen-Cilag, Andrómaco-Grünenthal, Esteve and Lundbeck. He receives fees to participate as a speaker at courses and conferences from the laboratories, Pfizer-Eisai, Novartis, Janssen Cilag, Andrómaco-Grünenthal, Esteve and Lundbeck.. He receives funding to deliver spring courses for neurology behaviour and dementia study groups of the SEN. From the Pfizer-Eisai laboratories. Funding to participate in the IMPACT (Important Perspectives on Alzheimer's Care and Treatment) research study from the Pfizer-Eisai laboratories. Consultancy for a pharmaceutical company: National advisory committee, international advisory committee, NEURONET group-Dementia from the laboratories, Pfizer-Eisai, Novartis, Janssen-Cilag, Andrómaco-Grünenthal, Esteve and Lundbeck.

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M.ª Dolors Navarro Rubio, the type of work carried out at the Josep Laporte Foundation has at times counted on funding from different organisations and institutions to carry out research projects or specific training programmes that do not interfere in any way with the external review of this guideline. **Raimundo Mateos Álvare** has received funding to attend work meetings of the Executive Board of the Spanish Society of Psychogeriatrics from the Novartis laboratories.

As president of the Organising Committee of the IPA International Meeting/V Congress of the Spanish Society of Psychogeriatrics, he managed subsidies from official and private entities, receiving financial support from the laboratories, Angelini, Esteve, Novartis, GE Health Care, Almirall, AstraZeneca, Bristol-Myers-Squibb, Otsuka, Pfizer, Eisai, Ferrer, Grünenthal, Lilly, Janssen, Sanofi-Aventis, UCB Pharma. **José Francisco Horga de la Parte** has received financial support from several pharmaceutical laboratories to participate as a speaker at different courses, over the last three years.

Luis Ignacio Brusco has received financial support from the laboratories, Phoenix, Novartis, Eli Lilly, and Beta, to participate as a speaker in different courses.

Mercè Boada Rovira, has received fees to participate as a speaker at courses and conferences from the following institutions and laboratories: Institut Borja Bioètica; Discovery Cascade; Fundació Agrupació Mútua, Fundació Aequitas; Fundación Grünenthal; Fundació Parc Taulí; International University Menéndez Pelayo; Lundbeck España; Pfizer, SA; General Foundation of the Complutense University of Madrid; Araclon Biotech; Esteve laboratories; RPS Research Ibéria, SLU; Euromedice Ediciones Médicas; National Agency of Assessment and Pros of the MICINN; CIEN, Medinankeia foundation; Infociencia; ANEP; Bar Association of Barcelona; University of Burgos; Instituto de Salud Carlos III; General Council of the Judiciary; Omniprex; Uriach laboratories; Col·legi Psicòlegs de Catalunya. She has received financial support to participate in research from the laboratories, Wyeth, GlaxoSmithKline, Eisai, Roche Pharma, Araclon; Pharmaeutical Prodict Development Spain, AstraZeneca, Servier, Instituto Grifols, Phidea SL, Pfizer, SA, Neurochem Inc. Sanofi-Aventis SA. She has received financial support to fund a research study in the service of Hospital de la Vall d'Hebron, from the laboratories, Pfizer, Esteve and Novarits. And different pharmaceutical laboratories related to Alzheimer's disease have financially helped towards staff from the unit registering to attend educational courses or congresses. **Lluís Tárraga Mestre** has received financial support from the laboratories, Novartis, Esteve, Grünenthal, Lundbeck, Janssen and Pfizer to attend Congresses and Conferences and has received financial support from the laboratories, Esteve, SA, to participate as a speaker at several courses and congresses.

Juan R. García Rodríguez, Juan de Jesús Libre Rodríguez, José M. Martínez Lage, Micheline Antoine Selmes, Javier Tirapu, Raúl F. Gutiérrez have declared absence of conflict of interest.

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Appendix 6. Methodological aspects

Bibliographic search strategies

Phase 1: Strategy to identify CPG and SRCT

Search by terms: dementia, frontotemporal AND (Lobar OR degeneration), vascular AND dementia, Lewy AND bod*, alzheimer AND disease.

Search in the title, descriptors and/or key words fields, using the following terms:

#1 dementia OR (frontotempora AND (Lobar OR degeneration)) OR (vascular AND dementia) OR (lewy AND bod*) OR (alzheimer AND disease)

#2 practice guideline OR guideline OR consensus development conference OR recommend* OR consens* OR statement* OR (clinical AND protocol*) OR (medical AND protocol*)

#3 (systemat* AND review*) OR (systemat* AND overview*) OR (integrati* AND review*) OR (integrati* AND overview*) OR (quantitativ* AND review*) OR (quantitativ* AND overview*) OR (methodologic* AND review*) OR (methodologic* OR overview*) OR (manual AND search*) OR (collaborativ* AND review*) OR (collaborativ* AND overview*) OR (cochrane AND review) OR (Medline AND review) OR (Pubmed AND review) OR "hand searched" OR handsearch* OR "hand search" OR "hand searching" OR "pooled data" OR "review literature" OR meta-analy* OR metaanaly* OR meta analy* OR meta-analysis OR systematic OR (review AND random*) OR (review AND "clinical trials")

#1 AND #2
#1 AND #3

Phase 2: Strategy to identify RCT

Search by terms: dementia, frontotemporal AND (Lobar OR degeneration), vascular AND dementia, Lewy AND bod*, alzheimer AND disease.

Search in the title, descriptors and/or key words fields, using the following terms:

#1 dementia OR (frontotempora AND (Lobar OR degeneration)) OR (vascular AND dementia) OR (lewy AND bod*) OR (alzheimer AND disease)

#2 (random* OR trial* OR efficacy OR effectiv* OR blind* OR placebo* OR cohort* OR multicent* OR prospectiv* OR longitudinal OR follow*)fpt

#1 AND #2

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Main CPGs, consensus documents and positionings (recommendations) of scientific societies of use

1. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984;34(7):939-44.[131]

   Expert consensus
   Available at:
   www.neurology.org/cgi/content/abstract/34/7/939

2. McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Con¬sensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996;47(5):1113-24.[28]

   Expert consensus
   Available at:
   www.ncbi.nlm.nih.gov/pubmed/8909416

3. Kessel H, Marín N, Maturana N. Primera Conferencia Nacional de Consenso sobre el Anciano Maltratado. Rev Esp Geriatr Gerontol. 1996;31:367-72.[686]

   Expert consensus
   Available at:
   www.imsersomayores.csic.es/documentos/documentos/almeria-declaracion-01.pdf

4. Patterson CJ, Gauthier S, Bergman H, Cohen CA, Feightner JW, Feldman H, et al. The recognition, assessment and management of dementing disorders: conclusions from the Canadian Consensus Conference on Dementia. CMAJ. 1999;160(12 Suppl):S1-15.[195]

   Expert consensus
   Available at:
   http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1230425/pdf/cmaj_160_12_S1.pdf

5. Canadian Guide to Clinical Preventive Health Care. Ottawa (Canada): Canadian Task Force on the Periodic Health Examination; 2003.[199]

   AGREE evaluation: recommended
   Available at:
   http://www.phac-aspc.gc.ca/publicat/clinic-clinique/index-eng.php

6. Guideline for cognitive impairment: is this dementia? Symptoms to diagnosis. Edmonton, AB (Canada): Working group for Cognitive Impairment. Alberta Clinical Practice Guidelines Program; 2002 (revised 2004).[148]

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

AGREE evaluation: Recommended with changes
Available at: http://topalbertadoctors.org/informed_practice/clinical_practice_guidelines/complete%20set/Cognitive%20Impairment%20Symptoms%20to%20Diagnosis/ cognitive_impairment_symptoms_to_diagnosis_guideline.pdf

7. Guide to assessing and counselling older drivers. Chicago, IL (US): American Medical Association (AMA); 2004.[527]

Positioning (recommendations) of a scientific society
Available at: www.ama-assn.org/ama/pub/physician-resources/public-health/promoting-healthy- lifestyles/geriatric-health/older-driver-safety/assessing-counseling-older-drivers.shtml

8. Chamorro García L. Guía de manejo de los transtornos mentales en atención primaria. Barcelona: Psiquiatria editores; 2004.[412]

Expert consensus

9. Téllez JM, Villena A, Morena S, Pascual P, López-García C. El paciente agitado. Guías Clínicas. 2005;5(34).413

Expert consensus
Available at: www.enfermeriadeurgencias.com/documentos/recomendaciones/paciente_agitado.pdf

10. Feldman HH, Gauthier S, Chertkow H, Conn DK, Freedman M, Chris M. Progress in clinical neurosciences: Canadian guidelines for the development of antidementia therapies: a conceptual summary. Can J Neurol Sci. 2006;33(1):6-26.[416]

Expert consensus
Available at: http://cjns.metapress.com/app/home/contribution.asp?referrer=parent&backto=issu e,4,24;journal,33,75;linkingpublicationresults,1:300307,1

11. Management of patients with dementia. A national clinical guideline. Edinburgh, Scotland (United Kingdom): Scottish Intercollegiate Guidelines Network (SIGN); 2006. SIGN publication nº 86.[129]

AGREE evaluation: Recommended Available at:
http://www.sign.ac.uk/pdf/sign86.pdf

12. Chiu E, Chiu H. Dementia care in Asia-second consensus statement on quality services. Int Psychogeriatr. 2006;18(1):176.[687]

Expert consensus

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

13. Guidelines for a Palliative approach in residential aged care. Canberra: The National Palliative Care Program. National Health and Medical Research Council; 2006.[586]

    AGREE evaluation: recommended
    Available at: http://www.palliativecare.org.au/Portals/46/Guidelines%20for%20a%20palliative%20 approach%20in%20residential%20aged%20care%20-%20guide.pdf

14. Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. London (United Kingdom): National Institute for Clinical Excellence (NICE); February 2006. GCG32.[688]

    AGREE evaluation: Recommended Available at:
    www.nice.org.uk/guidance/CG32

15. Dementia. The NICE-SCIE guideline on supporting people with dementia and their caregivers in health and social care. London (United Kingdom): National Collaborating Centre for Mental Health. Social Care Institute for Excellence. National Institute for Health and Clinical Excellence (NICE); 2007. National Clinical Practice Guideline Number 42.[25]

    AGREE evaluation: recommended
    Available at:

16. Dementia. Singapore: Ministry of Health; 2007. MOH Clinical Practice Guidelines. Informe Núm. 3/2007.[140]

    AGREE evaluation: Recommended with changes
    Available at: www.moh.gov.sg/mohcorp/uploadedFiles/Publications/Guidelines/Clinical_ Practice_ Guidelines/Dementia.pdf

17. Guideline for cognitive impairment-dementia-diagnosis to management. Edmonton, AB (Canada): Working group for Cognitive Impairment. Alberta Clinical Practice Guidelines Program; 2007.[246]

    AGREE evaluation: Recommended with changes
    Available at: www.albertadoctors.org/bcm/ama/ama-website.nsf/AllDocSearch/87256DB000705C3F87256E05005534D5/$File/COGNITIVE_IMPAIRMENT_PART_2.PDF?OpenElement

18. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias. Second edition. Arlington, VA (US): American Psychiatric Association(APA); 2007.42

    AGREE evaluation: Recommended with changes
    Available at: www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=AlzPG101007

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

19. Arrieta Antón E, Fernández Pascual L, González Rodríguez V, Goñi Imizcoz M, Guerrero Díaz MT, López Merino P, et al. Guía de atención al paciente con demencia en atención primaria. Valladolid: Gerencia Regional de Salud. Junta de Castilla y León; 2007.[234]

AGREE evaluation: Recommended with changes
Available at: www.salud.jcyl.es/sanidad/cm/profesionales/images?locale=es_ES&textOnly=false& idMmedia=94952

20. Ayuso T, Ederra MJ, Manubens JM, Nuin MA, Vilar D, Zubicoa J. Abordaje de la demencia. Guía de actuación en la coordinación Atencion Primaria- Neurología. Pamplona: Servicio Navarro de Salud-Osasunbide; 2007.[204]

AGREE evaluation: Recommended with changes
Available at: http://www.navarra.es/NR/rdonlyres/90E6356A-73C3-4CA1-9291-834501AA4324/0/ Guiaabordajedelademencia.pdf

21. Chertkow H. Alzheimer's & Dementia: The journal of the alzheimer's association. Alzheimers Dement. 2007;3(4).[152]

AGREE evaluation: Recommended with changes

22. Waldemar G, Dubois B, Emre M, Georges J, McKeith IG, Rossor M, et al. Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. Eur J Neurol. 2007;14(1):e1-26.[5]

AGREE evaluation: recommended
Available at: http://www.efns.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2007_ management_of_disorders_associated_with_dementia.pdf

23. Guía de actuación compartida para el paciente con contención. Jaén: Subcomisión de cuidados. Área de Salud Mental de Jaén. Junta de Andalucía; marzo 2007.[556]

Positioning (recommendations) of a scientific society
Available at: http://www.juntadeandalucia.es/servicioandaluzdesalud/distritos/djaen/pdf/apcli/gact_compartida/S.%20MENTAL%20-%20GUIA%20DE%20ACTUACI%C3%93N%20COMPARTIDA%20PARA%20LA%20 CONTENCI%C3%93N%20DEL%20PACIENTE.pdf

24. Health care guidelines: Palliative care. Bloomington, MN (US): Institute for Clinical Systems Improvement (ICSI); 2007.[584]

AGREE evaluation: recommended
Available at
http://www.icsi.org/palliative_care/palliative_care_11918.html

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

25. Guideline for Alzheimer's disease management. Assessing cognitive function. En: Evidence-based geriatric nursing protocols for best practice. Delirium and acute problematic behavior in the long-term care setting. California (US): National Guideline Clearinghouse; 2008.[235]

    AGREE evaluation: Recommended with changes Available at:
    http://www.guideline.gov/content.aspx?id=12379

26. Guía de práctica clínica de la enfermedad de Alzheimer y otras demencias. Servicio Canario de la Salud. Gobierno de Canarias.[202]

    Expert consensus
    Available at: www2.gobiernodecanarias.org/sanidad/scs/content/5d1a6bd6-f9cc-11dd-9d99-e96480bea708/Alzheimer_1.pdf

27. Grupo de Trabajo de la Guía de Práctica Clínica sobre Cuidados Paliativos. Guía de Práctica Clínica sobre Cuidados Paliativos. Madrid: Plan Nacional para el SNS del MSC. Agencia de Evaluación de Tecnologías Sanitarias del País Vasco; 2008. CLINICAL PRACTICE GUIDELINES IN THE SNS: OSTEBA Nº 2006/08.[575]

    AGREE evaluation: recommended
    Available at: http://www9.euskadi.net/sanidad/osteba/datos/e_06_08_Cuidados_Paliat.pdf

28. Guía de recomendaciones clínicas. Demencia. Oviedo: Clínica Asturias; 2008.[517]

    AGREE evaluation: Recommended with changes Available at:
    www.princast.es/salud/pcais/pdfs/demencia.pdf

29. Molinuevo JL, Peña-Casanova J, Grupo de estudio de neurología de la conducta y demencias. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones. Barcelona: Sociedad Española de Neurología; 2009.[6]

    AGREE evaluation: Recommended with changes Available:
    http://www.imim.es/noticias/view.php?ID=121
    This CPG updated the guideline of 2002.[19]

30. La atención sociosanitaria en España: perspectiva gerontológica y otros aspectos conexos. Recomendaciones del Defensor del Pueblo e informes de la Sociedad Española de Geriatría y Gerontología y de la Asociación Multidisciplinaria de Gerontología. [consultado 9 octubre 2009]. Madrid: IMSERSO.[187]

    Positioning (recommendations) of a scientific society
    Available at: http://www.imsersomayores.csic.es/documentos/documentos/defensor-atencion-01.pdf

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

31. Antúnez C, Boada M, Alberca R, Bosch A, Berthier M, Alegret M. Documento Sitges 2009: Capacidad para tomar decisiones durante la evolución de una demencia: Reflexiones, derechos y propuestas de evaluación. Barcelona: Editorial Glosa; 2009.[206]

Expert consensus
Available at:
www.sen.es/pdf/2009/documento_sitges.pdf
This document updates the consensus of 2005.[5]

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

More than 5 years have passed since the publication of this Clinical Practice Guideline,and its validity has not been reviewed

Bibliography

1. Rocca WA, Hofman A, Brayne C, Breteler MM, Clarke M, Copeland JR, et al. Frequency and distribution of Alzheimer's disease in Europe: a collaborative study of 1980-1990 prevalence findings. The EURODEM-Prevalence Research Group. Ann Neurol. 1991;30(3):381-90.
2. Lobo A, Launer LJ, Fratiglioni L, Andersen K, Di CA, Breteler MM, et al. Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. Neurology. 2000;54(11 Suppl 5):S4-S9.
3. Qiu C, De RD, Fratiglioni L. The epidemiology of the dementias: an update. Curr Opin Psychiatry. 2007;20(4):380-5.
4. Berr C, Wancata J, Ritchie K. Prevalence of dementia in the elderly in Europe. Eur Neuropsychopharmacol. 2005;15(4):463-71.
5. Waldemar G, Dubois B, Emre M, Georges J, McKeith IG, Rossor M, et al. Recommendations for the diagnosis and management of Alzheimer's disease and other disorders associated with dementia: EFNS guideline. Eur J Neurol. 2007;14(1):e1-26.
6. Molinuevo JL, Peña-Casanova J, Grupo de estudio de neurología de la conducta y demencias. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones. Barcelona: Sociedad Española de Neurología (SEN); 2009. Guía Nº 8.
7. Casado I, Calatayud T. Epidemiología y factores de riesgo. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 23-50.
8. De Pedro-Cuesta J, Virués-Ortega J, Vega S, Seijo-Martínez M, Saz P, Rodríguez F, et al. Prevalence of dementia and major dementia subtypes in Spanish populations: a reanalysis of dementia prevalence surveys, 1990-2008. BMC Neurol. 2009;9:55.
9. Anuario Estadístico de España [página en Internet]. Madrid: Instituto Nacional de Estadística. [consultado 9 octubre 2009]. Disponible en: http://www.ine.es/prodyser/pubweb/anuarios_mnu.htm
10. Eurostat (Statistical Office of the European Communities). Disponible en: http://epp.eurostat.ec.europa.eu
11. Harvey RJ, Skelton-Robinson M, Rossor MN. The prevalence and causes of dementia in people under the age of 65 years. J Neurol Neurosurg Psychiatry. 2003;74(9):1206-9.
12. Grupo de trabajo sobre guías de práctica clínica. Elaboración de guías de práctica clínica en el Sistema Nacional de Salud. Manual metodológico. Madrid: Plan Nacional para el Sistema Nacional de Salud del Ministerio de Sanidad y Consumo: Instituto Aragonés de Ciencias de la Salud-I+CS; 2007. Guías de Práctica Clínica en el Sistema Nacional de Salud: I+CS Nº 2006/1.
13. Instrumento AGREE versión española [página en Internet]. The AGREE collaboration; 2005. Disponible en: http://www.agreecollaboration.org
14. Etxeberria A, Rotaeche R, Lekue I, Callén B, Merino M, Villar M. Descripción de la metodología de elaboración-adaptación-actualización empleada en la guía de práctica clínica sobre asma de la CAPV. Proyecto de Investigación Comisionada. Vitoria-Gasteiz. Departamento de Sanidad. Gobierno Vasco, 2005. Informe nº: Osteba D-05-03.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

15. Viñuela Fernández F, Olazarán Rodríguez J. Criterios para el diagnóstico del síndrome de demencia. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 1-8.
16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed., text revised) DSM-IV-TR. Washington, DC (US): American Psychiatric Association; 2000.
17. López-Ibor JJ, Valdés M. DSM-IV-TR Manual diagnóstico y estadístico de los trastornos mentales. Barcelona: Masson; 2005.
18. World Health Organization. The ICD-10 Classification of mental and behavioural disorders. Geneva (Switzerland): World Health Organization; 1992.
19. Robles A, Del Ser T, Alom T, Peña-Casanova J. Grupo asesor del grupo de neurología de la conducta y demencias de la Sociedad Española de Neurología. Propuesta de criterios para el diagnóstico clínico del deterioro cognitivo leve, la demencia y la enfermedad de Alzheimer. Neurología. 2002;17:17-32.
20. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. Lancet. 2005;366(9503):2112-7.
21. Fratiglioni L, Wang HX. Brain reserve hypothesis in dementia. J Alzheimers Dis. 2007;12(1):11-22.
22. Bermejo-Pareja F, Benito-León J, Vega S, Medrano MJ, Román GC. Incidence and subtypes of dementia in three elderly populations of central Spain. J Neurol Sci. 2008;264(1-2):63-72.
23. Hofman A, Rocca WA, Brayne C, Breteler MM, Clarke M, Cooper B, et al. The prevalence of dementia in Europe: a collaborative study of 1980-1990 findings. Eurodem Prevalence Research Group. Int J Epidemiol. 1991;20(3):736-48.
24. Gao S, Hendrie HC, Hall KS, Hui S. The relationships between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. Arch Gen Psychiatry. 1998;55(9):809-15.
25. Dementia. The NICE-SCIE guideline on supporting people with dementia and their carers in health and social care. London (United Kingdom): National Collaborating Centre for Mental Health. Social Care Institute for Excellence. National Institute for Health and Clinical Excellence (NICE); 2007. National Clinical Practice Guideline Number 42.
26. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Appendix C: Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review): Report of the quality standards subcommittee of the American academy neurology. CONTINUUM Lifelong Learning in Neurology. 2007;13(2):222-31.
27. Gascón-Bayarri J, Reñé R, Del Barrio JL, De Pedro-Cuesta J, Ramón JM, Manubens JM, et al. Prevalence of dementia subtypes in El Prat de Llobregat, Catalonia, Spain: the PRATICON study. Neuroepidemiology. 2007;28(4):224-34.
28. McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996;47(5):1113-24.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

29. Yamada T, Hattori H, Miura A, Tanabe M, Yamori Y. Prevalence of Alzheimer's disease, vascular dementia and dementia with Lewy bodies in a Japanese population. Psychiatry Clin Neurosci. 2001;55(1):21-5.
30. Rahkonen T, Eloniemi-Sulkava U, Rissanen S, Vatanen A, Viramo P, Sulkava R. Dementia with Lewy bodies according to the consensus criteria in a general population aged 75 years or older. J Neurol Neurosurg Psychiatry. 2003;74(6):720-4.
31. Del Ser T, Pondal M, Rodríguez E, Castro MD, Sánchez-Sánchez F, Muñoz D. Prevalence of probable dementia with Lewy bodies in a Spanish census-based elderly sample. Neurology. 2004;62(S5):A209.
32. Gislason TB, Sjogren M, Larsson L, Skoog I. The prevalence of frontal variant frontotemporal dementia and the frontal lobe syndrome in a population based sample of 85 year olds. J Neurol Neurosurg Psychiatry. 2003;74(7):867-71.
33. Stevens T, Livingston G, Kitchen G, Manela M, Walker Z, Katona C. Islington study of dementia subtypes in the community. Br J Psychiatry. 2002;180:270-6.
34. Qizilbach N. Introduction. En: Qizilbach N, Schneider LS, Chui H, Tariot P, Brodaty H, Kaye J, et al., editores. Evidence-based dementia practice. Oxford (United Kingdom): Blackwell; 2002. p. 3-5.
35. Baquero Toledo M, Carnero Pardo C, Martínez Lozano MD. Clasificación. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 51-60.
36. Pascual Millán LF. Tipos básicos y clasificación etiopatogénica de las demencias. En: Alberca R, López-Pousa S, editores. Enfermedad de Alzheimer y otras demencias. 3ª ed. Madrid: Editorial Médica Panamericana; 2006. p. 43-50.
37. Fernández M, Blesa R, Zarranz JJ. Demencia. En: Zarranz JJ, editor. Neurología. 4ª edición. Madrid: Elsevier Science; 2008.
38. Lyketsos CG, López O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. JAMA. 2002;288(12):1475-83.
39. McKhann GM, Albert MS, Grossman M, Miller B, Dickson D, Trojanowski JQ. Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. Arch Neurol. 2001;58(11):1803-9.
40. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology. 2005;65(12):1863-72.
41. Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, et al. Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord. 2007;22(12):1689-707.
42. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias. Second edition. Arlington, VA (US): American Psychiatric Association; 2007.
43. Seelaar H, Schelhaas HJ, Azmani A, Kusters B, Rosso S, Majoor-Krakauer D, et al. TDP-43 pathology in familial frontotemporal dementia and motor neuron disease without Progranulin mutations. Brain. 2007;130(Pt 5):1375-85.
44. Alberca R. Enfermedad de Alzheimer. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomen-

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

daciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 61-85.
45. Lladó Plarrumani A, Sánchez-Valle Díaz R. Degeneración lobular frontotemporal. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 117-32.
46. Martínez-Lage P, Frank A, Valentí Soler M. Demencia vascular. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 243-77.
47. Reñé R, Campdelacreu J, Gascón J. Demencia con cuerpos de Lewy. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 87-100.
48. González Gutiérrez JL, Manzano Palomo MS, García-Ramos García R. Enfermedad de Parkinson: demencia y trastornos cognitivos conductuales asociados. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 101-15.
49. Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol. 2003;60(3):387-92.
50. Reñé R, Campdelacreu J, Escrig A, Gascón-Bayarri J, Hernández-Pardo M, Jauma S, et al. Degeneración lobular frontotemporal: estudio descriptivo de 42 pacientes. Neurología. 2008;23(8):511-7.
51. Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology. 1998;51(6):1546-54.
52. Dobato Ayuso JL, Ponce MA. Degeneración corticobasal. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 133-42.
53. Mackenzie IR, Neumann M, Bigio EH, Cairns NJ, Alafuzoff I, Kril J, et al. Nomenclature and nosology for neuropathologic subtypes of frontotemporal lobar degeneration: an update. Acta Neuropathol. 2010;119(1):1-4.
54. García Ribas G, López Sendón J, García de Yébenes J. Enfermedad de Huntigton. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 169-91.
55. Jiménez Huete A, Guardado Santervás P, Valentí Soler M. Enfermedades priónicas. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 193-222.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

56. Carnero Pardo C. Parálisis supranuclear progresiva. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 143-54.
57. Kovacs GG, Alafuzoff I, Al-Sarraj S, Arzberger T, Bogdanovic N, Capellari S, et al. Mixed brain pathologies in dementia: the BrainNet Europe consortium experience. Dement Geriatr Cogn Disord. 2008;26(4):343-50.
58. Roman GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, García JH, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology. 1993;43(2):250-60.
59. Hachinski VC, Iliff LD, Zilhka E, Du Boulay GH, McAllister VL, Marshall J, et al. Cerebral blood flow in dementia. Arch Neurol. 1975;32(9):632-7.
60. Oslin D, Atkinson RM, Smith DM, Hendrie H. Alcohol related dementia: proposed clinical criteria. Int J Geriatr Psychiatry. 1998;13(4):203-12.
61. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol. 1999;56(3):303-8.
62. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56(9):1133-42.
63. Petersen RC. Mild cognitive impairment: Current research and clinical implications. Seminars in Neurology. 2007;27(1):22-31.
64. Portet F, Ousset PJ, Visser PJ, Frisoni GB, Nobili F, Scheltens P, et al. Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. J Neurol Neurosurg Psychiatry. 2006;77(6):714-8.
65. Olazarán Rodríguez J, Molinuevo Guix JL. Deterioro cognitivo ligero. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 15-21.
66. Stephan BC, Matthews FE, McKeith IG, Bond J, Brayne C. Early cognitive change in the general population: how do different definitions work? J Am Geriatr Soc. 2007;55(10):1534-40.
67. Busse A, Bischkopf J, Riedel-Heller SG, Angermeyer MC. Mild cognitive impairment: prevalence and incidence according to different diagnostic criteria. Results of the Leipzig Longitudinal Study of the Aged (LEILA75+). Br J Psychiatry. 2003;182:449-54.
68. Luck T, Luppa M, Briel S, Riedel-Heller SG. Incidence of mild cognitive impairment: a systematic review. Dement Geriatr Cogn Disord. 2010;29(2):164-75.
69. Chertkow H, Massoud F, Nasreddine Z, Belleville S, Joanette Y, Bocti C, et al. Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia. CMAJ. 2008;178(10):1273-85.
70. Lleó A, Menéndez González M. Marcadores diagnósticos en demencias degenerativas: pruebas de neuroimagen y laboratorio. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009.Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 337-54.

More than 5 years have passed since the publication of the Clinical Practice Guideline and its validity has not been reviewed

71. Rabinovici GD, Jagust WJ. Amyloid imaging in aging and dementia: testing the amyloid hypothesis in vivo. Behav Neurol. 2009;21(1):117-28.
72. Jack CR, Jr., Lowe VJ, Weigand SD, Wiste HJ, Senjem ML, Knopman DS, et al. Serial PIB and MRI in normal, mild cognitive impairment and Alzheimer's disease: implications for sequence of pathological events in Alzheimer's disease. Brain. 2009;132(Pt 5):1355-65.
73. Kemppainen NM, Aalto S, Wilson IA, Nagren K, Helin S, Bruck A, et al. PET amyloid ligand [11C]PIB uptake is increased in mild cognitive impairment. Neurology. 2007;68(19):1603-6.
74. Okello A, Koivunen J, Edison P, Archer HA, Turkheimer FE, Nagren K, et al. Conversion of amyloid positive and negative MCI to AD over 3 years: an 11C-PIB PET study. Neurology. 2009;73(10):754-60.
75. Yakushev I, Bartenstein P, Siessmeier T, Hiemke C, Scheurich A, Lotz J, et al. Cerebrospinal Fluid Tau Protein Levels and (18)F-Fluorodeoxyglucose Positron Emission Tomography in the Differential Diagnosis of Alzheimer's Disease. Dement Geriatr Cogn Disord. 2010;30(3):245-53.
76. Karow DS, McEvoy LK, Fennema-Notestine C, Hagler DJ, Jr., Jennings RG, Brewer JB, et al. Relative capability of MR imaging and FDG PET to depict changes associated with prodromal and early Alzheimer disease. Radiology. 2010;256(3):932-42.
77. Mattsson N, Zetterberg H, Hansson O, Andreasen N, Parnetti L, Jonsson M, et al. CSF biomarkers and incipient Alzheimer disease in patients with mild cognitive impairment. JAMA. 2009;302(4):385-93.
78. Diniz BS, Pinto Junior JA, Forlenza OV. Do CSF total tau, phosphorylated tau, and beta-amyloid 42 help to predict progression of mild cognitive impairment to Alzheimer's disease? A systematic review and meta-analysis of the literature. World J Biol Psychiatry. 2008;9(3):172-82.
79. Blennow K. CSF biomarkers for mild cognitive impairment. J Intern Med. 2004;256(3):224-34.
80. Andreasen N, Blennow K. CSF biomarkers for mild cognitive impairment and early Alzheimer's disease. Clin Neurol Neurosurg. 2005;107(3):165-73.
81. DeKosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA, Ives DG, Saxton JA, et al. Ginkgo biloba for prevention of dementia: a randomized controlled trial. JAMA. 2008;300(19):2253-62.
82. Fernández M, Blesa R, Zarranz J. Demencia. En: Zarranz J, editor. Neurología. 4ª edición. Ed. Elsevier. Madrid: 2008.
83. Carrillo-Alcalá ME, Bermejo-Pareja F. Demencia en nonagenarios. Revisión sistemática de estudios poblacionales con datos de España. Rev Neurol. 2008;47(7): 347-54.
84. Azad NA, Al Bugami M, Loy-English I. Gender differences in dementia risk factors. Gend Med. 2007;4(2):120-9.
85. van Duijn CM, Stijnen T, Hofman A. Risk factors for Alzheimer's disease: overview of the EURODEM collaborative re-analysis of case-control studies. EURODEM Risk Factors Research Group. Int J Epidemiol. 1991;20 Suppl 2:S4-12.
86. Waring SC, Rosenberg RN. Genome-wide association studies in Alzheimer disease. Arch Neurol. 2008;65(3):329-34.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

87. Patterson C, Feightner JW, García A, Hsiung GY, MacKnight C, Sadovnick AD. Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer disease. CMAJ. 2008;178(5):548-56.
88. Bertram L, McQueen MB, Mullin K, Blacker D, Tanzi RE. Systematic meta-analyses of Alzheimer disease genetic association studies: the AlzGene database. Nat Genet. 2007;39(1):17-23.
89. Serretti A, Olgiati P, De Ronchi D. Genetics of Alzheimer's disease. A rapidly evolving field. J Alzheimers Dis. 2007;12(1):73-92.
90. Huang X, Chen P, Kaufer DI, Troster AI, Poole C. Apolipoprotein E and dementia in Parkinson disease: a meta-analysis. Arch Neurol. 2006;63(2):189-93.
91. Llorca J, Rodríguez-Rodríguez E, Dierssen-Sotos T, Delgado-Rodríguez M, Berciano J, Combarros O. Meta-analysis of genetic variability in the beta-amyloid production, aggregation and degradation metabolic pathways and the risk of Alzheimer's disease. Acta Neurol Scand. 2008;117(1):1-14.
92. Patterson C, Feightner J, García A, MacKnight C. General risk factors for dementia: A systematic evidence review. Alzheimer's & Dementia. 2007;3(4):341-7.
93. Kloppenborg RP, Van den Berg E, Kappelle LJ, Biessels GJ. Diabetes and other vascular risk factors for dementia: Which factor matters most? A systematic review. Eur J Pharmacol. 2008.
94. McGuinness B, Todd S, Passmore P, Bullock R. Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia. Cochrane Database Syst Rev. 2009;(4):CD004034.
95. Kennelly SP, Lawlor BA, Kenny RA. Blood pressure and the risk for dementia: a double edged sword. Ageing Res Rev. 2009;8(2):61-70.
96. Anstey KJ, Lipnicki DM, Low LF. Cholesterol as a risk factor for dementia and cognitive decline: a systematic review of prospective studies with meta-analysis. Am J Geriatr Psychiatry. 2008;16(5):343-54.
97. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. Lancet Neurol. 2006;5(1):64-74.
98. Arvanitakis Z, Wilson RS, Bennett DA. Diabetes mellitus, dementia, and cognitive function in older persons. J Nutr Health Aging. 2006;10(4):287-91.
99. Grodstein F. Cardiovascular risk factors and cognitive function. Alzheimer's and Dementia. 2007;3(Suppl 2):S16-S22.
100. Irie F, Fitzpatrick AL, López OL, Kuller LH, Peila R, Newman AB, et al. Enhanced risk for Alzheimer disease in persons with type 2 diabetes and APOE epsilon4: the Cardiovascular Health Study Cognition Study. Arch Neurol. 2008;65(1):89-93.
101. Peters R, Burch L, Warner J, Beckett N, Poulter R, Bulpitt C. Haemoglobin, anaemia, dementia and cognitive decline in the elderly, a systematic review. BMC Geriatr. 2008;8:18.
102. Ownby RL, Crocco E, Acevedo A, John V, Loewenstein D. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. Arch Gen Psychiatry. 2006;63(5):530-8.
103. Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. Am J Epidemiol. 2007;166(4):367-78.
104. Peters R, Poulter R, Warner J, Beckett N, Burch L, Bulpitt C. Smoking, dementia and cognitive decline in the elderly, a systematic review. BMC Geriatr. 2008;8:36.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

105. Issa AM, Mojica WA, Morton SC, Traina S, Newberry SJ, Hilton LG, et al. The efficacy of omega-3 fatty acids on cognitive function in aging and dementia: a systematic review. Dement Geriatr Cogn Disord. 2006;21(2):88-96.
106. Peters R, Peters J, Warner J, Beckett N, Bulpitt C. Alcohol, dementia and cognitive decline in the elderly: a systematic review. Age Ageing. 2008;37(5):505-12.
107. Barranco Quintana JL, Allam MF, Serrano Del Castillo A, Fernández-Crehuet Navajas R. Alzheimer's disease and coffee: a quantitative review. Neurol Res. 2007;29(1):91-5.
108. Beydoun MA, Beydoun HA, Wang Y. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. Obes Rev. 2008.
109. Gorospe EC, Dave JK. The risk of dementia with increased body mass index. Age Ageing. 2007;36(1):23-9.
110. Caamano-Isorna F, Corral M, Montes-Martínez A, Takkouche B. Education and dementia: a meta-analytic study. Neuroepidemiology. 2006;26(4):226-32.
111. Valenzuela MJ, Sachdev P. Brain reserve and cognitive decline: a non-parametric systematic review. Psychol Med. 2006;36(8):1065-73.
112. Paradise M, Cooper C, Livingston G. Systematic review of the effect of education on survival in Alzheimer's disease. Int Psychogeriatr. 2009;21(1):25-32.
113. Santibáñez M, Bolúmar F, García AM. Occupational risk factors in Alzheimer's disease: a review assessing the quality of published epidemiological studies. Occup Environ Med. 2007;64(11):723-32.
114. García AM, Sisternas A, Hoyos SP. Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis. Int J Epidemiol. 2008;37(2):329-40.
115. Hogervorst E, Yaffe K, Richards M, Huppert F. Hormone replacement therapy for cognitive function in postmenopausal women. Cochrane Database Syst Rev. 2002;(3):CD003122.
116. Low LF, Anstey KJ. Hormone replacement therapy and cognitive performance in postmenopausal women-a review by cognitive domain. Neuroscience & Biobehavioral Reviews. 2006;30(1):66-84.
117. Craig MC, Murphy DG. Oestrogen, cognition and the maturing female brain. Journal of Neuroendocrinology. 2007;19(1):1-6.
118. Henderson VW. Alzheimer's disease and other neurological disorders. Climacteric. 2007;10 Suppl 2:92-6.
119. Zhou B, Teramukai S, Fukushima M. Prevention and treatment of dementia or Alzheimer's disease by statins: a meta-analysis. Dement Geriatr Cogn Disord. 2007;23(3):194-201.
120. Rockwood K. Epidemiological and clinical trials evidence about a preventive role for statins in Alzheimer's disease. Acta Neurol Scand Suppl. 2006;185:71-7.
121. Lucca U, Tettamanti M, Quadri P. Homocysteine lowering and cognitive performance. N Engl J Med. 2006;355(13):1390.
122. Lim WS, Gammack JK, Van NJ, Dangour AD. Omega 3 fatty acid for the prevention of dementia. Cochrane Database Syst Rev. 2006;(1):CD005379.
123. Jedrziewski MK, Lee VMY, Trojanowski JQ. Physical activity and cognitive health. Alzheimer's & Dementia. 2007;3(2):98-108.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

124. Valenzuela M, Sachdev P. Can Cognitive Exercise Prevent the Onset of Dementia? Systematic Review of Randomized Clinical Trials with Longitudinal Follow-up. Am J Geriatr Psychiatry. 2009;17(3):179-87.
125. Breitner JC, Haneuse SJ, Walker R, Dublin S, Crane PK, Gray SL, et al. Risk of dementia and AD with prior exposure to NSAIDs in an elderly community-based cohort. Neurology. 2009;72(22):1899-905.
126. Sánchez-Valle Díaz R, Molinuevo Guix JL. Asesoramiento genético en demencias. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 355-67.
127. Ley 14/2007, de 3 de julio, de investigación biomédica. Madrid: Boletín Oficial del Estado (BOE); núm. 12945, de 4/07/2007. p. 28826.
128. Green RC, Roberts JS, Cupples LA, Relkin NR, Whitehouse PJ, Brown T, et al. Disclosure of APOE genotype for risk of Alzheimer's disease. N Engl J Med. 2009;361(3):245-54.
129. Management of patients with dementia. A national clinical guideline. Edinburgh (United Kingdom): Scottish Intercollegiate Guidelines Network (SIGN); 2006. SIGN publication nº 86.
130. Castilla-Rilo J, López-Arrieta J, Bermejo-Pareja F, Ruiz M, Sánchez-Sánchez F, Trincado R. Instrumental activities of daily living in the screening of dementia in population studies: a systematic review and meta-analysis. Int J Geriatr Psychiatry. 2007;22(9):829-36.
131. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984;34(7):939-44.
132. Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56(9):1143-53.
133. Dubois B, Feldman HH, Jacova C, DeKosky ST, Barberger-Gateau P, Cummings J, et al. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. Lancet Neurol. 2007;6(8):734-46.
134. Moroney JT, Bagiella E, Desmond DW, Hachinski VC, Molsa PK, Gustafson L, et al. Meta-analysis of the Hachinski Ischemic Score in pathologically verified dementias. Neurology. 1997;49(4):1096-105.
135. McKhann GM, Albert MS, Grossman M, Miller B, Dickson D, Trojanowski JQ. Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. Arch Neurol. 2001;58(11):1803-9.
136. Feldman HH, Jacova C, Robillard A, García A, Chow T, Borrie M, et al. Diagnosis and treatment of dementia: 2. Diagnosis. CMAJ. 2008;178(7):825-36.
137. Ham RJ. Confusion, dementia and delirium. En: Ham RJ, Sloane PD, editores. Primary Care Geriatrics: A Case Base Approach, 3rd edn. St Louis: Mosby, 1997: 217-259.
138. Reisberg B, Prichep L, Mosconi L, John ER, Glodzik-Sobanska L, Boksay I, et al. The pre-mild cognitive impairment, subjective cognitive impairment stage of Alzheimer's disease. Alzheimers Dement. 2008;4(1 Suppl 1):S98-S108.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

139. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56(9):1133-42.
140. Dementia. Singapore: Ministry of Health; 2007. MOH Clinical Practice Guidelines. Informe Núm. 3/2007.
141. Lara JP, Peña-Casanova J. Test neuropsicológicos en la evaluación de la demencia. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2010. p. 319-35.
142. Blesa R, Pujol M, Aguilar M, Santacruz P, Bertran-Serra I, Hernandez G, et al. Clinical validity of the 'mini-mental state' for Spanish speaking communities. Neuropsychologia. 2001;39(11):1150-7.
143. Lobo A, Ezquerra J, Gómez BF, Sala JM, Seva DA. El miniexamen, cognoscitivo (un «test» sencillo, práctico, para detectar alteraciones intelectuales en pacientes médicos). Actas Luso Esp Neurol Psiquiatr Cienc Afines. 1979;7(3):189-202.
144. Lobo A, Saz P, Marcos G, Día JL, De La Cámara C, Ventura T, et al. Revalidación y normalización del Mini-Examen Cognoscitivo (primera versión en castellano del Mini-Mental Status Examination) en la población general geriátrica. Med Clin (Barc). 1999;112(20):767-74.
145. Carnero Pardo C, Sáez-Zea C, Montiel NL, Del SP, Feria V, I, Pérez Navarro MJ, et al. Utilidad diagnóstica del Test de las Fotos (Fototest) en deterioro cognitivo y demencia. Neurología. 2007;22(10):860-9.
146. Rajmil L, Molinuevo JL, Sánchez-Valle R, Bosch B, Villar A. Screening for amnestic mild cognitive impairment and early Alzheimer's disease with M@T (Memory Alteration Test) in the primary care population. Int J Geriatr Psychiatry. 2007;22(4):294-304.
147. Clarfield AM. The decreasing prevalence of reversible dementias: an updated meta-analysis. Arch Intern Med. 2003;163(18):2219-29.
148. Guideline for cognitive impairment: is this dementia? Symptoms to diagnosis. Edmonton, AB (Canada): Working group for Cognitive Impairment. Alberta Clinical Practice Guidelines Program; 2002 (revised 2004).
149. Dementia-Diagnostic and therapeutic interventions. A systematic review. Stockholm (Sweden): The Swedish Council on Technology Assessment in Health Care; 2008.
150. Blomqvist ME, Reynolds C, Katzov H, Feuk L, Andreasen N, Bogdanovic N, et al. Towards compendia of negative genetic association studies: an example for Alzheimer disease. Hum Genet. 2006;119(1-2):29-37.
151. Papassotiropoulos A, Fountoulakis M, Dunckley T, Stephan DA, Reiman EM. Genetics, Transcriptomics, and Proteomics of Alzheimer's Disease. Journal of Clinical Psychiatry. 2006;67(4):652-70.
152. Chertkow H. Alzheimer's & Dementia: The journal of the alzheimer's association. Alzheimers Dement. 2007;3(4).
153. Mayeux R, Saunders AM, Shea S, Mirra S, Evans D, Roses AD, et al. Utility of the apolipoprotein E genotype in the diagnosis of Alzheimer's disease. Alzheimer's Disease Centers Consortium on Apolipoprotein E and Alzheimer's Disease. N Engl J Med. 1998;338(8):506-11.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

154. Formichi P, Battisti C, Radi E, Federico A. Cerebrospinal fluid tau, A beta, and phosphorylated tau protein for the diagnosis of Alzheimer's disease. J Cell Physiol. 2006;208(1):39-46.
155. Ben SW, Broers P, Devogelaer JP, Depresseux G, Kaufman JM, Goemaere S, et al. Interest of a prescreening questionnaire to reduce the cost of bone densitometry. Osteoporos Int. 2002;13(5):434-42.
156. Petzold A, Keir G, Warren J, Fox N, Rossor MN. A systematic review and meta-analysis of CSF neurofilament protein levels as biomarkers in dementia. Neurodegener Dis. 2007;4(2-3):185-94.
157. Zerr I, Kallenberg K, Summers DM, Romero C, Taratuto A, Heinemann U, et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain. 2009;132(Pt 10):2659-68.
158. Scheltens P, Leys D, Barkhof F, Huglo D, Weinstein HC, Vermersch P, et al. Atrophy of medial temporal lobes on MRI in «probable» Alzheimers disease and normal ageing: diagnostic value and neuropsychological correlates. J Neurol Neurosurg Psychiatry. 1992;55(10):967-72.
159. O'Brien JT. Role of imaging techniques in the diagnosis of dementia. Br J Radiol. 2007;80 Spec Nº 2:S71-S77.
160. McKeith I, O'Brien J, Walker Z, Tatsch K, Booij J, Darcourt J, et al. Sensitivity and specificity of dopamine transporter imaging with 123I FP-CIT SPECT in dementia with Lewy bodies: a phase III, multicentre study. Lancet Neurol. 2007;6(4):305-13.
161. Antonini A. The role of I-ioflupane SPECT dopamine transporter imaging in the diagnosis and treatment of patients with dementia with Lewy bodies. Neuropsychiatr Dis Treat. 2007;3(3):287-92.
162. Warren JD, Schott JM, Fox NC, Thom M, Revesz T, Holton JL, et al. Brain biopsy in dementia. Brain. 2005;128(Pt 9):2016-25.
163. Ley 14/1986, de 25 de abril, General de Sanidad. Madrid: Boletín Oficial del Estado (BOE); núm. 102, de 29/04/1986. p. 15207-24.
164. Ordre, de 19 de maig de 1986, de creació del Programa Vida als Anys d'atenció sociosanitària a la gent gran amb llarga malaltia. Barcelona: Diari Oficial de la Generalitat de Catalunya (DOGC); núm. 694, de 18/07/1986. p. 1753.
165. Plan gerontológico nacional 1992-2000.
166. Programa PALET de la Comunitat Valenciana; 1995.
167. Boletín sobre el envejecimiento: perfiles y tendencias. Madrid: Observatorio de Personas Mayores. Ministerio de Trabajo y Asuntos Sociales; Junio 2000 [consultado 10 octubre 2009]. Número 2. Disponible en: http://www.imsersomayores.csic.es/documentos/documentos/boletinsobreenvejec02.pdf
168. Plan de Calidad asistencial gerontológica 1998-2003.
169. Plan de servicios sociales de Andalucía 1993-1996.
170. Plan de atención a las personas mayores en Aragón; 1995.
171. Plan gerontológico del Principado de Asturias; 1997.
172. Plan integral de las personas mayores de Baleares; 1998.
173. Plan de acción sociosanitario para el mayor de Cantabria 1999-2005.
174. Plan de atención a las personas mayores en Castilla-La Mancha 1998-2002.
175. Plan de atención sociosanitario de Castilla y León.
176. Programa de Atención Sociosanitaria de Galicia; 1997.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

177. Plan de mayores de la comunidad de Madrid; 1996.
178. Plan gerontológico de La Rioja; 1994.
179. Plan gerontológico de Navarra 1997-2000.
180. Plan gerontológico de Euskadi; 1994.
181. Declaración de Alma-Ata. Conferencia Internacional sobre Atención Primaria de Salud convocada por la Organización Mundial de la Salud (OMS). Alma-Ata (actualmente Kazajstán); 6-12 septiembre 1978. Disponible en: http://www.paho.org/Spanish/dd/pin/alma-ata_declaracion.htm
182. Página en Internet. Asistenciasanitaria/RegimenGeneral/Contenido/Índex.htm. [consultado 9 octubre 2009]. Disponible en: http://www.segsocial.es/Internet_1/Trabajadores/prestacionesPension10935/
183. Atención especializada [página en Internet]. Barcelona: Departament de Salut. Servei Català de la Salut. Generalitat de Catalunya. [consultado 9 octubre 2009]. Disponible en: http://www10.gencat.cat/catsalut/esp/servcat_especialitzada.htm
184. Ley 2/1998, de Salud de Andalucía, Decreto 105/1986 de 11 de junio, sobre Ordenación de asistencia sanitaria especializada y órganos de dirección de los hospitales de la Asistencia Especializada, modificado por el Decreto 462/1996 de 8 de octubre.
185. Atención sociosanitaria [página en Internet]. Barcelona: Departament de Salut. Servei Català de la Salut. Generalitat de Catalunya. [consultado 9 octubre 2009]. Disponible en: http://www10.gencat.cat/catsalut/esp/servcat_sociosanitaria.htm
186. El model d'atenció sociosanitària a Catalunya. Barcelona: Pla de Salut. Departament de Sanitat i Seguretat Social. Generalitat de Catalunya; 1994. Quadern núm. 5.
187. La atención sociosanitaria en España: perspectiva gerontológica y otros aspectos conexos. Recomendaciones del Defensor del Pueblo e informes de la Sociedad Española de Geriatría y Gerontología y de la Asociación Multidisciplinaria de Gerontología. [consultado 9 octubre 2009]. Madrid: IMSERSO. Disponible en: http://www.imsersomayores.csic.es/documentos/documentos/defensor-atencion-01.pdf
188. Ritchie K, Kildea D. Is senile dementia «age-related» or «ageing-related»?-evidence from meta-analysis of dementia prevalence in the oldest old. Lancet. 1995;346(8980):931-4.
189. López-Pousa S. Informe sobre atenció primària. Girona.
190. Zunzunegui Pastor MV, Del ST, Rodríguez LA, García Yebenes MJ, Domingo J, Otero PA. Demencia no detectada y utilización de los servicios sanitarios: implicaciones para la atención primaria. Aten Primaria. 2003;31(9):581-6.
191. Guía de atención al paciente con demencia en atención primaria. Gerencia Regional de Salud. Junta de Castilla y León.
192. Pla operatiu d'atenció a les demències. Document de consens. Barcelona: Regió Sanitària de Barcelona. Departament de Sanitat i Seguretat Social. Generalitat de Catalunya; 2007.
193. Pla de Demències de Catalunya període 2010-2014. Barcelona: Pla Director Sociosanitari. Departament de Salut. Generalitat de Catalunya; 2010.
194. Screening for dementia. Rockville, MD (US): U.S. Preventive Services Task Force. Agency for Healthcare Research and Quality; 2003. Disponible en: http://www.ahrq.gov/clinic/uspstfix.htm
195. Patterson CJ, Gauthier S, Bergman H, Cohen CA, Feightner JW, Feldman H, et al. The recognition, assessment and management of dementing disorders: conclusions from the Canadian Consensus Conference on Dementia. CMAJ. 1999;160(12 Suppl):S1-15.

More than 5 years have passed since the publication of the Clinical Practice Guidelines and its validity has not been reviewed

196. Demencias desde la Atención Primaria. GdT de demencias de la SemFYC. 1ª edición. Barcelona: Sociedad Española de Medicina de Familia y Comunitaria (SemFYC); 2005.
197. Galasko D. Biomarkers for Alzheimer's disease-clinical needs and application. J Alzheimers Dis. 2005;8(4):339-46.
198. Hye A, Lynham S, Thambisetty M, Causevic M, Campbell J, Byers HL, et al. Proteome-based plasma biomarkers for Alzheimer's disease. Brain. 2006;129(Pt 11):3042-50.
199. Canadian Guide to Clinical Preventive Health Care. Ottawa (Canada): Canadian Task Force on the Periodic Health Examination; 2003.
200. Hoyos AMC, Fernández HJA. Diagnóstico sindrómico, diferencial y etiológico. En: Grupo de trabajo de Demencias de la SemFYC. Demencias desde la Atención Primaria. Barcelona: Sociedad Española de Medicina de Familia y Comunitaria (SemFYC); 2005.
201. Plan andaluz de Alzheimer 2007-2010. Sevilla: Consejería de Salud. Junta de Andalucía. Disponible en: http://www.juntadeandalucia.es/salud/export/sites/csalud/galerias/documentos/c_1_c_6_planes_estrategias/plan_alzheimer/plan_alzheimer_2007_2010/analisis_plan_alzheimer.pdf
202. Guía de práctica clínica de la enfermedad de Alzheimer y otras demencias. Servicio Canario de la Salud. Gobierno de Canarias. Disponible en: http://www2.gobiernodecanarias.org/sanidad/scs/content/623c0d43-f9cc-11dd-9d99-e96480bea708/Alzheimer_2.pdf
203. Demencia: proceso asistencial integrado. Sevilla: Consejería de Salud. Junta de Andalucía; 2002 [consultado 9 Octubre 2009]. Disponible en: http://www.juntadeandalucia.es/salud/servicios/contenidos/procesos/docs/inicio%5B1%5D.pdf
204. Ayuso T, Ederra MJ, Manubens JM, Nuin MA, Vilar D, Zubicoa J. Abordaje de la demencia. Guía de actuación en la coordinación Atencion Primaria - Neurología. Pamplona: Servicio Navarro de Salud-Osasunbide; 2007.
205. Newman AB, Fitzpatrick AL, López O, Jackson S, Lyketsos C, Jagust W, et al. Dementia and Alzheimer's disease incidence in relationship to cardiovascular disease in the Cardiovascular Health Study cohort. J Am Geriatr Soc. 2005;53(7):1101-7.
206. Antúnez C, Boada M, Alberca R, Bosch A, Berthier M, Alegret M. Documento Sitges 2009: Capacidad para tomar decisiones durante la evolución de una demencia: Reflexiones, derechos y propuestas de evaluación. Barcelona: Editorial Glosa; 2009.
207. Antúnez Almagro C, Hernández I, Morera Guitart J. Unidades de demencia. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 379-98.
208. Claire A, Kessels A, Dröksen C, Severens J, Verhey F. Integrated multidisciplinary diagnostic approach for dementia care: randomised controlled trial. Br J Psychiatry. 2008;192:300-5.
209. Salvà Casanovas A. La organización de servicios para la atención de personas con enfermedad de Alzheimer u otras demencias. Alzheimer. 2003;25:4-9.
210. Estrategia en Salud Mental del Sistema Nacional de Salud. Madrid: Sistema Nacional de Salud. Ministerio de Sanidad y Consumo; 2007.
211. Fantova F. Los sistemas de servicios sociales en España: intento de caracterización. Boletín CIES. 2004; 21.

More than 5 years have passed since the publication of this Clinical Practice Guideline, so its validity has not been reviewed

212. Fantova F. Sistemas públicos de servicios sociales. Bilbao: Universidad de Deusto; 2008.
213. Muñoz Luque J. Servicios sociales de atención primaria en España. En: Navarro V. La situación social de España. Madrid: Fundación F. Largo Caballero. Biblioteca Nueva. Programa de Políticas Públicas y Sociales de la Universidad Pompeu Fabra; 2009. Vol. III. p. 503-42.
214. López-Doblas J. Personas mayores viviendo solas. La autonomía como valor en alza. Madrid: IMSERSO; 2005.
215. Stone R, Cafferata GL, Sangl J. Caregivers of the frail elderly: a national profile. Gerontologist. 1987;27(5):616-26.
216. Estudio ECO: Carga y coste de la enfermedad de Alzheimer en España; 2003.
217. Coduras A, Rabasa I, Frank A, Bermejo-Pareja F, López-Pousa S, López-Arrieta JM, et al. Prospective one-year cost-of-illness study in a cohort of patients with dementia of Alzheimer's disease type in Spain: the ECO study. J Alzheimers Dis. 2010;19(2):601-15.
218. Jonsson L, Wimo A. The cost of dementia in Europe: a review of the evidence, and methodological considerations. Pharmacoeconomics. 2009;27(5):391-403.
219. Losada A, Montorio I, Moreno-Rodríguez R, Cigarán M, Peñacoba C. Análisis de programas de intervención psicosocial en cuidadores de pacientes con demencia. Informaciones Psiquiátricas. 2006;184(2):173-86.
220. Selwood A, Johnston K, Katona C, Lyketsos C, Livingston G. Systematic review of the effect of psychological interventions on family caregivers of people with dementia. J Affect Disord. 2007;101(1-3):75-89.
221. Coon DW, Ory MG, Schulz R. Family Caregivers: Enduring and Emergent Themes. En: Coon DW, Gallagher-Thompson D, Thompson LW, editores. Innovative Interventions to Reduce Dementia Caregivers Distress. New York, NY (US): Springer; 2003. p. 3-27.
222. Ley 13/2006, de 27 de julio, de Prestaciones Sociales de caracter económico. Madrid: Boletín Oficial del Estado (BOE); núm. 201, de 23/08/2006. p. 30951-8.
223. Martínez MC, Ramos P, Hernández G, Campos X, Linares del Río C, Yanguas JJ. Modelo de Centro de Día para personas con enfermedad de Alzheimer. Madrid: IMSERSO; 2008.
224. Yanguas JJ. Modelo de atención a las personas con enfermedad de Alzheimer. Madrid: IMSERSO; 2007.
225. Garre-Olmo J, Flaque M, Gich J, Pulido TO, Turbau J, Vallmajo N, et al. A clinical registry of dementia based on the principle of epidemiological surveillance. BMC Neurol. 2009;9:5.
226. Laakkonen ML, Raivio MM, Eloniemi-Sulkava U, Saarenheimo M, Pietila M, Tilvis RS, et al. How do elderly spouse care givers of people with Alzheimer disease experience the disclosure of dementia diagnosis and subsequent care? J Med Ethics. 2008;34(6):427-30.
227. Pinner G, Bouman WP. Attitudes of patients with mild dementia and their carers towards disclosure of the diagnosis. Int Psychogeriatr. 2003;15(3):279-88.
228. Holroyd S, Turnbull Q, Wolf AM. What are patients and their families told about the diagnosis of dementia? Results of a family survey. Int J Geriatr Psychiatry. 2002;17(3):218-21.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

229. Johnson H, Bouman WP, Pinner G. On telling the truth in Alzheimer's disease: a pilot study of current practice and attitudes. Int Psychogeriatr. 2000;12(2):221-9.
230. Marzanski M. Would you like to know what is wrong with you? On telling the truth to patients with dementia. J Med Ethics. 2000;26(2):108-13.
231. Dautzenberg PL, van Marum RJ, van Der HR, Paling HA. Patients and families desire a patient to be told the diagnosis of dementia: a survey by questionnaire on a Dutch memory clinic. Int J Geriatr Psychiatry. 2003;18(9):777-9.
232. Ryan RE, Prictor MJ, McLaughlin KJ, Hill SJ. Audio-visual presentation of information for informed consent for participation in clinical trials. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. Nº: CD003717. DOI: 10.1002/14651858.CD003717.pub2.
233. Derouesné C, Selmés J. Diagnosis discloure of Alzheimer's disease. En: Waldemar G, Burns A. Alzheimer's Disease. ONPL; 2009. p. 51-55.
234. Arrieta Antón E, Fernández Pascual L, González Rodríguez V, Goñi Imizcoz M, Guerrero Díaz MT, López Merino P, et al. Guía de atención al paciente con demencia en atención primaria. Valladolid: Gerencia Regional de Salud. Junta de Castilla y León; 2007.
235. Guideline for Alzheimer's disease management. Assessing cognitive function. En: Evidence-based geriatric nursing protocols for best practice. Delirium and acute problematic behavior in the long-term care setting. Columbia, MD (US): American Medical Directors Association (AMDA); 2008.
236. Rockwood K, Dai D, Mitnitski A. Patterns of decline and evidence of subgroups in patients with Alzheimer's disease taking galantamine for up to 48 months. Int J Geriatr Psychiatry. 2008;23(2):207-14.
237. Kavirajan H, Schneider LS. Efficacy and adverse effects of cholinesterase inhibitors and memantine in vascular dementia: a meta-analysis of randomised controlled trials. Lancet Neurol. 2007;6(9):782-92.
238. Ballard C, Sauter M, Scheltens P, He Y, Barkhof F, van Straaten EC, et al. Efficacy, safety and tolerability of rivastigmine capsules in patients with probable vascular dementia: the VantagE study. Curr Med Res Opin. 2008;24(9):2561-74.
239. Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. Nº: CD005593. DOI: 10.1002/14651858.CD005593.
240. Birks J, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. Nº: CD001190. DOI: 10.1002/14651858.CD001190.pub2.
241. Cholinesterase inhibitors in Alzheimer's disease. Cologne (Germany): German Institute for Quality and Efficiency in Health Care (IQWiG -Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen); 2007.
242. Wilcock G, Howe I, Coles H, Lilienfeld S, Truyen L, Zhu Y, et al. A long-term comparison of galantamine and donepezil in the treatment of Alzheimer's disease. Drugs Aging. 2003;20(10):777-89.
243. Bullock R, Passmore F, Potocnik F, Hock C. The tolerability, ease of use and efficacy of donepezil and rivastigmine in alzeimer's disease patients: a 12-week, multinational, comparative study. J Am Geriatr Soc. 2001;49(4):S19.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

244. Bullock R, Touchon J, Bergman H, Gambina G, He Y, Rapatz G, et al. Rivastigmine and donepezil treatment in moderate to moderately-severe Alzheimer's disease over a 2-year period. Curr Med Res Opin. 2005;21(8):1317-27.
245. López OL, Becker JT, Wahed AS, Saxton J, Sweet RA, Wolk DA, et al. Long-term effects of the concomitant use of memantine with cholinesterase inhibition in Alzheimer disease. J Neurol Neurosurg Psychiatry. 2009;80(6):600-7.
246. Guideline for cognitive impairment-dementia-diagnosis to management. Edmonton, AB (Canada): Working group for Cognitive Impairment. Alberta Clinical Practice Guidelines Program; 2007.
247. Greenberg SM, Tennis MK, Brown LB, Gómez-Isla T, Hayden DL, Schoenfeld DA, et al. Donepezil therapy in clinical practice: a randomized crossostudy. Arch Neurol. 2000;57(1):94-9.
248. Courtney C, Farrell D, Gray R, Hills R, Lynch L, Sellwood E, et al. Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial. Lancet. 2004;363(9427):2105-15.
249. Engedal K, Soininen H, Verhey F, Waldemar G, Winblad B, Wimo A, et al. Donepezil improved or stabilized cognition over one year in patients with mild and moderate Alzheimer's disease. Eur Neuropsychopharmacol. 2000;10(Suppl 3):S368.
250. Holmes C, Wilkinson D, Dean C, Vethanayagam S, Olivieri S, Langley A, et al. The efficacy of donepezil in the treatment of neuropsychiatric symptoms in Alzheimer disease. Neurology. 2004;63(2):214-9.
251. Beier M. Treatment strategies of behavioral symptoms of Alzheimer's disease: focus on early phatmacologic intervention. Pharmacotherapy. 2007;27(3):399-411.
252. Raina P, Santaguida P, Ismaila A, Patterson C, Cowan D, Levine M, et al. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: evidence review for a clinical practice guideline. Ann Intern Med. 2008;148(5):379-97.
253. Loy C, Schneider L. Galantamine for Alzheimer's disease and mild cognitive impairment. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. Nº: CD001747. DOI: 10.1002/14651858.CD001747.pub3.
254. Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, et al. The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine for Alzheimer's disease. Health Technol Assess. 2006;10(1):iii-xi.
255. Burns A, Bernabei R, Bullock R, Cruz Jentoft AJ, Frolich L, Hock C, et al. Safety and efficacy of galantamine (Reminyl) in severe Alzheimer's disease (the SERAD study): a randomised, placebo-controlled, double-blind trial. Lancet Neurol. 2009;8(1):39-47.
256. McShane R, Areosa SA, Minakaran N. Memantine for dementia. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. Nº: CD003154. DOI: 10.1002/14651858.CD003154.pub5. Cochrane Database Syst Rev. 2006;(2):CD003154.
257. Reisberg B, Doody R, Stoffler A, Schmitt F, Ferris S, Mobius HJ. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003;348(14):1333-41.
258. Gauthier S, Loft H, Cummings J. Improvement in behavioural symptoms in patients with moderate to severe Alzheimer's disease by memantine: a pooled data analysis. Int J Geriatr Psychiatry. 2008;23(5):537-45.
259. Morris JN, Hawes C, Fries BE, Phillips CD, Mor V, Katz S, et al. Designing the national resident assessment instrument for nursing homes. Gerontologist. 1990;30(3):293-307.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

260. Hansen RA, Gartlehner G, Lohr KN, Kaufer DI. Functional outcomes of drug treatment in Alzheimer's disease: A systematic review and meta-analysis. Drugs Aging. 2007;24(2):155-67.
261. Birks J. The evidence for the efficacy of cholinesterase inhibitors in the treatment of Alzheimer's disease is convincing. Int Psychogeriatr. 2008;1-7.
262. Hansen RA, Gartlehner G, Lohr KN, Kaufer DI. Functional outcomes of drug treatment in Alzheimer's disease: A systematic review and meta-analysis. Drugs Aging. 2007;24(2):155-67.
263. Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. Clin Interv Aging. 2008;3(2):211-25.
264. Diniz BS, Pinto JA, Jr., Gonzaga ML, Guimaraes FM, Gattaz WF, Forlenza OV. To treat or not to treat? A meta-analysis of the use of cholinesterase inhibitors in mild cognitive impairment for delaying progression to Alzheimer's disease. Eur Arch Psychiatry Clin Neurosci. 2009;259(4):248-56.
265. Kirby J, Green C, Loveman E, Clegg A, Picot J, Takeda A, et al. A systematic review of the clinical and cost-effectiveness of memantine in patients with moderately severe to severe Alzheimer's disease. Drugs Aging. 2006;23(3):227-40.
266. Llop R, Aguilera C, Bosch M, Espinàs J. Updating of the pharmacological treatment of dementia. Atencion Primaria. 2006;37(2):108-12.
267. Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. JAMA. 2004;291(3):317-24.
268. Cummings JL, Schneider E, Tariot PN, Graham SM. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. Neurology. 2006;67(1):57-63.
269. Fillit HM, Doody RS, Binaso K, Crooks GM, Ferris SH, Farlow MR, et al. Recommendations for best practices in the treatment of Alzheimer's disease in managed care. Am J Geriatr Pharmacother. 2006;4 Suppl A:S9-S24.
270. Porsteinsson AP, Grossberg GT, Mintzer J, Olin JT. Memantine treatment in patients with mild to moderate Alzheimer's disease already receiving a cholinesterase inhibitor: a randomized, double-blind, placebo-controlled trial. Curr Alzheimer Res. 2008;5(1):83-9.
271. Doody RS, Geldmacher DS, Gordon B, Perdomo CA, Pratt RD. Open-label, multicenter, phase 3 extension study of the safety and efficacy of donepezil in patients with Alzheimer disease. Arch Neurol. 2001;58(3):427-33.
272. Emre M, Aarsland D, Albanese A, Byrne EJ, Deuschl G, De Deyn PP, et al. Rivastigmine for dementia associated with Parkinson's disease. N Engl J Med. 2004;351(24):2509-18.
273. Aarsland D, Laake K, Larsen JP, Janvin C. Donepezil for cognitive impairment in Parkinson's disease: a randomised controlled study. J Neurol Neurosurg Psychiatry. 2002;72(6):708-12.
274. Leroi I, Brandt J, Reich SG, Lyketsos CG, Grill S, Thompson R, et al. Randomized placebo-controlled trial of donepezil in cognitive impairment in Parkinson's disease. Int J Geriatr Psychiatry. 2004;19(1):1-8.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

275. Ravina B, Putt M, Siderowf A, Farrar JT, Gillespie M, Crawley A, et al. Donepezil for dementia in Parkinson's disease: a randomised, double blind, placebo controlled, crossover study. J Neurol Neurosurg Psychiatry. 2005;76(7):934-9.
276. Aarsland D, Ballard C, Walker Z, Bostrom F, Alves G, Kossakowski K, et al. Memantine in patients with Parkinson's disease dementia or dementia with Lewy bodies: a double-blind, placebo-controlled, multicentre trial. Lancet Neurol. 2009;8(7):613-8.
277. McKeith I, Del ST, Spano P, Emre M, Wesnes K, Anand R, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet. 2000;356(9247):2031-6.
278. Wesnes KA, McKeith IG, Ferrara R, Emre M, Del ST, Spano PF, et al. Effects of rivastigmine on cognitive function in dementia with lewy bodies: a randomised placebo-controlled international study using the cognitive drug research computerised assessment system. Dement Geriatr Cogn Disord. 2002;13(3):183-92.
279. Yaffe K, Fox P, Newcomer R, Sands L, Lindquist K, Dane K, et al. Patient and caregiver characteristics and nursing home placement in patients with dementia. JAMA. 2002;287(16):2090-7.
280. Edwards K, Royall D, Hershey L, Lichter D, Hake A, Farlow M, et al. Efficacy and safety of galantamine in patients with dementia with Lewy bodies: a 24-week open-label study. Dement Geriatr Cogn Disord. 2007;23(6):401-5.
281. Molloy S, McKeith IG, O'Brien JT, Burn DJ. The role of levodopa in the management of dementia with Lewy bodies. J Neurol Neurosurg Psychiatry. 2005;76(9):1200-3.
282. Bonelli SB, Ransmayr G, Steffelbauer M, Lukas T, Lampl C, Deibl M. L-dopa responsiveness in dementia with Lewy bodies, Parkinson disease with and without dementia. Neurology. 2004;63(2):376-8.
283. Goldman JG, Goetz CG, Brandabur M, Sanfilippo M, Stebbins GT. Effects of dopaminergic medications on psychosis and motor function in dementia with Lewy bodies. Mov Disord. 2008;23(15):2248-50.
284. Boxer AL, Boeve BF. Frontotemporal dementia treatment: current symptomatic therapies and implications of recent genetic, biochemical, and neuroimaging studies. Alzheimer Dis Assoc Disord. 2007;21(4):S79-S87.
285. Vossel KA, Miller BL. New approaches to the treatment of frontotemporal lobar degeneration. Curr Opin Neurol. 2008;21(6):708-16.
286. Méndez MF, Shapira JS, McMurtray A, Licht E. Preliminary findings: behavioral worsening on donepezil in patients with frontotemporal dementia. Am J Geriatr Psychiatry. 2007;15(1):84-7.
287. Boxer AL, Lipton AM, Womack K, Merrilees J, Neuhaus J, Pavlic D, et al. An open-label study of memantine treatment in 3 subtypes of frontotemporal lobar degeneration. Alzheimer Dis Assoc Disord. 2009;23(3):211-7.
288. Demaerschalk BM, Wingerchuk DM. Treatment of vascular dementia and vascular cognitive impairment. Neurologist. 2007;13(1):37-41.
289. Black S, Roman GC, Geldmacher DS, Salloway S, Hecker J, Burns A, et al. Efficacy and tolerability of donepezil in vascular dementia: positive results of a 24-week, multicenter, international, randomized, placebo-controlled clinical trial. Stroke. 2003;34(10):2323-30.
290. Wilkinson D, Doody R, Helme R, Taubman K, Mintzer J, Kertesz A, et al. Donepezil in vascular dementia: a randomized, placebo-controlled study. Neurology. 2003;61(4):479-86.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

291. Malouf R, Birks J. Donepezil for vascular cognitive impairment. Cochrane Database Syst Rev 2004: CD004395.
292. Aguilar M, Roman G, Black S. Efficacy and safety of donepezil in vascular dementia: results from largest double-blind trial in vascular demntia. Proceedings of the 10th International Conference on Alzheimer's Disease and Related Disorders. Madrid. 15-20 julio 2006. p. 4-439.
293. Dichgans M, Markus HS, Salloway S, Verkkoniemi A, Moline M, Wang Q, et al. Donepezil in patients with subcortical vascular cognitive impairment: a randomised double-blind trial in CADASIL. Lancet Neurol. 2008;7(4):310-8.
294. Moretti R, Torre P, Antonello RM, Cazzato G, Bava A. Rivastigmine in subcortical vascular dementia: an open 22-month study. J Neurol Sci. 2002;203-204:141-6.
295. Erkinjuntti T, Kurz A, Small GW, Bullock R, Lilienfeld S, Damaraju CV. An open-label extension trial of galantamine in patients with probable vascular dementia and mixed dementia. Clin Ther. 2003;25(6):1765-82.
296. Erkinjuntti T, Kurz A, Gauthier S, Bullock R, Lilienfeld S, Damaraju CV. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. Lancet. 2002;359(9314):1283-90.
297. Cahill S. Educational workshops and decision support software increase detection of dementia in the elderly in primary care settings. Evid Based Ment Health. 2006;9:102.
298. Auchus A, Brashear H, Salloway S, Korczyn A, De Deyn P, Gassmann-Mayer C, et al. Galantamine treatment of vascular dementia: a randomized trial. Neurology. 2007;69(5):448-58.
299. Bullock R, Erkinjuntti T, Lilienfeld S. Management of patients with Alzheimer's disease plus cerebrovascular disease: 12-month treatment with galantamine. Dement Geriatr Cogn Disord. 2004;17(1-2):29-34.
300. Craig D, Birks J. Galantamine for vascular cognitive impairment. Cochrane Database Syst Rev. 2006;(1):CD004746.
301. Orgogozo JM, Rigaud AS, Stoffler A, Mobius HJ, Forette F. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). Stroke. 2002;33(7):1834-9.
302. Wilcock G, Mobius HJ, Stoffler A. A double-blind, placebo-controlled multicentre study of memantine in mild to moderate vascular dementia (MMM500). Int Clin Psychopharmacol. 2002;17(6):297-305.
303. Mobius HJ, Stoffler A. New approaches to clinical trials in vascular dementia: memantine in small vessel disease. Cerebrovasc Dis. 2002;13 Suppl 2:61-6.
304. Doody RS, Stevens JC, Beck C, Dubinsky RM, Kaye JA, Gwyther L, et al. Practice parameter: management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56(9):1154-66.
305. López-Arrieta J, Birks J. Nimodipina para la demencia degenerativa primaria, mixta y vascular. Reproducción de una revisión Cochrane, traducida y publicada en La Biblioteca Cochrane Plus, 2008, Número 2.
306. Pantoni L, Del ST, Soglian AG, Amigoni S, Spadari G, Binelli D, et al. Efficacy and safety of nimodipine in subcortical vascular dementia: a randomized placebo-controlled trial. Stroke. 2005;36(3):619-24.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

307. Olin J, Shneider L, Novit A, Luczak S. Hidergina para la demencia. Cochrane Database Syst Rev. 2001;(2):CD000359.
308. Fioravanti M, Yanagi M. Cytidinediphosphocholine (CDP-choline) for cognitive and behavioural disturbances associated with chronic cerebral disorders in the elderly. Cochrane Database Syst Rev. 2005;(2):CD000269.
309. Estimulació cognitiva. Consell Assessor de Psicogeriatria del Servei Català de la Salut. Grup de Treball d'Estimulació cognitiva; 2008.
310. Sitzer DI, Twamley EW, Jeste DV. Cognitive training in Alzheimer's disease: a meta-analysis of the literature. Acta Psychiatr Scand. 2006;114(2):75-90.
311. Amer Ferrer G, Torrealba Fernández E. Tratamiento no farmacológico. En: Molinuevo JL, Peña-Casanova J, editores. Guía oficial para la práctica clínica en demencias: conceptos, criterios y recomendaciones 2009. Barcelona: Prous Science, SAU. Thomson Reuters. Guías oficiales de la Sociedad Española de Neurología Nº 8; 2009. p. 399-416.
312. Olazarán J, Muñiz R, Reisberg B, Peña-Casanova J, Del Ser T, Cruz-Jentoft J, et al. Benefits of cognitive-motor intervention in MCI and mild to moderate Alzheimer disease. Neurology. 2004;63:2348-53.
313. Ito T, Meguro K, Akanuma K, Ishii H, Mori E. A randomized controlled trial of the group reminiscence approach in patients with vascular dementia. Dement Geriatr Cogn Disord. 2007;24(1):48-54.
314. Montagut N, Sánchez-Valle R, Castellví M, Rami L, Molinuevo JL. Reaprendizaje de vocabulario. Análisis comparativo entre un caso de demencia semántica y enfermedad de Alzheimer con afectación predominante del lenguaje. Rev Neurol. 2010;50(3):152-6.
315. Heiss WD, Kessler J, Mielke R, Szelies B, Herholz K. Long-term effects of phosphatidylserine, pyritinol, and cognitive training in Alzheimer's disease. A neuropsychological, EEG, and PET investigation. Dementia. 1994;5(2):88-98.
316. Tàrraga L, Boada M, Modinos G, Espinosa A, Diego S, Morera A, et al. A randomized pilot study to assess the efficacy of an interactive, multimedia tool of cognitive stimulation in Alzheimer's disease. J Neurol Neurosurg Psychiatry. 2006;77:1116-21.
317. Barnes DE, Yaffe K, Belfor N, Jagust WJ, DeCarli C, Reed BR, et al. Computer-based cognitive training for mild cognitive impairment: results from a pilot randomized, controlled trial. Alzheimer Dis Assoc Disord. 2009;23(3):205-10.
318. Baztán Cortés J, González Montalvo J, Del Ser Quijano T. Escalas de actividades de la vida diaria. En: Del Ser T, Peña-Casanova J, editores. Evaluación neuropsicológica y funcional de la demencia. Barcelona: JR Prous Editores; 1994. p. 137-64.
319. Peña-Casanova J. Escalas funcionales e instrumentales de las actividades de la vida diaria. Revista de Neurología. 1998;27(1):27-9.
320. Atención a las personas en situación de dependencia «Libro blanco». Madrid: Ministerio de Trabajo y Asuntos Sociales; 2004.
321. Asociación profesional de terapeutas ocupacionales de Navarra. Pamplona: Terapia Ocupacional; 2004.
322. Montorio Cerrato I. Intervenciones psicológicas en la prevención y atención a la dependencia. Intervención Psicosocial. 2007;16(1).
323. Osborn CL, Marshall MJ. Self-feeding performance in nursing home residents. J Gerontol Nurs. 1993;19(3):7-14.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

324. Vogelpohl TS, Beck CK, Heacock P, Mercer SO. «I can do it!» Dressing: promoting independence through individualized strategies. J Gerontol Nurs. 1996;22(3):39-42.
325. Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Olderikkert MG. Effects of community occupational therapy on quality of life, mood, and health status in dementia patients and their caregivers: a randomized controlled trial. J Gerontol A Biol Sci Med Sci. 2007;62(9):1002-9.
326. Tappen RM. The effect of skill training on functional abilities of nursing home residents with dementia. Res Nurs Health. 1994;17(3):159-65.
327. Scherder EJ, Eggermont LH. Physical activity and behaviour in dementia: a review of the literature and implications for psychosocial intervention in primary care. Dementia. 2006;5(3):411-28.
328. Rolland Y, Pillard F, Klapouszczak A, Reynish E, Thomas D, Andrieu S, et al. Exercise program for nursing home residents with Alzheimer's disease: a 1-year randomized, controlled trial. J Am Geriatr Soc. 2007;55(2):158-65.
329. Viggo HN, Jorgensen T, Ortenblad L. Massage and touch for dementia. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD004989. DOI: 10.1002/14651858.CD004989.pub2.
330. Cameron M, Lonergan E, Lee H. Transcutaneous Electrical Nerve Stimulation (TENS) for dementia. Cochrane Database of Systematic Reviews 2003, Issue 3. Art. Nº: CD004032. DOI: 10.1002/14651858.CD004032.
331. Vink AC, Birks JS, Bruinsma MS, Scholten RJPM. Music therapy for people with dementia. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. Nº: CD003477. DOI: 10.1002/14651858.CD003477.pub2.
332. Chung JCC, Lai CKY. Snoezelen for dementia. Cochrane Database of Systematic Reviews 2002, Issue 4. Art. Nº: CD003152. DOI: 10.1002/14651858.CD003152.
333. Finkel S, Costa e Silva J, Cohen G, Miller S, Sartoriu S. Behavioural and psychological sings and symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment. Int Psychogeriatr 1996;8(Supl 3): 497-500.
334. Assal F, Cummings JL. Neuropsychiatric symptoms in the dementias. Curr Opin Neurol. 2002;15(4):445-50.
335. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology. 1994;44(12):2308-14.
336. Aalten P, Verhey FRJ, Boziki M, Bullock R, Byrne EJ, Camus V, Caputo M. Neuropsychiatric Syndromes in Dementia. Results from the European Alzheimer Disease Consortium: Part I. Dement Geriatr Cogn Disord. 2007;24:457-63.
337. Katz I, De Deyn PP, Mintzer J, Greenspan A, Zhu Y, Brodaty H. The efficacy and safety of risperidone in the treatment of psychosis of Alzheimer's disease and mixed dementia: a meta-analysis of 4 placebo-controlled clinical trials. Int J Geriatr Psychiatry. 2007;22(5):475-84.
338. Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. Neurology. 1996;46(1):130-5.
339. Devanand DP, Sano M, Tang MX, Taylor S, Gurland BJ, Wilder D, et al. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. Arch Gen Psychiatry. 1996;53(2):175-82.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

340. Copeland JR, Dewey ME, Griffiths-Jones HM. A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. Psychol Med. 1986;16(1):89-99.
341. Vilalta J. Trastornos psiquiátricos asociados a las demencias. En: López-Pousa S, Vilalta-Franch J, Llinás-Reglá J, editores. Manual de Demencias. Barcelona: Prous Science; 1996. p. 473-492.
342. Leuchter AF, Spar JE. The late-onset psychoses. Clinical and diagnostic features. J Nerv Ment Dis. 1985;173(8):488-94.
343. Finkel S, Burns A. Introduction. En: Ames D, O'Brien J, eds. Behavioral and Psychological Symptoms of Dementia (BPSD): A Clinical and Research Update. Internacional Psychogeriatrics. 2000;12(Suppl. 13):9-12.
344. Gaugler JE, Kane RL, Kane RA, Newcomer R. The longitudinal effects of early behavior problems in the dementia caregiving career. Psychol Aging. 2005;20(1):100-16.
345. Roth M, Tym E, Mountjoy CQ, Huppert FA, Hendrie H, Verma S, et al. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. Br J Psychiatry. 1986;149:698-709.
346. Vilalta J, Llinàs J, López-Pousa S, Amiel J, Vidal C. CAMDEX. Validación de la adaptación española. Neurología. 1990;5:117-20.
347. Saz P, Díaz JL, De la Cámara C, Carreras S, Marcos G, Lobo A. Reliability and validity of the Spanish version of the GMS-AGECAT package for the assessment of dementia and cognitive disturbances. Int J Geriatric Psychiatry. 1996;11(8):721-8.
348. Manzano JM, Llorca G, Ledesma A, López-Ibor JJ. Adaptación Española de la Alzheimer's Disease Assessment Scale (ADAS). Actas Luso-Españolas de Neurología, Psiquiatría y Ciencias Afines. 1994;22(2):64-70.
349. Pascual LF, Saz P, Larumbe R, Martínez-Lage P, Muruzábal J, Morales F, Lobo A. Estandarización en una población española de la escala ADAS (Alzheimer's Disease Assessment Scale). Neurología. 1997;12(6):24-32.
350. Peña-Casanova J, Aguilar M, Santacruz P, Bertran-Serra I, Hernández G, Sol JM, Pujol A. Adaptación y Normalización españolas de la Alzheimer's Disease Assessment Scale (ADAS). Neurología. 1997;12(2):69-77.
351. Levin HS, High WM, Goethe KE. The Neurobehavioral Rating Scale: Assesment of the behavioral sequelae of head injury by the clinician. J Neurol Neurosurg Psychiatry. 1987;50:183-93.
352. Pelegrín Valero C, Martín Carrasco M, Tirapu Ustarroz J. La escala NRS: la versión española de la neurobehavioral rating scale. Anales de Psiquiatría. 1995;2(3):22-32.
353. Reisberg B, Auer SR, Monteiro IM. Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) Rating Scale. International Psychogeriatrics. 1997;8:301-8.
354. Boada M, Tárraga L, Modinos G, Diego S, Reisberg B. Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD): validación española. Neurología. 2006;21(1):19-25.
355. Vilalta-Franch J, Lozano-Gallego M, Hernández-Ferrándiz M, Llinàs-Reglà J, López-Pousa S, López OL. Neuropsychiatric Inventory. Propiedades psicométricas de su adaptación al español. Revista de Neurología. 1999;29(1):15-9.
356. Boada M, Cejudo JC, Tàrraga L, López OL, Kaufer D. Neuropsychiatric Inventory Questionnaire (NPI-Q): validación española de una forma abreviada del Neuropsychiatric Inventory (NPI). Neurología. 2002;17(6):317-23.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

357. Clinical and neuropathological criteria for frontotemporal dementia. The Lund and Manchester Groups. J Neurol Neurosurg Psychiatry. 1994;57(4):416-8.
358. Kaufer DI, Cummings JL, Ketchel P, Smith V, MacMillan A, Shelley T, et al. Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. J Neuropsychiatry Clin Neurosci. 2000;12(2):233-9.
359. Boada M, Tàrraga L, Modinos G, López OL, Cummings JL. Neuropsychiatric Inventory-Nursing Home version (NPI-NH): validación española. Neurología. 2005; 20(10):665-73.
360. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
361. Herrero MJ, Blanch J, Peri JM, De PJ, Pintor L, Bulbena A. A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. Gen Hosp Psychiatry. 2003;25(4):277-83.
362. Gale CR, Allerhand M, Sayer AA, Cooper C, Dennison EM, Starr JM, et al. The structure of the Hospital Anxiety and Depression Scale in four cohorts of community-based, healthy older people: the HALCyon program. Int Psychogeriatr. 2010;22(4):559-71.
363. Pujol J, de Azpiazu P, Salamero M, Cuevas R. Sintomatología depresiva de la demencia. Escala de Cornell: validación de la versión en castellano. Rev Neurol. 2001;33(4):397-8.
364. Martínez, I, Onis Vilches MC, Duenas HR, Aguado JC, Albert CC, Arias Blanco MC. Abreviar lo breve. Aproximación a versiones ultracortas del cuestionario de Yesavage para el cribado de la depresión. Aten Primaria. 2005;35(1):14-21.
365. Fernández-San Martin MI, Andrade-Rosa C, Molina JD, Munoz PE, Carretero B, Rodríguez M, et al. Validation of the Spanish version of the geriatric depression scale (GDS) in primary care. Int J Geriatr Psychiatry. 2002;17(3):279-87.
366. Wancata J, Alexandrowicz R, Marquart B, Weiss M, Friedrich F. The criterion validity of the Geriatric Depression Scale: a systematic review. Acta Psychiatr Scand. 2006;114(6):398-410.
367. Patel V, Hope RA. A rating scale for aggressive behaviour in the elderly--the RAGE. Psychol Med. 1992;22(1):211-21.
368. De Azpiazu P, Salamero M, Pujol J, Cuevas R. Conductas agresivas en la demencia. Escala RAGE, validación de la versión en castellano. Rev Neurol. 2001;33(10):928-30.
369. Eustace A, Bruce I, Coen R, Cunningham C, Walsh C, Walsh JB, et al. Behavioural disturbance triggers recognition of dementia by family informants. Int J Geriatr Psychiatry. 2007;22(6):574-9.
370. Assal F, Cummings JL. Neuropsychiatric symptoms in the dementias. Curr Opin Neurol. 2002;15(4):445-50.
371. Fernández MM, Castro FJ, Pérez de las HS, Mandaluniz LA, Gordejuela MM, Zarranz Imirizaldu JJ. Prevalence of neuropsychiatric symptoms in elderly patients with dementia in Mungia de County (Basque Country, Spain). Dement Geriatr Cogn Disord. 2008;25(2):103-8.
372. FM M, Molano A, Castro J, Zarranz JJ. Prevalence of neuropsychiatric symptoms in mild cognitive impairment and Alzheimer's disease, and its relationship with cognitive impairment. Curr Alzheimer Res. 2010;7(6):517-26.
373. Sparks MB. Inpatient care for persons with Alzheimer's disease. Crit Care Nurs Q. 2008;31(1):65-72.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

374. Fernández-Martínez M, Castro J, Molano A, Zarranz JJ, Rodrigo RM, Ortega R. Prevalence of neuropsychiatric symptoms in Alzheimer's disease and vascular dementia. Curr Alzheimer Res. 2008;5(1):61-9.
375. Nabalamba A, Patten SB. Prevalence of mental disorders in a Canadian household population with dementia. Can J Neurol Sci. 2010;37(2):186-94.
376. Di IF, Palmer K, Blundo C, Casini AR, Gianni W, Caltagirone C, et al. Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. Int Psychogeriatr. 2010;22(4):629-40.
377. Nagata T, Shinagawa S, Ochiai Y, Kada H, Kasahara H, Nukariya K, et al. Relationship of frontal lobe dysfunction and aberrant motor behaviors in patients with Alzheimer's disease. Int Psychogeriatr. 2010;22(3):463-9.
378. Rongve A, Boeve BF, Aarsland D. Frequency and correlates of caregiver-reported sleep disturbances in a sample of persons with early dementia. J Am Geriatr Soc. 2010;58(3):480-6.
379. Vecchierini MF. Les troubles du sommeil dans la demence d'Alzheimer et autres demences. Psychol Neuropsychiatr Vieil. 2010;8(1):15-23.
380. Anderson KN, Hatfield C, Kipps C, Hastings M, Hodges JR. Disrupted sleep and circadian patterns in frontotemporal dementia. Eur J Neurol. 2009;16(3):317-23.
381. McKeith I, Cummings J. Behavioural changes and psychological symptoms in dementia disorders. Lancet Neurol. 2005;4(11):735-42.
382. Levy JA, Chelune GJ. Cognitive-behavioral profiles of neurodegenerative dementias: beyond Alzheimer's disease. J Geriatr Psychiatry Neurol. 2007;20(4):227-38.
383. Bathgate D, Snowden JS, Varma A, Blackshaw A, Neary D. Behaviour in frontotemporal dementia, Alzheimer's disease and vascular dementia. Acta Neurol Scand. 2001;103(6):367-78.
384. The Expanded Prostate Cancer Index Composite (EPIC). Versión española del Expanded Prostate Cancer Index (EPIC), 2002 adaptada por M. Ferrer y cols. Barcelona: Institut Municipal d'Investigació Mèdica (IMIM-Hospital del Mar). Grupo de Investigación en Servicios Sanitarios; 2003.
385. Zetteler J. Effectiveness of simulated presence therapy for individuals with dementia: a systematic review and meta-analysis. Aging Ment Health. 2008;12(6):779-85.
386. O'Connell B, Gardner A, Takase M, Hawkins MT, Ostaszkiewicz J, Ski C, et al. Clinical usefulness and feasibility of using Reality Orientation with patients who have dementia in acute care settings. Int J Nurs Pract. 2007;13(3):182-92.
387. O'Connor DW, Ames D, Gardiner B, King M. Psychosocial treatments of psychological symptoms in dementia: a systematic review of reports meeting quality standards. Int Psychogeriatr. 2009;21(2):241-51.
388. Livingston G, Johnston K, Katona C, Paton J, Lyketsos CG. Systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. Am J Psychiatry. 2005;162(11):1996-2021.
389. Spijker A, Vernooij-Dassen M, Vasse E, Adang E, Wollersheim H, Grol R, et al. Effectiveness of nonpharmacological interventions in delaying the institutionalization of patients with dementia: a meta-analysis. J Am Geriatr Soc. 2008;56(6):1116-28.
390. Pla de salut de Catalunya 1996-1998. Barcelona: Departament de Salut. Generalitat de Catalunya; 1997.

More than 5 years have passed since the publication of the Clinical Practice Guideline, and its validity has not been reviewed

391. Verkaik R, van Weert JC, Francke AL. The effects of psychosocial methods on depressed, aggressive and apathetic behaviors of people with dementia: a systematic review. Int J Geriatr Psychiatry. 2005;20(4):301-14.
392. Woods B, Spector A, Jones C, Orrell M, Davies S. Reminiscence therapy for dementia. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. Nº: CD001120. DOI: 10.1002/14651858.CD001120.pub2.
393. Moran M, Lynch CA, Walsh C, Coen R, Coakley D, Lawlor BA. Sleep disturbance in mild to moderate Alzheimer's disease. Sleep Med. 2005;6(4):347-52.
394. Yesavage JA, Friedman L, ncoli-Israel S, Bliwise D, Singer C, Vitiello MV, et al. Development of diagnostic criteria for defining sleep disturbance in Alzheimer's disease. J Geriatr Psychiatry Neurol. 2003;16(3):131-9.
395. Lai CK, Arthur DG. Wandering behaviour in people with dementia. J Adv Nurs. 2003;44(2):173-82.
396. Althus DE, Mathews RM, Xaverius PK. Evaluating an electronic monitoring system for people who wander. Am J Alzh Dis. 2000;15(2):121-5.
397. Robinson L, Hutchings D, Corner L, Beyer F, Dickinson H, Vanoli A, et al. A systematic literature review of the effectiveness of non-pharmacological interventions to prevent wandering in dementia and evaluation of the ethical implications and acceptability of their use. Health Technol Assess. 2006;10(26):iii, ix-iii,108.
398. Hermans DG, Htay UH, McShane R. Intervenciones no farmacológicas para pacientes con demencia que deambulan en ámbitos domésticos (Revisión Cochrane traducida). En: La Biblioteca Cochrane Plus, 2007 Número 4. Oxford: Update Software Ltd. Disponible en: http://www.update-software.com. (Traducida de The Cochrane Library, 2007 Issue 4. Chichester, UK: John Wiley & Sons, Ltd.).
399. Carson S, McDonagh MS, Peterson K. A systematic review of the efficacy and safety of atypical antipsychotics in patients with psychological and behavioral symptoms of dementia. J Am Geriatr Soc. 2006;54(2):354-61.
400. Fischer C, Bozanovic R, Atkins JH, Rourke SB. Treatment of delusions in Alzheimer's disease-response to pharmacotherapy. Dement Geriatr Cogn Disord. 2006;22(3):260-6.
401. Ballard C, Waite J. The effectiveness of atypical antipsychotics for the treatment of aggression and psychosis in Alzheimer's disease. Cochrane Database Syst Rev. 2006;(1):CD003476.
402. Lonergan E, Luxenberg J, Colford J, Birks J. Haloperidol for agitation in dementia. Cochrane Database of Systematic Reviews 2002, Issue 2. Art. Nº: CD002852. DOI: 10.1002/14651858.CD002852.
403. Ozkan B, Wilkins K, Muralee S, Tampi RR. Pharmacotherapy for inappropriate sexual behaviors in dementia: a systematic review of literature. Am J Alzheimers Dis Other Demen. 2008;23(4):344-54.
404. Ballard C, Howard R. Neuroleptic drugs in dementia: benefits and harm. Nat Rev Neurosci. 2006;7(6):492-500.
405. Schneider LS, Dagerman K, Insel PS. Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. Am J Geriatr Psychiatry. 2006;14(3):191-210.
406. Wang PS, Schneeweiss S, Avorn J, Fischer MA, Mogun H, Solomon DH, et al. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. N Engl J Med. 2005;353(22):2335-41.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

407. Herrmann N, Lanctot KL. Do atypical antipsychotics cause stroke? CNS Drugs. 2005;19(2):91-103.
408. Burns A, De Deyn PP. Risperidone for the treatment of neuropsychiatric features in dementia. Drugs and Aging. 2006;23(11):887-96.
409. De Vugt ME, Stevens F, Aalten P, Lousberg R, Jaspers N, Winkens I, et al. Do caregiver management strategies influence patient behaviour in dementia? Int J Geriatr Psychiatry. 2004;19(1):85-92.
410. Zec RF, Burkett NR. Non-pharmacological and pharmacological treatment of the cognitive and behavioral symptoms of Alzheimer disease. NeuroRehabilitation. 2008;23(5):425-38.
411. Boeve BF. A review of the non-Alzheimer dementias. J Clin Psychiatry. 2006;67(12): 1985-2001.
412. Chamorro García L. Guía de manejo de los transtornos mentales en atención primaria. Barcelona: Psiquiatría editores; 2004.
413. Téllez JM, Villena A, Morena S, Pascual P, López-García C. El paciente agitado. Guías Clínicas. 2005;5(34). Disponible en: http://www.fisterra.com
414. Isaac MG, Quinn R, Tabet N. Vitamin E for Alzheimer's disease and mild cognitive impairment. Cochrane Database Syst Rev. 2008;(3):CD002854.
415. Miller ER, III, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med. 2005;142(1):37-46.
416. Feldman HH, Gauthier S, Chertkow H, Conn DK, Freedman M, Chris M. Progress in clinical neurosciences: Canadian guidelines for the development of antidementia therapies: a conceptual summary. Can J Neurol Sci. 2006;33(1):6-26.
417. Kessler H, Bayer TA, Bach D, Schneider-Axmann T, Supprian T, Herrmann W, et al. Intake of copper has no effect on cognition in patients with mild Alzheimer's disease: a pilot phase 2 clinical trial. J Neural Transm. 2008;115(8):1181-7.
418. Bent S, Goldberg H, Padula A, Avins AL. Spontaneous bleeding associated with ginkgo biloba: a case report and systematic review of the literature: a case report and systematic review of the literature. J Gen Intern Med. 2005;20(7):657-61.
419. Birks J, Grimley EJ. Ginkgo biloba for cognitive impairment and dementia. Cochrane Database Syst Rev. 2009;(1):CD003120.
420. Higgins JP, Flicker L. Lecithin for dementia and cognitive impairment. Cochrane Database Syst Rev. 2003;(3):CD001015.
421. Klugman A, Sauer J, Tabet N, Howard R. Alpha lipoic acid for dementia. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. Nº: CD004244. DOI: 10.1002/14651858.CD004244.pub2.
422. Chiu CC, Su KP, Cheng TC, Liu HC, Chang CJ, Dewey ME, et al. The effects of omega-3 fatty acids monotherapy in Alzheimer's disease and mild cognitive impairment: a preliminary randomized double-blind placebo-controlled study. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(6):1538-44.
423. Lee MS, Yang EJ, Kim JI, Ernst E. Ginseng for cognitive function in Alzheimer's disease: a systematic review. J Alzheimers Dis. 2009;18(2):339-44.
424. Mizukami K, Asada T, Kinoshita T, Tanaka K, Sonohara K, Nakai R, et al. A randomized cross-over study of a traditional Japanese medicine (kampo), yokukansan, in the treatment of the behavioural and psychological symptoms of dementia. Int J

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

Neuropsychopharmacol. 2009;12(2):191-9.
425. Dantoine T, Auriacombe S, Sarazin M, Becker H, Pere JJ, Bourdeix I. Rivastigmine monotherapy and combination therapy with memantine in patients with moderately severe Alzheimer's disease who failed to benefit from previous cholinesterase inhibitor treatment. Int J Clin Pract. 2006;60(1):110-8.
426. Harrell LE, Marson D, Chatterjee A, Parrish JA. The Severe Mini-Mental State Examination: a new neuropsychologic instrument for the bedside assessment of severely impaired patients with Alzheimer disease. Alzheimer Dis Assoc Disord. 2000;14(3):168-75.
427. Rodríguez-Rodríguez P. Residencias para personas mayores. Manual de orientación. Colección Gerontología Social SEGG. Madrid: SG Editores; 1995.
428. Ball K. How to develop a laser center. Indiana Med. 1988;81(4):332-6.
429. Graff J, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels W, Olde M. Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. BMJ. 2008;333:1196.
430. Charlesworth G, Shepstone L, Wilson E, Thalanany M, Mugford M, Poland F. Does befriending by trained lay workers improve psychological well-being and quality of life for carers of people with dementia, and at what cost? A randomised controlled trial. Health Technol Assess. 2008;12(4):1-78.
431. Reyes MC. Construyendo el concepto de cuidador de ancianos. IV Reunión de Antropología de Mercosul. Curitiba (Brasil). Diciembre 2001.
432. Valderrama H. Panel «La institución geriátrica como centro de servicios gerontológicos». Revista de la Asociación de Establecimientos Geriátricos. 1999;9(35).
433. Gallart A. Factores de riesgo del cansancio en el cuidador formal no profesional inmigrante en Barcelona. Revista de Administración Sanitaria Siglo XXI. 2004;2(2):299-316.
434. Conde-Sala JL, Garre-Olmo J, Turró-Garriga O, López-Pousa S, Vilalta-Franch J. Factors related to perceived quality of life in patients with Alzheimer's disease: the patient's perception compared with that of caregivers 3. Int J Geriatr Psychiatry. 2009;24(6):585-94.
435. Conde-Sala JL, Garre-Olmo J, Turró-Garriga O, Vilalta-Franch J, López-Pousa S. Quality of life of patients with Alzheimer's disease: differential perceptions between spouse and adult child caregivers 2. Dement Geriatr Cogn Disord. 2010;29(2): 97-108.
436. Conde-Sala JL, Garre-Olmo J, Turró-Garriga O, Vilalta-Franch J, López-Pousa S. Differential features of burden between spouse and adult-child caregivers of patients with Alzheimer's disease: An exploratory comparative design 1. Int J Nurs Stud. 2010;47(10):1262-73.
437. Marwit SJ, Meuser TM. Development and initial validation of an inventory to assess grief in caregivers of persons with Alzheimer's disease. Gerontologist. 2002;42(6):751-65.
438. Ankri J, Andrieu S, Beaufils B, Grand A, Henrard JC. Beyond the global score of the Zarit Burden Interview: useful dimensions for clinicians. Int J Geriatr Psychiatry. 2005;20(3):254-60.
439. Martín M, Salvadó I, Nadal S, Miji LC, Rico JM, Lanz P. Adaptación para nuestro medio de la escala de sobrecarga del cuidador (caregiver burden interview) de Zarit. Rev Gerontol. 1996;6(338):346.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

440. Turró-Garriga O, Soler-Cors O, Garré-Olmo J, López-Pousa S, Vilalta-Franch J, Montserrat-Vila S. Distribución factorial de la carga en curadores de pacientes con enfermedad de Alzheimer. Rev Neurol. 2008;46:582-8.
441. Higginson IJ, Gao W, Jackson D, Murray J, Harding R. Short-form Zarit Caregiver Burden Interviews were valid in advanced conditions. J Clin Epidemiol. 2010;63(5):535-42.
442. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893-7.
443. McHorney CA, Ware JE, Jr., Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care. 1994;32(1):40-66.
444. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33.
445. Schneider J, Murray J, Banerjee S, Mann A. EUROCARE: a cross-national study of co-resident spouse carers for people with Alzheimer's disease: I-Factors associated with carer burden. Int J Geriatr Psychiatry. 1999;14(8):651-61.
446. Rabins PV. The caregiver's role in Alzheimer's disease. Dement Geriatr Cogn Disord. 1998;9 Suppl 3:25-8.
447. Zabalegui A, Navarro M, Cabrera E, Gallart A, Bardallo D, Rodríguez E, Gual P, Fernández M, Argemí J. Eficacia de las intervenciones dirigidas a cuidadores principales de personas dependientes mayores de 65 años. Una revisión sistemática. Rev Esp Geriatr Gerontol. 2008;43(3):157-66.
448. Thompson C, Spilsbury K. WITHDRAWN: Support for carers of people with Alzheimer's type dementia. Cochrane Database Syst Rev. 1998;(3):CD000454.
449. Gallagher-Thompson D, Coon DW. Evidence-based psychological treatments for distress in family caregivers of older adults. Psychol Aging. 2007;22(1):37-51.
450. Brodaty H, Green A, Koschera A. Meta-analysis of psychosocial interventions for caregivers of people with dementia. J Am Geriatr Soc. 2003;51(5):657-64.
451. Thompson C, Briggs M. Support for carers of people with Alzheimer's type dementia. Cochrane Database Syst Rev. 2000;(2):CD000454.
452. Teri L, Mc Curry S, Logsdon R, Gibbons L. Training community consultants to help family members improve dementia care: a randomized controlled trial. Gerontologist 2005;45:802-11.
453. Gitlin LN, Corcoran M, Winter L, Boyce A, Hauck WW. A randomized, controlled trial of a home environmental intervention: effect on efficacy and upset in caregivers and on daily function of persons with dementia. Gerontologist. 2001;41(1):4-14.
454. Gitlin LN, Winter L, Corcoran M, Dennis MP, Schinfeld S, Hauck WW. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. Gerontologist. 2003;43(4):532-46.
455. Associacions de Salut i Grups d'Ajuda Mútua (GAM Barcelona) [Página en Internet]. Barcelona: Serveis Associatius Torre Jussana. Ajuntament de Barcelona. Disponible en: http://www.bcn.es/tjussana/gam
456. Álvarez D. Los grupos de ayuda mutua, un modelo social de salud [ponencia]. En: I Jornades d'Afectats de Neurofibromatosis a Catalunya. Revista AC NEfi. Asociación Catalana de las Neurofibromatosis. 1999. Disponible en: http://www.acnefi.com/revista/1999t35.htm

More than 5 years have passed since the publication of the Clinical Practice Guideline and its validity has not been reviewed

457. Moya MJ, Costa S. Manual de consulta sobre grups d'ajuda mútua de persones amb discapacitat física (experiències en GAM des de la Federació ECOM); 2007.
458. Bonet R, Ferrer MJ, Vilajoana JC. Estrategias de grupo y sida: ayuda mutua. Revista de Psicología General y Aplicada. 1994;47(2):193-200.
459. Villalbí J, Roca F. Un instrumento a desarrollar para la promoción de la salud entre nuestros pacientes y sus allegados: los grupos de ayuda mutua. Med Clin (Barc). 1989;11(93):427-30.
460. Barath A, Csepeli G. Self-Help aspects of sociology and psychology. En: Gielen P. Self-help and mutual aid in health. Leuven (Belgium): International Centre for Self-Help and Health; 1987;2-6.
461. Snyder L, Jenkins C, Joosten L. Effectiveness of support groups for people with mild to moderate Alzheimer's disease: an evaluative survey. Am J Alzheimers Dis Other Demen. 2007;22(1):14-9.
462. Acton GJ, Kang J. Interventions to reduce the burden of caregiving for an adult with dementia: a meta-analysis. Res Nurs Health. 2001;24(5):349-60.
463. Losada-Baltar A, Izal-Fernández de Trocóniz M, Montorio-Cerrato I, Márquez-González M, Pérez-Rojo G. Eficacia diferencial de dos intervenciones psicoeducativas para cuidadores de familiares con demencia. Rev Neurol. 2004;38(8):701-8.
464. López J, Crespo M. Intervenciones con cuidadores de familiares mayores dependientes: una revisión. Psicothema. 2007;19(1):72-80.
465. Conde-Sala JL. La familia y los cuidados informales en la demencia. Diferencias entre cónyuges e hijos cuidadores. En: Alberca R, López S. Enfermedad de Alzheimer y otras demencias. 4ª edición. Madrid: Editorial Médica Panamericana; 2010 (En prensa).
466. Ulstein ID, Sandvik L, Wyller TB, Engedal K. A one-year randomized controlled psychosocial intervention study among family carers of dementia patients-effects on patients and carers. Dement Geriatr Cogn Disord. 2007;24(6):469-75.
467. CEAFA. Confederación Española de Familiares de Enfermos de Alzheimer y Otras Demencias. Disponible en: www.ceafa.es
468. Villars H, Oustric S, Andrieu S, Baeyens JP, Bernabei R, Brodaty H, et al. The primary care physician and Alzheimer's disease: an international position paper. J Nutr Health Aging. 2010;14(2):110-20.
469. Kelley BJ, Boeve BF, Josephs KA. Cognitive and noncognitive neurological features of young-onset dementia. Dement Geriatr Cogn Disord. 2009;27(6):564-71.
470. Vilalta-Franch J, Garre-Olmo J, López-Pousa S, Turon-Estrada A, Pericot-Nierga I. Diferencias entre las demencias según la edad de inicio: estudio a partir de los datos de un registro de demencias. Neurología. 2008;23(3):145-51.
471. Sampson EL, Warren JD, Rossor MN. Young onset dementia. Postgrad Med J. 2004;80(941):125-39.
472. Koedam EL, Pijnenburg YA, Deeg DJ, Baak MM, Van Der Vlies AE, Scheltens P, et al. Early-onset dementia is associated with higher mortality. Dement Geriatr Cogn Disord. 2008;26(2):147-52.
473. Werner P, Stein-Shvachman I, Korczyn AD. Early onset dementia: clinical and social aspects. Int Psychogeriatr. 2009;21(4):631-6.
474. Shiino A, Watanabe T, Maeda K, Kotani E, Akiguchi I, Matsuda M. Four subgroups of Alzheimer's disease based on patterns of atrophy using VBM and a unique pattern for early onset disease. Neuroimage. 2006;33(1):17-26.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

475. Shiino A, Watanabe T, Kitagawa T, Kotani E, Takahashi J, Morikawa S, et al. Different atrophic patterns in early- and late-onset Alzheimer's disease and evaluation of clinical utility of a method of regional z-score analysis using voxel-based morphometry. Dement Geriatr Cogn Disord. 2008;26(2):175-86.
476. Jacobs D, Sano M, Marder K, Bell K, Bylsma F, Lafleche G, et al. Age at onset of Alzheimer's disease: relation to pattern of cognitive dysfunction and rate of decline. Neurology. 1994;44(7):1215-20.
477. Borroni B, Agosti C, Bellelli G, Padovani A. Is early-onset clinically different from late-onset frontotemporal dementia? Eur J Neurol. 2008;15(12):1412-5.
478. Shinagawa S, Toyota Y, Ishikawa T, Fukuhara R, Hokoishi K, Komori K, et al. Cognitive function and psychiatric symptoms in early- and late-onset frontotemporal dementia. Dement Geriatr Cogn Disord. 2008;25(5):439-44.
479. Orrell M, Spector A, Thorgrimsen L, Woods B. A pilot study examining the effectiveness of maintenance Cognitive Stimulation Therapy (MCST) for people with dementia. Int J Geriatr Psychiatry. 2005;20(5):446-51.
480. Winblad B, Jones RW, Wirth Y, Stoffler A, Mobius HJ. Memantine in moderate to severe Alzheimer's disease: a meta-analysis of randomised clinical trials. Dement Geriatr Cogn Disord. 2007;24(1):20-7.
481. Harvey RJ, Rossor MN, Skelton-Robinson M, Garralda E. Young onset dementia: epidemiology, clinical symptoms, family burden, support and outcome [monografia en Internet]. London (United Kingdom): The National Hospital for Neurology and Neurosurgery. Imperial College School of Medicine; 1998 [citado 8 marzo 2010]. Disponible en: http://home.kosha.net/~h1415c/report.pdf
482. Baker AA. Granny battering. Modern Geriatrics. 1975;5(8):20-4.
483. Burston GR. Granny-battering. Br Med J. 1975;3(5983):592.
484. Declaración de Almería. I Conferencia Nacional de Consenso sobre el Anciano Maltratado; 1996.
485. Organización Mundial de la Salud (OMS); 2002.
486. Cooper C, Selwood A, Livingston G. The prevalence of elder abuse and neglect: a systematic review. Age Ageing. 2008;37(2):151-60.
487. Cooper C, Selwood A, Livingston G. Knowledge, detection, and reporting of abuse by health and social care professionals: a systematic review. Am J Geriatr Psychiatry. 2009;17(10):826-38.
488. Gutiérrez RF. Maltrato geriátrico. En: Garza Elizondo T. Trabajo con familias. Nuevo León (Mexico): Universidad Autónoma de Nuevo León; 2009. p. 311-8.
489. Hudson MF. Elder mistreatment: a taxonomy with definitions by Delphi . Journal of Elder Abuse & Neglect. 1991;3(2):1-20.
490. Lowenstein A. Elder abuse and neglect-«old phenomenon»: new directions for research, legislation, and service developments. (2008 Rosalie S. Wolf Memorial Elder Abuse Prevention Award-International Category Lecture). J Elder Abuse Negl. 2009;21(3):278-87.
491. INPEA - Red Internacional para la prevención del maltrato hacia las personas mayores; 1995.
492. Rovi S, Chen PH, Vega M, Johnson MS, Mouton CP. Mapping the elder mistreatment iceberg: U.S. hospitalizations with elder abuse and neglect diagnoses. J Elder Abuse Negl. 2009;21(4):346-59.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

493. Biggs S, Manthorpe J, Tinker A, Doyle M, Erens B. Mistreatment of older people in the United Kingdom: findings from the first National Prevalence Study. J Elder Abuse Negl. 2009;21(1):1-14.
494. Acierno R, Hernández MA, Amstadter AB, Resnick HS, Steve K, Muzzy W, et al. Prevalence and correlates of emotional, physical, sexual, and financial abuse and potential neglect in the United States: the National Elder Mistreatment Study. Am J Public Health. 2010;100(2):292-7.
495. Vandeweerd C, Paveza GJ. Verbal mistreatment in older adults: a look at persons with Alzheimer's disease and their caregivers in the state of Florida. J Elder Abuse Negl. 2005;17(4):11-30.
496. Lachs MS, Williams CS, O'Brien S, Pillemer KA, Charlson ME. The mortality of elder mistreatment. JAMA. 1998;280(5):428-32.
497. Schiamberg LB, Gans D. Elder abuse by adult children: an applied ecological framework for understanding contextual risk factors and the intergenerational character of quality of life. Int J Aging Hum Dev. 2000;50(4):329-59.
498. Coma M, Muñoz J, Orfila F, Tabueña M. Prevenir y actuar contra los malos tratos a las personas mayores. Obra Social de Caixa Catalunya; 2009.
499. Aguar-Fernández M, Delgado-Sánchez A, Castellano Arroyo M, Luna del Castillo JD. Prevalencia de malos tratos en mujeres que consultan al médico de familia. Aten Primaria. 2006;37:241-2.
500. Usaola C. Maltrato a la mujer en la relación de pareja. Factores relacionados implicados [disertación doctoral no publicada]. Madrid: Universidad de Alcalá de Henares; 2001.
501. Alonso M, Bedoya JM, Cayuela A, Daurat M, Gómez M, Gentilhome D. Violència contra la dona. Resultats d'una enquesta hospitalària. Progressos en Obstetrícia i Ginecologia. 2004;47:511-20.
502. Fulmer T. Elder mistreatment. Annu Rev Nurs Res. 2002;20:369-95.
503. Vandeweerd C, Paveza GJ, Fulmer T. Abuse and neglect in older adults with Alzheimer's disease. Nurs Clin North Am. 2006;41(1):43-vi.
504. Pérez-Rojo G. Factores de riesgo asociados al maltrato hacia personas con demencia en el ámbito comunitario. Zerbitzuan: Gizarte zerbitzuetarako aldizkaria (Revista de servicios sociales). 2008;43:19-32.
505. Yaffe MJ, Wolfson C, Lithwick M, Weiss D. Development and validation of a tool to improve physician identification of elder abuse: the Elder Abuse Suspicion Index (EASI). J Elder Abuse Negl. 2008;20(3):276-300.
506. Reis M, Nahmiash D. Validation of the indicators of abuse (IOA) screen. Gerontologist. 1998;38(4):471-80.
507. Cohen M, Halevi-Levin S, Gagin R, Friedman G. Development of a screening tool for identifying elderly people at risk of abuse by their caregivers. J Aging Health. 2006;18(5):660-85.
508. Reis M, Nahmiash D. When seniors are abused: an intervention model. Gerontologist. 1995;35(5):666-71.
509. LEY 6/1999, de 7 de julio, de Atención y Protección a las Personas Mayores. Comunidad Autónoma de Andalucía: Boletín Oficial del Estado (BOE); núm. 233, de 29/09/1999. p. 19448.
510. Fernández-Alonso MC, Grupo de trabajo de salud mental PAPPS. Documento de actuación en malos tratos a ancianos. Barcelona: Sociedad Española de Medicina de

More than 5 years have passed since the publication of the Clinical Practice Guideline and its validity has not been reviewed

Familia y Comunitaria (SemFYC); 2001.
511. Hofmann JC, Wenger NS, Davis RB, Teno J, Connors AF, Jr., Desbiens N, et al. Patient preferences for communication with physicians about end-of-life decisions. SUPPORT Investigators. Study to Understand Prognoses and Preference for Outcomes and Risks of Treatment. Ann Intern Med. 1997;127(1):1-12.
512. Collins LG, Parks SM, Winter L. The state of advance care planning: one decade after SUPPORT. Am J Hosp Palliat Care. 2006;23(5):378-84.
513. Hirschman KB, Corcoran AM, Straton JB, Kapo JM. Advance care planning and hospice enrollment: who really makes the decision to enroll? J Palliat Med. 2010;13(5):519-23.
514. Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. Madrid: Boletín Oficial del Estado (BOE); núm 274, de 15-11-2002. p. 40126-32.
515. Real Decreto 124/2007, de 2 de febrero, por el que se regula el Registro nacional de instrucciones previas y el correspondiente fichero automatizado de datos de carácter personal. Barcelona: Boletín Oficial Del Estado (BOE); núm. 40, de 15-02-2007. p. 6591-6593.
516. Ley 39/2006, de 14 de diciembre, de promoción de la autonomía personal y atención a personas en situación de dependencia. Madrid: Boletín Oficial del Estado (BOE); núm. 299, de 15/12/2006. p. 44142-56.
517. Demencia. Guía de recomendaciones clínicas. Oviedo: Dirección General de Organización de las Prestaciones Sanitarias. Consejería de Salud y Servicios Sanitarios del Principado de Asturias; 2008.
518. Assessment of mental capacity: guidance for doctors and lawyers. 2nd edition. London: British Medical Association (BMA). Law Society. BMJ Books; 2004.
519. Sturman ED. The capacity to consent to treatment and research: a review of standardized assessment tools. Clin Psychol Rev. 2005;25(7):954-74.
520. Appelbaum PS. Clinical practice. Assessment of patients' competence to consent to treatment. N Engl J Med. 2007;357(18):1834-40.
521. Alzheimer Europe Report: End-of-life care for people with dementia. Luxembourg: Alzheimer Europe; 2008.
522. Boada M, Robles A. Documento Sitges 2005: Análisis y reflexiones sobre la capacidad de tomar decisiones durante la evolución de una demencia. Barcelona: Editorial Glosa; 2005.
523. Badenes-Guía D, Casas-Hernanz L, Cejudo-Bolívar J, Aguilar-Barberà M. Valoración de la capacidad de conducción de vehículos en pacientes con diagnóstico de deterioro cognitivo leve y demencia. Neurología. 2008;23(9):575-82.
524. Real decreto 1277/ 2003, de 10 de octubre, por el que se establecen las bases generales sobre autorización de centros, servicios y establecimientos sanitarios. Madrid: Boletín Oficial del Estado (BOE); núm. 254, de 23/10/2003. p. 37893.
525. Reglamento de centros de reconocimiento; 2010.
526. Deficits and fitness to drive. Leicester (United Kingdom): The British Psychological Society (BPS); 1999. Disponible en: http://www.bps.org.uk
527. Guide to assessing and counselling older drivers. Chicago, IL (US): American Medical Association (AMA); 2004. Disponible en: http://www.ama-assn.org
528. Ley 29/2006, de 26 de julio, de garantías y uso racional de los medicamentos y productos sanitarios. Madrid: Boletín Oficial del Estado (BOE); núm. 178, de 27/7/2006. p. 28122.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

529. Declaración de Helsinki. World Medical Association. WMA Ferney-Voltaire. Disponible en: http://www.wma.net
530. Council for International Organizations of Medical Sciences (CIOMS). Geneva (Switzerland).
531. Clinical practice. Assessment of patients competence to consent to treatment. N Engl J Med. 2007;357:1834-40.
532. Barrio M, Simón P, Pascau M. El papel de la enfermera en la planificación anticipada de las decisiones: más allá de las instruccciones previas o voluntades anticipadas. Enferm Clin. 2004;14(4):223-9.
533. Ley 1/2009, de 25 de marzo, de reforma de la Ley de 8 de junio de 1957, sobre el Registro Civil, en materia de incapacitaciones, cargos tutelares y administradores de patrimonios protegidos. Madrid: Boletín Oficial del Estado (BOE); núm. 73, de 26/3/2009. p. 29137.
534. Ley 41/2003 de 18 de noviembre, de protección patrimonial de las personas con discapacidad y de modificacion del Código Civil, de la Ley de Enjuiciamiento Civil y de la Normativa Tributaria con esta finalidad. Madrid: Boletín Oficial del Estado (BOE); núm. 277, de 19/11/2003. p. 40852.
535. Artículo 223 del Código Civil. En: Título X. De la tutela, de la curatela y de la guarda de los menores o incapacitados. Capítulo II. De la tutela. Sección I. De la tutela en general.
536. Artículo 1732 del Código Civil. En: Título IX. Del mandato. Capítulo IV. De los modos de acabarse el mandato.
537. Ley 13/1983, del 24 de octubre, de reforma del Código Civil en materia de tutela. Madrid: Boletín Oficial del Estado (BOE); núm. 256/1983, de 26 de octubre de 1983. (artículos 222, 223, 228, 229, 239, 243, ...).
538. Enciclopedia jurídica [página en Internet]. Disponible en: www.enciclopedia-juridica.biz14.com
539. Tutela. En: Wikipedia. La Enciclopedia Libre [Internet]. Disponible en: http://es.wikipedia.org/wiki/Tutela
540. La tutela, la curatela y el defensor judicial. En: iAbogado [Internet]. Disponible en: http://iabogado.com/guia-legal/familia/la-tutela-la-curatela-y-el-defensor-judicial/lang/es
541. Seguridad del paciente: Protocolo de contención mecánica e inmovilización de pacientes. Granada: Dirección de Enfermería. Hospital Universitario San Cecilio; 2007.
542. Protocolo de contención mecánica de movimientos. Madrid: Grupo de Trabajo de Contención Mecánica. Hospital Universitario 12 de Octubre; septiembre 2003.
543. Ramos Briera JA. Contención mecánica. Restricción de movimientos y aislamiento. Manual de uso y protocolos de procedimiento. Barcelona: Editorial Masson; 1999.
544. Evans D, Wood J, Lambert L, Fitzgerald M. Physical restraint in acute and residential care: a systematic review. Adelaide (Australia): Joanna Briggs Institute for Evidence Based Nursing and Midwifery; 2002. Systematic Review Number 22.
545. Grupo de trabajo estrategia para la seguridad del paciente. Consejería de Salud de la Junta de Andalucía; 2006. Disponible en: www.juntadeandalucía.es/salud
546. Andrés A. Vigilancia de las medidas de restricción física. En: VII Congreso de SEMEN. II Curso para Auxiliares de Residencias. Bilbao; 26 y 27 de octubre de 2007.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

547. Protocolo de contención de pacientes. Oviedo: Hospital Universitario de Asturias; abril 2005.
548. Secretaría del Plan Nacional sobre el Sida. Encuesta hospitalaria sobre la utilización de recursos y características de los pacientes VIH/sida. Madrid: Ministerio de Sanidad y Consumo; 1998.
549. Germond M, Dessole S, Senn A, Loumaye E, Howles C, Beltrami V. Successful in-vitro fertilisation and embryo transfer after treatment with recombinant human FSH [letter]. Lancet. 1992;339(8802):1170.
550. Convenio Europeo para la Protección de los Derechos Humanos y las Libertades Fundamentales. Artículo 5. Convenio para la Protección de los Derechos Humanos y de las Libertades Fundamentales (CEDH). Lisboa, 13 de diciembre de 2007.
551. Tribunal Europeo de Derechos Humanos (TEDH). Tribunal de Estrasburgo y Cortes Europea de Derechos Humanos.
552. Asamblea Parlamentaria del Consejo de Europa sobre Psiquiatría y Derechos Humanos del 12 de abril de 1994.
553. Ley orgánica 15/1999, de 13 de diciembre (RCL 1999, 3058), de Protección de Datos de Carácter General. Madrid: Boletín Oficial del Estado (BOE); núm. 298, de 14/12/1999. p. 43088-99.
554. Principios de Naciones Unidas. Puntos 9.1 y 11.1.
555. Ley de Enjuiciamiento Civil (artículo 758.2). Ley 1/2000, de 7 de enero. Madrid: Boletín Oficial del Estado (BOE); núm. 266, de 04-11-2009. p. 92103-313.
556. Guía de actuación compartida para el paciente con contención. Jaén: Subcomisión de cuidados. Área de Salud Mental de Jaén. Junta de Andalucía; marzo 2007.
557. Ley 1/2000, de 7 de enero, de enjuiciamiento civil. Madrid: Boletín Oficial del Estado (BOE); núm. 7, de 8/01/00. p. 575-728.
558. Instrucción 3/1990, de la Fiscalía General del Estado, sobre ingreso en centros geriátricos.
559. Reisberg B, Ferris SH, de Leon MJ, Crook T. Global Deterioration Scale (GDS). Psychopharmacol Bull. 1988;24(4):661-3.
560. Sclan SG, Reisberg B. Functional assessment staging (FAST) in Alzheimer's disease: reliability, validity, and ordinality. Int Psychogeriatr. 1992;4 Suppl 1:55-69.
561. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993;43(11):2412-4.
562. Robles Raya MJ. Toma de decisiones clínicas en pacientes con demencia avanzada. Rev Mult Gerontol. 2006;16(4):209-20.
563. Espaulella J. Criteris de definició de situació avançada i terminal en el pacient geriàtric. Barcelona: Màster de gerontologia clínica. Universitat Autònoma de Barcelona; 2001.
564. Cabarcos A. Valoración integral del enfermo en la fase terminal; 2000.
565. Gómez-Batiste X, Espinosa J, Porta-Sales J, Benito E. Modelos de atención, organización y mejora de la calidad para la atención de los enfermos en fase terminal y su familia: aportación de los cuidados paliativos. Med Clin (Barc). 2010;135(2):83-9.
566. Gómez-Batiste X, Pascual A, Espinosa J, Caja C. Diseño, implementación y evaluación de programas públicos de cuidados paliativos. Med Clin (Barc). 2010;135(4):179-85.
567. Medical guidelines for determinig prognosis in selected non-cancer diseases. 2nd edition. Arlington, VA (US): National Hospice Organization; 1996.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

569. National Gold Standards Framework Centre [página en Internet]. Disponible en: www.goldstandardsframework.nhs.uk
570. Dale J, Petrova M, Munday D, Koistinen-Harris J, Lall R, Thomas K. A national facilitation project to improve primary palliative care: impact of the Gold Standards Framework on process and self-ratings of quality. Qual Saf Health Care. 2009;18(3):174-80.
571. Currow DC, Abernethy AP, Fazekas BS. Specialist palliative care needs of whole populations: a feasibility study using a novel approach. Palliat Med. 2004;18(3): 239-47.
572. Mitchell SL, Teno JM, Kiely DK, Shaffer ML, Jones RN, Prigerson HG, et al. The clinical course of advanced dementia. N Engl J Med. 2009;361(16):1529-38.
573. ECP-SNS. Estrategia en cuidados paliativos del Sistema Nacional de Salud. Madrid: Ministerio de Sanidad y Consumo; 2007.
574. Sampson EL, Ritchie CW, Lai R, Raven PW, Blanchard MR. A systematic review of the scientific evidence for the efficacy of a palliative care approach in advanced dementia. Int Psychogeriatr. 2005;17(1):31-40.
575. Grupo de Trabajo de la Guía de Práctica Clínica sobre Cuidados Paliativos. Guía de Práctica Clínica sobre Cuidados Paliativos. Madrid: Plan Nacional para el SNS del MSC. Agencia de Evaluación de Tecnologías Sanitarias del País Vasco; 2008. Guías de Práctica Clínica en el SNS: OSTEBA Nº 2006/08.
576. Pasman HR, Onwuteaka-Philipsen BD, Kriegsman DM, Ooms ME, van der WG, Ribbe MW. Predictors of survival in nursing home patients with severe dementia in whom artificial nutrition and hydration are [corrected] forgone. Int Psychogeriatr. 2006;18(2):227-40.
577. Pilotto A, Sancarlo D, Panza F, Paris F, D'Onofrio G, Cascavilla L, et al. The Multidimensional Prognostic Index (MPI), based on a comprehensive geriatric assessment predicts short- and long-term mortality in hospitalized older patients with dementia. J Alzheimers Dis. 2009;18(1):191-9.
578. Coventry PA, Grande GE, Richards DA, Todd CJ. Prediction of appropriate timing of palliative care for older adults with non-malignant life-threatening disease: a systematic review. Age Ageing. 2005;34(3):218-27.
579. Scarmeas N, Albert M, Brandt J, Blacker D, Hadjigeorgiou G, Papadimitriou A, et al. Motor signs predict poor outcomes in Alzheimer disease. Neurology. 2005; 64(10):1696-703.
580. Lee M, Chodosh J. Dementia and life expectancy: what do we know? J Am Med Dir Assoc. 2009;10(7):466-71.
581. Gambassi G, Landi F, Lapane KL, Sgadari A, Mor V, Bernabei R. Predictors of mortality in patients with Alzheimer's disease living in nursing homes. J Neurol Neurosurg Psychiatry. 1999;67(1):59-65.
582. Wada H, Nakajoh K, Satoh-Nakagawa T, Suzuki T, Ohrui T, Arai H, et al. Risk factors of aspiration pneumonia in Alzheimer's disease patients. Gerontology. 2001;47(5):271-6.
583. McNamara B, Rosenwax LK, Holman CD. A method for defining and estimating the palliative care population. J Pain Symptom Manage. 2006;32(1):5-12.
584. Health care guidelines: Palliative care. Bloomington, MN (US): Institute for Clinical Systems Improvement (ICSI); 2007.

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

585. Hughes JC, Robinson L. General practice perspectives: co-ordinating end-of-life care. En: Hughes JC, ed. Palliative Care in Severe Dementia. Dinton (United Kingdom): Quay Books; 2005.
586. Guidelines for a palliative approach in residential aged care. Canberra (Australia): The National Palliative Care Program. National Health and Medical Research Council; 2006.
587. O'Brien T. Eur J Palliat Care. 2003;10(Suppl 2):7-9. Respuesta al artículo: Foley KM. How much palliative care do we need? Eur J Palliat Care. 2003;10(Suppl 2):5-7.
588. Herrera E, Rocafort J, Cuervo Pinna MA, Redondo Moralo MJ. Primer nivel asistencial en cuidados paliativos: evolución del contenido de la cartera de servicios de atención primaria y criterios de derivación al nivel de soporte. Aten Primaria. 2006;38(S2):85-92.
589. Goodman C, Evans C, Wilcock J, Froggat K, Drennan V, Sampson E, et al. End of life care for community dwelling older people with dementia: an integrated review. Int J Geriatr Psychiatry. 2010;25(4):329-37.
590. James R, Whitten MD. Diez mandamientos para el cuidado de los pacientes terminales. Am Fam Physician. 1999;6(2):61-3.
591. Ferris FD. Standards of Care. En: Bruera E, Higginson I, Ripamonti C, Von Gunten C, editores. Textbook of Palliative Medicine. London (United Kingdom): Hodder Arnold; 2006;217-30.
592. Ganguli M, Rodríguez EG. Reporting of dementia on death certificates: a community study. J Am Geriatr Soc. 1999;47(7):842-9.
593. Inouye SK, Van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990;113(12):941-8.
594. Casarett DJ, Inouye SK. Diagnosis and management of delirium near the end of life. Ann Intern Med. 2001;135(1):32-40.
595. Dasgupta M, Hillier LM. Factors associated with prolonged delirium: a systematic review. Int Psychogeriatr. 2010;22(3):373-94.
596. Jackson KC, Lipman AG. Drug therapy for delirium in terminally ill patients. Cochrane Database Syst Rev. 2004;(2):CD004770.
597. Summerssall J, Wight S. When it's difficult to swallow: the role of the speech terapist. En: Hughes JC, ed. Palliative Care in Severe Dementia. Dinton (United Kingdom): Quay Books; 2005.
598. Regnard C, Huntley ME. Managing the physical symptoms of dying. En: Hughes JC, ed. Palliative Care in Severe Dementia. Dinton (United Kingdom): Quay Books; 2005.
599. Palecek EJ, Teno JM, Casarett DJ, Hanson LC, Rhodes RL, Mitchell SL. Comfort feeding only: a proposal to bring clarity to decision-making regarding difficulty with eating for persons with advanced dementia. J Am Geriatr Soc. 2010;58(3):580-4.
600. Sampson EL, Candy B, Jones L. Enteral tube feeding for older people with advanced dementia. Cochrane Database Syst Rev. 2009 Apr;15;(2):CD007209.
601. Cook AK, Niven CA, Downs MG. Assessing the pain of people with cognitive impairment. Int J Geriatr Psychiatry. 1999;14(6):421-5.
602. Nygaard HA, Jarland M. Are nursing home patients with dementia diagnosis at increased risk for inadequate pain treatment? Int J Geriatr Psychiatry. 2005;20(8):730-7.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

603. Manfredi PL, Breuer B, Wallenstein S, Stegmann M, Bottomley G, Libow L. Opioid treatment for agitation in patients with advanced dementia. Int J Geriatr Psychiatry. 2003;18(8):700-5.
604. Scherder E, Oosterman J, Swaab D, Herr K, Ooms M, Ribbe M, et al. Recent developments in pain in dementia. BMJ. 2005;330(7489):461-4.
605. SIGN 2007. Edinburgh, Scotland (United Kingdom): Scottish Intercollegiate Guidelines Network (SIGN); 2007.
606. WHO's Pain Ladder [página en Internet]. World Health Organitzation; 2006. Disponible en: http://www.who.int/cancer/palliative/painladder/en/print.html
607. Fellowes D, Barnes K, Wilkinson S. Aromatherapy and massage for symptom relief in patients with cancer. Cochrane Database Syst Rev. 2004;(2):CD002287.
608. Chen JH, Lamberg JL, Chen YC, Kiely DK, Page JH, Person CJ, et al. Occurrence and treatment of suspected pneumonia in long-term care residents dying with advanced dementia. J Am Geriatr Soc. 2006;54(2):290-5.
609. Hurley AC, Volicer BJ, Volicer L. Effect of fever-management strategy on the progression of dementia of the Alzheimer type. Alzheimer Dis Assoc Disord. 1996;10(1):5-10.
610. Kwong E, Pang S, Wong T, Ho J, Shao-ling X, Li-jun T. Predicting pressure ulcer risk with the modified Braden, Braden, and Norton scales in acute care hospitals in Mainland China. Appl Nurs Res. 2005;18(2):122-8.
611. Thompson RS, Hall NK, Szpiech M, Reisenberg LA. Treatments and outcomes of nursing-home-acquired pneumonia. J Am Board Fam Pract. 1997;10(2):82-7.
612. Spruyt O, Kausae A. Antibiotic use for infective terminal respiratory secretions. J Pain Symptom Manage. 1998;15(5):263-4.
613. Clayton J, Fardell B, Hutton-Potts J, Webb D, Chye R. Parenteral antibiotics in a palliative care unit: prospective analysis of current practice. Palliat Med. 2003;17(1):44-8.
614. Cullum NA, McInnes E, Bell-Syer SEM, Legood R. Support surfaces for pressure ulcer prevention. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. Nº: CD001735. DOI: 10.1002/14651858.CD001735.pub2.
615. Reddy M, Gill SS, Rochon PA. Preventing pressure ulcers: a systematic review. JAMA. 2006;296(8):974-84.
616. The management of pressure ulcers in primary and secondary care. A clinical practice guideline. London (United Kingdom): Royal College of Nursing and National Institute for Health and Clinical Excellence. Royal College of Nursing; 2005.
617. Holloway M. Death the great leveller? Towards a transcultural spirituality of dying and bereavement. J Clin Nurs. 2006;15(7):833-9.
618. Bayés Sopena R, Borrás Hernández FX. ¿Qué son las necesidades espirituales? Med Paliat. 2005;12(2):99-107.
619. Lin HR, Bauer-Wu SM. Psycho-spiritual well-being in patients with advanced cancer: an integrative review of the literature. J Adv Nurs. 2003;44(1):69-80.
620. Stoltz P, Uden G, Wullman A. Support for family carers who care for an elderly person at home - A systematic literature review 10. Scand J Caring Sci. 2004;18(2):111-9.
621. Proot IM, bu-Saad HH, Crebolder HF, Goldsteen M, Luker KA, Widdershoven GA. Vulnerability of family caregivers in terminal palliative care at home; balancing between burden and capacity. Scand J Caring Sci. 2003;17(2):113-21.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

622. Fürst CJ, Doyle D. The terminal phase. En: Doyle D, Hanks G, Chreney N, Calman K, editores. Oxford Textbook of Palliative Medicine. Third edition. Oxford (United Kingdom): Oxford University Press; 2004;117-33.
623. Ellershaw J, Ward C. Care of the dying patient: the last hours or days of life. BMJ. 2003;326(7379):30-4.
624. Doyle D, Hanks G, Chreney N, Calman K. Oxford Textbook of Palliative Medicine. Third edition. Oxford (United Kingdom): Oxford University Press; 2004.
625. Dohrenwend BS, Krasnoff L, Askenasy AR, Dohrenwend BP. The Psychiatric Epidemiology Research Interview Life Events Scale. En: Mezzich JE, Jorge MR, Salloum IM, editores. Psychiatric Epidemiology. Assessment concepts and methods. Baltimore, MA (US): The Johns Hopkins University Press; 1994. p. 401-36.
626. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. J Psychosom Res. 1967;11(2):213-8.
627. Landa V, García-García J. Duelo. Guías Clínicas Fisterra. 2007;7(26). Disponible en: www fisterra com
628. Genevro JL, Marshall T, Millet T. Report on Bereavement an Grief Research. Washington, DC (US): Center for the Advancement of Health. Disponible en: http://www.cfah.org
629. Aranda S, Milne D. Guidelines for assessment of bereavement risk I family members of people receiving palliative care. Melbourne (Australia): Center for Palliative Care; 2000.
630. Kristjanson L, Lobb E, Aoun SA. A systematic review of the literature on complicate grief. Canberra (Australia): Department of Health and Ageing. Australian Government. Disponible en: http://www.health gov au
631. Allumbaugh DL, Hoyt W. Effectiveness of grief therapy: a meta-analysis. J Couns Psychol. 1999;46:370-80.
632. Wimpenny P, Unwin R, Dempster P, Grundy M, Work F, Brown A. Literature review on bereavement and bereavement care. Aberdeen (United Kingdom): The Robert Gordon University. Joanna Briggs Collaborating Centre for Evidence-based Multiprofessional Practice; 2006.
633. Gjerdingen DK, Neff JA, Wang M, Chaloner K. Older persons' opinions about life-sustaining procedures in the face of dementia. Arch Fam Med. 1999;8(5):421-5.
634. Anand S, Kurella Tamura M, Chertow GM. The elderly patients on hemodialysis. Minerva Urol Nefrol. 2010;62(1):87-101.
635. Conroy SP, Luxton T, Dingwall R, Harwood RH, Gladman JR. Cardiopulmonary resuscitation in continuing care settings: time for a rethink? BMJ. 2006;332(7539):479-82.
636. Ebell MH, Becker LA, Barry HC, Hagen M. Survival after in-hospital cardiopulmonary resuscitation. A meta-analysis. J Gen Intern Med. 1998;13(12):805-16.
637. British Medical Association. United Kingdom: The Resuscitation Council and the Royal College of Nursing; 2001.
638. Congedo M, Causarano RI, Alberti F, Bonito V, Borghi L, Colombi L, et al. Ethical issues in end of life treatments for patients with dementia. Eur J Neurol. 2010;17(6):774-9.
639. Martí Massó JF, Poza JJ, Olasagasti B. Avances en los cuidados paliativos de las enfermedades neurodegenerativas; 2005.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

640. Volicer L. End-of-life care for people with dementia in residential care settings; 2005.
641. Afzal N, Buhagiar K, Flood J, Cosgrave M. Quality of end-of-life care for dementia patients during acute hospital admission: a retrospective study in Ireland. Gen Hosp Psychiatry. 2010;32(2):141-6.
642. Fallowfield L. Communication with the patient and family in palliative medicine. En: Doyle D, Hanks G, Chreney N, Calman K, editores. Oxford Textbook of Palliative Medicine. Third edition. Oxford (United Kingdom): Oxford University Press; 2004.
643. Barbero J. El derecho del paciente a la información: el arte de comunicar. Anales del Sistema Sanitario de Navarra. 2006;29(S3):19-27.
644. Buckman R. Breaking bad news: why is it still so difficult? Br Med J (Clin Res Ed). 1984;288(6430):1597-9.
645. Enfermedad de Creutzfeldt-Jakob. Sistema de vigilancia de las EET en España [página en Internet]. Madrid: Instituto de Salud Carlos III. Disponible en: http://www.isciii.es/htdocs/centros/epidemiologia/eeb_vigilancia.jsp
646. BrainNet Europe [página web en Internet]. Disponible en: http://www.brainnet-europe.org.
647. Guía de estilo: Salud y medios de comunicación. Alzheimer. Madrid: Pfizer; 2006. Disponible en: www.pfizer.es/actualidad/Recursos/Guia_estilo_enfermedades/guia_estilo_salud_medios_comunicacion_alzheimer.html
648. Tratamiento informativo del Alzheimer en la prensa española entre los años 2003 y 2006. Observatorio Maren Salud y Comunicación. Disponible en: www.familialzheimer.org/prensa/articulos/ver/2530
649. Abizanda-Soler P, Romero-Rizos L, Sánchez-Jurado PM, Martín-Sebastiá E, Luengo-Márquez C. Necesidad de la enseñanza de pregrado en geriatría: aportaciones de un nuevo modelo educativo. Rev Esp Geriatr Gerontol. 2005;40:275-84.
650. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Psicología [monografia en Internet]. Madrid: ANECA; 2005 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150356/libroblanco_psicologia_def.pdf
651. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Enfermería [monografia en Internet]. Madrid: ANECA; 2004 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150360/libroblanco_jun05_enfermeria.pdf
652. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Trabajo Social [monografia en Internet]. Madrid: ANECA; 2004 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150376/libroblanco_trbjsocial_def.pdf
653. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Fisioterapia [monografia en Internet]. Madrid: ANECA; 2004 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150428/libroblanco_jun05_fisioterapia.pdf
654. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Logopedia [monografia en Internet]. Madrid: ANECA; 2004 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150352/libroblanco_logopedia_def.pdf

More than 5 years have passed since the publication of this Clinical Practice Guideline, and its validity has not been reviewed

655. Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). Libro Blanco. Título de grado en Terapia Ocupacional [monografia en Internet]. Madrid: ANECA; 2005 [consultado septiembre 2010]. Disponible en: http://www.aneca.es/media/150316/libroblanco_terapiaocupacional_def.pdf
656. Coll de Tuero G, Garré-Olmo J, López-Pousa S, Vilalta J, Limón E, Caja C. Percepción, actitudes y necesidades de los profesionales de atención primaria en relación al paciente con demencia. Aten Primaria. 2010 (en prensa).
657. Plan de especialidad según el modelo del Ministerio de Sanidad y Consumo de España. Disponible en: www.portalesmedicos.com/plan_programa_especialidad
658. Plan de especialidad según el modelo del Ministerio de Sanidad y Consumo de España: Neurología. Disponible en: www.portalesmedicos.com/plan_programa_especialidad/neurologia_1.htm
659. Plan de especialidad según el modelo del Ministerio de Sanidad y Consumo de España: Geriatría y Gerontología. Disponible en: www.portalesmedicos.com/plan_programa_especialidad/geriatria_gerontologia_1.htm
660. Plan de especialidad según el modelo del Ministerio de Sanidad y Consumo de España: Psiquiatría. Disponible en: www.portalesmedicos.com/plan_programa_especialidad/psiquiatria_1.htm
661. Santolaya F. Perfiles profesionales del Psicólogo. Madrid: Colegio Oficial de Psicólogos de España; 1998.
662. Villanueva A, Nebot C, Galán A, Gómez G, Cervera M, Mira JJ, et al. Puntos de vista de pacientes, ciudadanos, profesionales y directivos sobre cómo llevar a la práctica una atención sanitaria centrada en el paciente. Rev Calidad Asistencial. 2006;21(4):199-206.
663. Peña-Casanovas J. Máster en Neuropsicología y Neurología de la Conducta. Barcelona: Universitat Autònoma de Barcelona. Institut Municipal d'Assistència Sanitària.
664. Postgrado de Neuropsicología Clínica. Barcelona: Instituto Superior de Estudios de Psicología (ISEP).
665. Programa de Formación en el área de Salud: Especialista Universitario en Neuropsicología. Madrid: Fundación UNED. Universidad Nacional de Educación a Distancia (UNED). Disponible en: www.fundacion.uned.es
666. Instituto Europeo de Formación y Consultoría (INEFOC). Disponible en: www.inefoc.net
667. Guillen Grima F, Espin Ríos MI. [Cost-effectiveness analysis of different alternatives of universal vaccination against hepatitis B in the region of Murcia (see comments)]. Med Clin (Bar). 1995;104(4):130-6.
668. Grado de enfermería. Real Decreto 1393/2007, de 29 octubre, por el que se establece la ordenacion de las enseñanzas universitarias oficiales. Madrid: Boletín Oficial del Estado (BOE); núm. 260, de 30/10/2007.
669. Especialidad en Enfermería clínica avanzada: capacitación específica en cuidados neurológicos y de neurocirugía. Propuesta de programa de formación al Comité Asesor de Especialidades de Enfermería. Barcelona: Sociedad Española de Enfermería Neurológica (SEDENE). Disponible en: www.sedene.com
670. Sociedad Española de Enfermería Neurológica (SEDENE). Disponible en: www.sedene.com

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

671. Plan de cuidados de enfermería del Alzheimer. Salamanca: Universidad de Salamanca (USAL). Disponible en: www.usal.es/webusal
672. Guía de cuidados enfermeros a pacientes de Alzheimer y otros síndromes demenciales y a sus cuidadores. Grupo de Demencias de la Sociedad Española de Enfermería Geriátrica y Gerontológico (SEEGG).
673. Orden SAS/3225/2009, de 13 de noviembre, por la que se aprueba y publica el programa formativo de la especialidad de Enfermería Geriátrica. Madrid: Boletín Oficial del Estado (BOE); núm. 288, de 30/12/2009. p. 101976-101992.
674. Ministerio de Sanidad y Consumo. Resolución de la Secretaría Disponible en: http://www.msps.es/profesionales/formacion/docs/EnfermeriaSaludMental.pdf
675. Orden SAS/1729/2010, de 17 de junio, por la que se aprueba y publica el programa formativo de la especialidad de Enfermería Familiar y Comunitaria. Madrid: Boletín Oficial del Estado (BOE); núm. 157, de 29/06/2010. p. 57217-57250.
676. Colegios Oficiales de Diplomados en Trabajo Social y Asistentes Sociales. Disponible en: www.cgtrabajosocial.es
677. TrabajaSocial [página en Internet]. Disponible en: www.trabajasocial.com
678. Gómez A. Fisioterapia en Salud Mental. Murcia: Fundación AlzheimUr; 2009. Disponible en: www.fundacionalzheimur.org
679. Piqueras JA, Campillo JM, Guilabert MI. Terapia ocupacional aplicada basada en la evidencia científica. UMH 2009/2010 [blog en Internet]. Disponible en: http://terapiaocupacionalaplicadaumh.blogspot.com
680. Plan Nacional de Investigación Científica, Desarrollo e Innovación Tecnológica 2008-2011. Madrid: Ministerio de Educación y Ciencia; 2007 [consultado 12 diciembre 2007]. Disponible en: www.plannacionalidi.es
681. Séptimo Programa Marco Europeo (2007-2013). Bruselas; 2006. Disponible en: http://europa.eu/legislation_summaries/energy/european_energy_policy/i23022_es.htm
682. Robles A. La investigación en la neurología del envejecimiento. Rev Esp Geriatr Gerontol. 2001;36(Supl 3):39-40.
683. Vilardell M. Ser metge. L'art i l'ofici de curar. Barcelona: Plataforma Editorial; 2009.
684. Donabedian A. The quality of care. How can it be assessed? JAMA. 1988;260(12):1743-8.
685. Serveis Sociosanitaris: Indicadors per mesurar els criteris de qualitat de l'atenció al pacient i la família. Barcelona: Direcció General de Planificació i Avaluació. Pla Director Sociosanitari. Departament de Salut. Generalitat de Catalunya; setembre 2006.
686. Kessel H, Marín N, Maturana N. Primera Conferencia Nacional de Consenso sobre el Anciano Maltratado. Rev Esp Geriatr Gerontol. 1996;31:367-72.
687. Chiu E, Chiu H. Dementia care in Asia-second consensus statement on quality services. Int Psychogeriatr. 2006;18(1):176.
688. Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. London (United Kingdom): National Institute for Clinical Excellence (NICE); February 2006. GCG32.

More than 5 years have passed since the publication of this Clinical Practice Guideline and its validity has not been reviewed

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