Clinical Practice Guideline on Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents

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 GUIDELINES IN THE SPANISH NATIONAL HEALTHCARE SYSTEM
MINISTRY OF HEALTH, SOCIAL POLICY, AND EQUALITY

MINISTERIO DE CIENCIA E INNOVACIÓN
MINISTERIO DE SANIDAD, POLÍTICA SOCIAL E IGUALDAD
Plan de Calidad para el Sistema Nacional de Salud
Generalitat de Catalunya Departament de Salut

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MINISTRY OF HEALTH AND SOCIAL POLICIES

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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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This guideline must be quoted:

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Presentation

Healthcare practice is becoming more and more complicated due to many different factors. One of the most relevant factors is the increase of scientific information available to us.

For the clinical decisions to be adequate, efficient and safe, professionals need to permanently update their knowledge, to which end a great deal of effort has been invested.

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

At the beginning of 2006, the Directorate General of the Quality Agency of the SNS prepared the Quality Plan for the National Health System, 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. As part of the Plan, different agencies and expert groups in prevalent pathologies related to the health strategies were asked to prepare eight CPG.Furthermore, the definition of a common CPG preparation methodology was requested for the SNS, which has been prepared among the expert groups in CPGs in our country, combining their efforts and coordination.This methodology has been the basis to prepare this CPG on ADHD.

In 2007, the GuiaSalud Project was renewed, creating the Clinical Practice Guideline Library. This project goes deeper into the preparation of CPGs and includes other evidence-based medicine products and services.Furthermore, its aim is to favour the implementation and assessment of the use of CPGs in the National Health System.Later, another fourteen guidelines have been addressed, with the collaboration of the same institutions and participation of the scientific societies involved.This *Clinical Practice Guideline on attention deficit hyperactivity disorder (ADHD) in Children and Adolescentsis* the fruit of this request.

ADHD is a disorder that has a neurobiological origin, starting in childhood and whose symptoms can last until adult age.It is one of the psychiatric disorders with greatest prevalence and the one that records the largest number of consultations due to the enormous consequences in the different aspects of the patient's life.Over the last few years, it has been one of the most highly-researched disorders, due to the potential repercussions that it has on the personal and family development of the person affected.

The aim of this CPG is to give citizens, health and education professionals, a useful instrument that will provide answers to the basic questions about the disorder, especially those related to the diagnostic assessment and the different types of treatment of ADHD in children and adolescents.

This guideline is the result of a group of professionals associated with ADHD and experts in the methodology of CPGs and its aim is to detect and become aware of the disorder, assessing it correctly as well as proposing therapeutic objectives and strategies for the family and teachers.

This CPG has been reviewed by Spanish experts in ADHD and has the backing of associations of patients and Spanish scientific societies involved in its care.

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We trust that this work will undoubtedly result in higher quality care of children and adolescents with ADHD and the carers.

PABLO RIVERO CORTE
D. G. of the Quality Agency of the SNS

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Societat Catalana de Psiquiatria Infanto-Juvenil (SCPIJ)

Spanish Society of Paediatric Neurology (SENEP)

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Declaration of interest: All the members of the development group as well as the people who have participated as collaborators and external reviewers (either individually or as representatives of entities) have made the declaration of conflict of interests via a form designed for this purpose. Appendix 6 includes the summary of the declaration.

This guideline is editorially independent from the financing entity

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Questions to be answered

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ADHD

1. How is ADHD defined? What clinical manifestations does the disorder have?
2. Etiopathogeny of ADHD. What are the main risk factors?
3. In ADHD: Are there neuropsychological dysfunctions?
4. What is the natural course of ADHD?
5. In ADHD: What is the long-term prognosis? What factors have an influence on a good or bad prognosis? To what extent does early diagnosis and intervention improve the prognosis of ADHD?
6. In ADHD: What are the most frequent comorbid disorders?

DIAGNOSIS

7. What are the diagnostic criteria for ADHD in children and adolescents?
8. How is ADHD diagnosed in children and adolescents? Who must diagnose it?
9. Which evaluation areas must be included in the diagnosis of ADHD?
10. In the diagnosis of ADHD in children and adolescents? Is the neuropsychological assessment necessary?
11. In the diagnosis of ADHD in children and adolescents? Is the psychopedagogical assessment necessary?
12. In the diagnosis of ADHD in children and adolescents? Are supplementary examinations necessary?
13. In the diagnosis of ADHD in children and adolescents? Which entities would the differential diagnosis have to be carried out with?

ASSESSMENT INSTRUMENTS

14. Which screening instruments and specific scales of ADHD in children and adolescents are useful/recommendable for the diagnosis? Which have been validated in the Spanish population?
15. In ADHD in children and adolescents? Which general or broad spectrum pyschopathology scales are useful/recommendable? Which have been validated in the Spanish population?
16. In ADHD in children and adolescents? Which interviews are useful/recommendable for the diagnosis? Which have been validated in the Spanish population?
17. In ADHD in children and adolescents? Which neuropsychological and intelligence tests are useful/recommendable? Which have been validated in the Spanish population?
18. In ADHD in children and adolescents? Which psychopedagogical assessment tools are useful/recommendable? Which have been validated in the Spanish population?

TREATMENT

Psychological treatment

19. Psychological treatment: What does it consist of? What must it include?
20. Which psychological treatment is effectiveto treat ADHD in children and adolescents?
21. Psychological treatment of children and adolescents: Has it proved to be efficient/effective in the short and long term?
22. How effective is psychological treatment of ADHD in children and adolescents?
23. In ADHD in children and adolescents? What clinical variables and standardised instruments exist to evaluate the efficacy of psychological treatment?At what moment of the treatment should its efficacy be evaluated?

Psychopedagogical Treatment

24. Psychopedagogical intervention: What does it consist of? What must it include?
25. Which psychopedagogical interventions are efficient/effective to treat ADHD?
26. Psychopedagogical re-education: What does it consist of? What must it include?
27. In ADHD in children and adolescents? What adaptations are useful/recommendable in the school context?
28. Is the training given to teachers efficient/effective? What must it include?
29. In ADHD in children and adolescents? What clinical variables and standardised instruments exist to evaluate the efficacy of psychopedagogical treatment? At what moment of the psychopedagogical treatment should its efficacy be evaluated?

Pharmacological Treatment

30. What drugs are available for ADHD in Spain?
31. In ADHD: What pharmacological treatments are efficient/effective? How safe are the pharmacological treatments?
32. In ADHD: How effective are pharmacological treatments in the short and long term?
33. In ADHD: When and with what criteria must pharmacological treatment be started?
34. In ADHD: What criteria are used to choose the drug? What are the start, suppression and maximum dose guidelines?Which are the first and second choice drugs?
35. What are the most frequent (short term) side effects? How must the side effects be addressed?
36. In ADHD: How long should the pharmacological treatment last?
37. In ADHD: Are supplementary examinations required before starting the pharmacological treatment in children and adolescents?
38. What is the pharmacological strategy when there is a partial response, side effects or contraindication?How are the different methylphenidate presentations combined? How to make the transition from stimulants to atomoxetine?

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39. In which ADHD subtypes is pharmacological treatment more efficient?

40. Are there differences in response depending on the gender or age?

41. Which physical parameters must be controlled before starting the pharmacological treatment and during it?

42. What scientific evidence exists about the long-term effects in pharmacological treatment? Is it associated with growth retardation?

43. Pharmacological treatment of ADHD: Does it cause addiction? Does it increase the risk of consumption of substances?

44. Does the efficacy of pharmacological treatment decrease with time?

45. Do the effects remain after the pharmacological treatment has been withdrawn?

46. Is it recommendable to leave stimulant-free periods during the pharmacological treatment ("therapeutic holidays")?

47. What clinical variables and standardised instruments exist to evaluate the efficacy of pharmacological treatment?At what moment of the treatment should its efficacy be evaluated?

Combined Treatment

48. Combined treatment: What does it consist of? What must it include?

49. In ADHD in children and adolescents? Which intervention or combination of interventions has proved to be more efficient in the short and long term?

Comorbidity Treatment

50. In children and adolescents with ADHD: What must be done with comorbid epilepsy?

51. In children and adolescents with ADHD: What must be done with comorbid autism spectrum disorders?

52. In children and adolescents with ADHD: What must be done with comorbid mood disorders?

53. In children and adolescents with ADHD: What must be done with comorbid bipolar disorder?

54. In children and adolescents with ADHD: What must be done with comorbid substance abuse disorder?

Complementary and alternative medicine

55. Complementary and alternative medicine: What does it consist of?

56. To treat ADHD in children and adolescents:Are complementary and alternative therapies efficient?

ETHICAL AND LEGAL ASPECTS

57. Which ethical principles must be taken into account in relationship with minors or adolescents with ADHD?

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58. What precautions must be taken, from the ethical viewpoint, in the field of ADHD diagnosis?

59. What are the correct ethical standards for the start of therapeutic intervention in ADHD?

60. How involved must the minor be in the decision-making in the context of the diagnosis and treatment of ADHD?

61. What are the minor's rights in the field of information and confidentiality related to the diagnosis and treatment of ADHD?

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Recommendations of the CPG

The CPGs are a series of 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.

This *Clinical Practice Guideline on Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents* is a healthcare decision aid in the field of the Spanish SNS.It is not mandatory and it is not a substitute for the clinical judgement of healthcare personnel.

The CPG has detection, diagnosis and treatment algorithms, which must be followed when the successive clinical situations that arise are recognised.

When making out the prescriptions, the costs must also be taken into account by the clinician given their impact on the sustainability of the system.

The recommendations are presented in this section, following the structure of the guideline. Chapters 1, 2 and 3 of the CPG include the Introduction, Scope and Objective, and Methodology, respectively. Chapter 4 deals with ADHD. All these chapters are descriptive and, consequently, no recommendations for clinical practice have been formulated. Chapter 5, Diagnosis, is the first to contain recommendations. The clinical questions that do not present recommendations have been omitted from this section.

The letters corresponding to the degrees of recommendations and quality of the scientific evidence are listed below:

Degree of recommendation: A, B, C or D, depending on whether the quality of the scientific evidence is very good, good, moderate or low **(Appendix 1)**.
√ Good clinical practice: Recommendation by consensus of the development group.

5. Diagnosis

5.1. What are the diagnostic criteria for ADHD in children and adolescents?

D	5.1.1.	To diagnose ADHD in children and adolescents the use of the diagnostic criteria of DSM-IV-TR or ICD-10 is recommended.

5.2. How is ADHD diagnosed in children and adolescents? Who must diagnose it?

Recommendations		
D	5.2.1.	The diagnosis of ADHD in children and adolescents is exclusively clinical.
D	5.2.2.	The diagnosis of ADHD in children and adolescents must be carried out by a health professional with training and experience in the diagnosis of ADHD and its most frequent comorbidities.

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5.3. Which evaluation areas must be included in the diagnosis of ADHD?

Recommendations		
D	5.3.1.	The diagnosis of ADHD in children and adolescents must be done via clinical interviews with parents and the patient, obtaining information from the school, reviewing family and personal background as well as the physical and psychopathological examination of the patient.

5.4. In the diagnosis of ADHD in children and adolescents: Is the neuropsychological assessment necessary?

Recommendations		
C	5.4.1.	The neuropsychological assessment is not essential for the diagnosis of ADHD in children and adolescents.
√	5.4.2.	The neuropsychological examination of ADHD in children and adolescents is useful to get to know the profile of skills and difficulties in cognitive functioning and comorbidity with specific learning disorders.
C	5.4.3.	To diagnose ADHD it is not necessary for there to be an alteration in the results of the neuropsychological tests that assess executive functions.

5.5. In the diagnosis of ADHD in children and adolescents? Is the psychopedagogical assessment necessary?

Recommendations		
D	5.5.1.	The psychopedagogical assessment is useful to evaluate the learning style and difficulties and to establish the re-education intervention objectives.

5.6. In the diagnosis of ADHD in children and adolescents? Are supplementary examinations necessary?

Recommendations		
B	5.6.1.	To diagnose ADHD in children and adolescents supplementary laboratory, neuroimage or neurophysiological tests are not indicated unless the clinical evaluation justifies this.

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6. Assessment instruments

6.1. Which screening instruments and specific scales of ADHD in children and adolescents are useful/recommendable for the diagnosis?Which have been validated in the Spanish population?

Recommendations		
C	6.1.1.	The specific scales for ADHD in children and adolescents can be used in a complementary manner but never as substitutes for the clinical interview, to detect the presence and assess the intensity of the nuclear symptoms.
√	6.1.2.	The information provided by parents and teachers, via the assessment scales, is useful to diagnose ADHD in children and adolescents and to assess the evolution of the symptoms and the response to the treatment.

6.2. In ADHD in children and adolescents:Which general or broad spectrum psychopathology scales are useful/recommendable?Which have been validated in the Spanish population?

Recommendations		
√	6.2.1.	The general psychopathology questionnaires can be used to screen comorbidity.

6.3. In ADHD in children and adolescents:Which interviews are useful/ recommendable for the diagnosis? Which have been validated in the Spanish population?

Recommendations		
√	6.3.1.	Structured and semi-structured interviews are useful to establish the diagnosis of ADHD and its comorbidities in children and adolescents.

7. Treatment

7.1. Psychological treatmen

7.1.2. Which psychological treatment is effective to treat ADHD in children and adolescents?

Recommendations		
B	7.1.2.1.	The application of a behavioural training programme is recommended for parents of children and adolescents diagnosed with ADHD, with or without comorbidity.

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D	7.1.2.2.	Cognitive behavioural therapy is recommended as an initial treatment for ADHD in children and adolescents in any of the following situations: • The ADHD symptoms are mild • The impact of ADHD is minimal • There is considerable discrepancy about the frequency and intensity of symptoms between parents, or between these and the teachers • The diagnosis of ADHD is uncertain • Parents reject the use of medication • Children under 5 (although this age group is outside the scope of this guide).

7.1.5. In ADHD in children and adolescents:What clinical variables and standardised instruments exist to evaluate the efficacy of psychological treatment? At what moment of the treatment should its efficacy be evaluated?

Recommendations		
√	7.1.5.1.	The efficacy, possible adverse effects and therapeutic compliance must be assessed in the psychological treatment programmes of children and adolescents with ADHD. The assessment of the treatment will be carried out 3 months after the start, at the end (in case of having a defined time limit), or when the clinician deems this appropriate.

7.2. Psychopedagogical Treatment

7.2.2. Which psychopedagogical interventions are efficient/effective to treat ADHD?

Recommendations		
B	7.2.2.1.	Children and adolescents with ADHD require a personalised intervention programme at school that will include academic, social and behavioural aspects (adapted from SIGN 4.1.2)[1].
√	7.2.2.2.	The school programmes for ADHD must involve the majority of the teaching staff to facilitate its efficacy.
√	7.2.2.3.	School programmes for ADHD may include: Adaptations in the classroom, training for teachers, behaviour modification techniques and other strategies to manage ADHD in the classroom (application of rules and limits, presentation of tasks, student assessment systems for students with ADHD, etc.).

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7.2.3. Pyschopedagogical re-education: What does it consist of? What must it include?

Recommendations		
√	7.2.3.1.	Personalised and specific treatment of teaching in academic competences and skills is recommended for children and adolescents with ADHD and repercussion on academic performance.

7.2.4. In ADHD in children and adolescents:What adaptations are useful/recommendable in the school context?

Recommendations		
B	7.2.4.1.	When ADHD has a significant impact on the child's or adolescent's academic competence, the schools should make adaptations to help them in the classroom.

7.2.5. Is the training given to teachers efficient/effective? What must it include?

Recommendations		
√	7.2.5.1.	It is recommendable for teachers to receive training that enables them to detect ADHD alert signals and to manage ADHD in children and adolescents at school.

7.2.6. In ADHD in children and adolescents:What clinical variables and standardised instruments exist to evaluate the efficacy of psychopedagogical treatment? At what moment of the psychopedagogical treatment should its efficacy be evaluated?

Recommendations		
√	7.2.6.1.	The efficacy and possible adverse effects of the psychopedagogical intervention that is being carried out must be assessed in the psychopedagogical treatment programmes of children and adolescents with ADHD at least once every school year whilst the treatment lasts.

7.3. Pharmacological Treatment

7.3.2. In ADHD: What pharmacological treatments are efficient/effective? How safe are the pharmacological treatments?

Recommendations		
A	7.3.2.1.	Methylphenidate and atomoxetine are the recommended drugs today to treat ADHD in children and adolescents based on their efficacy and safety at recommended doses (adapted from NICE 10.18.5.1)[2].

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7.3.3. In ADHD: How effective are pharmacological treatments in the short and long term?

Recommendations		
A	7.3.3.1.	Long-term treatment with methylphenidate and atomoxetine can be recommended as its effectiveness is not reduced.

7.3.4. In ADHD: When and with what criteria must pharmacological treatment be started?

Recommendations		
D	7.3.4.1.	Pharmacological and/or behavioural treatment must be considered as first choice for ADHD in children and adolescents bearing in mind the age of the patient, the seriousness of the symptoms, their functional repercussion and the family's characteristics and preferences.
D	7.3.4.2.	Pharmacological treatment must be started by a properly qualified physician who is an expert in treating ADHD and its most frequent comorbidities.

7.3.5. In ADHD: What criteria are used to choose the drug? What are the start, suppression and maximum dose guidelines?Which are the first and second choice drugs?

Recommendations		
D	7.3.5.1.	The decision about which drug to choose must be based on (adapted from NICE 10.18.5.2)[2]: • The presence of comorbid conditions (for example, tic disorders, Tourette's syndrome, epilepsy and anxiety). • The different adverse effects of the drugs • Previous experiences of lack of efficacy • Issues regarding compliance, for example, problems created by the need to administer a treatment dose at school • Potential misuse • The preferences of the child/adolescentand his or her family

7.3.6. What are the most frequent (short term) side effects? How must the side effects be addressed?

Recommendations		
D	7.3.6.1.	Periodic follow-ups and monitoring of the possible adverse effects of methylphenidate and atomoxetine are recommended.

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7.3.7. In ADHD: How long should the pharmacological treatment last?

Recommendations		
√	7.3.7.1.	The duration of the treatment must be established on a personal basis depending on the symptoms and functional repercussion.In some cases the treatment can last for several years.
√	7.3.7.2.	It is advisable to periodically evaluate the persistence or remission of the symptoms.An accepted practice is to suspend the pharmacological treatment for short periods of 1 or 2 weeks a year, obtaining information about the functioning of the child or adolescent by the family and from the school.

7.3.8. In ADHD: Are supplementary examinations required before starting the pharmacological treatment in children and adolescents?

Recommendations		
D	7.3.8.1.	The systematic execution of supplementary examinations is not recommended, unless indicated by the physical exploration or anamnesis.

7.3.9. What is the pharmacological strategy when there is a partial response, side effects or contraindication? How are the different methylphenidate presentations combined? How to make the transition from stimulants to atomoxetine?

Recommendations		
√	7.3.9.1.	If there is a partial response to the drug, increase the dose until the maximum indicated or tolerated. If there is no response with maximum doses, consider the alternative drug that has not been used with this child or adolescent (another methylphenidate presentation or atomoxetine)
√	7.3.9.2.	If side effects appear, address them adequately. If they persist or are not tolerated, evaluate a change in medication.
√	7.3.9.3.	In the case of contraindication, evaluate the use of the alternative drug.
√	7.3.9.4.	If extended release methylphenidate is used with osmotic technology and an adequate adjustment of the dose is not achieved, a dose of immediate release methylphenidate can be added to the treatment at breakfast and/or mid-afternoon, to thus adjust the total dose of methylphenidate in agreement with the weight of the child or adolescent with ADHD and with the clinical response.If a 12-hour therapeutic action is required and the child or adolescent with ADHD is not able to swallow tablets, extended release methylphenidate can be administered with pellet technology in the morning (opening the capsule) and in the afternoon, after school, a dose of immediate release methylphenidate can be administered.This latter pattern can also be followed if there is a rebound effect in the afternoon with extended release methylphenidate with pellet technology.

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7.3.10. In which ADHD subtypes is pharmacological treatment more efficient?

Recommendations		
C	7.3.10.1.	Methylphenidate and atomoxetine are recommended as pharmacological treatments of choice for ADHD in children and adolescents regardless of the ADHD subtype.

7.3.11. Are there differences in response depending on the gender or age?

Recommendations		
B	7.3.11.1.	Methylphenidate and atomoxetine are recommended as pharmacological treatments of choice for ADHD in children and adolescents regardless of the age and gender.

7.3.12. Which physical parameters must be controlled before starting the pharmacological treatment and during

Recommendations		
D	7.3.12.1.	A physical examination must be performed before starting the pharmacological treatment, which will include taking the blood pressure, measuring heart rate, height and weight.Personal and family history of cardiac diseases must be sought, as well as history of exercise syncope or other cardiovascular symptoms (adapted from NICE, 10.18.4.1)[2].
D	7.3.12.2.	A preliminary cardiovascular study must be carried out at the start of the pharmacological treatment if there is a personal and/or family history of cardiac diseases, a history of serious cardiac problems, of sudden death in the family or abnormal findings in the initial physical examination (adapted from NICE, 10.18.4.1.)[2].
√	7.3.12.3.	In children and adolescents with ADHDreceiving treatment with methylphenidate or atomoxetine:The height must be measured every 6 months, the weight must be controlled 3 and 6 months after starting the pharmacological treatment, and every 6 months during the administration of the treatment.
√	7.3.12.4.	The height and weight in children and adolescents with ADHD receiving pharmacological treatment must be plotted on a growth chart and reviewed by the physician responsible for the treatment.
√	7.3.12.5.	The heart rate and blood pressure must be monitored in children and adolescents with ADHD receiving pharmacological treatment, plotting them before and after every change in dose, and systematically every 3 months.

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7.3.13. What scientific evidence exists about the long-term effects in pharmacological treatment? Is it associated with growth retardation?

Recommendations		
C	7.3.13.1.	Regular monitoring of the growth of children and adolescents with ADHD is recommended during the pharmacological treatment with methylphenidate and atomoxetine.
√	7.3.13.2.	The assurance of an adequate nutritional intake is recommended in children and adolescents receiving pharmacological treatment for ADHD with secondary anorexia to the treatment.

7.3.14. Pharmacological treatment of ADHD: Does it cause addiction? Does it increase the risk of consumption of substances?

Recommendations		
B	7.3.14.1.	The use of methylphenidate and atomoxetine is recommended to treat ADHD in children and adolescents, at the right doses, as it does not cause addiction or increase the risk of substance abuse.

7.3.15. Does the efficacy of pharmacological treatment decrease with time?

Recommendations		
B	7.3.15.1.	Pharmacological treatment with methylphenidate and atomoxetine for ADHD in children and adolescents should be continued in time whilst the clinical effectiveness is demonstrated.

7.3.17. Is it recommendable to leave stimulant-free periods during the pharmacological treatment ("therapeutic holidays")?

Recommendations		
√	7.3.17.1.	Pharmacological treatment rest periods ("therapeutic holidays") are not systematically recommended during treatment of ADHD.
√	7.3.17.2.	In some cases, periods without pharmacological treatment or with a lower dose can be included, when agreed between the family, the physician and child or adolescent, with the specific objective of: • Assessing the need to maintain the treatment or not. • Reduce adverse effects (lack of appetite, slowing-down in height growth, etc.).

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7.3.18. What clinical variables and standardised instruments exist to evaluate the efficacy of pharmacological treatment?At what moment of the treatment should its efficacy be evaluated?

Recommendations		
√	7.3.18.1.	The assessment of the efficacy and tolerability of the intervention will be carried out in the pharmacological treatment of children and adolescents with ADHD at least 1, 3 and 6 months after the start of the treatment, and then, every 6 months whilst it lasts, or else whenever adjustments are made in the dose or changes are made in the drug.

7.4. Combined Treatment

7.4.2. In ADHD in children and adolescents? Which intervention or combination of interventions has proved to be more efficient in the short and long term?

Recommendations		
B	7.4.2.1.	In children and adolescents with moderate or serious ADHD, combined treatment is recommended, which includes behavioural psychological treatment, pharmacological treatment and psychopedagogical intervention at school.

7.5. Comorbidity Treatment

7.5.1. In children and adolescents with ADHD: What must be done with comorbid epilepsy?

Recommendations		
C	7.5.1.1.	The use of methylphenidate is not contraindicated in children and adolescents with ADHD and comorbid epilepsy.

7.5.2. In children and adolescents with ADHD: What must be done with comorbid autism spectrum disorders?

Recommendations		
D	7.5.2.1.	The use of methylphenidate and atomoxetine is not contraindicated in children and adolescents with ADHD and comorbid autism spectrum disorders. However, they must be used with caution.

7.5.3. In children and adolescents with ADHD: What must be done with comorbid mood disorders?

Recommendations		
D	7.5.3.1.	In children and adolescents with ADHD and comorbid mood disorders, it is advisable to firstly treat the more intense disorder and that might have greater repercussion on the patient.

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B	7.5.3.2.	In children and adolescents with ADHD and associated anxiety, the use of atomoxetine is recommended as treatment of first choice, as it has proved to be efficient to treat both disorders.

7.5.4. In children and adolescents with ADHD: What must be done with comorbid bipolar disorder?

Recommendations		
D	7.5.4.1.	In the cases of clear comorbidity of bipolar disorder and ADHD in children and adolescents, stimulant medication may be useful to treat ADHD once the mood symptoms have been adequately controlled with other drugs.

7.5.5. In children and adolescents with ADHD: What must be done with comorbid substance abuse?

Recommendations		
B	7.5.5.1.	In the case of comorbidity of ADHD and substance use disorder in children and adolescents, treatment with non-stimulants or with long acting stimulants is indicated.

7.6. Complementary and alternative medicine

7.6.2. To treat ADHD in children and adolescents:Are complementary and alternative therapies efficient?

Recommendations		
D	7.6.2.1.	The elimination of artificial colouring agents and additives from the diet is not recommended as general treatment applicable in children and adolescents with ADHD.
D	7.6.2.2.	A supplementary diet of fatty acids is not recommended as general treatment applicable in children and adolescents with ADHD.
√	7.6.2.3.	Treatment with optometry, auditory stimulation, osteopathy and psychomotricity is not recommended to treat ADHD in children and adolescents.
B	7.6.2.4.	Treatment with homeopathy, herbal medicine and encephalogrambiofeedbackis not recommended to treat ADHD in children and adolescents.
√	7.6.2.5.	Health professionals must place emphasis, as with any other child and adolescent, on the importance of a balanced diet and regular exercise for children and adolescents with ADHD.
√	7.6.2.6.	Health professionals must ask the families about the use of complementary and alternative therapies to identify and informabout their possible risks or side effects to treat ADHD in children and adolescents.

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8. Prevention

Recommendations		
√	8.1.	It is advisable to pay special attention to the risk populations: • Family history of ADHD • Preterm infants • Low birthweight • Toxic consumption during pregnancy. • Serious craniocerebral (CCT) trauma.

9. Ethical and legal aspects

9.1. Which ethical principles must be taken into account in relationships with minors or adolescents with ADHD?

Recommendations		
√	9.1.1.	In the specific context of this guide, the ethical principles of nonmaleficence, beneficence, autonomy and justice are worth taking into account, in connection with aspects associated with the diagnosis and treatment of ADHD, distinguishing the area that refers to very young children, when it is the parents or guardians who must necessarily assume an essential and almost exclusive leading role, from the area of young adolescents or pre-adolescents, where patients must be involved much more, insofar as they are developing individuals, with certain rights that must be preserved.

9.2. What precautions must be taken, from the ethical viewpoint, in the field of ADHD diagnosis?

Recommendations		
√	9.2.1.	In the diagnosis of ADHD, the professional must be cautious, always respecting the criterion of nonmaleficence, in order to avoid pernicious effects for the child or adolescent in his or her school, social and family environment.

9.3. What are the correct ethical standards for the start of therapeutic intervention in ADHD?

Recommendations		
√	9.3.1.	The professional who assumes responsibility for the diagnosis and treatment of ADHD must act in agreement with criteria of suitability, necessityand proportionality, restricting those more restrictive interventions of the minor's rights to what is strictly necessary.

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9.4. How involved must the minor be in the decision-making in the context of the diagnosis and treatment of ADHD?

Recommendations		
√	9.4.1.	When the parents' consent must be given, if there is clear discrepancy between the two, consensus and mediation must be sought for the greater benefit of the minor, after informing the two about the risks derived from taking or not taking actions for the diagnosis and treatment of ADHD.If it is not possible to conciliate positions, the professionals responsible for the diagnosis and treatment will second the decision of the progenitor that adapts to criteria of greater benefit for the minor.Faced with a situation of doubt or special conflict, it is recommended to resort to the judicial authorisation to protect the minor.
Applicable legislative framework	9.4.2.	In all the cases, even in situations of subrogated decision of parents or guardians due to immaturity or incompetence of the minor, the latter must be informed of the situation and possible alternatives, in the appropriate language and understandable by him or her, clarifying any doubts that might arise, in order for him or her to form a valid criterion and cooperate in this situation.

9.5. What are the minor's rights in the field of information and confidentiality related to the diagnosis and treatment of ADHD?

Recommendations		
Applicable legislative framework	9.5.1.	Minors with ADHD must always be listened to and they must always be informed in the most complete way possible in agreement with their level of comprehension, comparing with them the different options and doubts they may have, and sharing the information with the parents or guardians in agreement with the degree of maturity and the need to complement the information process carried out with the minor.
Applicable legislative framework	9.5.2.	In the care of minors with ADHD, the professionals must respect professional secrecy and confidentiality in all those data referring to the context of the therapeutic relationship, except in the case of clear risk for the minor or for third parties.
Applicable legislative framework	9.5.3.	Between the ages of 12 and 16, confidentiality of the information and health data about the ADHD of the mature minor and with sufficient judgement must be respected, insofar as possible, especially when explicitly demanded by them.In this process the risks and benefits of transferring or communicating that information to parents or guardians will be considered, as well as its possible transcendence in other areas of the minor, and the minor will be advised on the advisability of dialogue and communication with parents or guardians about their health, avoiding presenting the clinical documentation to third parties without their consent, with the exception of properly justified serious risk situations.

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Applicable legislative framework	9.5.4.	From 16 years up, the minor's confidentiality must be preserved, as if he or she were of full legal age, leaving to their personal criterion, the decision about communicating the information to parents or guardians, unless there is a situation of serious risk or clear incompetence.

List of abbreviations of the recommendations

ICD10	International Classification of Diseases, tenth version
DSM –IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th version, revised text
CPG	Clinical Practice Guideline
NICE	*National Institute for Health and Clinical Excellence*
SIGN	*Scottish Intercollegiate Guidelines Network*
SNS	National Health System
ADHD	Attention deficit hyperactivity disorder

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1. Introduction

Background

The "Evidence-based Clinical Practice Guideline (CPG) Development Programme for the entire National Health System" is being carried out within the framework of the preparation of the Quality Plan of the Ministry of Health and Consumer Affairs, through the Quality Agency of the National Health System.

The guidelines must address the main public health and healthcare problems, focusing on those disorders where there is considerable variability in the clinical practice. Their main objective is to help take clinical decisions and they are aimed at the different professionals involved in healthcare, patients and their family members.

The majority of the guidelines available for ADHD in Spain come from the Anglo-Saxon world and do not adapt very well to our social and healthcare reality.

This CPG on Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents, written by experts who work in Spain and who are aware of the idiosyncrasy of our health system and of its professionals, aims to cover that vacuum, giving valid recommendations for our environment, based on the best scientific evidence available to date, and systematically developed to help professionals and carers intervene in the management of these patients and the decision-making about the most appropriate care.It is the first CPG on ADHD in children and adolescents carried out with this methodology in Spain.

The Sant Joan de Déu Foundation (FSJD), together with the Agencia d'Informacio, Avaluacio I Qualitat (AIAQS) of Catalonia are responsible for the development of this guideline.

Justification

G. Still[3] gave the first definition of ADHD in 1902, describing 43 children who had serious problems with sustained attention and self-regulation, to whom a defect in moral behavioural control was attributed.In 1914, Dr. Tredgold[4] argued that the causes were due to brain dysfunction, lethargic encephalitis that affects the area of behaviour, hence the subsequent compensatory hyperkinesis, explosivity in voluntary activity and impulsivity.In 1937, Bradley[5] discovered by chance the therapeutic effects of amphetamines in hyperactive children.The term "minimal brain dysfunction" was coined by Strauss and Lehtinen in 1947, applied to those children with behavioural disorders in whom there was not sufficient scientific evidence of brain pathology (Barkely, 2006)[6]. Lauferr and Denhoff (1957)[7] referred for the first time to hyperkinetic syndrome.In 1968, the *Diagnostic and Statistical Manual of Mental Disorders*, known by its English initials as DSM-II[8] included it as a hyperkinetic reaction ofchildhood and, later, the DMS-III (1980)[9] used the term of attention deficit disorder. Finally, the DMS-IV.TR (2001)[10] reached the term of attention deficit hyperactivity disorder.

ADHD is a disorder that starts in childhood and is characterised by a persistent pattern of inattention, hyperactivity and impulsivity.The disorder is considered to be present when this behaviour occurs more often than normal in agreement with the age and development of the person, and these manifestations significantly interfere with school or work performance and their daily activities (DSM-IV-TR, 2001)[10].

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ADHD represents a public health problem due to its high prevalence, which is estimated, according to epidemiological sources, at between 3 and 7% of the school population (DMS-IV-TR, 2001)[10]. Children with this disorder are at a greater risk of school failure, behavioural problems and difficulties in social and family relations, as a result of the symptoms of ADHD.The course of the disorder is chronic and requires long-term treatment, with the relative social cost.

Over the last few years, it has been one of the most highly researched disorders, due to the potential repercussions that it has on the child's personal and family development. Given the enormous number of bibliographic references that exist on the topic, the professionals who work in the fields of paediatrics, neurology, psychology and psychiatry in children and adolescents must have a practical guideline on the assessment and treatment of ADHD. This guideline must include the best scientific evidence and must be helpful to select the best option in the diagnosis and treatment of this disorder.

There is no agreement in our medium about which instruments must be used to assess children with possible ADHD. There is also controversy about the criteria that must be used to diagnose it.These difficulties in the detection, the diagnostic process and methodology, give rise to considerable variations (geographic and demographic), which lead an underdiagnosis or overdiagnosis of ADHD. There are no biological markers that enable us to diagnose ADHD, so the diagnosis is clinical. The instruments that are normally used to assess children, in whom the disorder is suspected, have not always been validated in the Spanish population.With reference to therapeutic options with drugs, there is controversy about whether to use stimulants or non-stimulants as a first choice, if the efficacy persists in treatments lasting for longer than 12 weeks, if it is recommendable to suspend the medication during holiday periods or at weekends, as well as the duration of the pharmacological treatment.Insofar as psychosocial treatment is concerned, the data are contradictory with respect to efficacy, duration and the generalisation of the results.There is no consensus, either, about measuring the therapeutic response, the side effects of the treatment or about the frequency of follow-up visits.The great variability in the treatment and controversy in the areas mentioned justify the preparation of a CPG that includes the best scientific evidence available to date.

Magnitude of the problem

ADHD is one of the most frequent reasons for children being referred to the paediatrician, neuropaediatrician, or to the mental health team, because they present behavioural problems.In fact, ADHD is one of the most prevalent psychiatric (neurobiological) disorders in children and adolescents (Barkley, 2006)[6].

The prevalence rates are markedly different depending on the diagnostic criteria used, the origin of the samples (clinical or population), the methodology and the ages and gender chosen (Benjumea, 2006)11. The prevalence ranges from 1.9 to 14.4% (DuPaul *et al*., 2001)12. The DSM-IV-TR refers to an estimated prevalence of 3 to 7% of the school-aged population10. Polanczyk *et al*. (2007)13 informed of a world prevalence of 5.29%. In Spain, as in other European studies, the prevalence rates are similar (see **Table 1**).

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Table 1. ADHD prevalence studies in Spain

Authors and year	Age (years)	Prevalence (%)
Cardo *et al*., 2007[14] (Mallorca)	6-11	4.57
Andrés *et al*., 1999[15] (Valencia)	10	3.6
Gómez-Beneyto et al., 1994[16] (Valencia)	8	14.4
	11	5.3
	15	3
Benjumea & Mojarro, 1993[17] (Seville)	6-15	4-6
Farré & Narbona, 1989[18] (Navarre)	5-10	1-2

An isolated presentation of the disorder is not very common. In one clinical sample, Jensen *et al*. (2001)[19] found that more than 85% of the patients presented at least one comorbidity, and about 60% had at least two comorbidities, the most frequent being oppositional defiant disorder, anxiety disorder and conductdisorder.

In non-clinical community samples, Szatmari et al.(1989)[20] indicated that around 44% of the patients presented at least one comorbidity, 32% two comorbidities, and 11% three or more comorbidities.

It is commonly accepted that the disorder occurs more frequently in males than in females, with ranges that vary from 2.5:1 to 5.6:1 (Criado *et al*., 2003)[21]. In both sexes, the combined subtype is the most frequent, but in the inattentive subtype there appears to be a greater percentage of girls, in whom the impulsivity and hyperactivity symptoms can appear with less intensity.The differences with respect to gender have more to do with the psychopathological and/or behavioural evaluation scales, which do not include specific items for girls, than with a specificity depending on the gender (Knellwolf et al., 2008)[22].

The average age of onset of the symptoms is between 4 and 5 years old; the children present impulsivity, hyperactivity, disobedience and are more prone to having accidents (Bonati *et al*., 2005)[23]. Diagnosis in preschool age can be more difficult as the symptoms are typical of the age; in this case it will be the intensity, frequency and repercussion on the environment which would orientate about an ADHD.Beitchman et al.,(1987)[24] found that preschool patients diagnosed with ADHD were more likely to receive the same diagnosis 5 years later or even for the same hyperactivity and disobedience symptoms to persist.

The diagnosis is usually made when they start primary education, when problems appear in school performance (incomplete and badly organised homework, as well as with mistakes), the child is easily distracted, talks impulsively, answers before the question ends, and social dysfunction is observed (disadaptive behaviour in the classroom, difficulties to accept rules, aggressiveness, interrupting and meddling with everything, etc.) (Johnston *et al*., 2001)[25].

Not all patients who have ADHD are correctly identified and treated. This fact will have important personal and family repercussions as well as an influence on public health.The North American Centers for Disease Control and Prevention (CDC) analysed the data of a national health survey on children and found that only 56.3% of them within the age group of 4 to 17, diagnosed with ADHD, received correct pharmacological treatment. No differences were found respect to gender (Goldman *et al*., 1998)[26].

In a study conducted by Jensen *et al*.(1999)[27] whose aim was to evaluate the possibility of overdiagnosis and overtreatment with stimulants, 5.1% prevalence of ADHD was found. Only

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12.5% of the children diagnosed with ADHD received treatment with stimulants.On the contrary, some of the prescriptions of stimulants were administered to children that did not satisfy all the ADHD criteria although they had high symptom levels, so they conclude that overdiagnosis does not exist.

Over the last few years, we have observed an increase in the number of patients treated with stimulants.Prescriptions for the treatment of ADHD have multiplied by five in the United States since 1991, which would mean that one out of every eight North American children takes methylphenidate (Dopfner *et al*., 2004)[28]. A similar situation occurs in Spain, between the years 1992 and 2001, the use of methylphenidate multiplied by six (Criado *et al*., 2003)[21], a lower increase than that experienced in the United States.

It is estimated that the increase in the use of methylphenidate is partly due to the larger number of ADHD consultations, to the extension of the pharmacological treatment and to the current use of stimulants in girls, in adolescents and in young adults, too, and to the case of predominantly inattentive ADHD (Pomerleau *et al*, 1995)[29].

Variability in clinical practice

Patients with ADHD represent quite a heterogeneous group, presenting considerable variations in the intensity of the symptoms, the onset age and the presence of symptoms in different situations. ADHD symptoms can be affected by situational factors, such as the time of day or tiredness, and motivational factors, the possibility of supervision, etc. (Barkley *et al*., 2006)[30].

This situation has led some professionals to question its existence and to wonder why more and more people present ADHD symptoms, suggesting that this may be a passing fashion in psychiatric diagnosis. Social critics and some professionals, who are not experts in the topic, say that ADHD is a myth or, more specifically, that children diagnosed with ADHD are normal but that they are "labelled" as suffering a mental disorder due to the intolerance of parents and teachers, due to the cultural and parental anxiety about the education of children and due to an unspecific or undocumented conspiracy between the medical community and pharmaceutical companies (Barkley *et al,* 2006)[30].

More specifically, in the United States, lobby groups have taken advantage of this situation to promote important media campaigns which have managed to generate considerable alarm among parents of children and adolescents with ADHD due to the use of psychotropic drugs. Focusing on infrequent reactions of methylphenidate, they label it as a hazardous and addictive drug, used by intolerant parents and educators and "physicians without scruples", which can cause death or violent acts, suicide, Tourette's syndrome, permanent brain injury, epileptic crises, increase in blood pressure, confusion, agitation and depression (Barkley *et al*., 2006)[6].

The American Medical Association (AMA) ordered a study to be carried out, which concludes that "ADHD is one of the best studied disorders in medicine and the general data about its validity are more convincing that in the majority of mental disorders and even in many other diseases" (Goldman *et al*., 1998)[26].

Based on the clinical experience in the assessment of people diagnosed with ADHD, it has been observed that the symptoms of the disorder have a great impact on the development of the individual and interfere in his or her social, emotion and cognitive functioning. They also cause important morbidity and dysfunctionality in children, in the group of companions and in their families (Cardo & Servera, 2008)[31].

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Health Repercussions

The repercussions of ADHD not only affect patients, but also their families. If ADHD is not treated or it is undertreated, in the long term it is associated with a wide range of adverse results, such as lower academic performance, an increase in school expulsions or school drop-out, lower professional category, more car accidents, an increase in visits to emergency services due to accidents, a greater incidence of divorce and even an increase in delinquency (Barkley *et al*., 2006; Mannuzza *et al*., 1993; 1998; 1997; 1991; 1991)[32-37]. Comorbidity with other psychiatric disorders is frequent, such asoppositional defiantdisorder and learning disorders, tic disorders and anxiety disorders (Jensen *et al*., 1997[38]; MTA, 1999[39]). Problems of low self-esteem and lack of social skills are frequent both in adolescents and in adult age (Wilens *et al*., 1995[40]; Klomerleau et al, 1995[29], Biederman *et al*., 1997[41]).The consumption of substances starts earlier on, too, in these patients, and abstinence in adult age is less likely.The risk of presenting an antisocial personality disorder is five times greater in patients with a history of ADHD, a risk that is associated with comorbidity with previous conductdisorders (Faraone *et al*, 1998)[42].

In a study prepared by Escobar *et al*.(2005)[43] that compared the quality of life between patients with ADHD and asthmatic patients, the authors concluded that ADHD interferes in the daily lives of children, parents and families more than asthma, mainly in those aspects related to psychosocial functioning. It also involves a subsequent impairment in physical functioning. Delays in the recognition, evaluation and treatment of ADHD can have a negative effect on the quality of life of these children.This same study observed that, on average, almost 6 years passed between the onset of symptoms and the diagnosis of ADHD.

In families, we find ideas of self-blame, social isolation, marriage conflicts, affective and anxiety symptoms, and less productivity as well as an increase in occupational absenteeism (Johnston *et al*., 2001[25]; Mash *et al*., 1983[44]).

Economic Repercussions

On the other hand, the impact of the disease on public health and its cost for the health system are considerable. The health costs of children with ADHD are almost double that of children without this disorder, so, in general, the cost of the disease is estimated to be more than 40 billion dollars a year in the United States (Schlander *et al*., 2007)[45].

The costs in that country have risen due to the increase in diagnosis and treatment of ADHD. The annual economic expenditure in children and adolescents amounted to approximately 14,000 dollars per person in 2005 prices (ranging from 12,000 to 17,500 dollars). This expenditure can be broken down into health costs (18%), education costs (34%) and costs associated with crime and delinquency (48%) (NICE, 2009)[2].

It can be deduced from this information that ADHD is significantly associated with financial costs and emotional overload that are reflected in the health system, education services, carers, families and society in general.An adequate treatment could improve the quality of life of people with ADHD, of their carers and family members, and at the same time, would reduce their psychological wear, as well as the financial implications and overload of ADHD for society.

The impact of ADHD and the associated costs in our medium are an unknown factor, but it is estimated that they are different to those of other societies due to the differences in the attention and treatment pattern, so they cannot be pervasive or compared. The costs to be studied in our medium should include:Accidents, health service costs, comorbidity with other disorders, substance abuse, antisocial behaviour, school failure, dysfunctions in the family and society, among others.

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2. Scope and objectives

Target population

This CPG focuses on the following groups:

a) Children and adolescents aged between 6 and 18 years old.

b) With main diagnosis of ADHD (any of the subtypes) according to DSM-IV-TR criteria or comparable criteria, with and without psychiatric and learning comorbidity.

This CPG has been limited to ADHD in school-aged children and does not deal with children in pre-school age (from 3 to 5), or adults (over 18). These age groups can be addressed in future reviews of the guide.

Scope and healthcare process

The guideline describes the healthcare that primary care and specialised care health professionals of the SNS provide children and adolescents with ADHD, as well as the clinical decision-making in its diagnosis and treatment.Although the assessment of scientific evidence includes questions related to the organisation of the disorder, planning the health services of the autonomous communities is not the aim of this guideline.

This CPG does not aim to be a substitute for clinical judgement.

The guideline examines the following aspects of the management of ADHD in children and adolescents:prevention, detection and screening, diagnosis, assessment instruments, types of treatment and their assessment (psychological, psychopedagogical, pharmacological, combined, comorbidity and special situations, complementary and alternative medicine), as well as ethical and legal aspects.

Psychiatric and non-psychiatric comorbidities that may require another type of care have been included in the CPG:epilepsy, autism spectrum disorders, mood disorders, bipolar disorder and substance use disorder.It does not include specific interventions for psychiatric and non-psychiatric comorbid disorders of ADHD.

Main Objective

To develop a scientific evidence-based CPG about ADHD in children and adolescentsthat will provide the professionals responsible for caring for patients, parents and educators, with a tool that will enable them to take the best decisions about the problems posed by their care.

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Secondary objectives

a) To generate recommendations about the diagnosis, treatment and evaluation of the therapeutic response of the patient with ADHD.

b) To generate recommendations about the detection and screening instruments of ADHD.

c) To generate recommendations about the diagnostic assessment instruments of ADHD.

d) To generate recommendations on the optimal use of the health resources in ADHD healthcare.

e) To give useful information to professionals from the clinical area to help them detect and take decisions about the management of ADHD.

f) To give information and clinical counselling to parents and educators that will enable them to learn, collaborate and take decisions regarding the treatment of ADHD.

g) To establish recommendations for future research in ADHD that will permit making progress in its knowledge.

h) To develop indicators that can be used to assess the recommendations.

Main users

This CPG is aimed at professionals from the clinical and education areas, and others, and at parents who intervene in the management of ADHD in children and adolescents.

The CPG provides information for patients, family members and educators that can also be used by the general population.

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3. Methodology

The methodology used is contained within the **CPG Development Manua**[146] of the Ministry of Health and Consumer Affairs.

The steps below have been followed:

- **Formation of the CPG development group**, comprised of specialists in neuropaediatrics, psychiatry, psychology and psychopedagogy, involved in the study and care of ADHD in children and adolescents.There have been two coordinators in the development group, one clinician, Jose Angel Alda, and one technician, Monica Fernandez, who, together with a member of the development group, Anna Torres, have carried out the systematic review of the bibliography.The development group has received advice on the methodology from a member of the AIAQS with experience in preparing scientific evidence-based CPGs and critical reading, and support from a documentation officer from the AIAQS.

  Collaborators have participated with the development group to prepare the chapter on ethical and legal aspects.

  With respect to the collaboration of experts, a group of Spanish professionals selected for their prestige in the area have also participated.External reviewers have also collaborated in preparing the guideline, including patients' representatives, who have been incorporated into the external review.

  All the members of the development group, collaborators, experts and external reviewers presented a declaration of interest (**Appendix 6**).

  Table 2 describes the different phases in the preparation of the guideline and the distribution of functions among the group of authors and collaborators.

Table 2. Description of the functions of authors and collaborators

	Clinical coordinator	Technical coordinator and systematic review	Clinicians	Methodological advice AIAQS	Documentation officer AIAQS	Ethical and legal aspects collaboration	Expert collaborator	External reviewers and patients' representatives
Definition of the scope	+++	+++	+++	++	-	-	++	-
Clinical questions	+++	++	+++	+	-	-	++	-
Bibliographic search	+	+++	+	+	+	+	-	-
Assessment and synthesis	+	+++	+	+	-	+	-	-
Recommendations	+++	++	+++	+	-	+	-	-
Drafting	++	+++	+	+	-	+	+	-
Review	++	++	++	+++	+	+	+++	+++

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- **Formulation of clinical questions** following the format, Patient/Intervention/Comparison/Outcome (PICO).
- **The search and selection of scientific evidence** for this guideline has given priority to identifying CPGs, SRs, MAs and other critical synthesis documents from quality scientific literature.

The search was organised as follows:

1. The following generic databases, metasearch engines and guideline preparation and compilation organisations were consulted: US National Guidelines Clearinghouse, US National Library ofMedicine (NLM), Tripdatabase, CMA Infobase, National Institute for Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), Institute for Clinical System Improvement (ICSI), New Zealand Guidelines Group (NZGG), Centre for Reviews and Dissemination (CRD), Cochrane Library, ISI web of knowledge, Psycinfo and PubMed.
2. A main systematic search was carried out, based on a strategy that combined the main terms related to ADHD, with CPG, SR and MA in the title, or else the MeSH /Medical Subject Headings) terms were used.The strategy depended in each case on whether the information source accepted a simple syntax or not.Studies published for children and adolescents in the age groups from 6 to 18 years old were sought.
3. The time window to search for the databases that permitted this was restricted from 1993 to February 2008. Later, to answer the questions not solved by the available references, or to update them if necessary, additional and supplementary searches were made in Pubmed/Medline and Psycinfo until March 2009.
4. To complete the search, sources suggested by members of the development group were used, as well as a manual investigation of secondary information sources.
5. The most relevant documents were selected by applying inclusion and exclusion criteria.

Inclusion criteria:

- Studies from journals published in Spanish, English or French.
- CPG, SR, MA, RCT, diagnostic test assessment studies, cohort studies, case-control studies and non-systematic (or narrative) reviews were selected.
- Studies were selected that dealt with the assessment and/or treatment of ADHD in children and adolescents.
- Guidelines prepared no more than 3 years ago or updated and valid ones to date.
- Guidelines classified as highly recommended or recommended according to the AGREE instrument (Appraisal of Guidelines for Research and Evaluation) with a score of more than 60 in the respective area in the rigour of development.
- Age range of participants included went from 6 to 18 years (average age).
- Availability of search strategies, scientific evident classification scales used, the recommendation formulation process and the scientific evidence tables.

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Exclusion criteria:

- Studies on description of cases, summaries, lectures, papers at congresses or case designs without control group.
- Studies that did not include results.
- Studies where the majority of the individuals in the sample were outside the inclusion age.
- Unavailable documents/guidelines (erroneous electronic address or reference).
- References not directly related to the objectives set out.

Two reviewers independently examined the titles and/or summaries of the documents identified by the search strategy. If any of the inclusion criteria were not satisfied, the document was excluded. Otherwise, the full document was requested and assessed to decide on its inclusion or exclusion.Discrepancies or doubts that occurred during the process were solved by consensus of the reviewers.

- **Scientific evidence quality assessment.** The quality assessment of the CPGs was done through the AGREE instrument by three assessors from the development group.The guidelines classified as recommended in the respective section in the rigour of development were considered as quality guidelines (**Appendix 7**).

  For the SR. MA and RCT, critical SIGN (**Scottish Intercollegiate Guidelines Network**) reading templates were used by the two assessors following the recommendations established in the **CPG Preparation Manual** of theMinistry of Health and Consumer Affairs46. The scientific evidence has been classified with the SIGN system (**Appendix 1**).

  Synthesis documents have been included with quality 1++, 1+, 2++ and 2+, considering those with quality 1- only in the cases where there was no scientific evidence of a better quality.

  The quality of the individual studies considered in the CPGs and SRs has been assumed by the development group on considering them quality studies.When the evaluation scale used by the CPGs or SRs differed from SIGN (followed in this guideline), the equivalent was sought.

- **Synthesis and analysis of the scientific evidence**. Information was taken from the main characteristics of the studies, which was summed up in scientific evidence tables for later qualitative analysis and weighting of the recommendations. When the CPGs informed about the results of individual studies, these were described in the "Scientific Evidence" section.

  With reference to the CPGs, apart from using the guidelines selected for their methodology quality, specific sections have been used from other guidelines to inspire specific aspects of this CPG, or scientific evidence has been compiled from them (**Appendix 7**).

  Observational studies were used for those questions where no quality scientific evidence was found.

- **Formulation of recommendations based on the "formal assessment" or "considered judgement" of SIGN**.The recommendations have been ranked according to the SIGN system (**Appendix 1**).The recommendations have been made during meetings of the development group.Any controversial recommendations or with a lack of scientific

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evidence have been solved by consensus of the development group.On some occasions, and for greater transparency, those recommendations that have been adapted from other guidelines and contextualised in our medium are explicitly established, so that the user can easily identify in which cases this has occurred. A total of 28 meetings of the development group have been held during the entire guideline preparation process.

- **Collaborators in the chapter on ethical and legal aspects**.They have participated with their experience in reviewing the legislation in force in our medium for children and adolescents with ADHD.

- **Expert collaborators:**They have participated in the preparation process of the scope and clinical questions to be answered, as well as in the review of the guideline.

- **External reviewers:**Different relevant professionals in the subject have participated in the review of the draft guideline, as well as scientific societies and representatives of patients and family members involved in ADHD in children and adolescents.

- To prepare the **information for patients, family members and educators (Appendix 3),** the development group agreed upon an index based on the complete guideline, which includes the most relevant aspects that might be of interest to patients, family members and educators.A summary of the sections of the guideline and of its main recommendations was prepared based on that index, adapting the information provided, the style and the language for this section.Although this information forms part of the CPG and must be presented and explained by the physicians, personalised leaflets to facilitate its dissemination are hoped to be published.

- The CPG is organised into chapters, where answers are given to the questions that appear at the beginning.Following each question, the documents and quality on which the answer is based are described.Afterwards, the results of the scientific evidence are presented in two blocks:scientific evidence and summary of the scientific evidence. The scientific evidence section presents the results of the individual studies described in the CPGs, SRs and MAs included. The results/conclusions of the CPGs, SRs, and MAs are included in the scientific evidence summary section. In some questions, to avoid repetitions, only one of these two sections is presented. Finally, the recommendations of the development group of this CPG are presented.Although the first author and the year of the individual publications are described in the scientific evidence tables, the results that appear correspond to the reviewed CPGs, SRs or MAs, except when RCTs have been identified in the update.The type of study and the quality of the reviewed literature is given in the right-hand margin, throughout the text.In the case of the CPGs, this is not indicated as they are all quality ones.

- The expression "children and adolescents" is constantly repeated throughout this CPG, referring to both sexes.

- This CPG is available on the portal of GuiaSalud (www.guiasalud.es). As well as on the web page of the AIAQS (www.aiaqs.net) and of the Sant Joan de Deu Hospital (www.hsjdbcn.org).

- **This CPG**, published in 2009, will **be updated** after evaluating any new scientific evidence that might appear over the next 3 years.Any modification during that time will be reflected in electronic format, which can be consulted on the portal of GuiaSalud and on the web page of the AIAQS.The methodology proposed in the Manual, *Update of Clinical Practice Guidelines in the National Health System* will be applied to carry out this update. *Methodology Manual*[47] of the Ministry of Health and Consumer Affairs.

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4. ADHD

Questions to be answered:

4.1. How is ADHD defined? What clinical manifestations does the disorder have?

4.2. Etiopathogeny of ADHD. What are the main risk factors?

4.3. In ADHD: Are there neuropsychological dysfunctions?

4.4. What is the natural course of ADHD?

4.5. In ADHD: What is the long-term prognosis? What factors have an influence on a good or bad prognosis?To what extent does early diagnosis and intervention improve the prognosis of ADHD?

4.6. In ADHD: What are the most frequent comorbid disorders?

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4.1. How is ADHD defined? What clinical manifestations does the disorder have?

Attention deficit hyperactivity disorder (ADHD) is a neurobiological disorder that starts during childhood and affects between 3 and 7% of school-aged children.It is characterised by a level of impulsivity, activity and attention that are not adequate for the development age.Many children and adolescents with ADHD find it difficult to regulate their behaviour and adjust to the rules expected for their age and, consequently, they find it difficult to adapt in their family and school environment, and in their relationships with their peers.They often perform below their capabilities and may present emotional and behavioural disorders (APA, 2001)[10].

What are the nuclear symptoms and how are they clinically manifested?

The data or behaviours that are taken into consideration to evaluate ADHD are dimensional. They are distributed continuously going from normality to pathology.The nuclear symptoms are: inattention, hyperactivity and impulsivity, to which comorbidity side effects are often added.

According to the DSM-IV-TR (APA, 2001)[10], the clinical manifestations of the nuclear symptoms refer to:

Hyperactivity

This is manifested by excess movement, motor and/or cognitive activity, in situations in which it is inappropriate to do so. These children show a high motor activity in different areas. They have difficulty keeping quiet when situations require this, both in structured contexts (the classroom or table at mealtime), and in non-structured contexts (playtime).

The developmental moment has a significant influence on the manifestation of the hyperactivity.Thus, the pervasive hyperkinesis of pre-school children is less dependent on the environ-

ment.At school age, the hyperactive behaviour of the child may be limited to certain situations, especially when these are not very structured. They talk too much and make too much noise during quiet activities. Hyperactivity in adolescents is usually less obvious, an internal feeling of restlessness prevailing, trying to do several things at the same time and going from one activity to another without finishing any.

Inattention

This refers to the difficulties to pay attention during a period of time, both in academic and in family tasks, as well as social tasks. Children find it difficult to give priority to the tasks, persist until they are finished and they avoid activities that represent sustained mental effort. They often tend to change tasks without finishing any of them. They often appear not to be listening.They do not follow orders or instructions and they have difficulties in organising tasks and activities, often tending to forget things and lose things.They are usually easily distracted by irrelevant stimuli.

In social situations, inattention is usually manifested by frequent changes in conversation, with difficulties to follow the rules or details in activities and/or games.

On a developmental level, inattention usually appears more frequently during the school stage, when a more complex cognitive activity is required, and it significantly persists during the teens and adult age.

Impulsivity

This is manifested by impatience, difficult to postpone answers and to await their turn, often interrupting others.The children often blurt out answers before the questions have been completed, letting themselves be taken away by the high-handed answer (spontaneous and dominant).

During the first years, impulsivity makes children appear "to be controlled by stimuli" so they have a tendency to touch everything.During school age, they constantly interrupt others and have difficulties awaiting their turn.

Impulsivity in adolescents leads to a greater conflict with adults and a tendency towards more risky behaviour (toxic substance abuse, early sexual activity and car accidents).

The behavioural manifestations described above usually take place in multiple contexts (home, school, work and social situations). As they grow older, the apparent hyperactivity usually decreases, but the impulsivity and inattention persist.

Are there any differences between the clinical manifestations of boys and girls?

With reference to nuclear symptoms, boys and girls with ADHD present different behavioural patterns.Girls tend to present greater inattention and the boys a greater hyperactivity-impulsivity component.

According to Lahey *et al*. (1994)[48], the proportion of boys/girls is greater for the combined type (7.3:1), followed by the hyperactive-impulsive type (4:1) and less so for the inattentive type (2.7:1).

More recently, Biederman *et al*.(2002)[49] presented the frequency, in percentage terms, of the ADHD subtypes according to sexes, determining that:

- ADHD-C: The combined subtype appeared more often in boys than in girls (80% compared with 65%, respectively).

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- ADHD-I: The inattentive subtype was more frequent in girls than in boys (30% compared with 16%, respectively).
- ADHD-HI: The hyperactive-impulsive subtype is the least frequent of the three and is found both in girls (5%) and in boys (4%).

There are studies, such as the Quinn study (2004)[50], that point out that teachers detect girls with ADHD less than boys with ADHD.

How do the clinical manifestations affect the school performance?

It is worthwhile bearing in mind, too, that school children with ADHD find learning more difficult than the rest of the child population. This fact is one of the main reasons for consultation and school failure (Spencer J, 2007)[51].

The low academic performance is partly due to the actual organisational, planning, prioritisation and attention difficulties, as well as hastiness in providing answers, that are due to the alterations of the executive functions (working memory and response inhibition) typical of ADHD, and to the specific difficulties entailed by the specific learning disorders that are often associated such as dyslexia.

In general, girls with ADHD have less associated learning disorders and better reading skills, which often lead to underdiagnosis.

How do the clinical manifestations affect the comorbid disorders?

There are different clinical manifestations of psychiatric comorbidity in boys and girls with ADHD (Spencer, J, 2007)[51].

- Boys are diagnosed more often with oppositional defiant disorders, behavioural disorders and major depression.In the classroom, they present a higher percentage of disruptive behaviour and hyperactivity.
- Girls with ADHD are less aggressive and impulsive and present less behavioural disorder symptoms.They have a greater risk of suffering anxiety disorders.At school level, they have fewer problems and participate in more out-of-school activities.

These sex differences disappear after puberty (Seidman L.J, 2006)[52].

4.2. Etiopathogeny of ADHD.

What are the main risk factors? Which etiopathogenic model is proposed in ADHD?

The etiopathogeny of ADHD entails the interrelationship of multiple genetic and environmental factors. ADHD is considered as a heterogeneous disorder with different subtypes resulting from different combinations of the risk factors that act at the same time.

It has been suggested that ADHD originates in a dysfunction of the prefrontal crust and of its fronto-striatal connections.

Different data support this etiopathogenic model, including the beneficial effect of stimulants and animal models that involve the dopaminergic pathways,which are very important in the functioning of the prefrontal lobe (Shaywitz *et al*., 1978; Arnsten, 2006)[53;54].

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Volumetric brain studies have shown deviations in the development of the cortical structures in individuals with ADHD with respect to the controls.These studies suggest that ADHD is a cortical maturation disorder more than a deviation in the development (Shaw *et al*., 2007)[55].

What structures and brain circuits are involved in ADHD?

On a structural level, in the paediatric population with ADHD, significantly lower volumes have been found at dorsolateral prefrontal cortex level and in regions connected to this, such as the caudate nucleus, pale nucleus, anterior cingulated gyrus and cerebellum (Castellanos, 2002[56]; Seidman *et al*., 2005[57]). The functional neuroimage studies, especially in adults, also consistently involve the prefrontal cortex and the anterior cingulate (Bush *et al*., 2005[58]; Pliszka *et al*., 2006[59]).

Is there a genetic component in ADHD?

There is scientific evidence of the importance of genetic aspects in ADHD. In 20 independent studies performed on twins, it has been verified that the inheritability of ADHD amounts to 76% (Faraone *et al*., 2005)[60]. Recent genomic studies show the genetic complexity of ADHD, which has been associated with markers in chromosome4, 5, 6, 8, 11, 16 and 17 (Faraone *et al*., 2005[60]; Smalley *et al*., 2002[61]). Faraone *et al*. (2005)[60] have identified 8 genes that have been investigated in at least three more studies; 7 of these genes have shown a statistically significant association with ADHD. These genes are related to receptors DR4, DR5 and the dopamine transporter (DAT), the dopamine – hydroxylase enzyme, the transporter (DBH) and serotonin receptor 1B (HTR1B) and the synaptosomal-associated protein 25 gene (SNAP25).

In a study performed by Spanish researchers, the participation of the so-called neurotrophic factors (NTF) has been verified in the genetic susceptibility of ADHD (Ribases *et al*., 2008)[62].

Are there other neurobiological factors in the origin of ADHD?

The presence of non-genetic neurobiological factors in the genesis of ADHD has been referred to in different studies: prematurity, hypoxic-ischemic encephalopathy and low birthweight (Botting *et al*., 1997)[63], consumption of tobacco and alcohol during pregnancy, basically (Linnet *et al*., 2003)[64]. The consumption of other substances such as heroin and cocaine during pregnancy has also been associated with ADHD (Ornoy *et al*., 2001)[65]. Intrauterine exposure to substances such as lead and zinc has also been indicated as a risk factor to suffer from ADHD (Tuthill, 1996)[66]. Moderate and serious craniocerebral traumas (CCT) in early childhood, as well as infections of the central nervous system (CNS) have also been associated with a greater risk of ADHD (Millichap, 2008)[67]. These non-genetic neurobiological factors are generically called environmental factors.

Are there non-neurobiological factors involved in the origin of ADHD?

Psychosocial risk factors, which would affect the development of the emotional and cognitive control capacity, have also been described. Problems in family relationships are more frequent in families with children with ADHD. This may be a consequence or a risk factor per se (Biederman *et al*., 2002)[68].

Today, gene-environment interaction is accepted as possible, so the presence of certain genes would affect the individual sensitivity to certain environmental factors (Lehn *et al*., 2007[69]; Thapar *et al*., 2007[70]).

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Dietetic factors such as the type of food, the use of food additives, sugar and sweeteners have also given rise to controversy, but, for the moment, there are no conclusive studies that associate them with ADHD (Mc Ardle *et al*., 2004)[71].

4.3. In ADHD: Are there neuropsychological dysfunctions?

Functional neuroimage and neuropsychological studies have shown that boys and girls with ADHD have a cognitive alteration in different components of the executive functions (AACAP, 2007[72]; Willcut *et al*., 2005[73]).

Which are these dysfunctions?

More specifically, a MA of 83 studies with more than 6000 patients indicates that the population with ADHD has alterations in different executive function components, such as response inhibition, vigilance, working memory and planning.

Pennington (2005)74 performed a review of the explanatory neuropsychological models of cognitive dysfunctions of ADHD, which would refer to:

- a deficit in executive functions (Barkley, 199775; Nigg *et al*., 2005[76]);
- a motivational deficit, also called imposition of delay/"delay aversion" (Sonuga-Barke *et al*., 2005)[77], and
- finally, the cognitive-energetic regulation model (Sergeant, 2005)[78].

It is not known exactly if these three cognitive models form independent circuits and/or interrelated circuits.

Thomas Brown also developed a model on complex cognitive capacities that are affected in ADHD.Apart from the executive functions, already mentioned by Barkley, Brown adds two important aspects, motivation and emotion regulation. Brown places more emphasis on these cognitive capacities as a cognitive basis of the disorder (Soutullo, 2007)[79].

Is there one single neuropsychological profile present in all the individuals?

Doyle (2006)[80] carried out a MA that reviews the knowledge about the relationship of ADHD and the problems in executive functions. On the one hand, he considered that there is scientific evidence about the alteration of executive functions (especially response inhibition and working memory), but, on the other hand, he finds considerable neuropsychological variability among the ADHD samples and within them, which makes it difficult to conceptualise the problem.

Along the same line, Seidman (2006)[52] reviewed the effect of the executive functions on ADHD throughout the entire life cycle, bearing in mind variables such as comorbidity, sex, psychopharmacology, etc. In this case, the conclusion was that "future research should clarify the multiple sources of ADHD impairments, continue to refine and optimise neuropsychological tools for their assessment and incorporate longitudinal, developmental designs to understand the disorder across the life cycle".

By way of a conclusion, as Doyle says, "ADHD can be conceptualised as a neuropsychologically heterogeneous condition".

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4.4. What is the natural course of ADHD?

The assessment of the developmental changes in the symptoms of ADHD has been considerably complicated by the changes in diagnostic systems, so studies prior to 1994 and many published after that date are often based on the unitary model of the DSM-III-R. Barkley (1997)[75] summed up the evidence that hyperactivity-impulsivity symptoms appear earlier on (at 3 to 4 years of age), inattention is obvious later on, when they start school (at 5 to 7 years of age), and the problems associated with inattention even later on.In fact, the predominantly hyperactive type is diagnosed more easily in younger children and the predominantly inattention type later on, as the ADHD develops. The hyperactivity-impulsivity symptoms decline more during childhood than the inattention symptoms (Gjone *et al*., 1996[81]; Hart *et al*., 1995[82]; Hechtman, 1996[83]; Levy *et al*., 1996[84]). This reduction of the hyperactivity-impulsivity symptoms is not the consequence of medication or any other treatment, but it is possible that it is developmental (Hart *et al*., 1995)[82]. Inattention could also decrease in intensity, and attention would last for longer with age, but it tends to be lower than the attention of unaffected people, than the level expected at that age and that is needed for the demands of daily life (NICE, 2009)[2].

4.5. In ADHD: What is the long-term prognosis? What factors have an influence on a good or bad prognosis?To what extent does early diagnosis and intervention improve the prognosis of ADHD?

The long-term prognosis of ADHD

The best summary of the developmental perspective of ADHD is that there is not one single prognosis. Hetchman (1996)[83] summed up the results, identifying three groups in adult age: 1) Those whose functioning is as good as that of those without a childhood history of ADHD; 2) those with important psychopathology; and 3) the largest group, those that have some difficulties with concentration, impulse control and social functioning. The percentages mentioned vary considerably among the different studies. Hetchman (1996)[83] analysed many of the relevant methodological questions, and a key question is the way in which the adults have been identified (by their own children, via follow-up studies based on their own behaviour in childhood, by self-referral, via clinical trials, etc.).

The risk of subsequent disadaptation also affects children who have not been referred to the practice clinic and to those not treated in any way. Longitudinal population studies (Moffitt, 199085; Taylor *et al*., 1996[86]) have shown that hyperactive-impulsive behaviours are a risk for several types of dysfunctions inadolescents.It has been informed that the lack of friends, of work and of constructive leisure activities is prominent and affects the quality of life. Varying levels of hyperactivity and impulsivity also lead to a greater probability of children developing an antisocial evolution and it also increases the probability of personality disorders, or substance abuse in late adolescence and in adult age (NICE, 2009)[2].

In the Milwaukee study, Barkley *et al*. (2002)[87] found that in young adults (average age of 20) 42% of the patients continued to satisfyDSM-III-R criteria for ADHD, based on the interview with parents.

Mannuzza *et al*. (1998)[34] found that ADHD in children predicted specific psychiatric disorders in adults, an antisocial personality disorder and drug abuse. Lambert (1988)[88] informed that

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hyperactive children had significantly lower educational results and more behavioural disorders than their peers of the same age. Lie (1992)[89] informed that criminality was related to school and behavioural problems in childhood more than ADHD per se, with a greater role for comorbid behavioural disorder in the final prognosis.

The psychiatric comorbidity studies in adults with ADHD by Biederman *et al*. (1993)[90] found major depression, bipolar disorder, anxiety and personality disorders. They also informed of high rates of antisocial disorder and substance abuse, as well as lower scores in total intellectual quotient (IQ), vocabulary and reading.

Although the symptoms of ADHD persist in the majority of the cases, it is important to recall that many adolescents with ADHD will also adapt well in adult age and will be free from mental problems.The prognosis will probably be better when inattention prevails more than hyperactivity-impulsivity, no antisocial behaviour is developed and relationships with family and with other children are correct.More studies must be carried out on the evolution of ADHD in children and adolescents until adult age, which should include the long-term prognosis together with possible benefits (and risks) of early diagnosis and treatment (NICE, 2009)[2].

Good or bad prognosis factors

Age

In general, it can be stated that in many individuals, the excess of motor activity decreases significantly the older the people get, whilst impulsivity and inattention tend to remain (Hart *et al*., 1995)[82]. Longitudinal studies show very different prevalence rates regarding the persistence of ADHD symptoms in adolescence and in adult age, due to the methodology differences in inclusion criteria and in the tools used to measure the symptoms. In general terms, we can say that the ADHD symptoms persist in adolescence in almost 80% of the people affected, where almost one third of the patients fully satisfy the disorder criteria (Klein & Mannuzza 1991[91]; Mannuzza *et al*., 1998[34]; Biederman *et al*., 1996[92], 1998[93]). In adult age, between 30% and 65% of the patients will present the disorder or will maintain clinically significant symptoms (Weiss et al., 1985[94]; Biederman *et al*., 1996[92], 1998[93]).

Gender

There is only one prospective study on the prognosis of ADHD depending on gender. A cohort of 17 girls with ADHD was compared with a cohort of 24 boys with ADHD and 24 control boys (Manuzza & Klein, 2000)[95]. The results indicated worse scores in academic, behaviour and social functioning measures in girls compared with boys. On the contrary, in adult age, the girls had better results than the boys, especially regarding prevalence of antisocial personality and substance abuse (Manuzza y Klein, 2000)[95]. These results must be taken with caution, given the size of the sample studied.

Cognitive level

Loney *et al*. (1982)[96] found that IQ was a predictive factor for antisocial personality and alcohol abuse disorder. Weiss & Hechtman (1993)[97] indicated that the cognitive level in children, combined with other factors, is a predictive factor of the prognosis of ADHD in adult age.

ADHD Subtype

According to several authors, factors of bad prognosis of ADHD exist if the symptoms are serious or predominantly hyperactive-impulsive (Moffitt, 1990; Lynskey & Fergusson, 1995; Babinski *et al*., 1999; Merrell & Tymms, 2001)[85; 98-100].

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Parents' psychopathology

In the study by Biederman (2001)101 patients with ADHD whose parents have an antisocial personality disorder had more anxiety, major depressive disorder, antisocial behaviour and aggressiveness in the follow-up.

The psychopathology of parents, especially the family history of ADHD, is associated with a greater risk of psychiatric and emotional problems of children in adolescence (August *et al*., 1983[102]; Biederman *et al*., 1996[92]; Fergusson *et al*., 1996[103]; Fischer *et al*., 1993[104]; Lambert *et al*., 1987[105]; Paternite & Loney, 1980[106]; Taylor *et al*., 1996[86]; Weiss & Hechtman, 1993[97]). Families with a history of ADHD with comorbid behaviour problems, antisocial behaviour, and substance dependence and abuse, are also associated with a worse prognosis in children with ADHD in adolescence.

Parent-children relationship

The level of conflict and/or hostility in the parent-child interaction is associated with aggressive behaviour in adolescence (August *et al*., 1983[102]; Biederman *et al*., 1996[92]; Fergusson *et al*., 1996[103]; Fischer *et al*., 1993[104]; Lambert *et al*., 1987[105]; Paternite & Loney, 1980[106]; Taylor **et al.,** 1996[86]; Weiss & Hechtman, 1993[97]).

A conflictive and/or hostile emotional climate in the home is associated with a bad prognosis of ADHD in adult age (Weiss y Hechtman, 1993)[97].

Socio-economic status

The low academic level and the presence of antisocial behaviour in adult age are associated with a low social and economic status of the parents (Weiss & Hechtman, 1993)[97].

Comorbidity

The conductdisorder increases the probability of substance use disorder (August *et al*., 1983)[102.]

In the New York study, the perpetration of criminal acts was almost exclusively explained by the prevalence of antisocial and substance use disorder (Manuzza & Klein, 2008)[107]. Criminality in adult age is associated more with antisocial behaviour than just with ADHD (Satterfield *et al*., 1997)[108].

The persistence of ADHD is associated with comorbidity with behaviour disorder and antisocial personality disorder (Biederman *et al*., 1996[92], 1998[93]). A worse prognosis of ADHD is associated with comorbidity with behavioural disorder, bipolar disorder, oppositional defiant disorder and substance abuse (Biederman *et al*., 2001)[101].

Influence of early diagnosis and intervention in the prognosis of ADHD

Despite not having found scientific evidence about the extent to which early diagnosis and intervention improve the prognosis of ADHD, the guideline development group considers that the prognosis is variable depending on how serious the symptoms are and on the problems and/or disorders that may co-exist with ADHD.In general, an early diagnosis and correct treatment will have a decisively positive influence on its development.

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4.6. In ADHD: What are the most frequent comorbid disorders?

The term, comorbidity, refers to the existence of two or more different disorders or illnesses in one same individual. ADHD is frequently associated with other psychiatric disorders (Pliszka *et al*., 1999)[109]. A study conducted in Sweden by the group of Kadesjo and Gillberg (2001)[110], showed that 87% of children that satisfied all the ADHD criteria had at least one comorbid diagnosis and that 67% satisfied the criteria for at least two comorbid disorders.

Oppositional defiant disorder and learning disorders, tic disorders and anxiety disorders are among the most frequent comorbidities(Jensen *et al*., 1997[38]; MTA, 1999[39], Barkley, 2006[30]).

A complete appraisal of ADHD in children and adolescents must include an evaluation of the associated learning and psychiatric disorders.The presence of comorbidity determines the clinical presentation, the prognosis, the therapeutic plan and the response to the treatment.

Table 3 shows the most frequent comorbidities in children and adolescents with ADHD.

Table 3. Comorbidity with ADHD

Disorder	Approximate rate in children with ADHD
Learning disorders (reading disorder, arithmeticdisorder)	Between 8 and 39% reading disorder, 12 to 30% arithmetic disorder [30]
Developmental Coordination Disorder (DCD) / motor coordination retardation	47% satisfy DCD criteria / 52% have motor coordination retardation [30]
Speech development disorders, expressive disorders (pragmatic)	Up to 35% start to talk late / between 10-54% have expressive difficulties, mainly pragmatic ones[30]
Pervasive developmental disorders*	UP to 26% of the children with pervasive developmental disorder (PDD) may have combined type ADHD [30]
Oppositionaldefiant disorder	Between 40 and 60% [30, 39]
Conductdisorder	14.3%[39]
Tics disorder / Tourette's syndrome	10.9%[39]
Substance use disorder	In adolescence, the risk is 2 to 5 times greater than in normal controls, if there is comorbidity with conductdisorder [30]
Mood disorder: Major depression / bipolar disorder	3.8%/2.2%[39]
Anxiety disorder (panic, phobia, compulsive obsessive, pervasive anxiety, separation anxiety)	Between 25 and 35%[30, 39]
Sleep disorder	Between 30 and 35%[30, 39]

* Despite the fact that today's diagnostic criteria do not permit the diagnosis of ADHD in children and adolescents with pervasive developmental disorders, a significant number of these patients also present compatible symptoms with ADHD, which requires specific appraisal and treatment.

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5. Diagnosis

Questions to be answered:

5.1. What are the diagnostic criteria for ADHD in children and adolescents?

5.2. How is ADHD diagnosed in children and adolescents? Who must diagnose it?

5.3. Which evaluation areas must be included in the diagnosis of ADHD?

5.4. In the diagnosis of ADHD in children and people: Is the neuropsychological assessment necessary?

5.5. In the diagnosis of ADHD in children and adolescents: Is the psychopedagogical assessment necessary?

5.6. In the diagnosis of ADHD in children and adolescents: Are supplementary examinations necessary?

5.7. In the diagnosis of ADHD in children and adolescents: Which entities would the differential diagnosis have to be carried out with?

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

5.1. What are the diagnostic criteria for ADHD in children and adolescents?

Summary of scientific evidence

There are two international classification systems:

– Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (APA, 2001)[110]

– International Classification of Mental Disorders (ICD-10) (WHO, 1992)[111].

The diagnostic criteria of DSM-IV-TR and ICD-10 are found in **Appendix 2**.

The specific criteria that are included in DSM-IV-TR and in ICD-10 include a similar list of 18 symptoms, referring to inattention, hyperactivity and impulsivity behaviour.

The codes of the attention deficit hyperactivity disorder (314.xx), are:

– F90.0. Combined type (314.01).

– F98.8 Predominantly inattentive type (314.00).

– F90.0 Predominantly hyperactive-impulsive type (314.01).

– F90.0 Attention-Deficit/Hyperactivity Disorder NOS (314.9).

Both classification systems coincide on several important points: – Onset of symptoms before the age of 6 (ICD-10) or 7 years (DMS-IV-TR). The NICE guideline (2009)2 recommends that ADHD can be diagnosed in some cases when the onset of symptoms takes place between the age of 7 and 12 years. – the symptoms must be maintained throughout time (persist for at least 6 months). – must be present in different situations of the child's life, – must cause a functional impairment, and – the symptoms cannot be explained any better by other disorders. Despite the similarities described, there is not total agreement between the two classifications. A specific characteristic of ICD-10 not shared by DSM-IV-TR is the requirement of the presence of three essential symptoms to make a diagnosis of ADHD referring to inattention, hyperactivity and impulsivity behaviours. It requires at least six inattention, three hyperactivity and one impulsivity symptoms, establishing four diagnostic categories: 1. Activity and attention disorder. 2. Hyperkinetic conductdisorder, in this case, hyperkinetic disorder is accompanied by a behaviour disorder. 3. Other hyperkinetic disorders. 4. Hyperkinetic disorders NOS. However, in agreement with DSM-IV-TR, both the attention difficulties and the hyperactivity-impulsivity, can produce a positive diagnosis. Thus, the current phenotype classification, according to DSM-IV-TR, poses the existence of three different subtypes of ADHD. It distinguishes a "combined subtype" (ADHD-C), when all the criteria for attention deficit and hyperactivity-impulsivity are satisfied; a "predominantly attention deficit subtype" (ADHD-I) and a "hyperactive-impulsive subtype" (ADHD-HI), when six or more criteria of one type and less than six criteria of the opposite factor are satisfied.It also distinguishes a "NOS subtype". Another specific characteristic of ICD-10 and not shared by DSM-IV-TR is that the presence of anxiety or mood alterations is a diagnostic exclusion criterion. DSM-IV-TR permits the presence and diagnosis of comorbid anxiety and/or mood alterations.	Experts' opinion 4 Experts' opinion 4

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A SR conducted by the NICE guideline (2009)[2] identified clinical, genetic, environmental and neurobiological factors associated with ADHD or that associate it with high levels of ADHD symptoms in the general population, which are sufficient to validate the diagnostic construct of ADHD.The review concludes that ADHD is contextualised as the extreme of a continuous trait that is distributed through the population; the distinction from normality being made by the presence of high levels of ADHD symptoms when they are accompanied by significant impairments in the functioning of the child, as defined by the diagnostic criteria of DMS-IV-TR and of ICD-10. Among the limitations presented by the DSM-IV-TR and ICD-10 classifications, the non-inclusion of necessary modifications for different age groups and sexes must be mentioned.	SR of cohort control case studies 2++
Despite the fact that today's diagnostic criteria do not permit the diagnosis of ADHD in children and adolescents with pervasive developmental disorders, a significant number of these patients also present compatible symptoms with ADHD, which requires specific appraisal and treatment. Currently, both the DSM-IV-TR criteria and the ICD-10 criteria are undergoing review, as DSM-V and ICD-11 are being prepared.	Experts' opinion 4

Recommendations

D	5.1.1.	To diagnose ADHD in children and adolescents the use of the diagnostic criteria of DSM-IV-TR or CIE-10 are recommended.

5.2. How is ADHD diagnosed in children and adolescents? Who must diagnose it?

The answer is based on the AAP (2000)[112], SIGN (2005)[1], AACAP (2007)[72] and NICE (2009)[2] guidelines.

Summary of scientific evidence

The diagnosis of ADHD is exclusively clinical, and must be based on the presence of the typical symptoms of the disorder, backed by a clear functional repercussion in the personal, family, academic and/or social areas, and after having excluded other disorders or problems that might be justifying the observed symptoms. (AAP, 2000[112]; SIGN, 2005[1]; AACAP, 2007[72]; NICE, 2009[2]).	Experts' opinion 4

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Recommendations

D	5.2.1.	The diagnosis of ADHD in children and adolescents is exclusively clinical.
D	5.2.2.	The diagnosis of ADHD in children and adolescents must be carried out by a health professional with training and experience in the diagnosis of ADHD and its most frequent comorbidities.

5.3. Which evaluation areas must be included in the diagnosis of ADHD?

The answer is based on the AAP (2000)[112], SIGN (2005)[1], AACAP (2007)[72] and NICE (2009)[2] guidelines, the MA of Biederman *et al*.(2006)[113] and the review of Linnet *et al*. (2003)[64].

Summary of scientific evidence

The diagnosis must be made based on the information obtained through the clinical interview with the child or adolescent, and with the parents. The information from the school must be evaluated as well as the physical examination of the child. The family background must also be appraised (given the genetic influences of the disorder) and the family functioning. Information must be obtained about the pregnancy, birth and perinatal period, about the psychomotor development, pathological background and mental health history of the child (especially previous psychiatric treatments). Although the majority of children with ADHD do not have an outstanding medical history and the physical examination is normal, both the anamnesis and physical examination can help rule out associated neurological processes and other causes that might justify the symptoms (AAP, 2000[112]; SIGN, 2005[1]; AACAP, 2007[72]; NICE, 2009[2]).	Experts' opinion 4

History of the current disease

Summary of scientific evidence

Parents must be interviewed regarding the child's current problems, the nature of the symptoms (frequency, duration, situational variation of the symptoms), age of onset and degree of functional impairment(AAP, 2000[112]; SIGN, 2005[1]; AACAP, 2007[72]).	Experts' opinion 4
The information obtained from the parents has proved, in general, to be validand reliable for the appraisal and diagnosis (SIGN, 2005)[1]. A recent MA of two RCTs has shown that the information obtained from the parents in the appraisal of ADHD symptoms during clinical trials is just as feasible as the information obtained from the teachers (Biederman *et al*., 2006)[113].	MA of RCT 1+

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Family background

Summary of scientific evidence

Questions must be asked about the history of psychiatric and specific disorders of ADHD in the family.Scientific evidence has clearly been established with respect to the contribution of genetic factors in ADHD (SIGN, 2005)[1].	Cohort and control case studies 2+

See chapter 4. *ADHD*, where the genetic factors of ADHD are described.

Personal background

Obstetric and perinatal history

Summary of scientific evidence

Previous guidelines recommend requesting information from the parents about the obstetric and perinatal history, as obstetric complications have been found that are associated with ADHD, such as intrauterine growth retardation, prematurity and toxic habits during pregnancy –alcohol and tobacco- (SIGN, 2005[1]; Linnet *et al*., 2003[65]).	SR cohort and control case studies 2+

See chapter 4. *ADHD*, where the risk factors of ADHD are described.

Developmental history

Summary of scientific evidence

Apart from the patient's perinatal history, the clinician must obtain information about the physical and motor development, the keydevelopmental milestones, the medical and mental health history (above all respect to any previous psychiatric treatment) (SIGN, 2005)[1].	Experts' opinion 4

Physical examination

Summary of scientific evidence

In patients with ADHD, the aim of the physical examination is to appraise other medical diseases that may be the cause or contribute to the symptoms that give rise to the consultation, as well as potential contra-indications for pharmacological intervention. Neurological signs and minor physical anomalies do not exclude or confirm the diagnosis of ADHD (SIGN, 2005)[1].	Experts' opinion 4

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Psychopathological examination

Summary of scientific evidence

The clinician must perform a complete psychopathological examination, appraising the aspect, perceptive capacity, mood, affection and cognitive processes (AACAP, 2007)[72].	Experts' opinion 4

School history

Summary of scientific evidence

Given that the majority of patients with ADHD have difficulties at school, it is important to pose specific questions about this field, examining the possible presence of learning disorders and reviewing the patient's academic performance over time (SIGN, 2005)[1].	Experts' opinion 4

See chapter 6. *Assessment tools*, where the school learning assessment tools used in our medium for the diagnostic appraisal of ADHD in children and adolescents are reviewed.

Data collection tools

Summary of scientific evidence

The development group considers that there are specific tools to appraise the symptoms of ADHD and of general psychopathology that facilitate screening or detection, an appraisal by intensity of the disorder and the response to treatment.Questionnaires must not, under any circumstances, be used as the only method to establish the diagnosis, nor as a substitute for a correct clinical interview with parents and with the child or adolescent.	Experts' opinion 4

See chapter 6. *Assessment tools*, where the school learning assessment tools used in our medium for the diagnostic appraisal of ADHD in children and adolescents are reviewed.

Recommendations

D	5.3.1.	The diagnosis of ADHD in children and adolescents must be done via clinical interviews with parents and the patient, obtaining information from the school, reviewing family and personal background as well as the physical and psychopathological examination of the patient.

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5.4. In the diagnosis of ADHD in children and adolescents: Is the neuropsychological assessment necessary?

The answer is based on the AACAP guideline (2007)[72], the reviews of Nigg *et al*. (2005)[76], Sergeant *et al*. (2005)[78], Sonuga-Barke *et al*. (2005)[77] and the studies of Jakobson *et al*. (2007)[114] and Geurts *et al*. (2005)[115].

Summary of scientific evidence

The neuropsychological study is not essential to diagnose ADHD.The neuropsychological examination enables us to discover the detailed profile of cognitive functioning, and it is also useful to carry it out when the presence of a comorbid learning disorder is suspected (Jakobson *et al*., 2007[114]; AACAP, 2007[72]).	Control case study 2+
The neuropsychological profiles in ADHD are not homogeneous and the most frequent cognitive deficits cover a broad spectrum of skills considered to be executive functions (Nigg *et al*., 2005[76]; Sergeant *et al*., 2005[78]; Sonuga-Barke *et al*., 2005[77]). The variability in the neuropsychological profiles in children with ADHD is probably due to a not very precise definition of these executive functions and the use of not very specific neuropsychological tests.	Narrative reviews 3
There are currently no well-defined neuropsychological profiles that permit distinguishing different subtypes of ADHD (Geurts *et al*., 2005)[115].	Control case study 2+

See chapter 6. *Assessment tools*, where the neuropsychological tests used in our medium for the diagnostic appraisal of ADHD in children and adolescents are reviewed.

Recommendations

C	5.4.1.	The neuropsychological assessment is not essential for the diagnosis of ADHD in children and adolescents.
√	5.4.1.	The neuropsychological examination of ADHD in children and adolescents is useful to get to know the profile of skills and difficulties in cognitive functioning and comorbidity with specific learning disorders.
C	5.4.1.	To diagnose ADHD it is not necessary for there to be an alteration in the results of the neuropsychological tests that assess executive functions.

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5.5. In the diagnosis of ADHD in children and adolescents: Is the psychopedagogical assessment necessary?

The answer is based on the AACAP (2007)[72] and SIGN (2005[1] guidelines.

Summary of scientific evidence

Academic impairment is frequently due to ADHD per se. In other cases, learning problems are present and the reason for these cannot be explained by ADHD. In these cases, the examination will be necessary in order to rule out specific learning disorders (AACAP, 2007)[72].	Experts' opinion 4
An appraisal by academic performance is essential for the diagnostic evaluation of the child or adolescent with ADHD /SIGN, 2005)1.	Experts' opinion 4

See chapter 6. *Assessment tools*, where the psychopedagogical tests used in our medium for the diagnostic appraisal of ADHD in children and adolescents are reviewed.

Recommendations

D	5.5.1.	The psychopedagogical assessment is useful to evaluate the learning style and difficulties and to establish the re-education intervention objectives.

5.6. In the diagnosis of ADHD in children and adolescents:Are supplementary examinations necessary?

The answer is based on the AAP (2000)[112], SIGN (2005)[1] and AACAP (2007)[72] guidelines.

Summary of scientific evidence

There is no specific biological marker to be able to diagnose ADHD (SIGN 2005[1], AAP 2000)[112]. Although differences have been found in some studies in neuroimage and neurophysiologic tests between ADHD cases and control cases, these tests do not permit identifying individual cases (AACAP, 2007[72]; AAP 2000[112]).	Case and control studies 2++
Blood analyses, neuroimage studies (CT and brain MRI, SPECT or PET) or neurophysiologic studies (EEG, evoked potentials) are not indicated in the diagnostic assessment of ADHD (AAP 2000[112], SIGN 2005[1]; AACAP 2007[72]). These examinations will only be used if justified by the physical examination and the clinical history.	Experts' opinion 4

Recommendations

B	5.6.1.	To diagnose ADHD in children and adolescents supplementary laboratory, neuroimage or neurophysiological tests are not indicated unless the clinical evaluation justifies this.

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5.7. In the diagnosis of ADHD in children and adolescents: Which entities would the differential diagnosis have to be carried out with?

The answer is based on the AAP (2000)[112], AACAP (2007)[72], NICE (2009)[2] guidelines, as well as on the reviews of Soutullo & Diez (2007)[79] and Culpepper (2006)[116].

Summary of scientific evidence

Within the clinical evaluation of children with ADHD it must be taken into account that not all lively and absent-minded children have ADHD; a differential diagnosis must be made with other entities that can be confused with the disorder (AAP, 2000[112]; Culpepper, 2006[116]; Soutullo y Diez, 2007[79]; AACAP, 2007[72]; NICE, 2009[2]). The first step, however, will be to rule out that the child's behaviour falls within normality. Thus, it is important to evaluate the quantity and intensity of the symptoms, the permanence in time and their functional impact on the different situations. The symptoms of hyperactivity, impulsivity and attention deficit may appear in a wide range of disorders: • mental retardation • learning disorders, • pervasive developmental disorders, • behavioural disorders, • anxiety disorders, • mood disorders, • substance abuse. • Environmental factors: • stress, • negligence/child abuse, • malnutrition, • inconsistency in education patterns. • Medical disorders: • Posttraumatic or postinfectious encephalopathies, • Epilepsy, • Sleep disorders (sleep apnoea, restlessleg syndrome, regular extremity movement syndrome, • Perceptualdisorders (significant auditory and sight deficits), • Side effect of drugs (bronchodilators, antiepileptics), • Thyroid dysfunction, • Lead intoxication, • Ferropenic anaemia. The majority of these disorders can be detected with a complete clinical evaluation.	Narrative reviews 3

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6. Assessment instruments

Questions to be answered:

6.1. Which screening instruments and specific scales of ADHD in children and adolescents are useful/recommendable for the diagnosis?Which have been validated in the Spanish population?

6.2. In ADHD in children and adolescents? Which general or broad spectrum psychopathologyscales are useful/recommendable?Which have been validated in the Spanish population?

6.3. In ADHD in children and adolescents? Which interviews are useful/recommendable for the diagnosis? Which have been validated in the Spanish population?

6.4. In ADHD in children and adolescents? Which neuropsychological and intelligence tests are useful/recommendable?Which have been validated in the Spanish population?

6.5. In ADHD in children and adolescents? Which psychopedagogical assessment tools are useful/recommendable? Which have been validated in the Spanish population?

Assessing ADHD requires obtaining information from the child or adolescent, from parents and carers, as well as from teachers about the nuclear symptoms of ADHD in several areas, the duration of the symptoms and the degree of impactof this situation.The information about the behaviour symptoms can be obtained by several methods, which include: open-ended questions, specific questions, semistructured interviews, questionnaires and scales (AAP, 2000)[112].

The ADHD assessment instruments are a means of obtaining standardised information about the parents' and teachers' perceptions of the child's problems.The results should be interpreted with caution when the scales used derive from other different populations to the Spanish population.

The aim of this section of the guideline is to review the detection and assessment tools available in the Spanish population (specific ADHD scales, broad spectrum scales and structured and semistructured interviews), as well as about the use of neuropsychological and psychopedagogical tests.

The lists presented include the main tools to assess ADHD in children and adolescents that are available in our medium.There are other types of questionnaires, scales and tests that have not been included as no translation or comparative scales have been found for the Spanish population.

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6.1. Which screening instruments and specific scales of ADHD in children and adolescents are useful/recommendable for the diagnosis?Which have been validated in the Spanish population?

6.2. In ADHD in children and adolescents? Which general or broad spectrum psychopathologyscales are useful/recommendable?Which have been validated in the Spanish population?

6.3. In ADHD in children and adolescents? Which interviews are useful/recommendable for the diagnosis? Which have been validated in the Spanish population?

The answer is based on the technical review of the Agency for Health Care Policy and Research (AHCPR) (Technical Review n.3, 1999)[117], the AAP guideline (2000)[112], and questionnaire validation studies.

Summary of scientific evidence

A technical review conducted by the Agency for Health Care Policy and Research (AHCPR) (Technical Review n.3, 1999)[117] has reviewed the reliability and validity of the screening and assessment tools for the diagnosis of ADHD compared with the gold standard. It can be concluded from the report that broad spectrum questionnaires do not permit an adequate distinction of the psychiatric patients (AAP, 2000)[112].	Questionnaire validation studies 2+
Likewise, the specific ADHD scales, more specifically the Conners scales, 1997 version, permit discriminating children with ADHD in community studies (sensitivity and specificity of over 94%), although their discrimination capacity decreases in less ideal situations (primary care compared with community studies) (AAP, 2000)[112].	Questionnaire validation studies 2+
The development group considers that there are useful structured and semistructured interviews to compile information, both in clinical practice and in research.However, the considerable application time and the preliminary training necessary mean that their use is not very feasible in normal clinical practice.	Experts' opinion 4
Table 4 presents the main specific scales, general psychopathology scales, and structured and semistructured interviews used in our medium to assess ADHD in children and adolescents.	Questionnaire validation studies 2+

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Table 4. Specific scales, general psychopathology scales, and structured and semi-structured interviews for the assessment of ADHD in

Title	Authors	Year	Description	Age range	Psychometric properties	Comments
Specific AdHD Scales:						
ADHD Rating Scale - IV	DuPaul *et al*.	1997[118], 1998[119]	– ADHD screening and assessment scale. – 18 4-point Likert type items – Two subscales: Inattention and Hyperactivity, and one total score – Each item represents each one of the ADHD symptoms according to DSM-IV criteria – Two versions: parents and teachers	– 6-16 years (Ortiz, not published). – 5-11 years (Servera 2007)[120] – 5-18 years (DuPaul, 1997; 1998)[118;119]	– Reliability by internal consistency: from 0.85 to 0.95 (Servera, 2007[120]; Ortiz, not published) – Adequate concurrent validity with Achenbarch scale attention problems (Ortiz, not published)	– Version translated and validated into Spanish (Servera & Cardo, 2007)[120] – Version translated and validated into Catalan (Ortiz et al., not published)
Conners Scales	Keith Conners, *et al*.	1989[18], 1997[121], 2008[122]	– ADHD screening and assessment scale. – Sensitive to changes in treatment – 3 versions: – 1989: two scales for parents, long (CPRS-93, 93 items) and short (CPRS-48, 48 items); two scales for teachers, long (CTRS-39, 39 items) and short (CTRS-28, 28 items – 1987: two scales for parents, long (CPRS-R: L 80 items) and short (CPRS-R, L 28 items); two scales for teachers, long (CTRS-R:L 59 items) and short (CTRS-R:2 27 items – 2008: two scales for parents, long (Conners 3-P(L) and short (Conners 3-P(S); two scales for teachers, long (Conners 3-T(L) and short (Conners E-T(S) and one self-administered version (Conners 3-SR) – The long scales include general psychopathology items. The short scales are basically comprised of 4 subscales: Oppositionism, inattention, hyperactivity and ADHD Index	– 3-17 years (1989[18], 1997121) – 6-18 years (2008)[122] – 8-18 years the (self-report 2008)[121]	– Reliability by internal consistency: 0.73 to 0.94 (Conners et al., 1998)[123] – Criterion validity: sensitivity 92.3%, specificity 94.5% (Conners et al, 1998)[124] – CPRS-48 in the Spanish population it does not reach satisfactory psychometric properties (Farre and Narbona, 1997)[121]	– Version translated to Spanish by MSH [122] – There are no normative data corresponding to the Conners Scales for Spanish population.

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Title	Authors	Year	Description	Age range	Psychometric properties	Comments
ADHD Questionnaire	Juan Antonio Amador, *et al*.	2005[125], 2006[126]	– ADHD symptom screening and assessment scale – 18 4-point Likert type items – Two subscales: Inattention – and hyperactivity and a total score – Each item represents each one of the ADHD symptoms according to DMS-IV criteria – Two version: Parents and teachers	– 4-12 years	– Reliability due to internal consistency: 0.94 to 0.95. Teachers, 0.85 to 0.89 parents – Adequate validity concurrent with Achenbach scales attention problems.	– Bilingual version, Spanish-Catalan – Spanish population – Normative data
EDAHscales	Anna Farré and Juan Narbona	1997[121]	– ADHD symptom screening and assessment scale – 20 4-point Likert type items – Two scales: Hyperactivity-Attention deficit (which is subdivided from – Two subscales) and behavioural disorders – One single version for teachers	– 6-12 years	– Reliability due to internal consistency: 0.84 to 0.93 – Adequate validity concurrent with DSM-III criteria	– Spanish population normative data – It has cut-off points
Magallian Scales	García-Pérez & Magaz-Lago	2000[127]	– ADHD screening scale – 17 items – 3 subscales: Hyperkinesis-Hyperactivity, Attention deficit, – Reflexivity deficit – Two versions: Parents and teachers	– 6-16 years (parents) – 6-12 years (teachers)	– Reliability due to internal consistency: 0.60 to 0.71	– Spanish population normative data – The scores indicate the probability of having ADHD or not
SNAP-IV	Swanson, Nolan and Pelma	2003[125]	– ADHD symptom screening and assessment scale – Sensitive to changes in treatment – 18 4-point Likert type items – 2 subscales: Inattention and Hyperactivity/Impulsivity, and a total score – Two version: Parents and teachers	– 5-11 years	– Reliability due to internal consistency: Not published – Reliability test-retest. 0.77 to 0.80	– There are no normative data for the Spanish population.

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Title	Authors	Year	Description	Age range	Psychometric properties	Comments
Specific AdHD Scales:						
Achenbach Scales	Achenbach *et al*.	1991[129], 2001[130]	– General psychopathology scale – 112 3-point Likert type items – 8 subscales: Inattention, Anxiety-Depression, Withdrawal-Depression, Somatic complaints, Social problems, thought problems, rule breaking behaviour, aggressive behaviour. They are grouped into two 2-tier factors: internalizing and externalizing. – Three versions: for parents (CBCL), teachers (TRF) and self-report (YSRF)	– 1.5-5 years (CBCL, TRF) – 6-18 years (CBCL, TRF) – 11-18 years (YSRF)	– Reliability by internal consistency: 0.84 to 0.94)	– Spanish translation by the UAB (Epidemiology and diagnosis unit in developmental psychopathology)[130] – There are no normative data for Spanish population
Behavioural Assessment System of children and adolescents BASC	Reynolds & Kamphaus	1992[131],	– Set of instruments that permits assessing the adaptative and disadaptative aspects of children's and adolescents' behaviour. – From 106 to 185 items (depending on version) 2 or 4-point Likert type – Scales: Externalizing problems (aggressiveness, hyperactivity, behavioural problems), Internalizing problems (anxiety, depression, somatisation), School problems (attention problems, learning problems), Other problems (atypical development, withdrawal), Adaptatiive skills (adaptability, leadership, social skills), other adaptative skills (skills for study), Behavioural symptoms index. – Five components: a self-report (S); two evaluation questionnaires, one for parents (P) and another for tutors (T); a Structure history of the development and an observation system of the student.	Parents and teachers: – 3-6 years – 6-12 years – 12-18 years	– Reliability by internal consistency: 0.79 to 0.90 – Test-retest reliability at 3 months: 0.78, 0.82 and 0.84 – Inter-rater agreement: teachers of 0.83 and parents 0.63 and 0.71 – Adequate concurrent validity with Achenbach and Conners scales (Spanish adaptation and validation)[132]	– Spanish adaptation and validation by Research Team of the Complutense University of Madrid (Javier Gonzalez Marques, Sara Fernandez Guinea, Elena Perez Hernandex) and R D department of TEA Ediciones (Pablo Santamaria Fernandez)[132]

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Title	Authors	Year	Description	Age range	Psychometric properties	Comments
SDQ Skills and Difficulties Questionnaire	Robert Goodman	1997[133]	– General psychopathology screening questionnaire – 25 3-point Likert type items – 5 scales: Emotional symptoms, Behavioural problems, hyperactivity/Inattention, relationship problems with peers and prosocial behaviour – Versions: Parents, teachers and adolescents	Parents and teachers: – 3 to 16 years Selfrport: – 11 to 16 years	– Area under the ROC curve to discriminate psychiatric patients: 0.87 (CI 95%: 0.83-0.91) for Parents and 0.85 (95% CI: 0.78-0.93) for teachers (Goodman, 1997)[133] – Useful in discrimination of psychiatric patients (Johnston et al., 2000)[134].	– Versions translated to Spanish, Catalan, Gallego and Basque (www.sdqinfo.com) – Preliminary validation In Gallego (García-Cortizar, et aL, 2000)[134] – There are no normative data for the Spanish population.
Structured and semistructured interviews						
Diagnostic Interview for Children and Adolescents DICA-IV	Herjanic & Reich	1982[135]	– Most recent semistructured version – Assesses an extensive group of psychopathological disorders in the child and adolescents population according to DMS-II and DSM-IV criteria – Versions: Children, adolescents and parents	– 6-17 years (parents) – 6-12 years (parents) – 13-17 years (adolescents)	– Reliability between interviewers (K between 0.65 and 1.00) (de la Osa, et al., 1996)[136]. – Reliability test-retest: 0.78 to 0.86 in parents; 0.24 to 0.43 in self-report	– Version translated and validated into Spanish (Ezpeleta, et al., 1997)[137] – Requires previous training
Schedule for Affective Disorders and Schizophrenia in School Age Children KSADS	Chambers *et al.*	1985[138]	– Semistructured diagnostic interview – Assesses past and present episodes of psychopathology in children and adolescents, according to DSM-IV and DSM-II-R criteria – Several sections: Sociodemographic, screening questions for 46 diagnostic categories, diagnostic supplements and functioning	– 6-17 years	– Reliability between interviewers (K between 0.76 and 1.00) (Ulloa, etaL, 2006)[139]	– Version translated to Spanish (de la Peña, et al., 2002[140]; Cesar Soutullo, Universidad de Navarra) (www.cun.es/laclinica/servicios-medicos/psiquiatria/mas-sobre-eldepartamento/unidades/ psiquiatria-infantil-y-adolescente) – Requires clinical training and experience of the interviewer

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Title	Authors	Year	Description	Age range	Psychometric properties	Comments
Diagnostic Interview Schedule for Children DISC	Shaffer, *et al*.	1999[141]	– Structured interview – Assesses psychopathological disorders in children and adolescents according to DSM-IV criteria – Administered to parents (DISC-P) and to patients (DISC-C)	– 4-17 years (DISC-P) – 11-7 years (DISC-C)	– Reliability between Interviewers (K between 0.42 and 0.70 for parents; K between 0.10 and 0.80 for child/adolescent) (Bravo, et al, 2001) 142	– Version translated to Spanish and validated in Puerto Rico (Bravo, et aL, 2001)[142] – Non-clinical personnel can administer it

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Recommendations

C	6.1.1.	The specific scales for ADHD in children and adolescents can be used in addition but never as substitutes for the clinical interview, to detect the presence and assess the intensity of the nuclear symptoms.
√	6.1.2.	The information provided by parents and teachers, via the assessment scales, is useful to diagnose ADHD in children and adolescents and to assess the evolution of the symptoms and the response to the treatment.
√	6.2.1.	The general psychopathology questionnaires can be used to screen comorbidity.
√	6.3.1.	Structured and semi-structured interviews are useful to establish the diagnosis of ADHD and its comorbidities in children and adolescents.

6.4. In ADHD in children and adolescents: Which neuropsychological and intelligence tests are useful/recommendable? Which have been validated in the Spanish population?

The answer is based on the AACAP (2007)[72] ,SIGN (2005)[1] and AAP (2000)[112] guidelines.

Summary of scientific evidence

The neuropsychological examination is not essential as part of the normal assessment of ADHD, but it can be indicated to get to know the profile of the cognitive functioning and comorbidity with specific learning disorders (AACAP, 200772; SIGN, 20051; AAP, 2000112).	Experts' opinion 4
Children and adolescents with ADHD are no different from the general population in the majority of the traditional psychological tests.Neuropsychological attention and concentration measurements do not differentiate ADHD children from other disorders or controls (SIGN, 2005)1.	Case and control studies 2++

Table 5 presents the major intelligence and neuropsychological tests most frequently used and validated in our medium.

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Table 5. Intelligence and neuropsychological tests most frequently used and validated in our medium

Name	Author / publishing house / year	What does it assess?	Ages
WISC-IV	David Weschler / TEA Ediciones (2005)	Intelligence	6-16 years
WAIS-III	David Weschler / TEA Ediciones (1999)	Intelligence	16-94 years
K ABC	Kaufman / TEA Ediciones (1997)	Intelligence	2.5-12.5 years
K BIT	Alan S. Kaufman, Nadeen L., Kaufman / TEA Ediciones (2000)	Intelligence	4-90 years
McCarthy (MSCA), revised version	Dorothea McCarthy / TEA Ediciones (2006)	Intelligence, development level	2.5-8.5 years
STROOP, Colour and word test	Golden / TEA Ediciones (2001)	Executive functions	7-80 years
MFF_20	E. D. Cairns y J. Cammock / TEA Ediciones (2002)	Cognitive reflexive-impulsive style	6-12 years
FACES (Perception of differences)	Thurstone & Yela. Narbona (3 & 6 minutes) / TEA Ediciones (1985)	Attention, perception of differences	>6 years
RCF (Rey Complex Figure)	Rey / TEA Ediciones (2003)	Visospatial, visoconstructive skills, visual memory, executive functions	4-adults
D2 (Attention test)	Brickenkamp & Zillmer,/ TEA Ediciones (2004)	Attention	8-18 years
CSAT (Children Sustained Attention Task)	Servera & Llabres / TEA Ediciones (2004)	Attention	6-11 years
CPT II (Conners' Continuous Performance Test II)*	Conners y Staff / MHS (2004)	Attention	>6 years
TP (Toulouse-Pieron)	Toulouse y Pieron / TEA Ediciones (2007)	Attention	>10 years

* There are no scales for the Spanish population.

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6.5. In ADHD in children and adolescents: Which psychopedagogical assessment tools are useful/recommendable? Which have been validated in the Spanish population?

The answer is based on the SIGN guideline (2005)[1].

Summary of scientific evidence

The psychopedagogical assessment consists in evaluating the level of the child or adolescent in basic areas such as reading, writing and mathematics to determine if they are in agreement with their age, schooling and skills. Qualitative information can be obtained about the child's learning style (SIGN, 2005) [1].	Experts' opinion 4

Table 6 presents the major psychopedagogical tests most frequently used and validated in our medium..

Table 5. Intelligence and neuropsychological tests most frequently used and validated in our medium

Name	Author / publishing house / year	Who assesses?	Levels
T.A.L.E. (Reading and writing analysis test) and T.A.L.E.C. (Analysis test On reading and writing in Catalan)	Cervera & Toro / TEA Ediciones Cervera y Toro / TEA Ediciones (1990)	Writing: Calligraphy, copy, dictation and drafting Reading letters, syllables, words and text. Reading comprehension	Up to 4th year primary
CANALS (instrumental learning psychopedagogical tests). Version in Spanish and Catalan	Canals, Bosch, Monreal, Perera, Rius / Editorial Onda (1988)	Reading speed. Reading comprehension Dictation Mathematics:+ calculation and problem-solving	Primary Secondary
PROESC (writing process assessment, primary)	Cuetos, Ramos, Ruano / TEA. Ediciones (2002	Dictation of syllables, words, pseudowords and phrases.Story-writing and drafting	Primary

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Name	Author / publishing house / year	Who assesses?	Levels
PROLEC-R (reading process assessment, primary)	Cuetos, Rodríguez, Ruano, Arribas / TEA Ediciones (2007)	Identification of letters: Name and sound of letters and differentiate words and pseudo-words. Lexical processes. Syntactic processes. Semantic processes	Primary
PROLEC-SE (reading process assessment, secondary)	Ramos, Cuetos / TEA Ediciones (2003)	Matching drawing-sentence. Text comprehension. Structure of a text Reading words. Reading pseudowords Punctuation signs	Secondary
IHE (Study habits inventory)	Fernández Pozar / TEA Ediciones (1994)	Environmental conditions Study planning. Use of materials. Assimilation of contents. Sincerity	Secondary
CHTE (Habits and study technique questionnaire) Version in Spanish and Catalan	Álvarez González, Fernández Valentín / TEA Ediciones (1990)	Attitude towards studying. Situation. Physical status of scholar Work plan Study techniques. Exams and exercises. Works	Primary Secondary
DIE (Integral study diagnosis)	Pérez Avellaneda, Rodríguez Corps, Cabezas Fernández & Polo Mingo / TEA Ediciones (1999)	Attitude towards studying. Academic self-concept. Results	Primary, Secondary, Baccalaureate

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7. Treatment

7.1. Psychological treatment

Questions to be answered:

7.1.1. Psychological treatment: What does it consist of? What must it include?

7.1.2. Which psychological treatment iseffective to treat ADHD in children and adolescents?

7.1.3. Psychological treatment of children and adolescents: Has it proved to be efficient/effective in the short and long term?

7.1.4. How effective is psychological treatment of ADHD in children and adolescents?

7.1.5. In ADHD in children and adolescents? What clinical variables and standardised instruments exist to evaluate the efficacy of psychological treatment? At what moment of the treatment should its efficacy be evaluated?

7.1.1. Psychological treatment: What does it consist of? What must it include?

The psychological interventions that have shown some scientific evidence of efficacy for ADHD are based on the principles of cognitive behavioural therapy (CBT).The type of interventions that are applied are described briefly below.

Behavioural therapy

The behaviours to be changed are defined based on a functional analysis of behaviour, which identifies the factors that are maintaining the maladaptative behaviour. These are then observed and recorded, analysing the existing contingencies, and a new contingency system is constructed in agreement with the objectives proposed; a reinforcement programme is planned and the programme is assessed during treatment.Positive reinforcements can include praise, positive attention, rewards and privileges.The techniques to reduce undesired behaviours include response cost, isolation timeout, overcorrection, extinction and punishment.Other behaviour modification techniques are token economy that combines positive reinforcement, response cost and contingency contract.

Parent Training Programs

This is a behavioural treatment programme whose aim is to provide information about the disorder, to train parents in behaviour modification techniques to help them manage their children better, to increase the parents' competence, to improve the parent-child relationship via better communication and attention to the child's development.The programmes are structured and developed in a specific number of sessions and are normally carried out in groups. Examples of programmes are: Triple P (Sanders, 2004)143; The Incredible Years (Webster-Stratton, 2004)144; Barkley, 199775; The Community Parent Education Program (Cunningham, 1998)145.

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Cognitive therapy with children

The aim of cognitive therapy is to identify and modify the maladaptivecognitions, emphasising the impact on behaviour and emotions to replace them with other, more adequate cognitions.These objectives are carried out through different procedures, highlighting training in self-instruction, self-control and problem-solving techniques.

Social Skills Training

Children and adolescents with ADHD often have relationship problems with the family; they have social skills difficulties and relationship problems with peers.Social skills training uses CBT techniques and is normally carried out in group format.

7.1.2. Which psychological treatment is effectiveto treat ADHD in children and adolescents?

The answer is based on the NICE (2009)2 and SIGN (2005)1 guidelines, a Cochrane SR with 1++ quality by Bjornstad & Montgomery (2008)[146], and a MA with 1+ quality by Van der Oord *et al*. (2008)[147]. The search has been updated with a RCT published in 2007 (Pfiffner, 2007)[148].

Practically all the scientific evidence shown studies the efficacy of psychological interventions based on behavioural therapy (BT) or cognitive behavioural therapy (CBT):

In the SR and MA conducted in the NICE CPG (2009)[2] 10 RCTs of studies published between 1997 and 2007 were included. The psychological interventions of all the studies included are based on cognitive behavioural therapy (CBT). Two RCTs only included preschool children and the intervention consisted in parenttraining(Bor, 2002[149]; Sonuga-Barke, 2001[150]), as in the two RCTs on children with ADHD with an average age of under 8 (Hoath, 2002[151]; Hoofdakker, 2007[152]). Four RCTs included children with ADHD with an average age of over 8 and the psychological intervention consisted in parenttraining and children (Bloomquist, 1991[153]; Fehlings, 1991[154]; Pfiffner, 1997[155]; Tutty, 2003[156]). Finally, 2 RCTs on children with an average age of over 8 included psychological interventions with children (Antshel, 2003[157]; González, 2002[158]). The comparison groups included waiting list, control without treatment and normal treatment.

In the Cochrane MA and SR carried out by Bjornstad & Montgomery (2008)[146] all those quality studies that included family therapy were included. Only 2 RCTs based on CBT satisfied the quality criteria: 1 RCT lasting for 14 months conducted by NIMH-MTA (Jensen, 1999)[39], and 1 RCT by Horn (1991)[159]. In the NIMH-MTA study (1999)[39] a training condition was included for parents + social skills training for the child + intervention at school.In this study, the relevant comparison condition for the MA was the attention group in the community.Horn's study (1991)[159] included the placebo medication alone and placebo medication + family BT intervention conditions in the MA.

Van der Oort, *et al*. (2008)[147] performed a MA that included those quality RCTs that assessed the efficacy of the psychological treatments published between 1985 and 2006, and in which the patients with ADHD has an average age of between 6 and 12. 12 RCTs satisfied the criteria, which included a psychological treatment condition based on CBT principles: Anastopoulos, 1993[160]; Antshel, 2003[157]; Brown, 1985[161], 1986[162]; Fehlings, 1991[154]; Hom, 1990[163]; Hoath, 2002[151]; Klein, 1997[164]; Miranda, 2000[165], 2002[166]; NIMH-MTA, 1999[39]; Pfiffner, 1997[155]; Tutty, 2003[156].

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Variable: ADHD symptoms

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in ADHD symptoms (4 RCTs, N=163, Tutty, 2003[156]; Fehlings, 1991[154]; Hoath, 2002[151]; Bloomquist, 1991[153]) (SMD: -0.25 [95% CI: -0.56 to 0.07]). RCT 1++

There is limited scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in ADHD symptoms (5 RCT, N=288, Tutty, 2003[156]; Sonuga-Barke,2001[150]; Fehlings, 1991[154]; Hoath, 2002[151]; Hoofdaker, 2007[152]) (SMD: =0.57 [CI 95): -1.00 to -0.14]) RCT 1+

There is not sufficient scientific evidence to suggest a positive effect of the psychological intervention compared with treatment in the community on the parents' scores in ADHD inattention symptoms (1 RCT, N=259; Jensen, 199939) (SMD: -0.09 [95% CI: -0.25 to 0.07]), nor hyperactivity/impulsivity (1 RCT, N=259; Jensen, 1999[39]) (SMD: -0.11 [95% CI: -0.29 to 0.07]). RCT 1++

There is not sufficient scientific evidence to suggest a positive effect of the psychological intervention compared with treatment in the community on the teachers' scores in ADHD inattention symptoms (1 RCT, N=247; Jensen, 1999[39]) (SMD: -001 [95% CI: -0.21 to 0.19]), nor hyperactivity/impulsivity (1 RCT, N=247; Jensen, 1999[39]) (SMD: -0.15 [95% CI: -0.35 to 0.05]). RCT 1++

There is limited scientific evidence to suggest a positive effect of the psychological intervention compared with placebo treatment on the teachers' scores in ADHD inattention symptoms (1 RCT, N=25; Horn, 1991[159]) (SMD: -1.98 [95% CI: -6.01 to 2.05]). RCT 1++

In studies with ADHD in school age (6-12), there is limited scientific evidence to suggest a positive effect of the psychological intervention on the parents' scores in ADHD symptoms (13 RCT,N=402; Anastopoulos, 1993[160]; Antshel, 2003[157]; Brown, 1985[161], 1986[162]; Fehlings, 1991[154]; Horn, 1990[163]; Hoath, 2002[151]; Klein, 1997[164]; Miranda, 2000[165], 2002[166]; NIMH-MTA, 1999[39]; Pfiffner, 1997[155]; Tutty, 2003[156]) (SMD: 0.87 [95% CI: -0.73 to 1.01]). RCT 1+

In studies with ADHD in school age (6-12), there is limited scientific evidence to suggest a positive effect of the psychological intervention on the teachers' scores in ADHD symptoms (12RCT, N=381; Anastopoulos, 1993[160]; Antshel, 2003[157]; Brown, 1985[161], 1986[162]; Fehlings, 1991[154]; Hoath, 2002[151]; Klein, 1997[164]; Miranda, 2000[165], 2002[166]; NIMH-MTA, 1999[39]; Pfiffner, 1997[155]; Tutty, 2003[156]) (SMD: 0.75 [95% CI: -0.49 to 1.01]). RCT 1+

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Variable: Behavioural symptoms (ODD, CD)

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in behavioural problem symptoms (3 RCT, N=63 ,Pfiffner, 1997[155]; Hoath, 2002[151]; Bloomquist, 1991[153]) (SMD: -012 [95% CI: -0.61 to 0.38]). RCT 1+

There is limited scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in behavioural problem symptoms (5 RCT, N=231, Bor, 2002149; Sonuga-Barke, 2001[150]; Hoofdaker, 2007[152]; Pfiffner, 1997[155]; Hoath, 2002[151]) (SMD: -0.54 [95% CI: -1.05 to =0.04]). RCT 1+

In studies with ADHD in school age (6-12), there is limited scientific evidence to suggest a positive effect of the psychological intervention on the parents' scores in behavioural problem symptoms (7 RCT, N=381; Brown, 1986[162]; Horn, 1990[163], 1987[167]; Klein, 1997[164]; Miranda, 2000[165], 2002[166]; MTA, 1999[39]) (SMD: 0.43 [95% CI: -0.26 to 0.60]). RCT 1+

Variable: Social skills

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychologica intervention has positive effects on the teachers' scores in the child's social skills (1 RCT, N=18, Pfiffner, 1997[155]) (SMD: -0.40 [95% CI: -033 to 0.54]). RCT 1+

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in the child's social skills (2 RCT, N=138, Antshel, 2003[157]; Pfiffner, 1997[155]) (SMD: -0.59 [95% CI: -1.80 to 0.61]). RCT 1++

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the children's scores in social skills (1 RCT, N=120, Antshel, 2003[157]) (SMD: -0.23, (95% CI: -0.61 to 0.15]). RCT 1++

In studies with ADHD in school age (6-12), there is limited scientific evidence to suggest a positive effect of the psychological intervention on the parents' scores in the child's social skills (5 RCT, N=292; Antshel, 2003[157]; Brown, 1986[162]; Klein, 1997[164]; MTA, 1999[39]; Pfiffner, 1997[155]) (SMD: 0.54 [95% CI: 0.37 to 0.70]). RCT 1+

In studies with ADHD in school age (6-12), there is limited scientific evidence to suggest a positive effect of the psychological intervention on the teachers' scores in the child's social skills (5 RCT, N=203; Brown, 1986[162]; Miranda, 2000[165], 2002[166]; MTA, 1999[39]; Pfiffner, 1997[155]) (SMD: 0.71 [95% CI: 0.51 to 0.92]). RCT 1+

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Variable: Internalized symptoms

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores ininternalizing symptoms (1 RCT, N=18, Pfiffner, 1997[155]) (SMD: -0.20 [95% CI: -1.12 to 0.73]). RCT 1+

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores ininternalizingsymptoms (2 RCT, N=112, Hoofdaker, 2007[152]; Pfiffner, 1997[155]) (SMD: -0.36 [95% CI: -0.73 to 0.01]). RCT 1++

Variable: self-efficacy

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the children's scores in self-efficacy (3 RCT, N=78, Bloomquist, 1991[153]; Fehlings, 1991[154]; González, 2002[158]) (SMD: -0.03 [95% CI: -0.48 to 0.42]). RCT 1++

Variable: academic functioning

Scientific evidence

There is limited scientific evidence to suggest that the psychological intervention has positive effects on the academic functioning in children at school age (6 RCT, N=274, Brown, 1985[161]; Horn, 1990[163], 1987[167]; Miranda, 2002[166]; MTA, 1999[39]; Klein, 1997[164]) (SMD: 0.19 [95% CI: 0.03 to 0.36]). RCT 1+

More results

Scientific evidence

One RCT that studies the efficacy of the therapeutic programme "Child Life and Attention Skills Program" (mixed house/school implementation), by Linda Pfiffner for inattention subtype ADHD, randomised a sample of 69 school children with ADHD-HI (recruited from school population, not clinical), showing that the treatment group, compared with the control group, presented an improvement in inattention symptoms, "sluggish cognitive tempo", social and organisational skills (Pfiffner, 2007)[148]. RCT 1+

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In 2006, NICE[168] published an assessment report on the efficacy of parenttraining in children with behavioural disorders. Seven of the studies included patients with ADHD.It was concluded that the parents training programmes for of children with behavioural disorders, mainly oppositional defiant disorder (ODD), were efficient under the following conditions: - Structured and based on social learning theory principles. Including strategies to improve the parent-child relationship. Optimal number of sessions: 8-12. - In group or individual format. - It would enable parents to identify their own objectives. - Incorporated *role-playing* sessions and *homework to* improve the generalisation. - Led by properlytrained professionals. - Based on manual and standardised materials.	SR of RCT 1++
In the NICE Technology Assessment report (2006)[168] scientific evidence was found of the efficacy of training for parents in children with behavioural disorder based on the results of the SR of quality 1++ assessed: Barlow & Stewart-Brown, 2000[169]; Richardson & Joughin, 2002[170]; Serketich, 1996[171]. They also found scientific evidence of the medium and long-term effectiveness (Dimond y Hyde, 1999)[172].	SR of RCT 1++,
In the studies included in the analysis of the scientific evidence of the psychological intervention on ADHD, both parenttrainiand (social and self-control) skills training for children appeared in a predominant way, it being difficult to determine which of the components has a greater impact on the efficacy; if one of them or the combination of both NICE[2].	MA of RCT 1++
In the MA by Van der Oord *et al*. (2008)[147], in general, greater efficacy effects on the ADHD symptoms have been found in those studies with a mainly behavioural treatment, compared with cognitive-behavioural type studies; these differences are not statistically significant. Although there are statistically significant differences in the efficacy of the behavioural interventions compared with the behavioural cognitive interventions on the scores for ADHD symptoms or behavioural problems according to the teachers, they do find differences in the ADHD symptom scores according to the parents, in favour of behavioural interventions.	MA of RCT 1+
The cognitive-behavioural interventions for school-age children with ADHD must ideally last for 8 to12 sessions of 50-90 minutes of CBT/SK for children + 8 sessions of 50 to 120 minutes for parents (NICE, 2009)[2].	Experts opion 4

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Summary of scientific evidence

There is scientific evidence from several RCTs of quality (1+) about the efficacy of psychological interventions (CT/CBT) on ADHD and behavioural symptoms referred by parents (NICE-2009)[2].	SR of RCT 1+
There is not sufficient scientific evidence or there is only limited scientific evidence about the efficacy of psychological interventions on ADHD and behavioural symptoms referred by teachers (NICE, 2009)[2].	SR of RCT 1+

The scientific evidence about the efficacy of psychological interventions on social skills from studies of quality (1+) (NICE, 2009)[2].	SR of RCT 1+
There is not sufficient scientific evidence about the efficacy of psychological therapy oninternalizedand self-efficacy symptoms (NICE, 2009)[2].	SR of RCT 1++
There is limited scientific evidence from studies of quality 1+ about the efficacy of psychological therapy on academic functioning (NICE, 2009)[2].	SR of RCT 1+
One RCT offers results with respect to the efficacy of psychological treatment on inattention symptoms, sluggish cognitive tempo, social and organisational skills in a subgroup of school children with ADHD-HI (Pfiffner, 2007)[148].	RCT1+
There is strong evidence that training for parents is effective for behavioural disorder, including a population with ADHD (NICE, 2006)[168]	SR of RCT 1++
The inclusion of training programmes for parents also increases the acceptability of the treatments and relieves parental malaise (SIGN, 2005)[1].	Experts' opinion 4

Recommendations

B	7.1.2.1.	The application of a behavioural training programme is recommended for parents of children and adolescents diagnosed with ADHD, with or without comorbidity.
D	7.1.2.2.	Cognitive-behavioural therapy is recommended as an initial treatment for ADHD in children and adolescents in any of the following situations: • The ADHD symptoms are mild • The impact of ADHD is minimal • There is considerable discrepancy about the frequency and intensity of symptoms between parents, or between these and the teachers • The diagnosis of ADHD is uncertain • Parents reject the use of medication • Children under 5 (although this age group is outside the scope of this guide).

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7.1.3. Psychological treatment of children and adolescents: Has it proved to be efficient/effective in the short and long term?

The answer is based on the NICE (2009)2, SIGN (2005)[1] guidelines, and on the study by NIMH-MTA (2004)[173]. The search has been updated with a RCT published in 2007 (Pfiffner, *et al*., 2007)[148].

Variable: ADHD symptoms

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in ADHD symptoms 6 months after treatment (2 RCT, N=101, Tutty, 2003[156]; Fehlings, 1991[154]) (SMD: -0.05 [95% CI: -0.4 to 0.35]). RCT 1++

There is scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in ADHD symptoms 6 months after the intervention (3 RCT, N=174, Tutty, 2003[156]; Sonuga-Barke, 2001[150]; Fehlings, 1991[154]) (SMD: -0.91 [95% CI: -1.23 to -0.59]). RCT 1++

No differences were found in the NIMH-MTA study in the ADHD symptoms after one year's follow-up between the group of patients with ADHD who received behavioural treatment and the group of patients with ADHD that received normal community treatment (MTA, 2004)[173]. RCT 1+

Variable: Behavioural symptoms (ODD, CD)

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in behavioural problem symptoms 3 to 4 months after treatment (1 RCT, N=18, Pfiffner, 1997[155]) (SMD: -0.13 [95% CI:-1.05 to 0.80]). RCT 1+

There is scientific evidence to suggest that the psychological intervention has positive effects on the parent's scores in behavioural problem symptoms, 3 to 5 months after treatment (2 RCT, N=68, Sonuga-Barke, 2001[150]; Pfiffner, 1997[155]) (SMD: -0.51, (95% CI: -1.01 to -0.01]). RCT 1++

No differences were found in the NIMH-MTA study in behavioural disorder symptoms after one year's follow-up between the group of patients with ADHD that received behavioural treatment and the group of patients with ADHD that received normal community treatment (MTA, 2004)[173]. RCT 1+

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Variable: Social skills

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in the child's social skills 3 months after treatment (1 RCT, N=18, Pfiffner, 1997[155]) (SMD: -0.06 [95% CI: -0.98 to 0.18]). RCT 1+

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in the child's social skills 3 months after treatment (2 RCT, N=138, Antshel, 2003[157]; Pfiffner, 1997[155]) (SMD: 0.06 [95% CI: -0.29 to 0.42]). RCT 1++

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the children's scores in social skills 3 months after treatment (1 RCT, N=120, Antshel, 2003[157]) (SMD: 0.04 [95% CI: -1,11 to 0.74]). RCT 1++

Variable: Internalized symptoms

Scientific evidence

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the teachers' scores in internalizedsymptoms 3 months after treatment (1 RCT, N=18, Pfiffner, 1997[155]) (SMD: -0.19 [95% CI: -1.11 to 0.74]). RCT 1+

There is not sufficient scientific evidence to suggest that the psychological intervention has positive effects on the parents' scores in internalizedsymptoms 3 months after treatment (1 RCT, n=18, Pfiffner, 1997[155]) (SMD: 0.04 [95% CI: -0.89 to 0.96]). RCT 1+

Variable: Self-efficacy

Scientific evidence

There is limited scientific evidence to suggest that the psychological intervention has positive effects on the children's scores in self-efficacy 5 months after treatment (1 RCT, N=26, Fehlings, 1991154) (SMD: -0.89 [95% CI: -1.70 to 0.08]). RCT 1+

More results

Scientific evidence

In the 2007 RCT that studies the efficacy of the therapeutic programme "Child Life and Attention Skills Program" (mixed home/school implementation), by Linda Pfiffner for inattention subtype ADHD, the improvement in the symptoms of inattention, sluggish cognitive tempo, social and organisational skills, was maintained 3 months after treatment (Pfiffner, *et al*., 2007)[148]. RCT 1+

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Summary of scientific evidence

There is strong scientific evidence to suggest that psychological intervention maintains positive effects on ADHD and behavioural problem symptoms referred to by parents in the short-medium term follow-up (3-6 months) (NICE, 2009)[2].	RCT 1++
There is limited scientific evidence to suggest that the psychological intervention has positive effects on self-efficacy in the short-medium term follow-up (3-6 months). However, positive results were not obtained in the post-treatment assessment, so it is difficult to attribute the improvement to the specific psychological intervention on self-efficacy; this may possibly be due to a secondary benefit of the behavioural intervention on ADHD and behavioural alterations (NICE, 2009)[2].	RCT 1++
There is no scientific evidence that the psychological intervention has positive effects on the short-term follow-up (3-6 months) on ADHD and behavioural problem symptoms referred to by teachers, social skills and internalized symptoms (NICE, 2009)[2].	RCT 1++

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7.1.4. How effective is the psychological treatment of ADHD in children and adolescents?

The answer is based on the NICE guideline (2009)[2] and on the RCT by Hoofdaker (2007)[152].

Summary of scientific evidence

The NICE guideline has conducted a cost-effectiveness study of the training interventions for parents of children with ADHD, both in group format and individually (NICE, 2009)[2]. Those quality studies that included a behavioural intervention for parents were included, both at group level (Hoath, 2002)[151], and individually (Sonuga-Barke, 2001[150]; Bor, 2002[149]). The analysis concludes that the behavioural training treatment for parents in group format is more cost-effective than in individual format.	Cost-effectiveness study 1++
A recent study has assessed the effectiveness in clinical practice of the training treatment for parents, as a contribution to the normal community treatment in patients and families (Hoofdaker, 2007[152]). The study randomly distributed 96 patients into two groups:training for parents + normal treatment compared with normal treatment.The results of the effectiveness in post-treatment and at the 6-month follow-up were analysed.The normal treatment + parenttrainingwas superiorto normal treatment inreducingbehavioural problems and internalizedsymptoms.No differences were found in ADHD symptoms and parental stress.The improvement in behavioural and internalizedsymptoms was maintained in the mid-term follow-up (6 months)	RCT 1+

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7.1.5. In ADHD in children and adolescents:What clinical variables and standardised instruments exist to evaluate the efficacy of psychological treatment?At what moment of the treatment should its efficacy be evaluated?

The response is based on the experts' opinions.

Summary of scientific evidence

The development group considers that to evaluate the efficacy of the psychological treatment, clinical variables will be taken into account, such as the intensity of the nuclear and associated symptoms, the family, academic and social repercussion.The information of the teachers and/or the information obtained via the standardised tools will be assessed based on the clinical interview with the child and parents.	Experts' opinion 4

See chapter 6. *Assessment tools*, where the main assessment tools for ADHD in children and adolescents used in our medium are reviewed.

Recommendations

√	7.1.5.1.	The efficacy, possible adverse effects and therapeutic compliance must be assessed in psychological treatment programmes of children and adolescents with ADHD. The assessment of the treatment will be carried out 3 months after the start, at the end (in case of having a defined time limit), or when the clinician deems this appropriate.

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7.2. Psychopedagogical Treatment

Questions to be answered:

7.2.1. Psychopedagogicalintervention: What does it consist of? What must it include?

7.2.2. Which psychopedagogical interventions are efficient/effective to treat ADHD?

7.2.3. Psychopedagogicalre-education: What does it consist of? What must it include?

7.2.4. In ADHD in children and adolescents? What adaptations are useful/recommendable in the school context?

7.2.5. Is the training given to teachers efficient/effective? What must it include?

7.2.6. In ADHD in children and adolescents: What clinical variables and standardised instruments exist to evaluate the efficacy of psychopedagogical treatment? At what moment of the psychopedagogical treatment should its efficacy be evaluated?

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7.2.1. Psychopedagogical intervention: What does it consist of? What must it include?

The psychopedagogical intervention represents a series of institutionalised intervention practices in the learning field, either as prevention and treatment of disorders, or as a modification of the school learning process (Castorina et al., 1989)[174]. The psychopedagogical intervention seeks to understand the teaching-learning processes in school and in out-of-school contexts, and efficiently intervene in their improvement, allowing the student to address the learning situations in a more efficient manner.

7.2.2. Which psychopedagogical interventions are efficient/effective to treat ADHD?

The answer is based on the SIGN guideline (2005)[1], the review by Wells et al. (2000)[175] on Irvine's Paraprofessional Programme (used in the MTA study), the study of the programme by Langberg et al. (2008)[176] and the MA by DuPaul *et al*. (1997)[177].

Many experiments have been carried out with interventions in schools to improve the academic functioning of children and adolescents with ADHD, some of them with a multimodal or multisystemic nature such as Irvine's Paraprofessional Programme, used in the MTA study, which includes individual interventions with the children and also training for teachers and parents, all of which has the aim of improving the general academic performance.

Scientific evidence

The Irvine Paraprofessional Program (Wells, *et al*., 2000)[175] is an educational intervention based on behaviour modification techniques, designed to treat problems at school for children with ADHD. The results of Wells, et al. (2000)[175] show the importance of generalising intervention programmes in the classrooms.

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More specific interventions have also shown an improvement in general academic performance.A specific teaching system in academic skills and competences is relatively easier and simpler to execute than other multi-programmes. RCT 1+

One of these systems would be the individual intervention proposed by Langberg *et al*.(2008)[176] to teach academic skills to children with ADHD to held them be successful in the school environment, covering the organisation and management of tasks, and fostering adequate behaviours to carry them out (working in silence, raising their hands, persistence in the task, etc.).

The MA by DuPaul, *et al*. (1997)[177] on psychosocial interventions in the school context points out that contingency management strategies and academic interventions are more effective for behavioural change than cognitive-behavioural strategies for children with ADHD. MA of RCT 1+

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Summary of scientific evidence

The SIGN guideline (2005)[1] indicates that children with ADHD require a personalised school intervention programme that includes both academic or instruction actions, and behavioural actions.	MA of RCT1+
The psychopedagogical interventions have shown an improvement in general academic performance (Langberg, et al., 2008)[176]	RCT 1+

Recommendations

B	7.2.2.1.	Children and adolescents with ADHD require a personalised intervention programme in school that will include academic, social and behavioural aspects (adapted from SIGN 4.1.2)[1].
√	7.2.2.2.	The school programmes for ADHD must involve the majority of the teaching staff to facilitate its efficacy.
√	7.2.2.3.	School programmes for ADHD may include: Adaptations in the classroom, training for teachers, behaviour modification techniques and other strategies to handle ADHD in the classroom (application of rules and limits, presentation of tasks, assessment systems for students with ADHD, etc.)

7.2.3. Psychopedagogicalre-education: What does it consist of? What must it include?

Psychopedagogical re-educationis personalised school tutoring that is provided during or after school hours and whose aim is to palliate the negative effects of ADHD in children or adolescents who suffer from it, in connection with their academic competence or learning.Emphasis is placed on the negative impactof the attention deficit, impulsivity and hyperactivity in the school learning process.

Psychopedagogical re-education must include actions aimed at:

- Improving the academic performance in the different areas, instrumental areas and the more specific areas for each school year.

- Working on habits that foster appropriate behaviour for learning (such as managing the timetable and controlling the school agenda) as well as study techniques (prereading, careful reading, analysis and underlining, synthesis and diagrams or summaries).
- Preparing and teaching strategies to prepare for exams.
- Improving self-esteem with respect to the tasks and study, identifying positive skills and increasing motivation for achievement.
- Teaching and promoting appropriate and facilitating behaviour for correct study and compliance with tasks.
- Reducing or eliminating maladaptativebehaviour such as defiant behaviour and bad organisation habits.
- Maintaining coordination actions with the specialist that is treating the child or adolescent and with the school, to establish common goals and offer the teacher strategies to manage the child or adolescent with ADHD in the classroom.
- Intervening with parents to teach them to put into practice, monitor and foster the continued use of study organisation and management tasks at home.

The response is based on the study of the programme of Langberg *et al*. (2008)[176].

Summary of scientific evidence

Langberg, et al. (2008)[176] examined the efficacy of a psychopedagogical organisational skill intervention programme for children with ADHD (n=37). Participations in the intervention group achieved a significant improvement, unlike the control group, in organisation and competences to do homework during the intervention.The improvement was maintained for 8 weeks.The children in the intervention group also showed improvements in the teachers' scores in academic performance (SMD:87) and lower parents' scores in problems in doing homework (SMD: 71). This study suggests that applying interventions focused on organising competences has the potential of improving general academic performance in children with ADHD.	RCT 1+

Recommendations

√	7.2.3.1.	Personalised and specific treatment of teaching in academic competences and skills is recommended for children and adolescents with ADHD and repercussion on academic performance.

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7.2.4. In ADHD in children and adolescents: What adaptations are useful/recommendable in the school context?

Interventions carried out at school must contemplate any adaptations considered necessary, which should include some or all of the following (Mena, et al., 2007)178:

- Use behaviour modification techniques: positive tutoring, token economy systems, modelling, extinction, response cost, time-out technique, overcorrection, etc.
- Teach the child or adolescent training techniques in self-control, problem-solving, social skills training or relaxation techniques.
- Clearly define, together with the child or adolescent, the short and long-term goals, both referring to curricular contents and to their behaviour at school.
- Adapt the environment and control the level of distracting elements in the classroom, situating the child or adolescent in a place where they can easily be supervised and at a distance from any stimuli that might distract them.
- Adapt the tasks and expectations to the child's or adolescent's traits, and, if necessary, reduce the requirement level or simply the instructions given to them to carry out the tasks, using short, simple and clear instructions.
- Adapt the assessment method, modifying the way of administering and assessing the tests and examinations.
- Supplement the oral instructions with visual instructions and reminders.
- Offer the child or adolescent aid systems to control their tasks every day, and complete short and long-term tasks (control of agenda, reminders, etc.).
- Achieve an adequate level of motivation in students, offering frequent feedback about their improvements in behaviour and effort.

The answer is based on the NICE (2009)[2], ICSI (2007)[179] and AAP (2001)[180] guidelines.

The NICE CPG (2009)[2] has conducted a SR and MA of studies that assess the efficacy of the teacher's interventions (academic and environmental adaptations), and only one study was found that compared the intervention of the teacher with non-invention (Kapalka, 2005)[181].

Scientific evidence

The ICSI guideline (2007)[179] indicates that non-pharmacological interventions, such as managing contingencies and educational modifications and adaptations in the classroom, have shown that they help children with ADHD cope and compensate for their academic and social difficulties associated with the disorder. Experts' opinion 4

The AAP guideline (2001)[180] indicates that when ADHD has a significant impact on the child's academic competence, schools must make adaptations to help them in the classroom. Experts' opinion 4

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Teacher's adaptations

Scientific evidence

There is limited scientific evidence to the extent that the adaptations in the school context have positive effects on the behaviour problems in the classroom (1 RCT, N=86, Kapalka, 2005[181]) (SMD: -1.47 [95% CI: -1.94 to -0.99]). RCT1+

Summary of scientific evidence

The NICE guideline (2009)[2] indicates that children and adolescents with ADHD require a school intervention programme that includes academic and behavioural actions, and recommends that teachers who have received training in ADHD should provide them with behavioural interventions in the classroom (Kapalka, 2005)[181]	RCT 1+

Recommendations

B	7.2.4.1.	When ADHD has a significant impact on the child's or adolescent's academic competence, the schools should make adaptations to help them in the classroom.

7.2.5. Is the training given to teachers efficient/effective? What must it include?

Teachers are often the first to identify a child or adolescent with ADHD. Anyone who does not have proper training in the disorder may not suitably appraise the alert signals.

The training programmes for teachers should include:

- General information about the disorder: symptoms, comorbidity, nature, incidence, development, prognosis, treatment and impacton behaviour and learning.
- Behavioural modification techniques aimed at increasing or maintaining desirable behaviour and at eliminating or reducing undesirable behaviour in children or adolescents with ADHD.
- Cognitive techniques: For learning and practice of self-instructions and training in self-control in children and adolescents with ADHD.
- Educational strategies with adaptations aimed at improving functioning in the classroom and learning.

The answer is based on the NICE guideline (2009)[2], the review by Miranda, et al. (2006)[182] and the study by Ohan, et al. (2008)[183].

Information to teachers about ADHD

The NICE CPG (2009)[2] has conducted a SR and MA on studies that assess the efficacy of giving information to teachers about ADHD. 3 studies have been included from the search. In one study, a leaflet was sent to the teachers with information about ADHD, as well as management strategies in the classroom that had previously proved to be efficient (DuPaul & Eckert, 1997[177]; Purdie,

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2002[184]; Tymms, 2006)[185]. This same study also assessed the effectiveness of this intervention, adding explicit information about which of their students may have ADHD (via a screening questionnaire in the classroom) (Tymms, 2006)[185]. In a third study, information was sent to teachers at the start of the year (CHADD Educators' Manual; Fowler, *et al*., 1992)[186], and updates were sent of this same information, accompanied by suggestions from parents that emerged from the parents' training (Corkum, *et al*., 2005)[187].

Scientific evidence

There is not sufficient scientific evidence about whether informing teachers via a leaflet on ADHD has possible effects on the ADHD symptoms (1 RCT, N=25.482; Tymms, 2006)[185] (SMD: -0.19 [95% CI: -0.39 to 0.01]), performance in mathematics (1 RCT, N=25,482; Tymms, 2006)[185] (SMD: -0.05 [95% CI: -0.18 to 0.09]), and reading (1 RCT, N=25.482; Tymms, 2006[185]) (SMD: -0.02 [95% CI: -0.17 to 0.12]). RCT 1+

There is limited scientific evidence about whether information to teachers via a leaflet on ADHD, adding explicit informationabout which of their students may have ADHD (via a screening questionnaire in the classroom) may have positive effects on performance in mathematics (1 RCT, N=25,482; Tymms, 2006[185]) (SMD: 0.15 [95% CI:-0.01 to 0.28]), and reading (1 RCT, N=25.482; Tymms, 2006[185]) (SMD:0.19 [95% CI: -0.04 to 0.34]). On the contrary, there is not sufficient scientific evidence about the effect on ADHD symptoms (1 RCT, N=25,482; Tymms, 2006)[185] (SMD: -0.13 [95% CI: -0.32 to 0.07]). RCT 1+

There is limited scientific evidence about whether information to teachersaccompanied by training for parents has positive effects on the ADHD symptoms (1 RCT, N=30, Corkum, 2005[187]) (SMD: -1.15 (CI 95%: -2.03 to -0.28]), not on behavioural symptoms (1 RCT, N=30; Corkum, 2005[187]) (SMD: 0.08 [95% CI: -0.88 to 0.72]). RCT 1+

Ohan *et al*. (2008)[183] conducted a study with teachers (n=140), which investigated their knowledge of ADHD and its impact on behaviour reports, and their perceptions of children with ADHD. The results suggest that the teachers showed a good general knowledge of ADHD, knowledge of the symptoms and diagnosis, and limitation in the knowledge of the etiology and treatment. Observational study 2+

The results suggest that a high percentage of teachers have a good knowledge of ADHD and that this has a positive impact on their behaviour and perceptions (e.g. to seek help for children with ADHD and/or perceive the benefit of treating a child) and cooperate with the ADHD professionals.

However, they also predicted that these children would have a more disruptive behaviour in the classroom, and they informed of less confidence in their skills to manage these children.

Training teachers

Training teachers includes psychoeducation about the disorder, modification of dysfunctional opinions with respect to it, and training in behavioural patterns.

The NICE CPG (2009)[2] has conducted a SR and MA on studies that assess the efficacy of training teachers, finding one single quality study (Bloomquist, 1991)[153].

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Scientific evidence

There is not sufficient scientific evidence that training for teachers compared with non-intervention has positive effects on the scores in ADHD symptoms (1 RCT, N=52, Bloomquist, 1991)[153] (SMD: -0.13 [95% CI: -0.82 TO 0.57]), or on behavioural problems (1 RCT, N=52, Bloomquist, 1991[153]) (SMD: -0.33 [95% CI: -1.03 to 0.37]). RCT 1+

There is not sufficient scientific evidence that training for teachers in multimodal treatment, compared with non intervention, has positive effects on the scores in ADHD symptoms (2 RCT, N=361, Bloomquist, 1991[153]; Braswell, 1997[188]) (SMD: -0.13 [95% CI: -0.80 to 0.53]), or on behavioural problems (2 RCT, N=361, Bloomquist, 1991[153]; Braswell, 1997[188]) (SMD: -0.49 [95% CI: -1.16 to 0.18]). RCT 1-

There is not sufficient scientific evidence that training for teachers in multimodal treatment, compared with training for teachers, has positive effects on the scores in ADHD symptoms (1 RCT, N=52, Bloomquist, 1991153) (SMD:0.05 [95% CI:-0.39 to 0.50]), or on behavioural problems (1 RCT, N=52, Bloomquist, 1991153) (SMD: -0.09 [95% CI: -0.57 to 0.56]). RCT 1+

A recent study conducted in Spain (Miranda, 2006)[182] emphasises the importance of training teachers in the management of ADHD combined subtype, achieving by way of a psychopedagogical intervention (based mainly on a training programme of 8 sessions lasting for 3 hours each) a significant reduction in the hyperactivity and impulsivity symptoms in agreement with the teachers' scores.In addition, an improvement was observed in the lack of attention and disorganisation, although it was not significant with respect to the control group. RCT 1+

Recommendations

√	7.2.5.1.	It is recommendable for teachers to receive training that enables them to detect ADHD alert signals and to manage ADHD in children and adolescents at school.

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7.2.6. In ADHD in children and adolescents
What clinical variables and standardised instruments exist to evaluate the efficacy of psychopedagogical treatment
At what moment of the psychopedagogical treatment should its efficacy be evaluated?

The response is based on the experts' opinions.

Summary of scientific evidence

The development group considers that to evaluate the efficacy of the psychopedagogical treatment, clinical variables will be taken into account, such as the intensity of the nuclear and associated symptoms, the family, academic and social repercussion.The information from the teachers and/or the information obtained via the standardised tools will be assessed based on the clinical interview with the child and parents.	Experts' opinion 4

See chapter 6. *Assessment tools*, where the main assessment tools for ADHD in children and adolescents used in our medium are reviewed.

Recommendations

√	7.2.6.1.	The efficacy and possible adverse effects of psychopedagogical intervention that is being carried out must be assessed in the psychopedagogical treatment programmes of children and adolescents with ADHD at least once every school year whilst the treatment lasts.

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7.3. Pharmacological treatment

Questions to be answered:

7.3.1. What drugs for ADHD are available in Spain?

7.3.2. In ADHD: What pharmacological treatments are efficient/effective? How safe are the pharmacological treatments?

7.3.3. In ADHD: How effective are pharmacological treatments in the short and long term?

7.3.4. In ADHD: When and with what criteria must pharmacological treatment be started?

7.3.5. In ADHD: What criteria are used to choose the drug? What are the start, suppression and maximum dose guidelines? Which are the first and second choice drugs?

7.3.6. What are the most frequent (short term) side effects? How must the side effects be addressed?

7.3.7. In ADHD: How long should the pharmacological treatment last?

7.3.8. In ADHD: Are supplementary examinations required before starting the pharmacological treatment in children and adolescents?

7.3.9. What is the pharmacological strategy when there is a partial response, side effects or contraindication?How are the different methylphenidate presentations combined?How to make the transition from stimulants to atomoxetine?

7.3.10. In which ADHD subtypes is pharmacological treatment more efficient?

7.3.11. Are there differences in response depending on the gender or age?

7.3.12. Which physical parameters must be controlled before starting the pharmacological treatment and during it?

7.3.13. What scientific evidence exists about the long-term effects in pharmacological treatment? Is it associated with growth retardation?

7.3.14. Pharmacological treatment of ADHD: Does it cause addiction? Does it increase the risk of consumption of substances?

7.3.15. Does the efficacy of pharmacological treatment decrease with time?

7.3.16. Do the effects remain after the pharmacological treatment has been withdrawn?

7.3.17. Is it recommendable to leave stimulant-free periods during the pharmacological treatment ("therapeutic holidays")?

7.3.18. What clinical variables and standardised instruments exist to evaluate the efficient of pharmacological treatment?At what moment of the treatment should its efficacy be evaluated?

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7.3.1. What drugs for ADHD are available in Spain?

Introduction

The beneficial effect of stimulants to treat patients with hyperkinetic behaviours has been known for more than 70 years (Bradley, 1937)[5]. In the United States, both methylphenidate and dexamphetamine have been available since 1955. In Spain, the Rubio laboratories sold immediate release methylphenidate for the first time in 1981 (Taylor, 2004)[189]. Over the last 5 years, with the introduction into the market of extended release methods and of non-stimulant medication such as atomoxetine, an important change has occurred with respect to the pharmacological treatment strategies available for addressing ADHD in Spain.

There are other drugs that are not indicated for ADHD that clinicians use much less frequently to treat patients with ADHD, such as:clonidine, bupropion, modafinil reboxetine, imipramine, risperidone and aripiprazole.These drugs are listed in **Table 7**.

Table 7. Drugs used to treat symptoms of ADHD[190]

Chemical type	Active principle
Psychostimulants	Methylphenidate*
Selective Serotonin Reuptake Inhibitors	Atomoxetine**
Adrenergic agents	Clonidine***
Antidepressants	Bupropion*** Venlafaxine*** Tricyclic antidepressants*** OMAI (oxidase monoamine inhibitors)*** Reboxetine***
Dopaminergic agents	Modafinil***

* Indication approved for ADHD in Spain.

** Indication approved for ADHD in Spain on 07-04-2006. Pursuant to RD 1344/2007 which regulates the pharmovigilance of medicines for human use, the owner is obliged to include the pictogram in all the catalogues, promotional material and any other type of material for dissemination to health professionals, during the first five years following the authorisation.

*** On not having approved indication for ADHD, RD 1015/2009, which regulates the availability of medicines in special situations, will be complied with.

Methylphenidate

Methylphenidate is a CNS stimulant. The action mechanism that reduces the ADHD symptoms is not known with accuracy, although it is believed that it increases the concentrations of noradrenaline and dopamine in the front cortex and subcortical regions associated with motivation and reward (Volkow, *et al*., 2004)[191]. A selective inhibition of the presynaptic dopamine transporter occurs, inhibiting the reuptake for dopamine and noradrenaline (Bezchlibnyk *et al*., 2004)[192].

Methylphenidate is a drug indicated as part of the holistic treatment of ADHD in children over 6 and adolescents when other measures are insufficient (technical data sheet).In Spain, it is sold as immediate release and extended release formulations.

The absorption of methylphenidate is fast (less than 30 minutes) and almost complete. However, its absolute bioavailability is low, around 30%, due to a pronounced first step. The union

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to proteins is 15% and there are no active metabolites. It is metabolised by de-sterification to ritalinic acid (which is not found in the drug detection tests in urine) and parahydroxy-MPH. It is not affected by citochrome P450. It is excreted by renal way, and the absorption and bioavailability of methylphenidate vary from one individual to another.The maximum plasmatic concentrations are reached, on average, between 1 and 2 hours after administering immediate action products.It has a relatively short half-life, between 1 and 4 hours.Therefore, immediate release methylphenidate requires three doses a day to achieve maximum effective coverage 12 hours a day.

The need to administer multiple doses entails several problems, such as: Forgetting to take a dose, difficulties to administer the drug at school (when to administer it, where to store it) and the stigmatisation of the child on taking medicine in front of companions (NICE 2009[2].

These problems gave rise to the need to develop extended release methylphenidate products to achieve a longer duration of the effect with one single dose.These drugs are taken once a day in the morning, achieving an initial effect that is similar to that of the administration of a dose of immediate action methylphenidate, followed by a progressive release of methylphenidate whose duration varies between 8 and 12 hours depending on the product.

Dosage of methylphenidate

Immediate release methylphenidate

The treatment must start with low doses, which will progressively be increased. Start with 2.5 or 5 mg (depending on the weight of the child or adolescent), two or three times a day (breakfast, lunch and tea; no later than 5 pm) and increase 2.5 - 5mg a week depending on the clinical response and the presence of side effects.The dose ranges from 0.5 to 2 mg/kg/day with a maximum daily dose of 60 mg per day, according to the prospectus.The *plateau* effect is obtained 3 weeks after continuous treatment.To reduce anorexia, it can be administered with the meals or after them.

The presentations of immediate release methylphenidate available today in Spain are 5 mg, 10 mg and 20 mg.

Extended action products consist of a mixture of methylphenidate, of immediate action and extended release. The difference between them is the proportion of both components and in the release mechanism used (Taylor, *et al*., 2004)[192].

Extended release methylphenidate with osmotic technology (OROS)

This has been sold in Spain since April 2004. The active principle (methylphenidate) coats the tablet as well as being on the inside and its structure permits its gradual and progressive release over a period of 12 hours after one single morning dose.It must be taken in the morning, swallowed, not chewed or broken up.Although the technical data sheet in Spain recommends not exceeding the dose of 54 mg/day, in other countries, the technical data sheet of the product considers doses of up to 72 mg/day in adolescents. However, this recommendation does not take into account the patient's weight. Some authors (Banaschewski, *et al*., 2006)[193] and guidelines (NICE, 2009[2]; AACAP, 2007[72]) indicate higher maximum doses, up to 2 mg/kg/day, not exceeding 108 mg/day.

Extended release methylphenidate with pellet technology

It has been sold in Spain since the end of 2007. This is a drug manufactured in Germany that uses pellet technology.The therapeutic effect starts 30 minutes after administration, once the immediate release portion has dissolved in the stomach.The extended release part has a gastric protection coating that resists the acid medium, so the absorption taken place when it reaches the duodenum. It is administered in single doses in the morning, and its action lasts for 8 hours. The capsules can be opened, making them easy to administer to patients who have swallowing difficulties.

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This does not modify the bioavailability (Mardomingo, 2007)[194]. In this case, the content of the capsule is sprinkled onto a small spoonful of yoghurt, jam, etc., and is taken immediately with a little fluid.

In order to guarantee the plasmatic concentration curve, it must be taken after a meal, as the permanence in the acid medium of the stomach must be guaranteed for sufficient time for the extended action pellets, which have a gastric juic resistant coating, to dissolve in the small intestine.The decisive factor is not the fatty content of the food, but that the food should be solid (e.g. muesli, bread, hot meal).

It is advisable not to exceed the dose of 2 mg/kg/day or a total dose of 60 mg/day of extended release methylphenidate with pellet technology.

The presentation of psychostimulants with extended release available in Spain is listed in **Table 8**.

Table 8. Presentation of extended release psychostimulants in Spain.

Product	Osmotic technology	Pellet technology
Technology	OROS	Pellets
Presentation	18, 27, 36, 54 mg	10, 20, 30, 40 mg
Immediate action	22% 4, 6, 8,12 mg	50% 5, 10.15, 20 mg
Extended action	78% 14, 21, 28, 42 mg	50% 5, 10, 15, 20 mg

Adverse effects of methylphenidate (technical data sheet)

The most frequent adverse effects of methylphenidate are: loss of appetite and weight, insomnia, anxiety, restlessness, nervousness, headaches, stereotypal movements, tics, increase in heart rate and blood pressure. Psychoses and mania induced by the drug are much more rare (Wolraich [et al.], 2007)[195].

Contraindications of methylphenidate:

- Sensitivity to psychostimulants.
- Glaucoma.
- Cardiovascular disease.
- Hyperthyroidism.
- High blood pressure.
- Anorexia nervosa

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Atomoxetine

This is a non-stimulant drug indicated for treating children aged 6 years upwards and adolescents diagnosed with ADHD.

The action mechanism to treat ADHD is not at all clear, but it is believed that it works by selective noradrenaline reuptake inhibition in the synaptic space by blocking the noradrenaline presynaptic transporter.

It is believed that atomoxetine acts mainly in regions of the cortex and, unlike stimulants, it hardly acts in subcortical brain regions associated with motivation and reward (NICE, 2009)2.

Atomoxetine is taken in one single daily dose in the morning, although some patients may benefit from dividing the daily dose into twice a day, in the morning and afternoon or first thing at night.

The absorption of atomoxetine is fast and complete after the oral administration, reaching maximum plasmatic concentration (Cmax) approximately 1 to 2 hours after oral administration. The atomoxetine bioavailability after oral administration varies between 63% and 94%, depending on inter-individual differences, depending on the first-step metabolism.

The average half-life for the elimination of atomoxetine after oral administration is 3.6 hours in fast metabolising patients and 21 hours in slow ones.Approximately 7% of Caucasians have a genotype that corresponds to absence of the function of enzyme CYP2D6 (CYP2D6 slow metabolisers).Patients with this genotype (slow metabolisers) have several times greater exposure to atomoxetine compared with those who possess a functional enzyme (fast metabolisers).

Slow metabolisers may have a greater risk of adverse effects, and in these cases a much slower increase of the dose is recommended.

A low initial dose and a slow increase in dose may considerably reduce the appearance of side effects in the patient.

Dosage of atomoxetine

The initial dose is 0.5 mg/kg/day for 7-14 days, in one single daily dose in the morning. The recommended maintenance dose is approximately 1.2 mg/kg/day (depending on the patient's weight and on the available presentations of atomoxetine) in one single daily dose in the morning. If there are side effects, the total dose of atomoxetine can be administered in two doses (morning and evening-night) or in one single dose at night. This latter option is especially indicated in the case of daytime sleepiness.The maximum dose is 100 mg/day.The safety of administering single doses of more than 1.8 mg/kg/day and total daily doses of over 1.8 mg/kg/day has not been systematically assessed.

Adverse effects of atomoxetine

The main adverse effects of atomoxetine are: Sleepiness, abdominal pain, nausea and vomiting, loss of appetite and weight, dizziness, tiredness and slight increase in heart rate and blood pressure (Wolraich *et al*., 2007)[195]. The side effects are usually transient and rarely lead to the suppression of the treatment (NICE, 2009)[2].

Hepatotoxicity has been described, but very infrequently, which is manifested with an increase in hepatic enzymes and an increase in bilirubin and jaundice.If this side effect appears, its subsequent re-introduction is not advised (Atomoxetine technical data sheet, 2007).

Suicidal behaviour has been notified (suicide attempts and suicidal ideation) in patients treated with atomoxetine.In the double blind RCTs, the suicide attitudes occured with a frequency

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of 0.44% in patients treated with atomoxetine (6 of the 1357 patients treated, 1 case of attempted suicide and 5 suicidal ideations).There were no cases in the group treated with placebo (n=851). The age range of children who experienced these behaviours was 7 to 12 years.It must be pointed out that there were very few adolescent patients included in the RCT.

Contraindications of atomoxetine (technical data sheet)

- Glaucoma.
- It cannot be administered with MAOIs.
- Hypersensitivity with atomoxetine.

The atomoxetine presentations are capsules of 10, 18, 25, 40, 60 and 80 mg.

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7.3.2. In ADHD: What pharmacological treatments are efficient/ effective?How safe are the pharmacological treatments?

The answer is based on the NICE (2009)[2], SIGN (2005)[1], AACAP (2007)[72], AAP (2005)[196] guidelines; SR Quality 1+ and 1++ (Banaschewski, *et al*., 2006[193]; Connor, *et al*., 2002[197]; Cheng, *et al*., 2007[198]; Faraone, *et al*., 2006[199]), Technology Assessment Reports of NICE (2006)[200] and of King, *et al*. (2006)[201]. Two RCTs have been found in the update of scientific evidence (Newcorn, *et al*., 2008[202]; Wang, *et al*., 2007[203]).

Scientific evidence of studies of efficacy, safety and cost-effectiveness of pharmacological treatments

Methylphenidate

The NICE CPG has conducted a bibliographic review and MA of methylphenidate efficacy studies compared with placebo in school-age children and adolescents diagnosed with ADHD.From this review, 12 quality RCTs have been found for the MA: Butter, 1983204; Conners, 1980205; Findling, 2006206; Gittelman-Klein, 1976207; Greenhill, 2002208, 2006209; Ialongo, 1994210; Kollins, 2006211; Kurlan, 2002212; Lerer, 1977213; Pliszka, 2000214; Wilens, 2006215. The NICE guideline defines three ranges of methylphenidate dose: Low (≤0.4 mg/kg/day, medium (>0.4<0.8 mg/kg/day) and high (≥0.8 mg/kg/day.).

Variable: ADHD symptoms

Scientific evidence

There is strong scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) significantly reduces the teachers' scores in ADHD symptoms (5 RCT, N=806, Conners, 1980[205]; Greenhill, 2002[208]; Findling, 2006[206]; Ialongo, 1994[210]; Pliszka, 2000[214]) (SMD: -0.84 [95% CI: -1.06 to -0.62]). RCT 1++

There is strong scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) significantly reduces the parents' scores in ADHD symptoms (4 RCT, N=747, Conners, 1980[205]; Greenhill, 2002[208]; Findling, 2006[206]; Ialongo, 1994[210]; Pliszka, 2000[214]) (SMD: -0.79 [95% CI: -1.14 to -0.45]). RCT 1++

There is not sufficient scientific evidence that methylphenidate in low doses (≤0.4 mg/kg/day) significantly reduces the teachers' scores in ADHD symptoms (2 RCT, N=78, Butter, 1983[204]; Ialongo, 1994[210]) (SMD: -0.40 [95% CI: -0.95 to 0.15]) RCT 1++

There is not sufficient scientific evidence that methylphenidate in low doses (≤0.4 mg/kg/day) significantly reduces the parents' scores in ADHD symptoms (1 RCT, N=48, Ialongo, 1994[210]) (SMD: 0.66 [95% CI: -0.06 to 1.37]). RCT 1++

There is scientific evidence that methylphenidate in medium doses (>0.4- (<0.8 mg/kg/day) significantly reduces the teachers' scores in ADHD symptoms (1 RCT, N=136, Kurlan, 2002[212]) (SMD: -1.69 [95% CI: -2.24 to -1.14]), as well as the parents' scores in ADHD symptoms (1 RCT, N=136, Kurlan, 2002[212]) (SMD: -233 [95% CI: -1.94 to -1.73]). RCT 1++

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

Variable: Behavioural problems

Scientific evidence

There is strong scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) significantly reduces the teachers' scores in behavioural problem symptoms (4 RCT, N=485, Findling, 2006[206]; Ialongo, 1994[210]; Pliszka, 2000[214]; Conners, 1980[205]) (SMD: -0.58 [95% CI: -0.84 to -0.31]). RCT 1++

There is strong scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) significantly reduces the parents' scores in behavioural problem symptoms (2 RCT, N=378, Findling, 2006[206]; Conners, 1980[205]) (SMD: -0.73 [95% CI: -1.06 to -0.41]). RCT 1++

There is not sufficient scientific evidence that methylphenidate in low doses (≥0.4 mg/kg/day) significantly reduces the teachers' scores in behavioural problem symptoms (1 RCT, N=48, Ialongo, 1994[210]) (SMD: -0.43 [95% CI: -1.13 to 0.27]). RCT 1+

There is scientific evidence that methylphenidate in medium doses (>0.4- <0.8 mg/kg/day) significantly reduces the teachers' scores in behavioural problems symptoms (1 RCT, N=136, Kurlan, 2002212) (SMD: -1.21 [95% CI: -1.72 to -0.71]). RCT 1++

Variable: Clinical improvement (clinician)

Scientific evidence

There is strong scientific evidence that methylphenidate in medium doses (>0.4- <0.8 mg/kg/day) is associated with significant clinical improvement (2 RCT, N=186, Lerer, 1977[213]; Kurlan, 2002[212]) (RR: 3.08 [95% CI: -1.40 to 6.78]). RCT 1++

There is strong scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) is associated with significant clinical improvement (5 RCT, N=823, Wilens, 2006[215]; Gittelman-Klein, 1976[207]; Pliszka, 2000[214]; Findling, 2006[206]; Greenhill, 2006[209]) (RR: 1.81 [95% CI: -1.46 to 2.24]). RCT 1++

Safety

Scientific evidence

There is scientific evidence that methylphenidate in high doses (≥0.8 mg/kg/day) is associated with a greater presence of insomnia (3 RCT, N=318, Conners, 1980[205]; Greenhill, 2006[209]; Wilens, 2006[215]) (NNTH: 12 [95% CI: 7 toi33]) and anorexia (4 RCT, N=634, Conners, 1980[205]; Greenhill, 2002[208]; Greenhill, 2006[209]; Wilens, 2006[215]) (NNTH: 16 [95% CI: 11 to 50]) compared with placebo. RCT 1++

There is not sufficient scientific evidence that treatment with methylphenidate in high doses (2 RCT, N=424, Greenhill, 2002[208]; Wilens, 2006[215]), medium (2 RCT, N=186, Lerer, 1977[213]; Kurlan, 2002[212]) or low doses (1 RCT, N=30, Ialongo, 1994[210]), is associated with a higher premature abandonment of the treatment due to adverse effects compared with placebo. RCT 1++

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There is strong scientific evidence that the number of abandonments of the treatment, for any reason, is greater in the placebo group than in the treatment with methylphenidate in medium doses (2 RC, N=186, Lerer, 1977[213]; Kurlan, 2002[212]) (NNTB: 8; [95% CI: 4 to 50]) or high doses (4 RCT, N=767, Gittelman-Klein, 1976[207]; Greenhill, 2002[208], 2006[209]; Wilens, 2006[215]) (NNTB: 11; [95% CI: 6 to 25]). RCT 1++

Other adverse effects associated with treatment with methylphenidate that have been found in some RCTs have been: Abdominal pain, headaches, dizziness, and less frequently, anxiety, irritability and emotional lability (Ahmann, 1993[216]; Barkley, 1990[217]; SIGN, 2005[1]). CPG

The NICE CPG describes the presence of tics in long-term treatment with methylphenidate (NICE, 2009)[2], although the available scientific evidence suggests that it is safe treatment for children with ADHD and tics, and only a minority of children with tic disorder present worsening or do not tolerate the stimulants (Palumbo, 2004[218]; Poncin, 2007[219]). Observational studies 2+

More results

Connor, *et al*. (2002)[197] conducted a MA on studies that assessed the efficacy of stimulants in in reducing aggressions. They included a total of 28 RCTs.

Scientific evidence

There is scientific evidence that stimulants are associated with a reduction in aggressions according to the evaluation of clinicians (18 RCT, N=367, Aman, 1997[220]; Amery, 1984[221]; Gadow, 1990[222]; Hinshaw, 1984[223]; 1989[224]; 1989[225], 1992[226]; Kaplan, 1990[227]; Klein, 1997[164]; Kolko, 1999[228]; Murphy, 1992[229]; Pelham, 1985[230], 1987[231], 1989[232], 1990[233], 1991[234]; 1999[235]; Smith, 1998[236]) (SMD: 0.76 [95% CI: 0.63 to 0.88]), parents (13 RCT, N=381, Aman, 1991[237], 1997[220]; Arnold, 1972[238], 1976[239]; Barkley, 1989[240]; Barrickman, 1995[241]; Bostic, 2000[242]; Bukstein & Kolko, 1998[243]; Gadow, 1990[222]; Klein, 1997[164]; Klorman, 1988[244]; Pelham, 1999[235]; Taylor, 1987[245]) (SMD: 0.71 [95% CI: 0.42 to 1.14]), or teachers (16 RCT, N=381, Aman, 1991[237], 1997[220]; Arnold, 1972[238], 1976[239]; Barkley, 1989[240]; Barrickman, 1995[241]; Bostic, 1984[221]; Bukstein & Kolko, 1998[243]; Gadow, 1990[222]; Klein, 1997[164]; Klorman, 1988[244]; Pelham, 1999[235]; Taylor, 1987[245]) (SMD: 1.04 [95% CI: 0.79 to 1.32]). RCT 1+

Comparison between immediate release methylphenidate and extended release methylphenidate

Summary of scientific evidence

There is not sufficient scientific evidence of significant differences between extended release methylphenidate and immediate release methylphenidate (Fitzpatrick, 1992[247]; Wolraich, 2001[248]; Pelham, 1987[231]; 1990[233]; 2001[249]).	SR of RCT 1+

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Atomoxetine:

The NICE CPG has conducted a bibliographic review and MA of atomoxetine efficacy studies compared with placebo in school-age children and adolescents diagnosed with ADHD. 9 RCTs on atomoxetine compared with placebo have been found in the review: Wernicke, 2004[250]; Bohnstedt, 2005[251]; Brown, 2006[252]; Kelsey, 2004[253]; Michelson, 2001[254], 2002[255], 2004[256]; Spencer 2002[257]; Weiss, 2005[258]; and 2 RCTs of atomoxetine in ADHD children + tic disorder compared with placebo: Allen, 2005[259]; Spencer, 2002[257]. The NICE CPG defines three ranges of atomoxetine dose: low (<0.8 mg/kg/day, medium (>0.8-<1.6 mg/kg/day) and high (≥1.6 mg/kg/day.).

Cheng *et al*. (2007)[198] have performed a MA on atomoxetine efficacy studies compared with placebo in school-age children and adolescents. 7 RCTs of atomoxetine compared with placebo in ADHD children (with mixed comorbidity) have been found based on the review:Buitelaar, 2006[260]; Kelsey, 2004[253]; Michelson, *et al*., 2001[254], 2002[255], 2004[256]; Spencer 2002[257]; Weiss, 2005[258]; and 2 RCTs with ADHD children + DND: Kaplan, 2004[261]; Newcorn, 2005[262].

Variable: ADHD symptoms

Scientific evidence

There is scientific evidence that atomoxetine in medium doses (>0.8- <1.6 mg/kg/day) significantly reduces the teachers' scores in ADHD symptoms (1 RCT, N=171, Michelson, 2002[255]) (SMD: -0.43 [95% CI: -0.73 to -0.12]). RCT 1++

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/day) significantly reduces the teachers' scores in ADHD symptoms (4 RCT, N=738, Michelson, 2004[256]; Bohnstedt, 2005[251]; Weiss, 2005[258]; Brown, 2006[252]) (SMD: -0.37 [95% CI: -0.54 to -0.21]). RCT 1++

There is scientific evidence that atomoxetine in medium doses (>0.8- <1.6 mg/kg/day) significantly reduces the parents' scores in ADHD symptoms (2 RCT, N=468, Michelson, 2001[254]; 2002[255]) (SMD: -0.65 [95% CI: -0.87 to -0.43]). RCT 1++

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/day) significantly reduces the parents' scores in ADHD symptoms (6 RCT, N=916, Michelson, 2001[254]; Spencer, 2002[257]; Kelsey, 2004[253]; Michelson, 2004[256]; Bohnstedt, 2005[251]; Brown, 2006[252]) (SMD: -0.59 [95% CI: -0.71 to -0.47]). RCT 1++

There is scientific evidence that atomoxetine significantly reduces the teachers' scores in ADHD symptoms (3 RCT, N=738, Buitelaar, 2006260; Michelson, 2002255; 2004256) (SMD: -0.34 [95% CI: -0.63 to -0.05]). RCT 1++

There is scientific evidence that atomoxetine significantly reduces the parents' scores in ADHD symptoms (6 RCT, N=1,595, Buitelaar, 2006[260]; Michelson, 2001[254], 2002[255], 2004[256]; Spencer, 2002[257]; Weiss, 2005[258]) (SMD: -0.61 [95% CI: -0.84 to -0.38]). RCT 1+

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Variable: Behavioural problems

Scientific evidence

There is not sufficient scientific evidence that atomoxetine in medium doses (>0.8-<1.6 mg/kg/day) significantly reduces the teachers' scores in behavioural problems (1 RCT, N=416, Michelson, 2004256) (SMD: 0.00 [95% CI: -0.24 to 0.24]). RCT 1+

There is scientific evidence that atomoxetine in low doses (≤0.8 mg/kg/day) significantly reduces the parents' scores in behavioural problems (1 RCT, N=126, Michelson, 2001[254]) (SMD: -0.46 [95% CI: -0.83 to -0.08]). RCT 1++

There is scientific evidence that atomoxetine in medium doses (>0.8-<1.6mg/kg/day) significantly reduces the parents' scores in behavioural problems (1 RCT, N=126 N=713, Michelson, 2001[254]; 2004[256]) (SMD: -0.31 [95% CI: -0.49 to 0.14]). RCT 1++

Variable: Clinical improvement (clinician)

Scientific evidence

There is scientific evidence that atomoxetine is associated with a clinical improvement (5 RCT, N=1.165, Kelsey, 2004[253]; Michelson, 2002[255], 2004[256]; Spencer, 2002[257]; Weiss, 2005[258]) (SMD: -0.63 [95% CI: -0.82 to -0.44]). RCT 1+

Variable: Psychosocial functioning and quality of life

Scientific evidence

There is scientific evidence that atomoxetine is associated with an improvement inpsychosocial functioning and quality of life (3 RCT, N=863, Buitelaar, 2006[260]; Michelson, 2001[254], 2004[256]) (SMD: 0.46 [95% CI: -0.25 to 0.68]). RCT 1+

Populations with comorbidity

Scientific evidence

There is scientific evidence that atomoxetine in medium doses (>0.8-<1.6 mg/kg/day) significantly reduces the parents' scores in the ADHD symptoms in children with ADHD + tic disorder (1 RCT, N=148, Allen, 2005[259]) (SMD: -0.56, (95% CI: -0.89 to -0.23]). RCT 1++

There is limited scientific evidence that atomoxetine significantly reduces the parents' scores in ADHD symptoms in children with ADHD + ODD (2 RCT, N=213, Kaplan, 2004[261]; Newcorn, 2005[262]) (SMD: -0.75 [95% CI: -1.01 to -0.48]). RCT 1+

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There is limited scientific evidence that atomoxetine significantly reduces the parents' scores in behavioural problem symptoms in children with ADHD + ODD (2 RCT, N=213, Kaplan, 2004[261]; Newcorn, 2005[262]) (SMD: -0.42 [95% CI: -0.70 to -0.14]). RCT 1+

There is scientific evidence that atomoxetine is associated with clinical improvement in children with ADHD + ODD (2 RCT, N=213, Kaplan, 2004[261]; Newcorn, 2005[262]) (SMD: -0.59 [95% CI: -0.84 to -0.34]). RCT 1+

Safety and adverse effects

Scientific evidence

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/day) is associated with a greater presence of nausea (2 RCT, N=275, Michelson, 2001[254]; Kelsey, 2004[253]) (NNTH: 10 [95% CI: 5 to 33]) than the placebo. RCT 1+

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/día) (2 RCT, N=468, Michelson, 2001[254]; Kelsey, 2004[253]) (NNTH: 9 [95% CI: 5 to 25]) and medium doses (0.8-1.6 mg/kg/day) (2 RCT, N=494, Michelson 2001[254], 2002[255]) (NNTH: 11 [95% CI: 6 to 33]) is associated with a greater presence of loss of appetite than the placebo. RCT 1++

There is scientific evidence that atomoxetine in medium doses (>0.8- <1.6 mg/kg/day) is associated more often with dyspepsia (1 RCT, 1++ N=171, Michelson, 2002[255]) (NNTH: 11 [95% CI: 6 to 33]) compared with placebo. RCT 1++

There is scientific evidence that atomoxetine in medium doses (>0.8- <1.6 mg/kg/day) is associated with a greater presence of vomiting (2 RCT, N=468, Michelson, 2001[254]; 2002[255]) (NNTH: 12 [95% CI: 7 to 50]) than the placebo. RCT 1++

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/day) is associated with a greater presence of sleepiness (2 RCT, N=494, Michelson, 2001[254]; Kelsey, 2004[253]) (NNTH: 10 [95% CI: 6 to 20]) than the placebo. RCT 1++

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/kg/day) is associated with a greater presence of fatigue (1 RCT, N=197, Kelsey, 2004[253]) (NNTH: 12 [95% CI: 7 to 50]) than the placebo. RCT 1+

There is scientific evidence that atomoxetine is associated with a greater presence of emotional lability (1 RCT,, N=127, Spencer, 2002[257]) (NNTH: 9 [95% CI: 4 to 50]) than the placebo. RCT 1+

There is scientific evidence that atomoxetine in high doses (≥1.6 mg/Kg/day) is associated with greater abandonment of the treatment due to side effects (5 RCT, N=1.189, Michelson, 2001[254]; Spencer, 2002[257]; Kelsey, 2004[253]; Michelson, 2004[256]; Weiss, 2005[258]) (NNTH: 33 [95% CI: 20 to 100]) than the placebo. RCT 1++

There is not sufficient scientific evidence that treatment with atomoxetine in high doses (≥1.6 mg/kg/day) (7 RCT, N=1485, Michelson, 2001[254]; Spencer, 2002[257]; Kelsey, 2004[253]; Michelson, 2004[256]; Bohnstedt, 2005[251]; Weiss, 2005[258]; Brown, 2006[252]), medium doses (2 RCT, N=468, Michelson, 2001[254]; 2002[255]) or low doses (1 RCT N=297, Michelson, 2001[254]), is associated with a greater premature abandonment of the treatment due to any reason compared with the placebo. RCT 1++

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There is not sufficient scientific evidence that treatment with atomoxetine in children with ADHD + tic disorder is associated with a greater premature abandonment of the treatment due to side effects (1 RCT, N=148, Allen, 2005[259]) compared with placebo. RCT 1+

Clonidine

The NICE CPG performed a bibliographic review where it found one RCT on the efficacy of clonidine compared with placebo. Hazell, 2003[263]; and one RCT on the efficacy of clonidine in ADHD children + tic disorder (Kurlan, 2002)212.

Variable: ADHD symptoms

Scientific evidence

There is scientific evidence that clonidine is associated with a reduction in the ADHD symptoms referred to by teachers (1 RCT, N=67, Hazell, 2003[263]) (SMD: -0.57 [95% CI: -1.06 to -0.08]). RCT 1++

There is not sufficient scientific evidence to suggest that clonidine is associated with a reduction in ADHD symptoms referred to by parents (1 RCT N=67, Hazell, 2003[263]) (SMD: -0.16 [95% CI: -0.64 to 0.32]). RCT 1++

There is scientific evidence that clonidine is associated with a reduction in the ADHD symptoms referred to by teachers in patients with ADHD and tic disorder (1 RCT, N=136, Kurlan, 2002[212]) (SMD:-2.42, (95% CI: -3.07 to -1.76]). RCT 1++

There is limited scientific evidence that clonidine is associated with a reduction in the ADHD symptoms referred to by parents in patients with ADHD and tic disorder (1 RCT, N=136, Kurlan, 2002[212]) (SMD: -2.41, (95% CI: -3.07 to -1.75]). RCT 1++

A recent RCT (Palumbo, 2008)[264] has found significant differencesin the treatment with clonidine compared with placebo in the reduction of ADHD symptoms referred to by parents but not in that referred to by teachers. RCT 1+

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Variable: Behavioural problems

Scientific evidence

There is limited scientific evidence that clonidine is associated with a reduction in the behavioural problem symptoms referred to by the teachers (1 RCT N=67, Hazell, 2003[263]) (SMD: -0.68 [95% CI: -1.18 to -0.18]). RCT 1++

There is not sufficient scientific evidence to suggest that clonidine is associated with a reduction in behavioural problem symptoms referred to by parents (1 RCT N=67, Hazell, 2003[263]) (SMD: -0.31 [95% CI: -0.8 to 0.17]). RCT 1++

There is limited scientific evidence that clonidine is associated with a reduction in the behavioural problem symptoms referred to by the teachers in patients with ADHD and tic disorder (1 RCT, N=136, Kurlan, 2002[212]) (SMD:-1.11 (95% CI: -1.64 to -0.58]). RCT 1++

Variable: Clinical improvement (clinician)

Scientific evidence

There is scientific evidence that clonidine is associated with a clinical improvement in patients with ADHD + tic disorder (1 RCT, N=136, Kurlan, 2002[212]) (RR: 1.98 [95% CI: -1.11 to 3.52]). RCT 1++

Safety and adverse effects

Scientific evidence

Clonidine is associated with sedation and a reduction in heart rate (NICE, 2009)[2]. SR of RCT 1+

There is not sufficient scientific evidence about the existence of significant differences in the premature abandonment of the treatment for any reason between treatment with clonidine and placebo (1 RCT, N=67, Hazell, 2003[263]). RCT 1+

There is not sufficient scientific evidence about the existence of significant differences in the premature abandonment of the treatment for any reason between treatment with clonidine and placebo (1 RCT, N=136, Kurlan, 2002[212]). RCT 1++

In a recent RCT (Daviss, 2008)[265], the adverse effects most frequently associated with treatment with clonidine were:tiredness, dry mouth, sedation, sleepiness and reduction of heart rate. RCT 1+

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Bupropion

The NICE CPG performed a bibliographic review where it found two RCTs on the efficacy of bupropion compared with placebo. Casat, 1987[266]; Conners, 1996[267].

Variable: ADHD symptoms

Scientific evidence

There is not sufficient scientific evidence to suggest that bupropion is associated with a reduction in ADHD symptoms referred to by teachers (2 RCT, N=139; Casat, 1987[266]; Conners, 1996[267]). (SMD: -0.70 [95% CI: -1.11 to 0.29]). RCT 1++

There is not sufficient scientific evidence to suggest that bupropion is associated with a reduction in ADHD symptoms referred to by parents (2 RCT, N=139; Casat, 1987[266]; Conners, 1996[267]). (SMD: -0.88 [95% CI: -1.89 to 0.13]). RCT 1++

Variable: Behavioural problems

Scientific evidence

There is not sufficient scientific evidence to suggest that bupropion is associated with a reduction in behavioural problem symptoms referred to by teachers (1 RCT, N=30; Casat, 1987266) (SMD: -0,44 [95% CI -1.21 to 0.32]). RCT 1+

There is not sufficient scientific evidence to suggest that bupropion is associated with a reduction in behavioural problem symptoms referred to by parents (1 RCT, N=30; Casat, 1987266) (SMD: 0.00 (CI 95%: -0.76 to 0.76]). RCT 1+

Safety and adverse effects

Scientific evidence

Bupropion is associated with dry mouth, gastrointestinal disturbances, insomnia, concentration impairment, headaches, depression, anxiety, agitation, tremor, rash, pruritus, and to a lesser extent, cardiovascular and metabolic disturbances, confusion or serious hypersensitivity reactions (NICE, 2009)[2]. SR of RCT 1+

Bupropion has been associated with a dose-related presence of convulsions, with an estimated incidence of approximately 0.1% (NICE, 2009)[2]. SR of RCT 1+

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Modafinil

The NICE CPG performed a bibliographic review where it found 5 RCTs on the efficacy of modafinil compared with placebo. Biederman, 2005[268], 2006[269]; Greenhill, 2006[270]; Rugino, 2003[271]; Swanson, 2006[272]. Dose of modafinil used in the studies: from 264 to 425 mg/day.

Variable: ADHD symptoms

Scientific evidence

There is limited scientific evidence that modafinil is associated with a reduction in the ADHD symptoms referred to by teachers (2 RCT, N=438, Biederman, 2005[268]; Swanson, 2006[272]) (SMD: -0.63 [95% CI: -0.84 to -0.43]) — RCT 1++

There is limited scientific evidence that modafinil is associated with a reduction in the ADHD symptoms referred to by parents (2 RCT, N=438, Biederman, 2005[268]; Swanson, 2006[272]) (SMD: -0.54 [95% CI: 0.74 to-0.33). — RCT 1++

Variable: Behavioural problems

Scientific evidence

There is limited scientific evidence that modafinil is associated with a reduction in the behavioural problem symptoms referred to by parents (1 RCTA, N=248, Biederman, 2005[268]) (SMD: -0.31 [95% CI: 0.57 to-0.04). — RCT 1+

Variable: Clinical improvement

Scientific evidence

There is scientific evidence that modafinil is associated with a clinical improvement (3 RCT, N=686, Biederman, 2005[268]; 2006[269]; Swanson, 2006[272]) (RR: 2.79 [95% CI: -2.02 to 3.86]). — RCT 1+

Safety and adverse effects

Scientific evidence

There is scientific evidence that modafinil is associated with a greater presence of insomnia (2 RCT, N=438, Biederman, 2005268; Swanson, 2006272) (NNTH: 4 [95% CI: 3 to 5]) than the placebo. — RCT 1++

There is scientific evidence that modafinil is associated with a greater presence of loss of appetite than placebo (1 RCT, N=24, Biederman, 2005268) (NNTH: 8 [95% CI: 5 to 12]) — RCT 1+

There is not sufficient scientific evidence that treatment with modafinil is associated with a greater abandonment of the treatment due to side effects (4 RCT, N=720, Rugino, 2003[271]; Biederman, 2005[268], 2006[269]; Greenhill, 2006[270]) than the placebo. — RCT 1+

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There is not sufficient scientific evidence that treatment with modafinil is associated with a greater premature abandonment of the treatment due to any reason compared with placebo (4 RCT, N=662, Rugino, 2003[271]; Biederman, 2006[269]; Greenhill, 2006[270]; Swanson, 2006[272]). RCT 1+

Treatment with modafinil is normally associated with insomnia, loss of appetite, vomiting, abdominal pain, headaches, irritability, amygdalitis and pharyngitis (NICE, 2009)[2]. RCT 1+

Antidepressants

Imipramine, SSRIs or SNRIs are not considered of value to treat the symptoms of ADHD (NICE, 2009)2

Desipramine, not available in Spain, is not recommended by a recent guideline due to its potential cardiotoxicity (NICE, 2009)2

Scientific evidence

The SIGN CPG (2005)[1] refers to scientific evidence of the treatment with tricyclic antidepressants to treat ADHD in children and in adolescents. More specifically, more than 70% of children with ADHD treated with tricyclic antidepressants (TCAs) showed an improvement in the behavioural symptoms compared with 10% of the children with placebo (Spencer, 1996[273]; Green, 1992[274]; Biederman, 1989[275]). MA of RCT 1++,1+

The CPG of the AAP (Brown, 2005[196]; Jadad, 1999[276]) performed a review of scientific evidence with respect to the treatment of ADHD in children and in adolescents with TCAs.They found 9 RCTs that compared the efficacy of the treatment with TCAs compared with placebo: 6 that examined the effects of desipramine (Rapport, 1993[277]; Biederman, 1989[275], 1993[278], 1989[275]; Donnelly, 1986[279]; Gualtieri, 1991[280]; Singer, 1995[281]; Wilens, 1996[282]), and 3 that examined the effects of imipramine (Gualtieri, 1988283; Winsberg, 1980[284]; Werry, 1980[285]). The studies included are, in general, of regular quality (1+), showing a lack of consistent scientific evidence for imipramine, and limited scientific evidence for desipramine (Brown, 2005)[196]. RCT 1+

Arabgol, *et al*. (2009)[286] performed a 6-week RCT on the efficacy and tolerability of reboxetine compared with methylphenidate to treat ADHD in children and adolescents (n=33, 7-16 years). The adverse effects of reboxetine included sleepiness and anorexia its seriousness varying from light to moderate. RCT 1+

The authors of the study conclude that reboxetine may have beneficial effects to treat ADHD, although more studies are required to clarify the potential therapeutic effects in comorbidity and the adverse effects.

Antipsychotics

Scientific evidence

There is not scientific evidence that treatment with atypical antipsychotics are of value to treat the symptoms of ADHD (NICE, 2009)[2]

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Cost-effectiveness studiest

Scientific evidence

The NICE CPG (2009)[2] has made a summary of scientific evidence available on economic cost-effectiveness studies with methylphenidate, atomoxetine or dexamphetamine. Donnelly, *et al*., 2004[287]; Gilmore & Milne, 2001[288]; King, *et al*., 2006[201]; Narayan & Hay, 2004[289]; and Zupancic, *et al*., 1998[290]. The review of the scientific evidence suggests that the pharmacological treatment is cost-effective when compared with non-treatment in children with ADHD..

Cost-effectiveness studies 1++

Comparison between medications

Scientific evidence

In the MA by Faraone (2006)[199] the efficacy of the different medications for ADHD was compared.They included 29 RCTs that included immediate release stimulants, extended release stimulants and non-stimulants (atomoxetine, modafinil and bupropion). The results indicated that both the immediate and extended release stimulants had significantly greater efficacy than non-stimulant drugs after control by confusion variables (Faraone, 2006)[199].

MA of RCT 1++

In the MA by Banaschewski, *et al*.(2006)[193], the efficacy of the different extended release medications for ADHD was compared.The results indicate greater effects of extended release stimulants compared with the effects of non-stimulant drugs (atomoxetine and modafinil) (Banaschewski, *et al*., 2006)[193]

MA of RCT 1++

Two quality RCTs have been found that directly compared methylphenidate with atomoxetine (Newcorn, 2008 [202]; Wang, 2007[203]).In the study by Wang (2007)[203], no significant differences were found between the two medications; however, relative low doses of methylphenidate (0.2 to 0.6 mg/kg/day) were used.In the more recent study by Newcorn (2008)[202] a significantly higher percentage of responders to methylphenidate (56%) than to atomoxetine (45%) was found.

RCT1++

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

Summary of the scientific evidence on the efficacy of pharmacological treatments

Methylphenidate and atomoxetine are the only medicines that have shown to be clearly efficient in reducing ADHD symptoms (NICE, 2009)[2].	RCT1++
The MAs that compare stimulant drugs with non-stimulant drugs suggest greater efficacy of the treatment with stimulants compared with non-stimulant drugs (Faraone, 2006[199]; Banaschewski, *et al*., 2006[193]). In the RCTs conducted that compared methylphenidate with atomoxetine, very different results are found, with one study that suggests superiority of methylphenidate over atomoxetine (Newcorn, 2008)[202] and another where no significant differences were found (Wang, 2007)[203].	MA of RCT 1++
There is no scientific evidence that tricyclic antidepressants, SSRIs, SNRIs are useful to treat ADHD symptoms (NICE, 2009)[2].	Experts' opinion 4

Recommendations

A	7.3.2.1.	Methylphenidate and atomoxetine are the recommended drugs today to treat ADHD in children and adolescents based on their efficacy and safety at recommended doses (adapted from NICE 10.18.5.1)[2].

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

7.3.3. In ADHD: How effective are pharmacological treatments in the short and long term?

The answer is based on the studies of MTA (1999)[39], MTA (2004)[173], Jensen, *et al*. (2007)[291], Kratochvil, *et al*. (2006)[299] and Wilens (2006)[300], as well as on the NICE (2009)[2], AAP (2005)[196] and SIGN (2005)[1] guidelines.

Scientific evidence

The MTA study assessed the efficacy of the long-term treatment (14 months) with 3 doses of methylphenidate, compared with behavioural therapy, with methylphenidate + behavioural therapy, and with normal treatment in the community (MTA, 1999)[39]. After 14 months' treatment, the pharmacological treatment with methylphenidate proved to be efficient in reducing nuclear symptoms of the disorder (hyperactivity/impulsivity and inattention) compared with the intervention in the community (MTA, 1999)[39]. When the trial ended, a naturalistic follow-up was carried out with follow-up results after 2 and 3 years. In the 2-year results, the positive effect of the pharmacological treatment is maintained regarding the intervention in the community in the reduction of the nuclear symptoms of the disorder (MTA, 2004)[173]; however, in the 3-year follow-up no significant differences between the groups are obtained (Jensen, *et al*., 2007)[291]. These results must be interpreted with caution because the follow-up after the intervention is naturalistic, with no control over the intervention, and because of the lack of a control group without treatment.	RCT1++
The NICE guideline (2009)[2] indicates that the results of pharmacological intervention studies, regardless of the type of drug, and lasting for 2 weeks or more, suggest a clinical improvement tendency with continued treatment (MTA, 1999[39]; Kupietz, 1988[292]; Quinn, 1975[293]; Brown, 1985[161]; Conrad, 1971[294]; Firestone, 1986[295]; Brown, 1986[162]; Fehlings, 1991[154]; Gillberg, 1997[296]; Gittelman-Klein, 1976[297]; Schachar, 1997[298]).	RCT 1+, 1++
In the follow-up after 2 years' treatment with atomoxetine the improvement attained during the first months' treatment is maintained both in children (Kratochvil, *et al*., 2006)[299] and in adolescents (Wilens, 2006)[300].	Cohorts- Study 2+

Summary of the scientific evidence on the efficacy of pharmacological treatments

There is scientific evidence of long-term effectiveness (from 12 weeks to 24 months) of the pharmacological treatment if this is continuous (AAP, 2005[196]; SIGN, 2005)[1].	RCT1++

Recommendations

A	7.3.3.1.	Long-term treatment with methylphenidate and atomoxetine can be recommended as its effectiveness is not reduced.

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

7.3.4. In ADHD: When and with what criteria must pharmacological treatment be started?

The answer is based on the AACAP (2007)[72] and NICE (2009)[2] guidelines.

Summary of the scientific evidence

The AACAP guideline (2007)[72] recommends pharmacological treatment and/or behavioural treatment as first choice bearing in mind the treatments thathave proved to be effective as well as the family preferences.	Experts' opinion 4
The pharmacological treatment must be started by a suitably qualified physician who is an expert in treating ADHD (NICE, 2009)[2].	Experts' opinion 4

Recommendations

D	7.3.4.1.	Pharmacological and/or behavioural treatment must be considered as first choice for ADHD in children and adolescents bearing in mind the age of the patient, the seriousness of the symptoms, their functional repercussion and the family's characteristics and preferences.
D	7.3.4.2.	Pharmacological treatment must be started by a properly qualified physician who is an expert in treating ADHD and its most frequent comorbidities.

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

7.3.5. In ADHD: What criteria are used to choose the drug? What are the start, suppression and maximum dose guidelines?Which are the first and second choice drugs?

The answer is based on the NICE (2009)[2]; AACAP (2007)[72], AAP (2001[180]; 2005[196]) guidelines and on the SR by Faraone (2006)[199] and Banaschewski, *et al*. (2006)[193].

Summary of the scientific evidence

The scientific evidence available that compares the efficacy of methylphenidate compared with atomoxetine suggests greater efficacy of methylphenidate in the reduction of the nuclear symptoms of ADHD (NICE, 2009[2]; Faraone, 2006[199]; Banaschewski, *et al*., 2006[193]).	SR of RCT 1+
The AACAP guideline (2007)[72], and the AAP guidelines (2001[180]; 2005[196]) consider stimulants as a drug of first choice, especially if there is no comorbidity.	Experts' opinion 4
The choice of atomoxetine as a first line drug in patients with active substance abuse, comorbidity with anxiety or tics can be considered (AACAP, 2007[72]; NICE, 2009[2]). It must also be considered if the patient has experienced significant adverse effects with stimulants(AACAP, 2007[72]; NICE, 2009[2]).	Experts' opinion 4
The choice of extended release methylphenidate can be considered in order to improve therapeutic compliance, as it is easy to administer (it need not be taken at school) or due to its pharmacokinetic profiles (NICE, 2009)[2]. Immediate release formulas are normally used in small children (<16 kg), who require more flexible doses (NICE, 2009 [2]; AACAP, 2007[72]).	Experts' opinion 4
Although the use of methylphenidate is contraindicated in the technical data sheet for patients with ADHD and comorbidity with tic disorder, based on the clinical experience of the development group, methylphenidate can be used in these patients with certain caution, in lower initial doses, increasing them much more slowly and with a much closer follow-up.	Experts' opinion 4

Table 9 includes a list of the doses of the drugs for ADHD available in Spain.

Table 9. Doses of the drugs for ADHD

Drugs	Presentations	Initial dose	Maximum dose
Immediate release methylphenidate	5, 10, 20 mg	5 mg	2 mg/kg/day up to 60 mg/day
Extended release methylphenidate with osmotic technology	18, 27, 36, 54 mg	18 mg	2 mg/kg/day up to 108 mg/day
Extended release methylphenidate with pellet technology	10, 20, 30, 40 mg	10 mg	2 mg/kg/day up to 60 mg/day
Atomoxetine	10, 18, 25, 40, 60, 80 mg	0.5 mg/kg/day	1.8 mg/kg/day up to 100 mg/day

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

Methylphenidate

Summary of the scientific evidence

In general, there is a linear relationship between the dose and the clinical response (AACAP, 2007)[72]. Likewise, the adverse effects are also dose dependent (SIGN, 2005)[1]. The treatment should seek the minimum effective dose that would produce the maximum therapeutic effect, keeping the adverse effects to a minimum (SIGN, 2005)[1]. The response threshold to methylphenidate is variable in each patient, in other words, each one has a unique dose-response curve (SIGN, 2005[1]; AACAP, 2007[72]).	RCT 1+
Some patients may require higher doses than those recommended in **Table 9** to obtain a therapeutic response (AACAP, 2007)[72]. In these cases, suitable clinical monitoring is necessary (SIGN, 2005[1]; AACAP, 2007[72]).	Experts' opinion 4
Once the treatment has started with the initial dose, the physician should increase it every 1 to 3 weeks until the maximum dose has been reached, or the ADHD symptoms have disappeared, or the presence of adverse effects prevents an increase in dose (AACAP, 2007)[72].	Experts' opinion 4

Atomoxetine

Summary of the scientific evidence

Atomoxetine has greater effects than the placebo already in the first week of treatment, although the greatest effects are not observed until week 6 (AACAP, 2007)[72].	RCT 1++

Recommendations

D	7.3.5.1.	The decision about which drug to choose must be based on (adapted from NICE 10.18.5.2[32]: • The presence of comorbid conditions (tic disorders, Tourette's syndrome, epilepsy and anxiety). • The adverse effects of the drugs • Previous experiences of lack of efficacy • Issues regarding compliance, for example, problems associated with the need to administer a dose at school • Potential abuse • The preferences of the child/adolescent and his or her family

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

7.3.6. What are the most frequent (short term) side effects? How to address them?

The answer is based on the SIGN guideline (2005)[1].

Summary of the scientific evidence

The majority of the adverse effects of treatment with stimulants are dose-dependent and subject to individual differences (SIGN, 2005)[1]. Normally they decrease between weeks 1 and 2 after having started the treatment and they disappear if this is interrupted or the dose is reduced (SIGN, 2005)[1]	RCT 1+
A regular follow-up of the adverse effects is recommended between the physician and family to address problems that might appear when stimulants are introduced (SIGN, 2005)[1].	Experts' opinion 4
Once the effective dose has been reached, regular visits are necessary to assess the adverse effects, and monitoring the evolution of the height, weight, heart rate and blood pressure (SIGN, 2005)[1].	Experts' opinion 4

Table 10 shows the main adverse effects of methylphenidate and how to address them (SIGN, 2005)[1].

Table 10. Adverse effects of methylphenidate*

Adverse effects of methylphenidate	How to address them?
Anorexia, nausea, loss of appetite	Monitoring, administer medication with meals, prescribe dietetic supplements.
Effects on growth	If significant (rare in long term) or if it causes parental concern, try "therapeutic holidays"
Insomnia	Monitoring, reduction or omission of the last dose
Dizziness or headache	Monitoring (blood pressure), increase intake of fluids
Involuntary movements, tics	Reduction, and if it persists, suspension of medication, consider alternative
Loss of spontaneity, dysphoria, agitation	Reduction or suspension (suspend if psychosis is suspected –rare-).
Irritability	Monitoring, reduce dose, assess if comorbidity (ODD, emotional disorder)
Rebound effect	Increase afternoon dose

* Adapted from SIGN (2005)[1]

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Atomoxetine

Summary of the scientific evidence

In September 2005, the FDA alerted about the risk of suicidalideation with treatment with atomoxetine in children and adolescents(US Food and Drug Administration, 2005)[301]. In 12 RCTs that included 1357 patients, the risk of suicidalideation was 4/1000 in the group treated with atomoxetine compared with none in the placebo group (AACAP, 2007)[72].	RCT 1++

Table 11 shows the main adverse effects of atomoxetine and how to address them.

Table 11. Adverse effects of atomoxetine

Adverse effects of atomoxetine	How to address them?
Anorexia, nausea	Monitoring, administer medication with meals, prescribe dietetic supplements.
Abdominal pain	Slow scaling-down or reduction of dose
Effects on growth	If significant (rare in long term) or it it causes parental concern, try "therapeutic holidays"
Sleepiness	Night-time dose or divide into two doses
Dizziness or headache	Monitoring (blood pressure), increase intake of fluids. Slow scaling of dose
Ideation and/or suicidal behaviour	Suspend medication and observation
Hepatotoxicity	Suspension of medication and not reintroduce it again

Recommendations

D	7.3.6.1.	Periodic follow-up and monitoring of the possible adverse effects of methylphenidate and atomoxetine are recommended

7.3.7. In ADHD: How long should the pharmacological treatment last?

The answer is based on the SIGN (2005)[1] and AACAP (2007)[72] guidelines.

Summary of the scientific evidence

As ADHD tends to persist in adolescents, and in some cases in adult age, and due to the fast re-appearance of the symptoms if the treatment is suspended, the pharmacological treatment for ADHD should be long-term (SIGN, 2005)[1].	Experts' opinion 4
Periodic controls must be carried out to assess the persistence or disappearance of the symptoms (AACAP, 2007)[72].	Experts' opinion 4

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

One accepted practice is to leave short periods (1 to 2 weeks) each year without treatment, obtaining feedback about the child's behaviour from the family and school (SIGN, 2005)[1]. Another possibility would be for the period without treatment to coincide with holidays, trying to get the family to suggest tasks to the child that require a demand with respect to cognitive resources (reading a book, maths problems, etc.) (AACAP, 2007)[72].	Experts' opinion 4
The long-term effectiveness studies of pharmacological treatments support the positive effect of the long-term treatment, especially in those patients with greater compliance (AACAP, 2007[72]; Charach, 2004[302]; Barbaresi, 2006[303]).	Cohorts study 2+

Recommendations

√	7.3.7.1.	The duration of the treatment must be established on a personal basis depending on the symptoms and functional repercussion. In some cases the treatment can last for several years.
√	7.3.7.2.	It is advisable to periodically evaluate the persistence or remission of the symptoms.An accepted practice is to suspend the pharmacological treatment for short periods of 1 or 2 weeks a year, obtaining information about the functioning of the child or adolescent from the family and from the school.

7.3.8. In ADHD: Are supplementary examinations required before starting the pharmacological treatment in children and adolescents?

The answer is based on the study by the American Heart Association (AHA, 2008)[304], on the study by Perrin, *et al*. (2008)[306] and on the note from the Spanish Medicine and Health Products Agency (Ref. 2009/01).

The Spanish Medicine and Health Products Agency has published a note (Ref.2009/01) where it informs of the possible cardiovascular effects of methylphenidate (including an increase in blood pressure and heart rate disturbances), so a thorough cardiovascular examination should be carried out before starting the treatment and follow-up must also be carried out.

Summary of the scientific evidence

Methylphenidate has a statistically significant association with the presence of clinically insignificant haemodynamic alterations (AHA, 2008)[304]. Sudden deaths that are directly associated with the drug are very rare, although ventricular arrhythmias have been found as well as suppression of the cardiac function associated with abuse of methylphenidate (AHA, 2008)[304].	Cohorts study 2+
Short-term studies have associated a slight increase in systolic blood pressure in adults with atomoxetine as well as a marginal increase in diastolic blood pressure in adults and children, which decreases with the suspension of the medication (Wernicke, 2003[305]). Sudden deaths have been referred to in children receiving treatment with atomoxetine (AHA, 2008)[304].	Cohorts study 2+

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The consensus of the American Heart Association (2008)[304] recommends the execution of an anamnesis, of the family and of the patient, a physical examination and an electrocardiogram (ECG) before starting pharmacological treatment. The American Paediatrics Association (Perrin, *et al*., 2008)[306] considered later on that the ECG is not necessary due to the lack of clear scientific evidence that associated methylphenidate with sudden death (Perrin, *et al*., 2008)[306].	Experts' opinion 4

Recommendations

D	7.3.8.1.	The systematic execution of supplementary examinations is not recommended, unless indicated by the physical exploration or anamnesis.

7.3.9. What is the pharmacological strategy when there is a partial response, side effects or contraindication?

How are the different methylphenidate presentations combined? How to make the transition from stimulants to atomoxetine?

The answer is based on the AAP guidelines (2001)[180] and Banachewski, *et al*. (2006)[193], the study by Quintana (2007)[307] and the narrative review of Weiss (2006)[308].

Summary of the scientific evidence

The AAP CPG (2001)[180] indicates that in the cases of children in whom the highest possible dose of a stimulant medication does not work, the clinician should recommend another stimulant drug. In the cases of children with ADHD in whom the pharmacological intervention does not show positive effects or who present intolerable side effects, they should be administered another of the stimulant medications recommended. It should be noted that in Spain methylphenidate is only available as a stimulant drug with different presentations. The lack of response to the treatment may lead clinicians to re-assessthe initial diagnosis and the possibility of non-diagnosed comorbid disorders. The lack of response to the treatment may reflect: 1) not very realistic objectives; 2) lack of information about the behaviour of the child; 3) incorrect diagnosis; 4) a co-existent disorder that affects the ADHD treatment; 5) lack of complianceto the treatment regime, and 6) failure of the treatment. The treatment of ADHD decreases the frequency and intensity of the nuclear symptoms of the disorder but it may not eliminate them in their entirety. Similarly, children with ADHD may continue experiencing difficulties in their relationships with companions although the treatment is the right one, and there may be no association, either, with the improvement in academic performance.	Experts' opinion 4
It is possible to complete the effect of extended methylphenidate products with immediate release ones (Banachewski, et al., 2006)[193].	SR 1+

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

There is no scientific evidence to decide which pattern must be followed in those patients treated with stimulants, whose treatment must be changed to atomoxetine due to lack of response or side effects.Quintana (2007)[307] proposes a fast change from the stimulant to atomoxetine with the following pattern: • First week: full dose of the stimulant and atomoxetine in doses of 0.5 mg/kg/day. • Second week: Reduce the dose of stimulant to half and administer atomoxetine in doses of 1.2 mg/kg/day. • Third week: Suspend the stimulant and maintain the dose of atomoxetine at 1.2 mg/kg/day. However, other clinicians such as Weiss (2006)[308] believe that the transition should be made much more slowly, due to the time that elapses until the atomoxetine starts to take effect.	Open-ended Trial 1- Narrative review 3

Recommendations

√	7.3.9.1.	If there is a partial response to the drug, increase the dose until the maximum indicated or tolerated.If there is no response with maximum doses, consider the alternative drug that has not been used with this child or adolescent (another methylphenidate or atomoxetine presentation).
√	7.3.9.2.	If side effects appear, address them adequately. If they persist or are not tolerated, evaluate a change in medication.
√	7.3.9.3.	In the case of contraindication, evaluate the use of the alternative drug.
√	7.3.9.4.	If extended release methylphenidate is used with osmotic technology and an adequate adjustment of the dose is not achieved, a dose of immediate release methylphenidate can be added to the treatment at breakfast and/or mid afternoon, to thus adjust the total dose in agreement with the weight of the child or adolescent with ADHD and with the clinical response. If a 12-hour therapeutic action is required and the child or adolescent with ADHD is not able to swallow tablets, extended release methylphenidate can be administered with pellet technology in the morning (opening the capsule) and in the afternoon, after school, administer a dose of immediate release methylphenidate.This latter pattern can also be followed if there is a rebound effect in the afternoon with extended release methylphenidate with pellet technology.

7.3.10. In which ADHD subtypes is pharmacological treatment more efficient?

The answer is based on the studies by Barbaresi (2006)[303] and by Stein, (2003)[309].

Scientific evidence

The long-term effectiveness studies have not found any significant differences between the ADHD subtype and the effectiveness of the pharmacological treatment (Barbaresi, 2006)[303]. Cohorts study 2+

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

In a RCT that studied the efficacy of extended release methylphenidate, a group of patients with combined ADHD was compared with a group of patients with inattentive ADHD (Stein, 2003)[309]. It was found that methylphenidate was equally efficient in both groups; however, in the group with combined ADHD, a linear relationship was verified between the dose and therapeutic response; on the contrary, in the group of inattentive ADHD there was a therapeutic response with lower doses of methylphenidate (60% responded with 36 mg/day or less). RCT1+

Recommendations

Recommendations		
C	7.3.10.1.	Methylphenidate and atomoxetine are recommended as pharmacological treatments of choice for ADHD in children and adolescents regardless of the ADHD subtype.

7.3.11. Are there differences in response depending on the gender or age?

The answer is based on the AACAP guideline (2007)[72] and on the studies by Barbaresi (2006) [303], Smith, et al. (1998)[236], Wilens (2006)[310] and Cox, et al. (2004)[311].

Scientific evidence

Long-term effectiveness studies have not found any significant differences between the gender and the effectiveness of the pharmacological treatment (Barbaresi, 2006)[303]. Cohorts study 2+

The treatment with methylphenidate is equally efficient in children and in adolescents (Smith, *et al*., 1998)[236]. RCT1++

The treatment with atomoxetine is equally efficient in children and adolescents (Wilens, 2006)[310]. Cohorts study 2+

The AACAP CPG (2007)[72] indicates, related to the response in agreement with the age, that the use of immediate or extended action stimulations has proved to be equally efficient in children and in adolescents. In connection with the use of extended action drugs, it must be pointed that this is much more convenient for the patient who complies better with the treatment. RCT1++

In adolescents, extended action methylphenidate can improve the driving ability compared with the use of short action methylphenidate (Cox, *et al*., 2004)[311]. Cohorts study 2+

Summary of the scientific evidence

There are no differences in the response to the pharmacological treatment in agreement with the gender and age (Barbaresi, 2006[303]; Wilens, 2006[310]; Cox, 2004[311]).	Cohorts study 2+

Recommendations

Recommendations		
B	7.3.11.1.	Methylphenidate and atomoxetine are recommended as pharmacological treatments of choice for ADHD in children and adolescents regardless of the age and gender.

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

7.3.12. Which physical parameters (weight, height, blood pressure, etc.) must be controlled before starting the pharmacological treatment and during it?

The answer is based on the AACAP (2007)[72] and NICE (2009)[2] guidelines.

Summary of the scientific evidence

The AACAP[72] guideline indicates that for pharmacological interventions, the follow-up must be carried out several times a year. The procedures applied in each visit may vary depending on the clinical needs, but throughout the treatment, the clinician must review the child's academic and behavioural function. Regarding physical parameters, the height, weight, blood pressure and heart rate are determined regularly. In parallel, the possible appearance of comorbid disorders and health problems is evaluated.	Experts' opinion 4
There is consistency between previous guidelines in that in patients with ADHD a regular follow-up must be carried out to introduce adjustments in the medication that will guarantee that the treatment is still effective, that the dose is optimal and that the side effects lack clinical importance (NICE, 2009)[2].	Experts' opinion 4

Recommendations

D	7.3.12.1.	A physical examination must be performed before starting the pharmacological treatment, which will include taking the blood pressure, measuring heart rate, weight and height.Personal and family history of cardiac diseases must be sought, as well as a history of syncope related to exercise or other cardiovascular symptoms (adapted from NICE, 10.18.4.1)[2].
D	7.3.12.2.	A preliminary cardiovascular study must be carried out at the start of the pharmacological treatment if there is a personal and/or family history of cardiac diseases or history of serious cardiovascular problems or sudden death in the family or abnormal finding in the initial physical examination (adapted from NICE, 10.18.4.1.)[2].
√	7.3.12.3.	In children and adolescents with ADHDreceiving treatment with methylphenidate or atomoxetine:the height must be measured every 6 months, the weight must be controlled 3 and 6 months after starting the pharmacological treatment, and every 6 months during the administration of the treatment.
√	7.3.12.4.	The height and weight in children and adolescents with ADHD in pharmacological treatment must be plotted on a growth chart and reviewed by the physician responsible for the treatment.
√	7.3.12.5.	The heart rate and blood pressure must be monitored in children and adolescents with ADHD receiving pharmacological treatment, plotting them before and after every change in dose, and systematically every 3 months.

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

7.3.13. What scientific evidence exists about the long-term effects in pharmacological treatment?Is it associated with growth retardation?

The answer is based on the AACAP guideline (2007)[72] and on the studies by Charach (2006)[312]; MTA (2004)[313]; (2007)[314], Spencer, *et al*.

Scientific evidence

Treatment with methylphenidate has been associated with a growth retardation at 2 and 5 years' follow-up (Charach, 2006[312]; MTA, 2004[313]; 2007[314]).	Cohorts study 2++
In the MTA study, the average height found 2 years into follow-up was 1.38 cm less than that expected for the age, and an average weight of 1.3 kg. less (MTA, 2004)[313]. 3 years into the follow-up, the group that received pharmacological treatment showed a growth of 2 cm less than the non-medicated group and an average weight of 2.7 kg less (MTA, 2007)[314].	Cohorts study 2++
Charach (2006)[312] has found a relationship between the dose of methylphenidate and growth retardation; this was significant 4 years into the follow-up with higher doses than 2.5 mg/kg/day.	Cohorts study 2++
The growth retardation is greater during the first year's treatment but decreases afterwards (AACAP, 2007)[72].	Cohorts study 2++
In the treatment with atomoxetine, retardation was also found (0.44 cm less and 0.87 kg less than expected for the age) in growth 2 years into follow-up (Spencer, *et al*., 2005)[315]. After 5 years' follow-up a smaller growth was observed than expected only in patients situated in the higher height quartiles, whilst there was a reverse tendency in children situated in the lower height quartiles (Spencer, *et al*., 2007)[316].	Cohorts study 2+

Summary of the scientific evidence

There is no consensus related to the long-term repercussion on the growth of children and adolescents receiving pharmacological treatment with methylphenidate and atomoxetine. There may be a slight decrease in weight and height. These effects seem to fade with time (Spencer, et al., 2007[316]; AACAP, 2007[72]; Carach, 2006[312]; MTA, 2004[313]; 2007[314]).	Cohorts study 2+

Recommendations

C	7.3.13.1.	A regular follow-up of the growth of children and adolescents with ADHD is recommended during the pharmacological treatment with methylphenidate and atomoxetine.
√	7.3.13.2	The assurance of an adequate nutritional intake is recommended in children and adolescents receiving pharmacological treatment with ADHD with secondary anorexia to the treatment.

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

7.3.14. Pharmacological treatment of ADHD: Does it cause addiction? Does it increase the risk of consumption of substances?

The answer is based on the MA of Wilens (2005)[317], (2003)[318] and (2008)[319], and on the study by Biederman (2008)[320]

Scientific evidence

Wilens (2005)[317] has performed a MA on the efficacy of the treatment with stimulants in adults and adolescents with ADHD + SUD (substance use disorder).He found efficacy of the treatment with stimulants in patients with ADHD + SUD that was not upheld with the analysis performed exclusively with controlled studies.The treatment with stimulants was not associated with a worsening of the SUD.	MA open-ended studies and RCT
Treatment with stimulants in childhood is associated with a reduction in the risk of consuming alcohol, tobacco and other substances in adolescents with ADHD (Wilens, 2003[318]; 2008[319]).	MA Cohorts study 2++
Biederman (2008)[320], in the naturalistic 10-year follow-up, indicates that there is no association between treatment with methylphenidate in children with ADHD and the consumption of substances.	Cohorts' study 2++

Summary of the scientific evidence

The treatment with stimulants does not increase the risk of substance use (Wilens, 2003[318]; 2008[319]; Biederman, 2008[320]).	Cohorts study 2+

Recommendations

B	7.3.14.1.	The use of methylphenidate and atomoxetine is recommended to treat ADHD in children and adolescents, at the right doses, as it does not cause addiction or increase the risk of substance abuse.

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

7.3.15. Does the efficacy of pharmacological treatment decrease with time?

The answer is based on the studies of MTA (1999)[39], (2004)[313], Jensen, et al.(2007)[291] and Wilens, et al. (2006)[300].

Scientific evidence

The MTA study appraised the efficacy of the long-term treatment (14 months) with 3 doses of methylphenidate, compared with behavioural therapy, comparedwith methylphenidate + behavioural therapy, compared with normal treatment in community (MTA, 1999)[39]. After 14 months' therapy, the pharmacological treatment with methylphenidate proved to be efficient in reducing the nuclear symptoms of the disorder (hyperactivity/impulsivity and inattention) compared with the intervention in community (MTA, 1999[39]). When the trial ended, a naturalistic follow-up was performed with follow-up results after 2 and 3 years. The positive effect of the pharmacological treatment on the intervention in communityis maintained in the 2-year results, regarding the reduction of the nuclear symptoms of the disorder (MTA, 2004)[313]. However, in the 2-year follow-up no significant differences are found between the groups (Jensen, *et al*., 2007)[291]. These results must be interpreted with caution due to the fact that the follow-up after the intervention is naturalistic, not controlling the intervention, and to the lack of a control group without treatment. RCT 1+-

Wilens, et al. (2006)300 described the follow-up of 601 adolescents with ADHD treated with atomoxetine, of whom 219 had completed 2 years' treatment. A total of 99 (16.5%) patients suspended the treatment of atomoxetine due to the lack of efficacy. Cohorts study 2+

Recommendations

B	7.3.15.1.	Pharmacological treatment with methylphenidate and atomoxetine for ADHD in children and adolescents should be continued in time whilst the clinical effectiveness is demonstrated.

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

7.3.16. Do the effects remain after the pharmacological treatment has been withdrawn?

The answer is based on the AAP (2005)[196]; SIGN (2005)[1] guidelines, and on the study by Michelson (2004)[256].

Summary of the scientific evidence

There is scientific evidence of the long-term effectiveness (from 12 weeks to 24 months) of the pharmacological treatment if this is continued (AAP, 2005[196]; SIGN, 20051)[1].	RCT 1+, 1++
The patients then followed a relapse prevention RCT with two conditions: atomoxetine and placebo. The atomoxetine (22.3% relapse rate) was greater than the placebo (37.9% relapse rate) in the prevention of relapses after 9 months' follow-up.The low rate of relapses in the placebo group is worth pointing out. These results do, nevertheless, require further studies.	RCT 1+

7.3.17. Is it recommendable to leave stimulant-free periods during the pharmacological treatment ("therapeutic holidays ")?

The answer is based on the NICE guideline (2009)[2]

Summary of the scientific evidence

The NICE CPG (2009)[2] indicates that the use of the drug should be continued for as long as its clinical effectiveness lasts. The pharmacological treatment should be revised at least once a year. This revision should include an appraisal by clinical needs, benefits and side effects, taking into consideration the points of view of the child or adolescent, as well as those of their parents, carers and teachers.The effect of missed doses, planned reductions or short treatment-free periods must be taken into account, and the preferred pattern of use must be assessed. The comorbid disorders must be assessed as well as their treatment or relative referral, as well as possible needs for psychological treatment or social support."Therapeutic holidays" from the drug are not systematically recommended.However, parents or carers and health professional should work together to find the best pattern of use, which may include periods without pharmacological treatment. In children and adolescents with ADHD, whose growth is significantly affected by the pharmacological treatment, the option of resting from the drug during school holidays may be considered to permit reaching the right growth.	Experts' opinion 4

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

Recommendations

√	7.3.17.1.	Pharmacological treatment rest periods ("therapeutic holidays") are not systematically recommended during treatment of ADHD.
√	7.3.17.2.	In some cases, periods without pharmacological treatment or with a lower dose can be included, when agreed between the family, the physician and child or adolescent, with the specific objective of: • Assessing the need to maintain the treatment or not. • Reduce adverse effects (lack of appetite, slowing-down in height growth, etc.).

7.3.18. What clinical variables and standardised instruments exist to evaluate the efficacy of pharmacological treatment? At what moment of the treatment should its efficacy be evaluated?

The response is based on the experts' opinions.

Summary of the scientific evidence

To evaluate the efficacy of the pharmacological treatment, clinical variables will be taken into account, such as the intensity of the nuclear and associated symptoms, the family, academic and social repercussion. The information from the teachers and/or the information obtained via the standardised tools will be assessed based on the clinical interview with the child and parents.	Experts' opinion 4

See chapter 6. Assessment tools, which reviews the main assessment tools used in our medium to evaluate ADHD in children and adolescents.

Recommendations

√	7.3.18.1.	The assessment of the efficacy and tolerability of the intervention will be carried out in the pharmacological treatment of children and adolescents with ADHD at least 1, 3 and 6 months after the start of the treatment, and later every 6 months whilst it lasts, or else, whenever adjustments are made in the dose or changes are made in the drug.

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7.4. Combined treatment

Questions to be answered:

7.4.1. Combined treatment: What does it consist of? What must it include?

7.4.2. In ADHD in children and adolescents: Which intervention or combination of interventions has proved to be more efficient in the short and long term?

7.4.1. Combined treatment: What does it consist of? What must it include?

Combined treatment for ADHD refers to the use of a combination of treatments that make it possible to increase the effects of the interventions in different areas:the medication that addresses the nuclear symptoms and the psychological treatment of secondary as well as comorbid problems associated with ADHD.

The combination of pharmacological and psychological treatments has immediate effects on the symptoms of ADHD via the use of the medication, as well as long-term effects via the development of cognitive and behavioural skills and strategies.

Another area of interest related to combined treatment is the possibility of reducing the risk of side effects of the medication, if the effects of the combined treatment are equivalent to those of the pharmacological treatment alone but with lower doses of medication (NICE, 2009[2]; SIGN, 2005[1]).

7.4.2. In ADHD in children and adolescents:Which intervention or combination of interventions has proved to be more efficient in the short and long term?

In this section, the scientific evidence on the efficacy, safety and cost-effectiveness of combining psychological and pharmacological interventions to treat ADHD is described.

Psychological intervention refers to the cognitive behavioural or behavioural treatment. Pharmacological intervention refers to the intervention with stimulants.

The answer is based on the NICE (2009)[2], SIGN (2005)[1], AACAP (2007)[72] guidelines and the MA by Van der Oord, *et al*. (2008)[147].

The NICE Guideline (2009)[2] performs two SRs and MAs on combined treatment for ADHD.

In the first SR and MA, 7 RCTs of studies published between 1976 and 2004 were included (Abikoff 2004[321]; Brown 1985[161]; Firestone 1981[322], 1986[295]; Gittelman-Klein 1976[297]; Klein 1997[164]; MTA 1999[39]; n=544, ages 5-12 years). The first review includes trials that compare groups with combined treatment (medication for ADHD and concurrent psychological intervention) with pharmacological treatment alone.The trials that compared the combined treatment with the psychological treatment alone or with controls were not included.

Another analysis was performed to compare intensive combined treatment with normal treatment that could include medication. This analysis is based on the data of the MTA study (MTA, 1999)[39] with a view to comparing what could be considered today as the best treatment for ADHD with the highest standard level of care in clinical practice.

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Scientific evidence

The scientific evidence reviewed by the SIGN Guideline (2005)[1] suggests that the combination of non-pharmacological interventions only produces a slight additive effect. However, it indicates that it may be beneficial in those cases where there is comorbidity (Horn, et al., 1991[159]; MTA, 1999[39]). The study by Ialongo, et al. (1994)[210] did not find any additive effects for the combination of medication, intervention in self-control for the child and training for parents. With respect to the MTA study (1999)[39], it finds that the effects of methylphenidate were only equivalent to the combination of psychosocial and pharmacological intervention. The combined group, however, attained an equivalent degree of improvement with a significantly lower dose of medication. The SIGN guideline (2005)[1] expresses the methodological limitations of the MTA study and the need to carry out more research.	RCT 1++
Van der Oord, et al. (2008)[147] performed a MA that included those quality RCTs that assessed the efficacy of methylphenidate, psychosocial treatments and a combination of both to treat ADHD, published between 1985 and 2006. The participants with ADHD were aged, on average, between 6 and 12. The authors evaluated the efficacy in ADHD symptoms, oppositionism, behaviour, social skills and academic performance. 6 RCTs satisfied the inclusion criteria, and included a condition of psychological treatment based on the principles of CBT and methylphenidate that lasted for a short period of time: Abikoff, 2004[321]; Brown, 1985[161], 1986[162]; Klein & Abikoff, 1997[164]; MTA, 1999[39]; Van den Hoofdakker, 2007[152].	MA of RCT 1+
The conclusions of these authors suggest that both methylphenidate and the psychosocial treatments are effective in reducing ADHD symptoms.However, psychosocial treatment has less effect than the other treatment conditions. The psychosocial treatment has no additional value to methylphenidate to reduce ADHD or the oppositionist and defiant symptoms evaluated by the teachers. However, for the social skills and oppositionist and defiant symptoms evaluated by the parents, the three treatments were equally effective.No efficacy was proved in improving academic performance.	

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Variable: Clinical improvement at the end of the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in ADHD symptoms at the end of the treatment (7 RCT, N=482, Abikoff 2004[321]; Brown 1985[161]; Firestone 1981[322], 1986[295]; Gittelman-Klein 1976[297]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.06 [95% CI: -0.24 to 0.12]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' scores in ADHD symptoms at the end of the treatment (6 RCT, N=428, Abikoff 2004[321]; Brown 1985[161]; Firestone 1981[322], Gittelman-Klein 1976[297]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.12 [95% CI: -0.31 to 0.07]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in behaviour at the end of the treatment (6 RCT, N=461 Abikoff 2004321; Firestone 1981[322], 1986[295]; Gittelman-Klein 1976[297]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.07 [95% CI: -0.26 to 0.11]). RCT 1++

There is limited scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' scores in behaviour at the end of the treatment (3 RCT, N=378 Abikoff 2004[321]; Klein 1997[164], MTA 1999[39]) (SMD: -0.21 [95% CI: -0.41 to -0.01]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in social skills at the end of the treatment (3 RCT, N=333, Abikoff 2004[321]; Klein 1997[164], MTA 1999[39]) (SMD: -0.03 [95% CI: -0.11 to 0.05]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the scores of the parents in social skills at the end of the treatment (2 RCT, N=315, Abikoff 2004[321]; MTA 1999[39]) (SMD:0.14, (95% CI: -0.36 to 0.09]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the children's scores in social skills at the end of the treatment (1 RCT, N=68, Abikoff 2004[321]) (SMD: -0.07 [95% CI: -0.54 to 0.41]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in emotional symptoms (internalized) at the end of the treatment (2 RCT N=265, Klein 1997[164]; MTA 1999[39]) (SMD: 0.15 [95% CI: -0.09 to 0.39]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' scores in emotional symptoms (internalized) at the end of the treatment (3 RCT N=327, Firestone 1981[322]; Klein 1997[164]; MTA 1999[39]) (SMD:-0.03, (95% CI: -0.25 to 0.19]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the children's scores in emotional symptoms (internalized) at the end of the treatment (1 RCT N=689, Abikoff 2004[321]) (SMD:0.28 [95% CI: -0.20 to 0.76]). RCT 1++

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There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the children's scores in self-efficacy at the end of the treatment (1RCT, N=68, Abikoff 2004[321]) (SMD: -0.02 [95% CI: -0.50 to 0.45]). RCT 1+

Variable: Clinical improvement 3 to 6 months after the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in the ADHD symptoms 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD: -0.05, (95% CI: -0.93 to 0.82]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' scores in the ADHD symptoms 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD:0.25 [95% CI: -0.63 to 1.13]). RCT 1+

Variable: Clinical improvement 7 to 12 months after the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in ADHD symptoms 7-9 months after treatment (1 RCT, N=44, Firestone 1986295) (SMD: 0.00 [95% CI: -0.59 to 0.59]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' and teachers' scores in ADHD symptoms 10 months after treatment (1 RCT, N=264, MTA 1999[39]) (SMD: -0.06 [95% CI: -0.30 to 0.18]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in behaviour 7-9 months after treatment (1 RCT, N=37, Firestone 1986[295]) (SMD: 0.00 [95% CI: -0.65 to 0.65]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' and teachers' scores in ADHD symptoms 10 months after treatment (1 RCT, N=264, MTA 1999[39]) (SMD: -0.18, (95% CI: -0.42 to 0.06]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' and teachers' scores in social skills 10 months after treatment (1 RCT, N=264, MTA 1999[39]) (SMD: -0.21 [95% CI: -0.45 to 0.03]). RCT 1++

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Variable: Clinical improvement 13 to 24 months after the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in ADHD symptoms 19-21 months after treatment (1 RCT, N=21, Firestone 1986295) (SMD: -0.05 [95% CI: -0.90 to 0.81]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' and teachers' scores in ADHD symptoms 22 months after treatment (1 RCT, N=242, MTA 1999[39]) (SMD: -0.02 [95% CI: -0.27 to 0.23]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the teachers' scores in behaviour 19-21 months after treatment (1 RCT, N=21, Firestone 1986[295]) (SMD:-0.23IC95%: -1.09 to 0.63]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on the parents' and teachers' scores in ADHD symptoms 22 months after treatment (1 RCT, N=242, MTA 1999[39]) (SMD:-0.03, (95% CI: -0.27 to 0.20]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects (+ on the parents' and teachers' scores in social skills 22 months after treatment (1 RCT, N=242, MTA 1999[39]) (SMD: 0.04 [95% CI: -0.21 to 0.29]). RCT 1++

Variable: Educational aspects at the end of the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on reading after treatment (6 RCT, N=478, Abikoff 2004[321] Brown 1985[161]; Firestone 1981[322], 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: 0.04 [95% CI: -0.14 to 0.22]). RCT 1++

There is not sufficient scientific evidence to suggest that combined treatment compared with pharmacological treatment has positive effects on mathematics after treatment (5 RCT, N=437, Abikoff 2004[321]; Brown 1985[161]; Firestone 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.03 [95% CI: -0.22 to 0.15]).

Variable: Educational aspects 3 to 6 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on reading 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD: 0.19 [95% CI: -0.69 to 1.07]). RCT 1+

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There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on mathematics 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD: -0.52 [95% CI: -1.42 to 0.37]). RCT 1+

Variable: Educational aspects 7 to 12 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on reading 7-12 months after treatment (2 RCT, N=303, Firestone 19862[95], MTA 1999[39]) (SMD: -0.02 [95% CI: -0.25 to 0.20]). RCT 1++

Variable: Educational aspects 13 to 24 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with pharmacological treatment has positive effects on reading 13-24 months after treatment (2 RCT, N=261, Firestone 1986295, MTA 1999[39]) (SMD: -0.02 [95% CI: -0.26 to 0.23]). RCT 1++

Summary of the scientific evidence

The results of the trials included in the NICE review (2009)[2] on treatment of children with ADHD that compare the combined intervention with the pharmacological treatment alone indicate that there is little or no advantage of the combined intervention over medication alone. Compared with medication, there is no scientific evidence that the combined treatment provides advantages in measuring nuclear symptoms of ADHD, emotional state or self-efficacy.	MA of RCT 1++
The only scientific evidence of the benefit of the combined treatment over the medication alone is for the parents' scores in behavioural problems at the end of the treatment; however, the benefits are limited, depending on the results of the effect size.No benefits were detected for the combined treatment in subsequent follow-ups after the end of treatment. The MTA study (MTA 1999)[39] is the trial with the largest number of cases of combined treatments with ADHD. Although the MTA data suggest that there is a small beneficial effect of the combined treatment over medication for the parent's scores with respect to behavioural problems at the end of the treatment, the effect size is small.	RCT 1++

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Clinical evidence of intensive combined treatment compared with normal (community) treatment for children with ADHD

The MTA study

The comparison between the intensive combined treatment of the MTA study (medication plus a multimodal psychological treatment for ADHD that consisted of intervention with the child, parents and intervention in the classroom) and the treatment group in community or normal treatment, enables a comparison to be made between intensive treatment and standard care (MTA 1999)[39].

In the MTA study, children with ADHD were randomly assigned to the following four groups:pharmacological treatment, psychosocial treatment, a combination of pharmacological and psychosocial treatment, and normal treatment in community.The pharmacological treatment consisted of scheduled monthly visits when the medication dose was meticulously adapted in agreement with the evaluation scales of parents and teachers.A reduction in ADHD symptoms was shown in the children from the four treatment groups after 14 months, compared with the basal situation. The results of the two groups that had received pharmacological treatment (alone and combined) was better, regarding ADHD symptoms, than the results of the patients who only received psychosocial treatment or normal treatment in community (MTA, 1999)[39]. The improvement of patients who only received psychosocial treatment was not significantly greater than the improvement of the control group who received normal treatment in community (two thirds of the individuals from this group received treatment with stimulants). The normal treatment group in community had a more limited medical follow-up and was treated with lower daily doses of stimulants than those given to the group receiving pharmacological treatment.Almost a quarter of the individuals to whom the psychosocial treatment alone was assigned, required treatment with medication during the trial, due to the lack of effectiveness of the behavioural therapy.

The combined intervention of the MTA study gives an example of what could be considered as intensive care treatment for children with ADHD that continued for 1 year or more.

Variable: Benefits at the end of treatment

Scientific evidence

There is scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on the ADHD symptoms at the end of the treatment according to the teachers' appraisal (1 RCT, N=263, MTA 1999)[39] (SMD: -0.64 [95% CI: -0.89 to -0.39]). RCT 1++

There is scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on the ADHD symptoms at the end of the treatment according to the appraisal by parents (1 RCT, N=263, MTA 1999)39 (SMD: -0.74 [95% CI: -0.99 to -0.49]). RCT 1++

There is scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on behaviour at the end of the treatment according to the teachers' appraisal (1 RCT, N=263, MTA 1999)[39] (SMD: -0.51 [95% CI: -0.76 to -0.26]). RCT 1++

There is scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on behaviour at the end of the treatment according to the parents' appraisal (1 RCT, N=263, MTA 1999)[39] (SMD: -0.53 [95% CI: -0.78 to -0.29]). RCT 1++ 1++

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There is limited scientific evidence to suggest that the combined compared with normal treatment in community has positive effects on social skills at the end of the treatment according to the teachers' appraisal (1 RCT, N=213, MTA 1999)[39] (SMD:-0.14 [95% CI: -0.22 to -0.06]). RCT 1++

There is limited scientific evidence to suggest that the combined compared with normal treatment in community has positive effects on social skills at the end of the treatment according to the parents' appraisal (1 RCT, N=252, MTA 1999)[39] (SMD:-0.27, (95% CI: -0.52 to -0.02]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment with normal treatment in community has positive effects on emotional results at the end of the treatment according to the teachers' appraisal (1 RCT, N=213, MTA 1999)[39] (SMD: -0.02 [95% CI: -0.29 to 0.25]). RCT 1++

There is limited scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on emotional results at the end of the treatment according to the parents' appraisal (1 RCT, N=252, MTA 1999)[39] (SMD:0.27 [95% CI: -0.02 to 0.52]). RCT 1++

Variable: Benefits 7 to 12 months after treatment

Scientific evidence

There is limited scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on ADHD symptoms 10 months after treatment according to the combined score of parents and teachers (1 RCT, N=273, MTA 1999[39]) (SMD: -0.34, (95% CI: -0.58 to -0.10]). RCT 1++

There is limited scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on behaviour 10 months after treatment according to the combined score of parents and teachers (1 RCT,, N=273, MTA 1999[39]) (SMD: -0.31 (95% CI: -0.55 to -0.07]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment with normal treatment in community has positive effects on social skills 10 months after treatment according to the combined score of parents and teachers (1 RCT, N=273, MTA 1999[39]) (SMD: -0.17 [95% CI: -0.41 to 0.06]). RCT 1+

Variable: Benefits 13 to 24 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment with normal treatment in community has positive effects on ADHD symptoms 22 months after treatment according to the combined score of parents and teachers (1 RCT, N=243, MTA 1999[39]) (SMD: -0.11 [95% CI: -0.36 to 0.15]). RCT 1+

There is strong scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on behaviour 22 months after treatment according to the combined score of parents and teachers (1 RCT, N=243, MTA 1999[39]) (SMD: -0.82 [95% CI: -1.08 to -0.56]). RCT 1++

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There is not sufficient scientific evidence to suggest that the combined treatment with normal treatment in community has positive effects on social skills 22 months after treatment according to the combined score of parents and teachers (1 RCT, N=243, MTA 1999[39]) (SMD: 0.04 [95% CI: -0.21 to 0.29]). RCT 1++

Variable: Educational aspects at the end of treatment

Scientific evidence

There is little scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on reading after treatment (1 RCT, N=267, MTA 1999[39]) (SMD: -0.27 [95% CI: -0.51 to -0.03]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on mathematics after treatment (1 RCT, N=267, MTA 1999[39]) (SMD: -0.01 [95% CI: -0.25 to 0.23]). RCT 1++

Variable: Educational aspects 7 to 12 months after end of treatment

Scientific evidence

There is little scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on reading after treatment (1 RCT, N=267, MTA 1999[39]) (SMD: -0.27 [95% CI: -0.51 to -0.03]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on mathematics after treatment (1 RCT, N=267, MTA 1999[39]) (SMD: -0.01 [95% CI: -0.25 to 0.23]). RCT 1++

Variable: Educational aspects 7 to 12 months after end of treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive on reading 10 months after treatment (1 RCT, N=273, MTA 1999[39]) (SMD: -0.19 [95% CI: -0.43 to 0.05]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with normal treatment in community has positive effects on reading after treatment (1 RCT, N=243, MTA 1999[39]) (SMD: -0.12 [95% CI: -0.37 to 0.13]). RCT 1++

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The combined intervention of MTA is generally more efficient than normal treatment in the community according to the scores of parents and teachers for ADHD symptoms and behaviour problems.According to the joint appraisals of parents and teachers of ADHD symptoms in follow-ups, the combined treatment continues having better results than normal treatment in community 10 months after the intervention, but the effect size is small.In the 22-month follow-up, neither the combined treatment nor the normal treatment in the community obtained positive results according to the joint appraisals for ADHD symptoms. However, in the measurements of the behaviour problems, the combined treatment is more efficient than normal treatment. At the end of the intervention, according to scores of parents and teachers, the reduction of the behaviour problems was greater with the combined treatment than with the normal treatment, the effect size being moderate. The score of parents and teachers for behaviour problems in subsequent follow-ups indicated that the beneficial effect of the combined treatment was reduced to a small effect 10 months after the intervention, but this effect was greater 22 months after treatment.

The scores of parents and teachers on social skills at the end of the intervention show small improvements with the combined treatment compared with normal treatment in the community, but this small effect disappears in subsequent follow-ups, according to the joint appraisals for parents and teachers.

The parents' scores on the emotional state of the child show a small advantage of the combined treatment compared with the normal treatment at the end of the intervention.However, the teachers' scores do not show this advantage at the end of the intervention.

When the joint results are taken into consideration, it seems that there is some benefit of the combined treatment over the normal treatment in the community.The measurements of ADHD symptoms at the end of the intervention indicate that the combined treatment is moderately more effective in nuclear symptoms than the treatment in the community, and that it may have beneficial effects on behaviour problems.However, the key factor to generate the positive effects of the combined treatment may be the management of the medication.In any case, the comparison of the results of the MTA study on the combined intensive treatment group and the normal treatment in community does not offer a consistent indication that the intensive treatment is more effective than the normal treatment, which includes medication for ADHD.The advantage of the combined intensive treatment over the normal treatment should be considered in the context of the evaluation of whether the combined treatment is efficient compared with a specific pharmacological treatment.

Summary of the scientific evidence

The scientific evidence of the trials that compare combined treatment with pharmacological treatment alone shows no beneficial effects when adding psychological intervention to the medication protocol. The data suggest that if the pharmacological treatment for ADHD has already been established, and the child has responded positively, adding psychological intervention to treat ADHD (parenttraining programmeor directly for the child) show no additive effects over the nuclear symptoms of ADHD, disturbing behaviour, emotional state and/or self-efficacy(NICE, 2009)[2].	MA of RCT 1++
The psychological intervention is effective as a contribution to the normal medication. This may be because the medication is less effective in normal clinical practice than in the context of a clinical trial. The same occurs in the MTA study (MTA, 1999)[39], which suggests that the combination of interventions may help treat certain problems and favour some results. Several authors defined the usefulness of multimodal treatment to improve the symptoms.	RCT 1++

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Clinical evidence of intensive combined treatment compared with normal (community) treatment for children with ADHD

Summary of the scientific evidence

The NICE guideline (2009)[2] conducts a direct review of the efficacy of the psychological and pharmacological treatments for ADHD. 6 RCTs of studies published between 1976 and 1999 are included (Brown 1985161; Firestone 1981322, 1986[295]; Gittelman-Klein 1976[297]; Klein 1997[164]; MTA 1999[39]). Generally speaking, for children with ADHD, the scientific evidence of the trials that compare stimulant medication (predominantly methylphenidate) with psychological intervention given to a group without pharmacological treatment, generally favours stimulant medication, although in the cases where it reaches statistical significance, the effect sizes are not great. The quality of the trials is moderate to high.	MA of RCT 1+, 1++
The AACAP guideline (2007)[72] specifies the study by Jadad, et al. (1999)[276], that reviewed 78 ADHD treatment studies; 6 of these compared pharmacological and non-pharmacological interventions. The reviewers indicated that the studies unanimously backed the superiority of stimulants with respect to non-pharmacological treatment.	RCT 1++

Variable: Benefits at the end of treatment

Scientific evidence

There is strong scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on ADHD symptoms at the end of the treatment according to the teachers' appraisal (5 RCT, N=392, Brown 1985[161]; Firestone 1981[322], 1986295; Klein 1997[164]; MTA 1999[39]) (SMD: -0.72 [95% CI: -1.12 to -0.32]). RCT 1++

There is scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on ADHD symptoms at the end of the treatment according to the parents' appraisal(4 RCT, N=350, Brown 1985[161]; Firestone 1981[322], 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.45 [95% CI: -0.66 to -0.23]). RCT 1++

There is scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on behaviour at the end of the treatment according to the teachers' appraisal(3 RCT, N=321; Firestone 1981[322,] 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.48 [95% CI: -0.70 to -0.25]). RCT 1++

There is limited scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on behaviour at the end of the treatment according to the parents' appraisal(3 RCT, N=355; Firestone 1986[295], 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.22 [95% CI: -0.43 to -0.01]). RCT 1++

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There is limited scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on social skills at the end of the treatment according to the teachers' appraisal (2 RCT, N=258, Klein 1997[164]; MTA 1999[39]) (SMD:-0.33 [95% CI: -0.57 to -0.08]). RCT 1++

There is not scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on social skills at the end of the treatment according to the parents' appraisal (1 RCT, N=151, MTA 1999[39]) (SMD: -0.08 [95% CI: -0.33 to 0.17]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on (internalized) emotional symptoms at the end of the treatment according to the teachers' appraisal (2 RCT, N=158, Klein 1997[164]; MTA 1999[39]) (SMD: 0.14 [95% CI: -0.10 to 0.39]). RCT 1++

There is limited scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on (internalized) emotional symptoms at the end of the treatment according to the parents' appraisal(3 RCT, N=331; Firestone 1981[322], 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD: -0.23 [95% CI: -0.45 to -0.01]). RCT 1++

Variable: Benefits 3 to 6 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects effects on ADHD symptoms 3 months after treatment according to the score of teachers (1 RCT, N=20, Brown 1985[161]) (SMD:-0.20 [95% CI: -1.58 to 0.68]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on ADHD symptoms 6 months after treatment according to the score of parents (1 RCT, N=20, Brown 1985[161]) (SMD: -0,82[95% CI -1.74 to 0.11]). RCT 1+

Variable: Benefits 7 to 12 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on ADHD symptoms 7 to 9 months after treatment according to the score of teachers (1 RCT, N=35, Firestone 1986[295]) (SMD: -0.53 [95% CI: -1.23 to 0.17]). RCT 1+

There is limited scientific evidence to suggest that pharmacological treatment compared with psychological treatment has positive effects on on ADHD symptoms 10 months after treatment according to the combined score of parents and teachers (1 RCT, N=267, MTA 1999[39]) (SMD: -0.25 [95% CI: -0.49 to -0.01]). RCT 1++

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There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on behaviour 7 to 9 months after treatment according to the score of parents (1 RCT, N=34, Firestone 1986[295]) (SMD: -0.32 [95% CI: -1.02 to 0.38]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on behaviour 10 months after treatment according to the combined score of parents and teachers (1 RCT, N=267, Firestone 1986[295]) (SMD: -0.10 [95% CI: -0.34 to 0.14]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on social skills 10 months after treatment according to the combined score of parents and teachers (1 RCT, N=267, MTA 1999[39]) (SMD: -0.07 [95% CI: -0.31 to 0.17]). RCT 1++

Variable: Benefits 13 to 24 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on ADHD symptoms 19 to 21 months after treatment according to the score of teachers (1 RCT, N=30, Firestone 1986[295]) (SMD:0.00 [95% CI: -0.88 to 0.88]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on ADHD symptoms 19 to 21 months after treatment according to the score of parents (1 RCT, N=20, Brown 1985[161]) (SMD:0.58 [95% CI: -0.32 to 1.48]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on ADHD symptoms 13 to 24 months after treatment according to the combined score of parents and teachers (1 RCT, N=242, MTA 1999[39]) (SMD: -0.06 [95% CI: -0.21 to 0.09]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on behaviour 22 months after treatment according to the combined score of parents and teachers (1 RCT, N=243, MTA 1999[39]) (SMD: 0.00 [95% CI: -0.25 to 0.25]). RCT 1++

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on social skills 22 months after treatment according to the combined score of parents and teachers (1 RCT, N=243, MTA 1999[39]) (SMD: -0.04 [95% CI: -0.29 to 0.21]). RCT 1++

Variable: Educational aspects at the end of the treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on reading after treatment (5 RCT, N=397 Brown 1985[161]; Firestone 1981322, 1986[295]; Klein 1997[164]; MTA 1999[39]) (SMD:-0.10, (95% CI: -0.3' to 0.09]). RCT 1++

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There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on mathematics after treatment (4 RCT, N=358, Brown 1985[161]; Firestone 1981[322], Klein 1997[164]; MTA 1999[39]) (SMD:0.01 [95% CI: -0.20 to 0.22]). RCT 1++

Variable: Educational aspects 3 to 6 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on reading 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD: 0.11 [95% CI: -0.77 to 0.99]). RCT 1+

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on mathematics 3 months after treatment (1 RCT, N=20, Brown 1985[161]) (SMD: 0.57 [95% CI: -0.32 to 1.47]). RCT 1+

Variable: Educational aspects 7 to 12 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on reading 7-10 months after treatment (2 RCT, N=301, Firestone 1986[295], MTA 1999[39]) (SMD: -0.05 [95% CI: -0.27 to 0.18]). RCT 1++

Variable: Educational aspects 13 to 24 months after treatment

Scientific evidence

There is not sufficient scientific evidence to suggest that the combined treatment compared with psychological treatment has positive effects on reading 19-22 months after treatment (2 RCT, N=260, Firestone 1986[295], MTA 1999[39]) (SMD: 0.03 [95% CI: -0.22 to 0.27]). RCT 1++

For the scores of parents and teachers on the nuclear symptoms of ADHD and behaviour problems at the end of the treatment, stimulant medication provides better results than psychological intervention, with effect sizes that vary from small to moderate.However, the benefits of stimulant medication on psychological therapies for nuclear symptoms of ADHD and behaviour problems in general are not sustained in follow-up appraisals (3-6 months, 7-12 months and 13-24 months after the end of the treatment).The MTA study finds a benefit of medication over the psychological intervention in the combined measurements for parents and teachers on nuclear symptoms of ADHD 10 months after treatment, but the effect size was small.

Stimulant medication seems to be more effective than psychological intervention in the improvement of social skills appraised by teachers, but this effect was small at the end of the treatment and not sustained in the follow-ups.It was not reflected either in the parents'

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measurements of social skills, which indicates that there is no positive influence of the stimulant medication on the social skills at the end of the treatment or during follow-up.In the measurements of the emotional state (depression, anxiety, emotional adjustment and internalized symptoms), the stimulant medication was more effective than the psychological intervention at the end of the treatment, but the effect size was small and limited in the parents' measurements, with no effect in the teachers' measurements.

The lack of scientific evidence of the sustained superiority of the medication over psychological intervention for ADHD is difficult to interpret.For longer follow-ups in time, the results can be influenced by the treatment that the child has received since the end of the experimental intervention period.In particular, children that received psychological intervention and were not medicated for ADHD during the trial period were able to start to receive medication for ADHD later on.In the MTA study, 44% of the children of the group that only received psychological intervention during the study had started stimulant medication after the 10-month follow-up.22 months after the end of the treatment, 45% of the children had started stimulant medication.

Summary of the scientific evidence

Although there is scientific evidence about the superiority of the pharmacological intervention with respect to the psychological intervention, when stimulant medication is compared with complex psychological intervention (as offered in the MTA study), the benefits of the medication respect to the psychological treatment are weak (NICE, 2009)[2].	RCT 1++

Cost-effectiveness studies

Summary of the scientific evidence

The NICE CPG (2009)[2] has reviewed the available scientific evidence on economic cost-effectiveness studies for pharmacological and psychological treatment and a treatment combination in children with ADHD: Lord & Paisley 2000[323], Zupancic, *et al*., 1998[290]. The NICE economic model was also used, about the use of methylphenidate, atomoxetine and dexamphetamine in children with ADHD via a subanalysis that compared the combination of interventions with the medications evaluated (King, et al., 2006)[201]. An economic analysis of the interventions assessed in the MTA study was reviewed separately (MTA 1999)[39]: Jensen, et al., 2005[324]; Foster, *et al*., 2007325.	Cost-effectiveness studies 1+, 1++
Lord & Paisley (2000)[323] performed an economic analysis that compared the cost-effectiveness of the combination of interventions with psychological therapy alone for children with ADHD in the United Kingdom, based on the data of the MTA study(1999)[39], the results favour the combined treatment. However, due to methodological limitations, these results must be appraised with caution.	Cost-effectiveness studies 1+

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The scientific evidence of Zupancic, et al. (1998)[290] suggests that combined and psychological therapy is not a cost-effective option compared with medication for children with ADHD. However, there are limitations in the clinical effectiveness of the data used in the analysis.	Cost-effectiveness studies 1+
The review of the economic analysis of King *et al*.(2006)[201] suggests that group behavioural therapy is more cost-effective than combined treatment and medication for children with ADHD. On the other hand, medication is more cost-effective than individual behavioural therapy. Combined therapy was not cost-effective in the studies reviewed.	Cost-effectiveness studies 1++
The review by Jensen *et al*.(2005)[324] and Foster, et al. (2007)[325] on the MTA study (MTA 1999)[39] concludes that, for children with ADHD, the management of the medication, although not so effective as the combined therapy, is a more cost-effective option, above all for children with associated comorbid disorders. For children with comorbid ADHD with both internalizedand externalising disorders, they suggest that the combined treatment is relatively cost-effective. The medication management was the most suitable option from the cost-effectiveness viewpoint, compared with intensive behavioural treatment and combined treatment.	Cost-effectiveness studies 1++

Different reasons why it is advisable to use multimodal treatment for ADHD (NICE, 2009)[2]

There are several reasons why non-pharmacological treatment, normally psychological treatment, can be combined with pharmacological treatment:

- When psychological intervention is the option preferred by children and adolescents, and their families, but due to the seriousness of the symptoms, this may not be feasible at that time.However, the medication's potential to provide a fast initial improvement over the first few weeks of a combined intervention may help them benefit from the psychological techniques later on.
- In serious cases, it may be advisable to start the pharmacological treatment in order to offer more immediate improvement effects. This may be necessary if there is a marked social dysfunction, a lot of pressure from the family or companion, if the child is facing an impending school expulsion.
- Behavioural learning in psychological treatment may be favoured by the combined use of pharmacological treatment.
- Combining pharmacological treatment with psychological intervention may lead to a reduction in the drug doses and also in concerns about the use of the medication.

Recommendations

B	7.4.2.1	In children and adolescents with moderate or serious ADHD, combined treatment is recommended, which includes behavioural psychological treatment, pharmacological treatment and psychopedagogical intervention at school.

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7.5. Comorbidity treatment

Questions to be answered:

7.5.1. In children and adolescents with ADHD: What must be done with comorbid epilepsy?

7.5.2. In children and adolescents with ADHD: What must be done with comorbid autism spectrum disorders?

7.5.3. In children and adolescents with ADHD: What must be done with comorbid mood disorders?

7.5.4. In children and adolescents with ADHD: What must be done with comorbid bipolar disorder?

7.5.5. In children and adolescents with ADHD: What must be done with comorbid substance abuse?

This section describes the scientific evidence about the therapeutic strategy of ADHD in children and adolescents associated with the comorbidities that the guideline development group considers important, due to the possible change in treatment strategy or to doubts with respect to the intervention.

A description is given below of the treatment strategy for children and adolescents with ADHD with comorbidity:Epilepsy, autism spectrum disorders (ASD), emotional disorders and substance use disorder.

7.5.1. In children and adolescents with ADHD: What must be done with comorbid epilepsy?

The answer is based on the review by Torres, *et al*. (2008)[326]; Schubert (2005)[327] and Artigas-Pallarés (2003)[328].

Summary of the scientific evidence

The reviews by Torres, et al. (2008)[326] and Schubert (2005)[327] indicate that the available scientific evidence supports the use of methylphenidate for treating ADHD in children with epileptic crises. They also suggest that the treatment should be part of a biopsychosocial intervention.	SR of cases series and cohort studies 2+
Epilepsy is not in itself a contraindication for the use of methylphenidate if the crises are controlled (Artigas-Pallarés, 2003)[328].	Experts' opinion. 4
Atomoxetine does not increase the risk of epileptic crises in patients with ADHD. To date, there is no scientific evidence about the safety of atomoxetine in children and adolescents with ADHD and comorbid epilepsy(Schubert, 2005)[327].	SR of case series and cohort studies 2+

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Recommendations

C	7.5.1.1.	The use of methylphenidate is not contraindicated in children and adolescents with ADHD and comorbid epilepsy.

7.5.2. In children and adolescents with ADHD: What must be done with comorbid autism spectrum disorders?

The answer is based on the guidelines of the Autism Spectrum Disorders Study Group (Fuentes-Biggi, *et al*., 2006)[329]. Also on the studies by Posey, *et al*. (2006)[330] and Troost, *et al*. (2006)[331].

Summary of the scientific evidence

The guideline of the ASD Study Group (Fuentes-Biggi, *et al*., 2006)[329] indicates, in connection with people with ASD in whom ADHD has also been identified, that the treatment with stimulants decreases the stereotypes and inappropriate language.In these cases, the drug must be used with caution as its beneficial effect is less and adverse effects have been described more frequently than in the general population with ADHD. These effects include:withdrawal, irritability, weight loss and difficulty to get to sleep.	Experts' opinion 4
No quality studies have been found in the searches made to prepare this CPG on the efficacy and safety of atomoxetine for treating ADHD in children and adolescents, comorbid to ASD. Two open-ended trials have been found by Posey, *et al*. (2006)[330] and Troost, *et al*.(2006)[331] performed with small samples (n=16, n=12) on children and adolescents with ADHD (6 to 14 years old) that assess the tolerability and efficacy of atomoxetine for ADHD symptoms in children with ASD. The authors' conclusions suggest that atomoxetine can be an efficient treatment for ADHD symptoms in children with ASD.However, they may be more vulnerableto some of the known side effects of atomoxetine.WW	Open-ended trials 1–

Recommendations

D	7.5.2.1.	The use of methylphenidate and atomoxetine is not contraindicated in children and adolescents with ADHD and comorbid autism spectrum disorders. However, they must be used with caution.

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7.5.3. In children and adolescents with ADHD: What must be done with comorbid mood disorders?

The answer is based on the Texas Children's Medication Algorithm Project guideline (Pliszka, *et al*., 2006)[332]. Also in the review by Artigas-Pallarés (2003)[328].

Summary of the scientific evidence

The Texas Children's Medication Algorithm Project (Pliszka, *et al*., 2006)[332] indicates that in the cases of children and adolescents with comorbid ADHD anddepressive disorder, the physician must focus, to start with, on treating the most intense disorder and that affects the child the most. Establishing one single drug is recommended for one of the disorders, the most intense one.	Experts' opinion 4
The use of atomoxetine has been studied to treat patients with ADHD and associated anxiety (Sumner, *et al*., 2005)[333]. At the end of the treatment period, the atomoxetine had significantly reduced the score of symptoms of ADHD and anxiety compared with placebo. Another study indicated that there are no data to show that atomoxetine is efficient to treat major depressive disorder (Bangs, *et al*., 2005)[334].	RCT1+
Despite the fact that pharmacological indication is well established for ADHD and depression, doubts arise about which medication is the most suitable to start with, methylphenidate, an SSRI or the association between both.Depending on the most marked symptoms, the use of the stimulant medication of the SSRI will be decided (Artigas-Pallarés, 2003)[328]	Experts' opinion 4

Recommendations

D	7.5.3.1.	In children and adolescents with ADHD and comorbid mood disorders, it is advisable to firstly treat the more intense disorder and that might have greater repercussion on the patient.
B	7.5.3.2.	In children and adolescents with ADHD and associated anxiety, the use of atomoxetine is recommended as treatment of first choice, as it has proved to be efficient to treat both disorders.

7.5.4. In children and adolescents with ADHD: What must be done with comorbid bipolar disorder?

The answer is based on the AACAP guideline for bipolar disorder (2007)[335]. Also on the MA by Consoli, *et al*. (2007)[336] and the review by Kowatch (2005)[337].

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Summary of the scientific evidence

The practical parameters of AACAP (2007)[335] for bipolar disorder indicate that comorbidity with ADHD predicts a worse response to the treatment. So, although the drugs used in adults may be useful, adolescents may be more difficult to treat, and require other interventions apart from the pharmacological intervention (State, *et al*., 2004)[338]. For patients with a clear bipolar disorder, the stimulant medication may be useful to treat ADHD symptoms once the mood symptoms have been suitably controlled with other drugs.	Experts' opinion 4
In the MA by Consoli, *et al*. (2007)[336] 5 open-ended trials were assessed (n=273) on children and adolescents with bipolar disorder, divided into two subgroups: with or without ADHD The objective was to assess if the comorbid ADHD has an influence on the response to the treatment of adolescents with acute mania. The authors' conclusion suggests that children and adolescents with bipolar disorder and ADHD tend to respond less to the pharmacological treatment used for the acute mania. The treatment administered in the majority of the trials was lithium.	MA of controlled trials 1-
Kowatch (2005)[337] indicates that the ADHD symptoms may worsen and complicate the treatment of the bipolar disorder, so he recommends the careful use of stimulants, if they are clinically indicated, only when the bipolar symptoms have been controlled by a mood stabiliser.Non-stimulants such as atomoxetine and tricyclic antidepressants may, due to their activity, induce changes in mania/hypomania and rapid cycling (Biederman, 1999)[339].	Experts' opinion 4

Recommendations

D	7.5.4.1.	In the cases of clear bipolar disorder comorbidity with ADHD in children and adolescents, stimulant medication may be useful to treat ADHD once the mood symptoms have been adequately controlled with other drugs.

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7.5.5. In children and adolescents with ADHD: What must be done with comorbid substance abuse?

The answer is based on the reviews by Kollins (2008)[340], Upadhyaya (2007)[341] and Wilens, *et al*. (2003, 2005)[317,318].

Scientific evidence

Kollins (2008)[340] indicates that the abuse and inadequate use of the prescription of stimulants are especially concerning when treating adolescents and children. Short-term stimulants may have a greater potential for abuse or inadequate use, although more data are required to confirm this observation. Treatment with non-stimulant drugs may be considered for ADHD in patients with a high risk of substance abuse or improper use of stimulants.	Experts' opinion 4
The review by Upadhyaya (2007)[341] indicates that patients with ADHD and substance use disorder start to use substances at a younger age, they may take longer to reach remission, they have a longer course, worse results and higher rates of other psychiatric comorbidities. There is scientific evidence of the incorrect use of stimulant medication, which suggests safety concerns.The pharmacological treatment studies for ADHD comorbid to substance abuse are limited, but they have shown that stimulant medication does not favour the use of substances. Non-stimulant medication for ADHD and long-term stimulant formulas are available and using them incorrectly is less likely. According to these authors, the clinical recommendations to treat this dual diagnosis include the use of non-stimulants or long-term formulas combined with psychosocial therapy to treat ADHD and substance use disorder.	Narrative review 3
Wilens, *et al*. (2005)[317] performed a MA to assess the role of medication to treat ADHD in individuals with ADHD and substance abuse. 9 studies were included (4 of adolescents and 5 of adults, n = 222). The authors' conclusions suggest that the pharmacological treatment (stimulant or non-stimulant) in ADHD comorbid to substance use has a moderate impact on the result of both disorders.This improvement has not been observed in controlled tests with placebo. From the safety perspective, there is no scientific evidence of a worsening of the substance use or adverse interactions with the drug.	MA of open-ended studies and RCT 1+, 1++
Wilens, *et al*. (2003)[318] performed a MA with 6 long-term studies (prospective and retroprospective) that assessed children with ADHD (n = 1034) treated with and without medication to evaluate the results of substance use in adolescents or adults. These authors' conclusion suggests that stimulant therapy in childhood is associated with the reduction of the risk of disorders caused by the abuse of substances, alcohol and cigarettes, and that it has a greater protective effect (Wilens, 2008)[342].	MA of cohort studies 2++

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Summary of the scientific evidence

The treatment with stimulants and non-stimulants in children and adolescents with ADHD represents a protective factor against the consumption of substances(Wilens, *et al*., 2005[317]; 2003[318]).	MA of cohort studies 2++

Recommendations

B	7.5.5.1.	In the case of comorbidity of ADHD and substance use disorder in children and adolescents, treatment with non-stimulants or with long acting stimulants is indicated.

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7.6. Complementary and alternative medicine

Questions to be answered:

7.6.1. Complementary and alternative medicine: What does it consist of?

7.6.2. To treat ADHD in children and adolescents:Are complementary and alternative therapies efficient?

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7.6.1. Complementary and alternative medicine: What does it consist of?

The Cochrane Collaboration defines complementary and alternative medicine (CAM) as a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs.Complementary and alternative therapies are different to those established by traditional health system in a culture and period (Chan, 2002)[343].

The practices and products of complementary and alternative medicine are not considered to be an integral part of standard allopathic clinical practice. Alternative medicine refers to the use of treatments other than standard ones.Complementary medicine indicates the use of alternative treatments applied together with standard treatments (web page of the NIH, 2009)[344].

Due to the exponential increase of complementary and alternative medicine or therapies over the last few years, health professionals are continuously receiving doubts and questions from their patients and carers about their use.On the other hand, many patients do not disclose their use to their physicians, with the possible interference in the medical treatment or adverse effects.

Due to many different causes, such as a lack of knowledge of ADHD in the general public, the despair of parents, social pressure, fear of medication and the broad offer that exists, there is a great variety of alternative treatments that lack scientific basis, whose efficacy and safety has not been proved, and which are advertised as the panacea in ADHD (Soutullo & Diez, 2007)[79].

Some of the alternative therapies for ADHD in children and adolescents include: dietetic treatments, optometry treatments, homeopathy, herbal medicine, auditory stimulation (Tomatis method) and encephalogram biofeedback (EEG-biofeedback, neurofeedback or neurotherapy), psychomotricity and osteopathy.

7.6.2. To treat ADHD in children and adolescents:Are complementary and alternative therapies efficient?

The answer is based on the NICE (2009)[2], SIGN (2005)[1], AACAP (2007)[72] guidelines, the Cochrane 1++ quality SR by Coulter & Dean (2007)[345], 1+ quality RCT by Weber, *et al*. (2008)[346] and the RCT by Pintov, *et al*. (2005)[347].

Dietetic treatments

It is popularly believed that many reactions to food and drink lead to hyperactive behaviour. Dietetic treatments consist in including supplementary substances in the diet that are believed to be beneficial to palliate a deficit, or exclude substances that are believed to be harmful for the organism.

Elimination interventions include those that lead to the discovery and elimination of substances from the individual diet of each child, for example, the elimination of tartrazine, artificial colouring agents and preserving agents. The use of fatty acids is one of the most outstanding supplementary interventions (NICE, 2009)[2].

Summary of the scientific evidence

Research has encountered many difficulties in the methodology and feasibility to study dietetic treatments.The quality of the scientific evidence is generally poor, reflecting the limited amount of data.Therefore, these have been studied based on a narrative approach instead of a systematic approach, and no significant conclusion has been found.The scientific evidence that supplementary or elimination diets, when compared with placebo, can reduce the symptoms of ADHD is not conclusive (NICE, 2009)[2].	RCT1-
The SIGN guideline (2005)[1] found insufficient scientific evidence to support the normal use of this type of interventions to treat ADHD. So diet restrictions or eliminations are not recommended in children with ADHD.	Experts' opinion 4
The AACAP guideline (2007)[72] indicates that there is not scientific evidence to support these interventions in patients with ADHD.	Experts' opinion 4
The AAP guideline (2001)[180] indicates that these interventions are not supported by scientific evidence-based studies.	Experts' opinion 4

Optometry treatment

This consists of visual training sessions carried out by an optometrist in order to improve or develop visual skills or palliate deficiencies that affect ADHD. The treatment is carried out by way of visual exercises and the use of coloured lenses, personalised glasses, filters, prisms and light.

No quality studies have been found in the searches made to prepare this CPG on the efficacy of optometry treatments for treating ADHD in children and adolescents.

Homeopathy

Over the last few years, homeopathy has gained in importance as an alternative therapy. It is a therapeutic system founded by Samuel Hahnemann (1755-1843), based on the principle of similarity where "similars are cured by similars".The diseases are treated by highly diluted substances that, in healthy people, cause the symptoms of the disease to be treated.The dilutions are repeated as many times as there is less than one molecule per dose and it is suggested that the benefit comes from the vital energy force of the original substance. Homeopathy focuses on the unique traits of each patient, their experience and symptoms, and it uses this information to determine the prescription for each patient (Coulter & Dean, 2007)[345].

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Summary of the scientific evidence

The Cochrane review by Coulter & Dean (2007)[345] assesses the scientific evidence of the efficacy, effectiveness and safety/tolerability of homeopathy as an intervention for ADHD. 4 studies were included: Jacobs, 2005[348]; Lamont, 1997[349]; Strauss, 2000[350]; Frei, 2005[351]. No studies were found on safety/ tolerability. In general, the results of this review do not suggest scientific evidence of the effectiveness of homeopathy for the global symptoms of ADHD, nuclear symptoms or associated symptoms such as anxiety in ADHD. The conclusions of the authors of the review suggest that there is little scientific evidence of the efficacy of homeopathy to treat ADHD.	SR of RCT 1+

Herbal medicine

Use of medicines derived from botanical sources, using their therapeutic properties, flavour or essence. Herbal medicine products are dietetic supplements. They are sold in tablets, capsules, powder, infusions, extracts, and dry or fresh.However, some many cause health problems, some are not effective or they may interact with other medications.

Summary of the scientific evidence

The SIGN guideline (2005)[1] did not find any scientific evidence of an acceptable standard that backs these strategies, so, it makes no recommendations about their use.	Experts' opinion 4
The AAP guideline (2001)[180] indicates that these interventions are not supported by scientific evidence-based studies.	Experts' opinion 4
Weber, *et al*. (2008)[346] conducted a study on the efficacy and safety of Hypericum perforatum (St. John's Wort) in a group of children with ADHD (n=54, 6 to 17 years old) compared with placebo. The intervention lasted for 8 weeks. The results of the study did not show significant differences in the symptoms of ADHD between the intervention group and the placebo group. The authors conclude that the administration of Hypericum perforatum does not have greater beneficial effects than the placebo to treat the symptoms of ADHD in children and adolescents.	RCT1+
Pintov, *et al*. (2005)[347] conducted a study on the effectiveness of Bach flowersto treat a group of children with ADHD (n=40, 7 to 11 years old) compared with placebo. The intervention lasted for 3 weeks. The results of the study did not show significant differences in the symptoms of ADHD between the intervention group and the placebo group. The authors' conclusion is that their results do not support the hypothesis that Bach flowers are associated with a greater response than the placebo.	RCT1+

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Auditory stimulation

This is based on the hypothetical beneficial effect of different tones of music and sounds on children with ADHD. It is assumed that the Tomatis method, for example, produces an auditory re-education (Soutullo & Diez, 2007)[79].

No quality studies have been found in the searches made to prepare this CPG on the efficacy of auditory stimulation treatments for treating ADHD in children and adolescents.

Encephalogram biofeedback (EEG- biofeedback, neurofeedback or neurotherapy)

In this therapy, the person uses the information from the biofeedback to voluntarily gain control over the process of the functions that are under the control of the autonomous system. It aims to treat ADHD by raising the ratio between high frequency waves with respect to low frequency waves in the EEG. The studies are loaded with artefacts, placebo effect and the effect of other treatments used (Soutullo & Diez, 2007)[79].

Summary of the scientific evidence

The SIGN guideline (2005)[1] did not find any scientific evidence of an acceptable standard that backs these strategies, so, it makes no recommendations about their use.	Experts' opinion 4
The AACAP guideline (2007)[72] indicates that the efficacy of EEG retrofeedback has not been established as primary treatment of ADHD or as an addition to the pharmacological treatment (Loo, 2003)[352].	RCT1+
The AAP guideline (2001)[180] indicates that these interventions are not supported by scientific evidence-based studies.	Experts' opinion 4

Osteopathy

Osteopathy is based on the belief that all the body systems work together, they are related and, therefore, the disorders in a system may affect the functioning of others.According to its principles, by manipulating the musculoskeletal system, affections of the vital organs or diseases can be cured.

No quality studies have been found in the searches made to prepare this CPG on the efficacy of osteopathy treatments for treating ADHD in children and adolescents.

Psychomotricity

Psychomotricity is the technique or series of techniques that aim to have an influence on the intentional or significant act, to stimulate it or modify it, using corporal activity and its symbolic expression as mediators. The objective, therefore, of psychomotricity is to increase the individual's capacity to interact with the environment (Núñez & Fernández Vidal, 1994)[353].

No quality studies have been found in the searches made to prepare this CPG on the efficacy of psychomotricity treatments for treating ADHD in children and adolescents.

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Recommendations

D	7.6.2.1.	The elimination of artificial colouring agents and additives from the diet is not recommended as general treatment applicable in children and adolescents with ADHD.
D	7.6.2.2.	The supplementary diet of fatty acids is not recommended as general treatment applicable in children and adolescents with ADHD.
√	7.6.2.3.	Treatment with optometry, auditory stimulation, osteopathy and psychomotricity are not recommended to treat ADHD in children and adolescents.
B	7.6.2.4.	Treatment with homeopathy, herbal medicine and encephalogram biofeedbackare not recommended to treat ADHD in children and adolescents.
√	7.6.2.5.	Health professionals must place emphasis, as with any other child and adolescent, on the importance of a balanced diet and regular exercise for children and adolescents with ADHD.
√	7.6.2.6.	Health professionals must ask the families about the use of complementary and alternative therapies to identify and inform about their possible risks or side effects to treat ADHD in children and adolescents.

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8. Prevention

Given the mainly genetically based etiology of ADHD, primary prevention, namely, actions aimed at the disorder not occurring, would not be feasible.

What we can do is act upon some non-genetic biological factors, such as the consumption of toxic products during pregnancy (tobacco and alcohol), recommending that these products should be avoided during pregnancy.

Another level of prevention would be the early detection of this disorder, paying special attention, above all, to risk populations such as children with a family background of ADHD, premature children, with low birthweight, intake of toxic substances during pregnancy and with serious craniocerebral traumas (Spencer, 2007[51]; Mick, 2002[354]; Sonuga-Barke, 2005[77]; Dopfner, 2004[28]).

The early detection of the disorder will help us start the right treatment as soon as possible, which is basic to prevent associated problems (bad school performance, difficulties in social relations, behavioural disorders).In this sense, it is important to bear in mind that the majority of children with ADHD already show symptoms of hyperactivity and impulsivity in preschool age, they are usually more disobedient, they have more accidents, it is hard for them to pay attention, etc. (DuPaul, 2001[12]; Sonuga-Barke, 2005[77]; Connor, 2002[197]; Quintero, 2006[355]). Given that these symptoms are common in young age, the diagnosis of a possible ADHD in these children can be difficult and must be based on the intensity and persistence of the symptoms, behavioural problems and impacton the environment (family, school, community) (DuPaul, 2001[12]; Sonuga-Barke, 2005[77]; Connor, 2002[197]). Therefore, the role of the primary healthcare paediatricians and educational professionals is very important to identify and refer these children.

Recommendations

√	8.1.	It is advisable to pay special attention to the risk populations: • Family history of ADHD • Prematureinfants • Low birthweight • Toxic comsumption during pregnancy • Serious craniocerebral (CCT) trauma.

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9. Ethical and legal aspects

Questions to be answered:

9.1. Which ethical principles must be taken into account in relationships with minors or adolescents with ADHD?

9.2. What precautions must be taken, from the ethical viewpoint, in the field of ADHD diagnosis?

9.3. What are the correct ethical standards for the start of therapeutic intervention in ADHD?

9.4. How involved must the minor be in the decision-making in the context of the diagnosis and treatment of ADHD?

9.5. What are the minor's rights in the field of information and confidentiality related to the diagnosis and treatment of ADHD?

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9.1. Which ethical principles must be taken into account in relationships with minors or adolescents with ADHD?

Since the Convention on the Rights of the Child, promulgated by the UN in 1989, there has been a series of changes in how childhood is viewed, characterised by the recognition of the capacity to take part in the decision-making process on the health and disease of the actual child, which have endowed the healthcare of children and adolescents with peculiarities.

Children and adolescents are the age groups where the preventive model is more important, and the care is always modulated by the figure of a third party, the parents or guardians, who are the ones who are going to make or transmit the demand and are going to intervene in the diagnostic and therapeutic process together with the patient.

Our care work must be modulated based on basic principles that govern the bioethics: *Nonmaleficence, Justice, Beneficence and Autonomy*.These principles are considered as *prima facie* principles, in other words, morally compulsory if there is no conflict between them, but that they must be hierarchised for those situations where, if they do enter into conflict, not all of them can be preserved. According to this internal hierarchy, *Nonmaleficence* and *Justice* would be the first tier principles and they would mark the minimal ethics demandable, even defined by law.

Autonomy and *Beneficence* are related to the vital projects of people, with their ethical maxims and their own value hierarchies.But, however, these principles must not be understood in an isolated fashion, but as being closely related to the principles of *dignity, integrity and vulnerability*. Respect for the principle of autonomy inevitably requires the principles of *responsibility*. It is especially in asymmetric relationships, such as medical care, and especially in the psychiatric and psychological care of the child and adolescent, where the principle of autonomy must necessarily be interpreted within the framework of ethical responsibility, as otherwise, the health professional's decision may be irresponsible and extremely harmful.

Recommendations

√	9.1.1.	In the specific context of this guide, the ethical principles of nonmaleficence, beneficence and justice are worth taking into account in connection with aspects associated with the diagnosis and treatment of ADHD, distinguishing the area that refers to very young children, when it is the parents or guardians who must necessarily assume an essential and almost exclusive leading role, from the area of young adolescents or pre-adolescents, where patients must be involved much more, insofar as they are developing individuals, with certain rights that must be preserved.

9.2. What precautions must be taken, from the ethical viewpoint, in the field of ADHD diagnosis?

Based on a correct application of the technical criteria contained in this guideline, making a clear diagnosis that adapts to the child or adolescent with possible ADHD is extremely important. Awarding diagnoses is both a pragmatic and an ethical question.And in the case of children and adolescents, we can find negative effects, which may range from implications that compromise their educational future and their learning, to effects such as stigmatisation, both at school and within the family, with negative repercussions on the child's opportunities.The children's perceptions with respect to stigmatising attitudes are not only normal, but also more negative than those that occur in adults.

Recommendations

√	9.2.1.	In the diagnosis of ADHD, the professional must be cautious, always respecting the criterion of nonmaleficence, in order to avoid pernicious effects for the child or adolescent in his or her school, social and family environment.

9.3. What are the correct ethical standards for the start of therapeutic intervention in ADHD?

Starting a therapeutic intervention in children and adolescents with ADHD must respond to the following three parameters for it to adapt to correct ethical standards:

- *Suitability:* If it is likely to achieve the objective proposed.
- *Necessity:* If it is necessary, in the sense that there is no other more moderate therapeutic measure to achieve this purpose with equal efficacy.
- *Proportionality:* If it is weighted and balanced, as more benefits or advantages are derived from it than harm over other assets or values in conflict.

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In the extreme case of needing to admit the patient with ADHD, we must bear in mind the legal provisions applicable to the case (Spanish Civil Code, Art. 211)356: in psychic disorders of childrenand disabled, hospitalisation must be authorised by the judge and in a suitable mental health establishment for the age, following a report from the children'scare services.

Recommendations

√	9.3.1.	The professional who assumes responsibility for the diagnosis and treatment of ADHD must act in agreement with criteria of suitability, necessityand proportionality, restricting those more restrictive interventions of the minor's rights to what is strictly necessary.

9.4. How involved must the childbe in the decision-making in the context of the diagnosis and treatment of ADHD?

Competency, in the minor, is a gradual process that covers psychological and cognitive development and must be evaluated in agreement with the importance and relevance of the decision that is going to be taken. The current legislation on the patients' rights (Law 41/2002)[357] acknowledges the legitimacy of mature childrento participate in their health processes, although it delegates the evaluation of their maturity on health professionals according to each specific situation and context, who must suitably weigh up the risks and benefits.However, faced with situations of lack of maturity or insufficient maturity, the law foresees the subrogation of the parents or guardians in the decision-making (criterion of parental authority) (Spanish Civil Code Art. 154-163)[358], which must also be in benefit of the child, a situation that is not free from difficulties faced with possible discrepancies between the criteria of both parties.

Thus, Law 41/2002[357] related to the rights of the childin the health area, establishes, on a general basis, and applicable, therefore, to the diagnosis and treatment of ADHD, that:

1. Between 12 and 16 years of age, the adolescent's competency and the importance of the decision to be made must be evaluated, weighing up the risks and benefits well, in order to define if they are able, on their own, to accept or reject the treatment and evaluate the involvement of the parents in the decision-making.In the case of minors **with sufficient maturity**, their opinion must prevail in the event of a possible conflict with their parents or guardians.

2. In the case of childrenunder the age of 12 or between 12 and 16 **without sufficient maturity**, the decision about the diagnosis and treatment will correspond to the parents or guardians.

3. From 16 years up, the adolescentmust be considered as being of full legal age for all intents and purposes, with the exception of situations where their incompetence is clear, in which case we must resort to the subrogated decision (parents or guardians).

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Recommendations

√	9.4.1.	When the parents' consent must be given, if there is clear discrepancy between the two, consensus and mediation must be sought for the greater benefit of the minor, after informing the two parties about the risks derived from taking or not taking actions for the diagnosis and treatment of ADHD.If it is not possible to conciliate positions, the professionals responsible for the diagnosis and treatment will second the decision of the parent that adapts to criteria of greater benefit for the minor.Faced with a situation of doubt or special conflict, it is recommended to resort to judicial authorisation to protect the child.
Applicable legal framework	9.4.2.	In all the cases, even in a situation of subrogated decision of parents or guardians due to immaturity or incompetence of the child, the latter must be informed of the situation and possible alternatives, in the appropriate language and understandable by him or her, clarifying any doubts that might arise, in order for him or her to form a valid criterion and cooperate in this situation.

9.5. What are the child's rights in the field of information and confidentiality related to the diagnosis and treatment of ADHD?

The right to intimacy and respect for their private spheres is, in general, acknowledged for mature children. This entails confidentiality of their healthcare data, after weighing up the risks and benefits that this may entail, and with the exception of serious risk for them.However, this acknowledgement may, on occasions, enter into conflict with the parents' or guardians' obligations and willingness to have access to this information.

As a basic criterion, it can be established that breaking the confidentiality of the mature childby the professional with respect to third parties, such as parents and guardians, must be exceptional and be ethically and legally justified, and it is not valid to apply a merely paternalist criterion or one of parental authority.The first basic principle is respect for that confidentiality, always obtaining the approval of the childor adolescent with ADHD to give the information to parents and guardians.

Recommendations

Applicable legal framework	9.5.1.	Childrenwith ADHD must always be listened to and they must always be informed as fully as possible in agreement with their level of comprehension, comparing with them the different options and doubts they may have, and sharing the information with the parents or guardians in agreement with the degree of maturity and the need to complement the information process. carried out with the minor.
Applicable legal framework	9.5.2.	In the care of childrenwith ADHD, the professionals must respect professional secrecy and confidentiality with respect to all the information referring to the context of the therapeutic relationship, except in the case of clear risk for the childor for third parties.

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Applicable legal framework	9.5.3.	Between the ages of 12 and 16, confidentiality of the information and health data about the ADHD of the mature adolescentand with sufficient judgement must be respected insofar as possible, especially when explicitly demanded by him or her.In this process the risks and benefits of transferring or communicating that information to parents or guardians will be considered, as well as its possible transcendence in other areas of the adolescent, and it will be advised on the advisability of dialogue and communication with parents or guardians about his or her health, avoiding presenting the clinical documentation to third parties without his or her consent, with the exception of properly justified serious risk situations.
Applicable legal framework	9.5.4.	From 16 years up, the adolescent's confidentiality must be preserved, as if he or she were of full legal age, leaving to their personal criterion, the decision about communicating the information to parents or guardians, unless there is a situation of serious risk or clear incompetence.

International regulations

1. Convention on the Rights of the Child. Adopted and ratified by the United Nations General Assembly resolution 44/25, of 20 November 1989.
2. European Charter on Children's Rights, 1992.
3. Convention on Human Rights and Biomedicine, Oviedo, 4 April 1997.

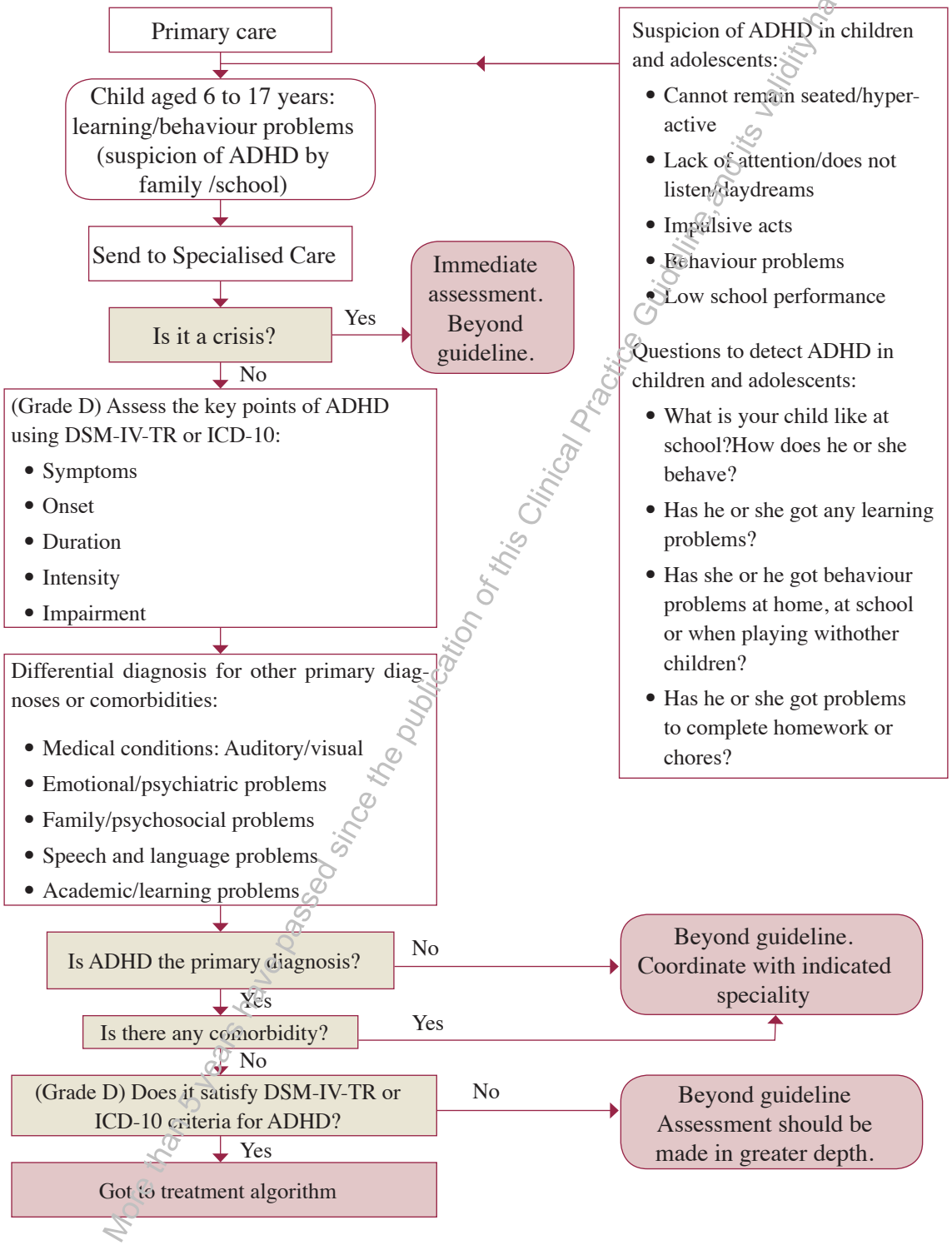
National regulations

1. Spanish Constitution (1978).
2. General Health Law 14/1986 (BOE no. 101 and 102, 28 and 29 April 1986).
3. Spanish Civil Code.
4. Instrument of Ratification of the Convention for the protection of human rights and dignity of the human being with respect to the applications of biology and medicine (Convention related to human rights and biomedicine), of the Council of Europe (BOE no. 251, 20 October 1999).
5. Organic Law 1/1996, 15 January, on Legal Protection of the Minor (BOE no. 235-249).
6. Law 41/2002, 14 November, regulatorybasisforpatient autonomy, rights and obligationswith respect toclinical information and documentation (BOE no. 274, 15 November 2002).
7. Code of Ethics and Deontology of the OMC(2003).

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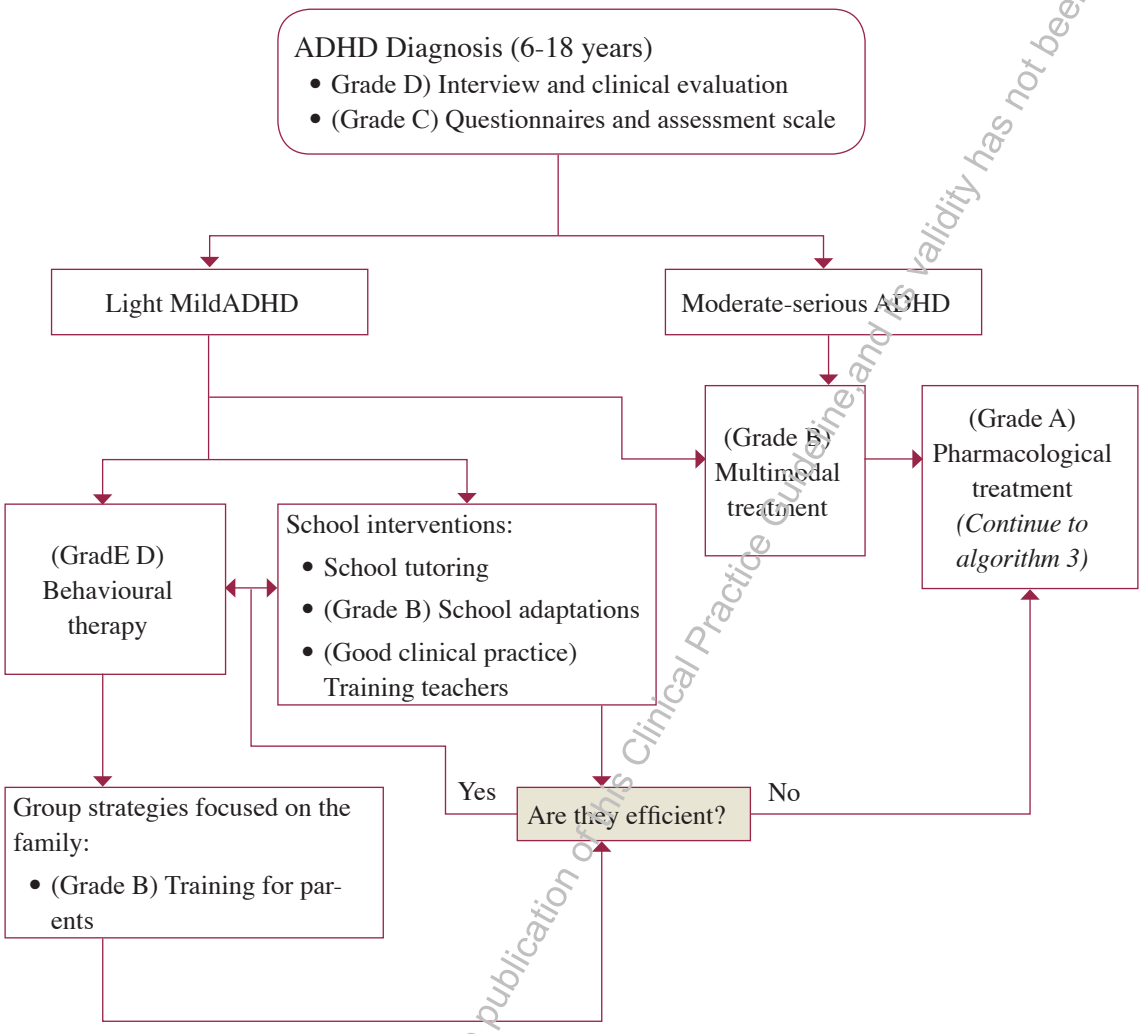
10. Diagnostic and therapeutic strategies

Algorithm 1. Detection and diagnosis of ADHD in children and adolescents



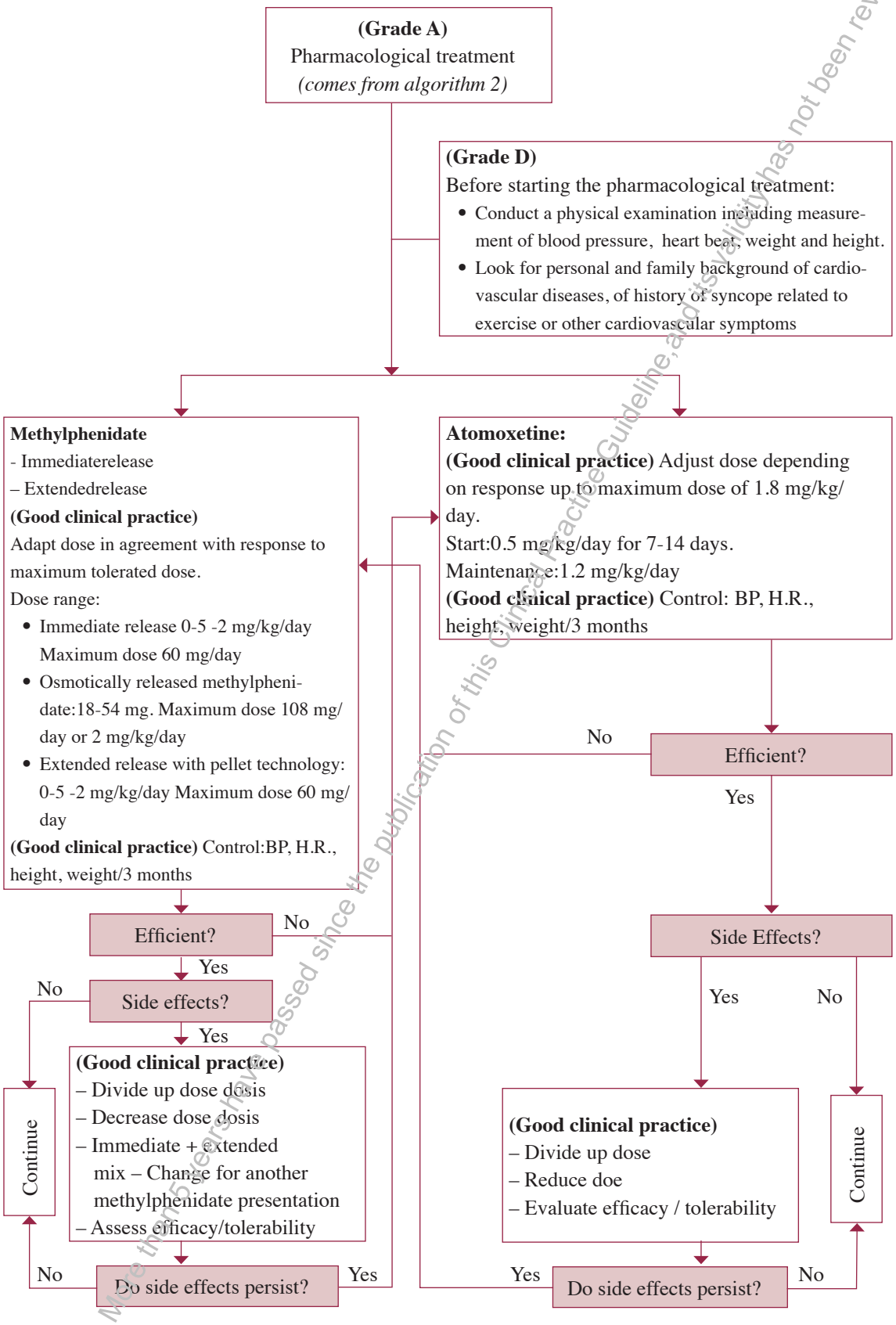
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Algorithm 2. Treatment of ADHD in children and adolescents



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Algorithm 3. Pharmacological treatment of ADHD in children and adolescents



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List of abbreviations of the algorithms

ICD-10	International Classification of Diseases, tenth version
DSM –IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th version, revised text
ADHD	Attention deficit hyperactivity disorder
BP	Blood pressure
HR	Heart rate
kg	kilograms
mg	milligrams

Annotations to Algorithm 3 of pharmacological treatment

1. If there is a family background of good response to a drug for ADHD, evaluate its use in the patient identified.

2. If it is impossible for patients to swallow capsules or tablets, immediaterelease methylphenidate can be used. This presentation can be crushed, or the capsule of extended release pellet technology methylphenidate can be opened, scattering the pellets over a small portion of food.

3. Ifextended extended release methylphenidate is used with osmotic technology and an adequate adjustment of the dose is not achieved, a dose of immediate release methylphenidate can be added to the treatment at breakfast and/or mid afternoon, to thus adjust the total dose of methylphenidate in agreement with the weight of the child or adolescent with ADHD and with the clinical response.

   If a 12-hour therapeutic action is required and the child or adolescent with ADHD is not able to swallow tablets, extended release methylphenidate can be administered with pellet technology in the morning (opening the capsule) and in the afternoon, after school, administer a dose of immediate release methylphenidate.This latter pattern can also be followed if there is a rebound effect in the afternoon with extended release methylphenidate with pellet technology.

4. If there has been a poor response to the treatment after having carried out training programmes for parents and/or psychological treatment and treatment with methylphenidate and atomoxetine in children and adolescents with ADHD, then it is advisable to re-assess the diagnosis, the comorbid disorders, the response to the treatment, the adverse effects, to the treatment, generation and use of psychological interventions by the children and their parents, the effects of the stigma to accept the treatment, concerns related to school and family, the motivation of the children and parents, and finally, the diet of the child or adolescent with ADHD.

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11. Dissemination and implementation

For this CPG to reach the health professionals of the SNS, it will be disseminated through the Catalogue of GuíaSalud (www.guiasalud.es).). As well as on the web pages of the AIAQSAAIAQS (www.aiaqs.net) and of the Sant Joan de Deu Hospital (www.hsjdbcn.org).

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.

The CPG has two versions for professionals, a full one and asummary, both with information for patients, families and educators **(Appendix 3)**. The CPG is published in digital version (full and summary) and it can be accessed in principle through the web pages of GuiaSalud, of AIAQS and of the Sant Joan de Deu Hospital, The summarizedversion is also published in book format, containing the CD-ROM of all the versions, to form part of the SNS CPG Library.

The measurement of the compliance and of the implementation of the CPG recommendations by monitoring and/or audit can improve its use. The AGREE instrument manual includes the importance of developing indicators, where item 21 on the applicability dimension is the one that deals with this aspect.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, used in this guideline is the Avedis Donabedian Foundation classification, 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.In the clinical evaluation of ADHD, measuring the key areas related to quality is recommendable. Some indicators are initially proposed for this, based on their apparent validity, reliability and feasibility of use at the different healthcare levels (primary care and specialised care).**Table 12** describes the eleven indicators proposed depending on the type of indicator, process or result.

It is important to bear in mind that, in practice, the available indicators are not perfect and are an approach to the real situation.Their objective is to provide useful information to make decision-making easier.They are quantitative measures that, if obtained on a regular basis, enable the analysis of the evolution in time (monitoring). Some indicators are common to those adopted in other guidelines, such as the SIGN guideline (2005)[1] and the ICSI guideline (2007)[179]. The development group has also proposed others.

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Table 12. Indicators proposed

Process indicators
• Evaluation percentage of the nuclear symptoms of ADHD • Percentage of use of the DMS-IV-TR and ICD-10 criteria to detect other conditions and co-morbidities in patients recently diagnosed with ADHD. • Evaluation percentage of the family functioning of the patient with ADHD • Evaluation percentage of the psychosocial functioning of the patient with ADHD • Percentage of patients with ADHD who are assessed with interviews, scales and questionnaires proposed in the guideline. • Percentage of patients with ADHD who receive psychological treatment according to proposed criteria • Percentage of patients with ADHD who receive psychopedagogical treatment according to proposed criteria • Percentage of patients with ADHD who receive pharmacological treatment according to proposed criteria • Percentage of the number of different health professionals and specialities involved to treat ADHD and nature of the interventions carried out
Result indicators
• Number of contacts with the primary or specialised care services. • Percentage of satisfaction of the patient with ADHD and family with the care received

It has not been the intention of the authors to design an exhaustive and detailed assessment that involves the use of all the indicators proposed. The aim is to provide stakeholders and clinicians with a tool that may be useful to specifically design the assessment of care of patients with ADHD.

The people responsible for assessing the impact of the CPG and of the care to patients with ADHD must choose the most suitable period of time that each indicator refers to.

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12. Future research recommendations

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Dimension of the problem

- Studies that define the real problem dimension in Spain, both in population and clinical samples.
- Epidemiological information on the prevalence of the disorder in children and adolescents, by age and gender, as well as the types of treatment used.
- Prevalence of ADHD in adolescents and adults with substance abuse, and other associated disorders.
- Prevalence of ADHD in adolescents and adults with school dropout.
- Groups with limited representation in the current bibliography of ADHD, such as girls, preschoolers, adolescents and adults.

Criteria and diagnosis assessment

- Applicability of the diagnostic criteria of ADHD to the different age intervals and genders.As well as for children and adults outside the age range of this CPG.
- In preschool children, the clear definition of the ADHD symptoms to be able to establish symptom onset age.
- Validity of the ADHD subtypes.
- Predictive value and clinical utility of the items to make a correct diagnosis.
- Developmental course of the ADHD symptoms.
- Influences that determine the impact of the symptoms on impairment and on the risk of future disorders, such as gender and level of development, age of detection and intervention that will estimate the benefits and risks of early diagnosis and intervention. The circumstantial environmental aspects: Family environment, group of friends, social-economic adversities. Additional research in this field should examine the same relationships through short-term designs that will include predictive elements.
- Methods used to establish the diagnosis of ADHD. As well as useful diagnostic methods to identity relevant comorbid disorders.
- On the adaptation and usefulness of the assessment instruments for ADHD validated in our medium.
- On the adaptation of diagnostic tests in our medium that might be applied in primary care.
- Development of validated clinical tools in our context to assess the degree of interference on adaptative functioning in two or more environments.

- Development of standardised neuropsychological tests, with practical utility and effectiveness for the diagnosis and for the psychological and psychopedagogical intervention.
- Discordance between informers due to the use of not very reliable or valid measures, or if the parents and teachers have different ways of conceptualising the behaviours, or they reflect the context diversity.

Neurobiological, genetic and executive functions studies

- Genetics, neuropsychological and neuroimage studies to clarify and integrate the relationships between the different theoretic models that seek to explain the origin of ADHD.
- Involvement of the prefrontal cortex and its connections in the ADHD.
- The relationship between ADHD and sleep problems.
- Genetic etiology of ADHD and the subsequent opportunities to prevent the disorder.
- Effect of executive functions on ADHD throughout the life cycle, bearing in mind variables such as comorbidity, sex, psychopharmacology.

Efficacy of the treatments

- Prescription process of an effective and comprehensive plan based on the traits of the child and adolescent with ADHD and the family, in terms of type, intensity and frequency, in order to improve the treatment plans, to achieve optimal results (immediate and long-term) based on clearly defined clinical indicators.
- Information about the social-demographic characteristics (age, gender) or clinical characteristics (ADHD subtype) that best respond to the medication or type of behavioural psychological treatment.
- About how ADHD and associated comorbid disorders interact, affecting the treatment and its results.
- Long-term results of the treatment in children and adolescents with or without comorbid disorders via longitudinal designs that consider the changes in time of the nuclear symptoms of ADHD, the co-existing ones and the functional results, such as occupational success or long-term relationships.
- Role of the pharmacological treatment and/or behavioural therapy in the evolution of the disorder.
- Effectiveness of parent training.If the group training interventions for parents are more effective than the pharmacological treatment in school age of children and adolescents with ADHD in terms of symptoms, quality of life and cost-effectiveness.
- Effectiveness of the environmental adaptations and out-of-school or recreational activities. Evaluate if there are benefits in making common sense environmental changes at

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home, at school or in the recreational atmosphere to reduce the nuclear symptoms of ADHD.Which out-of-school activities help reduce the symptoms of ADHD.

- Which are the optimal services and procedures considered for the success of ADHD treatment in real conditions, for example, in clinical practice and in the classroom.
- How are the drugs prescribed and which factors affect the clinical practice.
- To treat ADHD, which clinician is the most indicated to carry it out; the most efficient follow-up calendar; the most valid, sensitive and cost-effective way of monitoring the treatment.
- Assessment of the role of the education and primary care professionals in providing the treatment for ADHD.
- Description of the value of the efficacy of early intervention in childhood. Its results on the prevalence of ADHD, as well as the management of this type of patients.
- Effect of training on the behavioural management of children and adolescents with ADHD for teachers.If the training for teachers in behavioural management for children and adolescents with ADHD in primary and secondary education improves the symptoms of ADHD and the academic performance, the stress of the teacher in the classroom, and the impact of ADHD on students when compared with the traditional education methods.
- If the psychopedagogical interventions for primary and secondary differ in their effectiveness for each subtype of ADHD in behaviour, academic performance and attitude.
- Detection at school of children with problems related to ADHD and their referral for assessment.Studies on whether teachers having a knowledge of the ADHD symptoms leads to the detection, a better referral, diagnosis and implementation of adaptations, as well as to behavioural, academic and attitude improvement.
- Efficacy and generalisation of the psychopedagogical intervention.
- About when to interrupt the treatment of ADHD. If there are benefits or disadvantages of the long-term use of methylphenidate compared with its interruption 18 months after starting the treatment at least.Effect of continuing the pharmacological treatment beyond the 18 months, to improve the quality of life, nuclear symptoms of ADHD, associated emotional symptoms, side effects of the continued pharmacological treatment and the neuropsychological function.
- Well-designed rigorous studies on the efficacy of complementary and alternative therapies to ADHD.
- Development and assessment of new treatments for ADHD that will have greater efficacy in time of that have healing effects.

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Appendices

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Appendix 1: Evidence levels and recommendation degrees

Appendix 1: Evidence levels and recommendation degrees of SIGN

Level of evidence

1++	High quality meta-analysis, 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 performed clinical trials with a low risk of bias.
1-	Meta-analyses, systematic reviews of clinical trials, or clinical trials with high risk of bias.
2++	High-quality systematic reviews of case control or cohort studies. Well-conducted case control or cohort studies with a verylow risk of bias and a high probability that the relationship is causal.
2+	Well-conducted case control or cohort studies with a low risk of bias and a moderate probability that the relationship is causal.
2-	Case control or chort studies with a high risk of bias and a significant risk that the relationship is notcausal.
3	Non-analytical studies, such as case reports and case series.
4	Experts' 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 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 scientific evidence including studies rated as 2+, directly applicable to the target population of the guideline and demonstrating overall consistency of results; or extrapolated scientific evidence from studies rated as 2 ++
D	Scientific evidence level 3 or 4; or extrapolated scientific 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 bias possibility.

Good clinical practice

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

[1]At times, the development group realised that there were some important practical aspects that they wished to place emphasis on and for which there is probably no supporting evidence.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 assessed as points of good clinical practice.These messages are not an alternative to the scientific evidence-based recommendations, but they must only be considered when there is no other way to highlight this aspect.

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Appendix 2. Diagnostic criteria for ADHD

Diagnostic criteria for ADHD according to DSM-IV-TR (APA, 2001)[10]:

A. Either (1) or (2)

1. Six (or more) of the following symptoms of inattention have persisted for at lest 6 months to a degree that is maladaptive and inconsistent with developmental level:

Inattention

a) Often fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities.

b) Often has difficulty sustaining attention in tasks or play activities

c) Often does not seem to listen when spoken to directly.

d) Often does not follow through on instructions and fails to finish school work, chores or duties in the workplace (not due to oppositional behaviour or failure to understand instructions).

e) Often has difficulties organising tasks and activities.

f) Often avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework).

g) Often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books or tools).

h) Is often easily distracted by extraneous stimuli.

i) Is often forgetful in daily life activities.

2. Six (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at lest 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

a) Often fidgets with hands or feet or squirms in seat.

b) Often leaves seat in classroom or in other situations in which remaining seated is expected.

c) Often runs about or climbs excessively in situations in which it is in appropriate to do so.

d) Often has difficulty playing or engaging in leisure activities quietly.

e) Is often "on the go" or often acts as if "driven by a motor".

f) Often talks excessively.

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Impulsivity

a) Often blurts out answers before questions have been completed

b) Often has difficulty awaiting turn.

c) Often interrupts or intrudes on others.

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before the age of 7.

C. Some impairmentfrom symptoms is present in two or more settings (e.g. at school and at home).

D. There must be clear evidence of clinically significant impairment in social, academic or occupational functioning.

E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia or other psychotic disorder, and are not better accounted for by another mental disorder.

Diagnostic guidelines for hyperkinetic disorder according to ICD-10 (WHO, 1992)[111]:

Attention deficit

1. Often fails to give close attention to details, or makes careless errors in school work, or in other activities.
2. Often fails to sustain attention in tasks or play activities.
3. Often appears not to listen to what is being said to him or her.
4. Persistent impossibility to follow through on school work assigned or other missions.
5. Reduction in capacity to organise tasks and activities.
6. Often avoids or strongly dislikes tasks, such as homework, that require sustained mental effort.
7. Often loses things necessary for tasks and activities, such as school material, books, etc.
8. Is often easily distracted by external stimuli.
9. Is often forgetful in the course of daily activities.

Hyperactivity

1. Often fidgets with hands or feet or squirms in seat.
2. Leaves seat in classroom or in other situations in which remaining seated is expected.
3. Often runs about or climbs excessively in situations in which it is inappropriate.
4. Is often unduly noisy in playing or has difficulty in engaging quietly in leisure activities.
5. Exhibits a persistent pattern of excessive motor activity that is not substantially modified by social context or demands.

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Impulsivity

1. Often blurts out answers before questions have been completed.
2. Often fails to wait in lines or await turns in games or group situations.
3. Often interrupts or butts into others' matters.
4. Often talks excessively without appropriate response to social constraints.

- Onset of disorder is not later than the age of seven years.
- The criteria should be met for more than one situation.
- The hyperactivity, inattention and impulsivity symptoms cause clinically significant distress or impairment in social, academic or occupational performance.
- Does not meet the criteria for pervasivedevelopmental disorder, depressive episode or anxiety disorder.

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Appendix 3. Information for patients, family members and educators

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Learning to know and manage ADHD in children and adolescents

This guideline, aimed at patients, families and educators of children and adolescents with ADHD, is based on the *Practical Clinical Guideline on Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents*.Its aim is to provide information so that patients and their environments can have a better knowledge of the disorder and be involved in its detection, diagnosis and treatment.

The document makes recommendations based on the results of existing research to date.

It contains a list of addresses and reference bibliography where more information about ADHD can be obtained.

1. What is ADHD? How is it expressed in children and adolescents?

Attention deficit hyperactivity disorder (ADHD) is a neurobiological disorder that starts during childhood and affects between 3 and 7% of the children in school age.The main symptoms are **hyperactivity**, **impulsivity** and **inattention**.These symptoms occur with greater intensity and frequency than what is expected in children of their same age.

The nuclear symptoms of ADHD are the following:

Hyperactivity

Expressed by excessive movement in situations in which it is inappropriate to do so and in different areas (home and school).They have difficulty remaining quiet when situations require this, (they get up from the seat, touch everything, never keep still, seem driven by a motor).They talk too much and make too much noise during quiet activities.

Inattention

Characterised by difficulty to sustain attention in tasks that require sustained mental effort.They often seem not to listen, find it difficult to follow orders or instructions and they have difficulties in organising tasks and activities, often tending to forget and lose things. They are usually easily distracted by irrelevant stimuli. The attention difficulties usually appear more frequently during the school stage when the academic demand increases.

Impulsivity

Expressed by impatience, difficulty to postpone answers or await their turn. They often interrupt and blurt out answers before the questions have been completed.In general, they are characterised by acting without thinking, not assessing the consequences of their behaviour.

Children and adolescents with ADHD have problems in controlling their behaviour and adapting to the rules, thus presenting family, school and/or social adaptation difficulties.

Are there different types of ADHD?

The **DSM-IV-TR** (Diagnostic and Statistical Manual of Mental Disorders, fourth edition, revised text) of the American Psychiatric Association (2001) classifies ADHD into three types:

- **ADHD, combined type**:The three main symptoms are present (inattention, hyperactivity and impulsivity).
- **ADHD, predominantly inattentive type**:When the main symptom is inattention.
- **ADHD, predominantly hyperactive-impulsive type**: The predominant behaviour is hyperactivity and impulsivity.

Which disorders are present with ADHD?

Children with ADHD may often have other associated problems, such as behaviour disorders, anxiety or learning problems.

2. What causes ADHD? What factors intervene?

All the factors that intervene when ADHD appears are not known with accuracy, but it is clear that there is an interrelationship of multiple genetic and environmental factors.

Brain structures and circuits

There is scientific evidence that shows that the origin of ADHD is an alteration of the brain functioning, located in the areas of the prefrontal cortex and its connections with the basal ganglia. Different studies have found that that some of these brain areas are smaller in size in the paediatric population with ADHD.

Genetic component

There is scientific evidence about the genetic component of ADHD. Recent studies show the genetic complexity of ADHD, as different chromosomes and genes have been involved.The genetic component is perhaps the major predisposing factor for ADHD.

Neurobiological factors

The presence of non-genetic neurobiological factors in the appearance of ADHD has been referred to in different studies: Prematurity, hypoxic-ischemic encephalopathy, low birth weight and consumption of tobacco, alcohol and other drugs during pregnancy. At later ages, serious craniocerebral traumas (CCT) in early childhood, as well as infections of the central nervous system (CNS) have also been related to a greater risk of ADHD.These non-genetic neurobiological factors are generically called environmental factors.

Non-neurobiological factors

Psychosocial risk factors, which would affect the development of the emotional and cognitive control capacity, have also been described. Today, gene-environment interaction is accepted as possible, so the presence of certain genes would affect the individual sensitivity to certain environmental factors.

Diabetic factors such as the type of food, the use of food additives, sugar and sweeteners have also given rise to controversy, but, for the moment, there are no conclusive studies that associate them with ADHD.

Are there neuropsychological dysfunctions in ADHD?

Functional neuroimage and neuropsychological studies have shown that boys and girls with ADHD present a cognitive alteration in the so-called executive functions: response inhibition, surveillance, working memory and planning.

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3. How does ADHD evolve with age?

In many children the hyperactivity symptoms tend to decrease during childhood. Inattention and especially impulsivity remain in adolescents and adults.

The time that children can sustain attention increases with age; however, in many children with the disorder, this tends to be below the expected level and the level required to carry out daily life demands. **A high percentage of children with ADHD will continue to have symptoms during adolescence and adult age, so they must continue with the treatment.**

Although the inattention and hyperactivity symptoms may persist in many cases, it is important to remember that many adolescents with ADHD will adapt well in adult age and be free from mental health problems. A good prognosis will be more likely when inattention prevails more than hyperactivity-impulsivity, no behavioural disorders are developed and the relationships with family and with other children are correct.

4. How is ADHD diagnosed and who diagnoses it?

How is ADHD diagnosed?

The diagnosis of ADHD is exclusively clinical, in other words, by information obtained from the children or adolescents, their parents and educators, and it must be sustained in the presence of the typical symptoms of the disorder, with clear repercussion at a family, academic and/or social level, after having ruled out other disorders or problems that might justify the symptoms observed.

During the interview, information must be obtained about the child's current problems, nature of the symptoms (frequency, duration, situational variation of the symptoms), onset age and degree of repercussion on the different areas of the child's life.The family background must also be assessed (given the genetic nature of the disorder), the family functioning and the personal background (pregnancy, child-birth and perinatal period, psychomotor development, pathological background and child's mental health history).

A physical and a psychopathologicalexamination of the child must be carried out, collecting information from the school and about academic performance throughout the entire school history.

The neuropsychological and psychopedagogical examinations are not essential to diagnose ADHD in children and adolescents.However, the neuropsychological study is recommendable when the presence of a specific comorbid learning disorder is suspected, or it is important to evaluate the cognitive functioning profile.Likewise, a psychopedagogical assessment will permit evaluating the style of learning and establish the objectives of the re-educational intervention.

Additional laboratory, neuroimage or neurophysiological tests are not necessary to diagnose ADHD in children and adolescents, unless the clinical history and the physical examination show the presence of a disorder that requires their execution.

What assessment instruments are used?

To assess ADHD, information must be obtained about ADHD symptoms from the child or adolescent, from parents or carers and from the teachers.The information can be obtained by open-ended questions, specific questions, semi-structured interviews, questionnaires and scales.

The use of symptoms evaluation scales is always a complement to the clinical interview. Scales and questionnaires exist that are useful to evaluate the ADHD symptoms and their inten-

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sity, which are usually administered to parents or carers, and to the teachers.The use of broader and more general psychopathologicalscales is also frequent to detect if there are other associated disorders.

What is the differential diagnosis?

When examining and appraising a child with ADHD, it must be taken into account that not all lively and absent-minded children have ADHD.So a differential diagnosis with other diseases that may be confused with ADHD is necessary.

The symptoms of ADHD may appear in a wide variety of disorders:

- mental retardation
- learning disorders,
- pervasive developmental disorders,
- behavioural disorders,
- anxiety disorder,
- mood disorder,
- substance abuse,
- environmental factors,
- medical disorders.

The majority of these disorders can be ruled out with a complete clinical history and physical examination.

Who diagnoses ADHD?

The diagnosis of ADHD in children and adolescents must be carried out by a health professional (paediatrician, psychiatrist, neuropaediatrician, clinical psychologist or neuropsychologist) with training and experience in the diagnosis of ADHD and its most frequent comorbidities.

5. What is the treatment for ADHD?

The treatment of ADHD in children and adolescents can be personalised, in agreement with each patient and his or her family.The aim is to improve the symptoms and reduce the appearance of other associated disorders, as for the moment there is no cure for ADHD.

In children and adolescents with ADHD with moderate or severe impairment on their daily lives, **combined treatment** is recommended. This includes behavioural psychological, pharmacological treatment and psychopedagogical intervention.

The combination of pharmacological and psychological treatments has the potential to exercise immediate effects on the symptoms of ADHD via the use of medication, as well as long-term effects via the development of cognitive and behavioural skills and strategies, provided by the psychological treatment.

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5.1. Psychological treatment for ADHD in children and adolescents

The psychological interventions that have shown some scientific/positive evidence for ADHD treatment are based on the principles of cognitive behavioural therapy (CBT).

The types of interventions applied are described briefly below.

Behavioural therapy

This is a psychological therapy based on a behavioural analysis. The factors that are maintaining the inadequate behaviour are identified, the behaviours to be increased, decreased or eliminated are defined, observing and recording all of them. There are two types of techniques:

- To increase positive behaviour: Positive reinforcement such as praise, positive attention, rewards and privileges
- To reduce non-desired behaviours: Response cost, time out and extinction(not paying attention to the behaviour to be reduced or eliminated) are used.

Parent training

This is a behavioural treatment programme whose aim is to provide information about the disorder, teaching parents to modify the behaviour of their children, increasing the parents' competence, improving the parent-child relationship via better communication and attention to the child's development.

Cognitive therapy

Training in self-instructions, self-control and problem-solving techniques.

Social Skills Training

Children and adolescents with ADHD often have relationship problems with the family, social skills deficit and relationship problems with peers.Social skills training is usually done in small groups of similar ages, and CBT techniques are used.

5.2. Psychopedagogical treatment for ADHD in children and adolescents

Psychopedagogical intervention is a fundamental pillar in the combined treatment of ADHD, as it will range from interventions aimed at improving the academic performance of the child or adolescent (via psychopedagogical re-education) to those aimed at improving the school environment and, therefore, their adaptation to the school (via an intervention programme at school and teacher training).

Psychopedagogical re-education is personalised school tutoring that is provided after school hours and whose aim is to palliate the negative effects of ADHD in children or adolescents who suffer from it, in connection with their academic competence or learning.

Emphasis is placed on the negative repercussion of the attention deficit, impulsivity and hyperactivity in the school learning process.

Psychopedagogical re-education must include actions aimed at:

- Improving the academic performance in the different areas, instrumental areas and the more specific areas for each school year.

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- Working on habits that foster appropriate behaviour for learning (such as managing the timetable and controlling the school agenda) as well as study techniques (prereading, careful reading, analysis and underlining, synthesis and diagrams or summaries).
- Preparing and teaching strategies to prepare for exams.
- Improving self-esteem with respect to the tasks and study, identifying positive skills and increasing motivation for achievement.
- Teaching and promoting appropriate and facilitating behaviour for correct study and compliance with tasks.
- Reducing or eliminating improper behaviour such as defiant behaviour and bad organisation habits.
- Maintaining coordination actions with the specialist that is treating the child and with the school, to establish common goals and offer the teacher strategies to manage the child with ADHD in the classroom.
- Intervening with parents to teach them to put into practice, monitor and foster the continued use of study organisation and management tasks at home.

Children with ADHD require a personalised **intervention programme at school** for each one of them, which will include both academic actions or instruction, and behavioural actions.These programmes must involve the majority of the teaching staff to facilitate their efficacy, including:

- Those actions that refer to the methodology (the way of giving instructions, of explaining the academic contents, or the assignment of chores and tasks).
- Those that refer to the work environment (the physical situation of the child or adolescent in the classroom, structured and motivating environment or the elimination of distracting elements).
- Those that refer to the improvement of the child's or adolescent's behaviour (constant supervision, personalised tutorials and the use of behavioural techniques).

Training the teachers enables them to receive psychoeducation about the disorder, modify ideas and opinions about children and adolescents with ADHD, to train in behavioural patterns and be empowered to detect ADHD alert signals, thus favouring early detection.

5.3. Pharmacological treatment for ADHD in children and adolescents

Why use drugs to treat ADHD in children and adolescents?

The beneficial effect of drugs on hyperactive behaviour has been common knowledge for more than 70 years.The first drugs to treat ADHD were marketed in Spain more than 25 years ago.

These drugs are among the most **studied and safest** of all those that are used in children and adolescents, and all of them are **very efficient** to treat the symptoms of ADHD.Between 70 and 80% of the patients respond favourably to the first treatment used.

Therefore, due to its safety, high efficacy and limited side effects, pharmacological treatment is recommended to treat these patients.

With the drugs, **we reduce the ADHD symptoms, improving school performance and behaviour** of the child as well as their relationships both at home and at school. **At the same time, they foster the effect of psychological and psychopedagogical interventions.**

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What drugs are available in Spain?

At the present time, in our country we have two groups of medicines indicated to treat ADHD in children and adolescents: stimulants (methylphenidate) and non-stimulants (atomoxetine).

Methylphenidate is presented in three formats, depending on the way the drug is released:

- Immediate release: the effect lasts for about 4 hours so 2-3 doses must be administered throughout the day to adequately treat the patient.
- Extended release: this is a mixture of immediate release and extended release methylphenidate in one single daily dose.The difference between the two is the amount of immediate and extended action drug, and the release mechanisms used. All of this means that the length of the effect is different: about 12 hours for extended release methylphenidate with osmotic technology and about 8 hours for extended release methylphenidate with pellet technology.

In other countries of our environment, stimulant drugs are presented in other different formats:for example, in patches, association of stimulant salts, etc., not available in Spain for the time being.

What drug to choose?

Pharmacological treatment must be prescribed and controlled by a physician with experience in ADHD and in the management of these drugs and their possible side effects.The treatment must be **personalised**, that is, adapted to the needs of each patient and each family. The choice of one drug or another will depend on:

- The existence of associated problems, such as tics, epilepsy, anxiety, etc.
- The adverse effects of the medication.
- The existence of drug consumption in the adolescent.
- Prior experiences of lack of efficacy with a certain drug.
- The preferences of the child/adolescent and his or her family
- The administration ease.

Is it necessary to carry out tests before starting treatment with these drugs?

No additional test is required (blood analysis, electrocardiogram, etc.) unless advised by the history and/or examination of the patient.For example, in patients with a background of heart problems, a cardiological study will be necessary before starting treatment.

In the treatment control it is advisable to record the weight, height, pulse and blood pressure on a regular basis.

How is the pharmacological treatment started?

Once the drug has been chosen, it is started with low doses, which will then be increased every 1 to 3 weeks depending on the patient's response and the appearance of side effects. The physician will be responsible for assessing the efficacy and tolerability of the drug by periodic visits, which will be much more frequent at the start of treatment and more spread out in time (every 3-6 months) once the drug dose has been adequately adjusted.

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Although the treatment is personalised, the general patterns for each drug are:

- Immediate release methylphenidate, in 2-3 doses a day.
- Extended release methylphenidate, one dose in the morning.
- Atomoxetine, one single dose in the morning is recommended. If there are tolerance problems, administer at night or split the dose between morning and night.

Sometimes, if the improvement is not sufficient or there are other associated disorders, the dose will have to be increased to the maximum recommended or different types of drugs combined.

What are the most frequent side effects?

The side effects mainly occur when the treatment starts, they are not very frequent, or intense, they are temporary and are not very serious. In some very rare cases, the treatment has to be suspended. It is important to able to ask the physician responsible for the treatment about any adverse effects before suspending the administration of the drug.

The most frequent side effects of **stimulants (methylphenidate)** are:loss of weight and appetite, especially at start of treatment, difficulty to go to sleep (conciliation insomnia); headaches and much more infrequently, tics and restlessness.

The most frequent side effects of **non-stimulants (atomoxetine)** are:loss of weight and appetite, above all at the start of the treatment; sleepiness, gastrointestinal symptoms, such as abdominal pain, nausea and vomits, dizziness and tiredness.Very infrequently, jaundice may appear (the skin turns a yellowish colour due to the increase of bilirubin), reflecting hepatic damage meaning that the treatment must be ended.

How long does the pharmacological treatment last?

The duration of the treatment must be considered individually depending on the persistence of the symptoms and their repercussion on the life of the child or adolescent.

For patients who are taking stimulants, an accepted practice is for there to be short periods of time, from 1 to 2 weeks a year, without pharmacological treatment, in order to be able to evaluate the functioning of the child or adolescent both at home and at school.One of the best moments to carry out this appraisal without treatment is usually at the start of the school year.

Is it recommendable to have stimulant-free periods during the pharmacological treatment ("therapeutic holidays")?

Although stimulant drugs improve the symptoms of ADHD and school performance their effects are not only seen at school, but also at home and in other environments.Therefore, when treating ADHD in children and adolescents, **pharmacological treatment rest periods ("therapeutic holidays") are not recommended** as they may entail a worsening of the patient's symptoms.In any case, whether there are "therapeutic holidays" or not will be decided on jointly between the physician, family and patient, in order to assess the need to maintain the treatment or not, and reduce the adverse effects.

Does the pharmacological treatment produce addiction?

There is no scientific evidence to show that treatment with stimulants produces addiction.

But it has been clearly demonstrated that patients with ADHD receiving pharmacological treatment, have significantly less drug consumption problems in adolescence than patients with ADHD who do not receive pharmacological treatment.

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Is pharmacological treatment for ADHD related to growth retardation?

The studies available to date are not very conclusive. The latest data inform that the final height of children treated with stimulants will be 1 to 3 cm. less than expected. The growth regtardation is greater during the first year's treatment but tends to even out later on.

Does the efficacy of pharmacological treatment decrease with time?

The correct use of the drugs indicated to treat ADHD in children and adolescents administered in the way and dose prescribed, does not produce tolerance, continues to be efficient and it is not necessary to increase the dose, save for reasons of growth (increase in height and weight).There is scientific evidence that the treatment has a long-term effect if continued.

5.4. Complementary and alternative treatment for ADHD in children and adolescents

Due to the exponential increase of complementary and alternative medicine or therapies over the last few years, health professionals are continuously receiving doubts and questions from patients and their families about their use.On the other hand, many patients do not disclose their use to their physicians, with the possible interference in the medical treatment or adverse effects. **It is important to inform the physician responsible for the treatment if complementary or alternative treatments are used.**

Some of the alternative therapies without a general applicable recommendation for the treatment of ADHD in children and adolescents, include dietetic treatments, optometry, homeopathy, herbal medicine, auditory stimulation (Tomatis method) andencephalogram biofeedback(EEG-biofeedback, neurofeedback or neurotherapy), psychomotricity and osteopathy.

6. How are disorders associated with ADHD in children and adolescents treated?

Psychological therapy carried out with parents (parent training) is the most effective treatment for behavioural disorders in children. In addition, psychological therapies with children, such as social skills training, may be beneficial.

If necessary in children and adolescents with anxiety disorders and ADHD, the children's and adolescents's psychiatrist could also administer efficient and safe medication.

Learning problems require an assessment and a long-term psychopedagogical treatment plan.

7. How can ADHD be prevented?

Given the mainly genetically based etiology of ADHD, primary prevention, namely, actions aimed at the disorder not occurring, would not be feasible.

What we can do is act upon some non-genetic biological factors, such as the consumption of **toxic products during pregnancy** (tobacco and alcohol), recommending that they should be avoided during pregnancy.

Another level of prevention would be the early detection of this disorder, paying special attention, above all, to risk populations such as children with a family background of ADHD, prematurechildren, with low birthweight, intake of toxic substances during pregnancy and with serious craniocerebral traumas.

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The early detection of the disorder will help us start the right treatment as soon as possible, which is basic to prevent associated problems (bad school performance, difficulties in social relations, behavioural disorders).

8. What should be done if ADHD is suspected?

In the field of public health, if ADHD is suspected, the first step would be to consult the primary care paediatrician, who, depending on the availability of the area, may refer the child or adolescent to specialist child and adolescent mental health service, a children's psychology and psychiatry or neuropaediatrics service.

9. What can parents do to help children or adolescents with ADHD?

- Confirm the ADHD diagnosis with health professionals (paediatricians, clinical psychologists, child psychiatrists, neuropaediatricians, neuropsychologists), with experience and training in this disorder.
- Search for a professional assessment and personalised treatment.
- Start the treatment with professionals who have adequate training in ADHD.
- Search for adequate information about the disorder, which is also practical, realistic and is based on scientific data. This could be obtained from the professionals who attend them or ADHD associations.
- Get the closest family members involved in the education of ADHD.
- Learn to manage own negative emotions (anger, blame, bitterness) and maintain a positive attitude.
- Try to give the child immediate and frequent positive reinforcements
- Use long-lasting and efficient rewards.
- Use rewards before punishments.
- Improve the child's or adolescent's self-esteem, use positive messages.
- Make thoughts and problem solution tangible.
- Simplify the rules of the house or place where they are.
- Help the child do things step by step.
- Make sure their instructions are understood.
- Teach the child or adolescent to be organised and foster their social skills.
- Be understanding.

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10. What can be done from school to help children or adolescents with ADHD?

The interventions carried out at school must contemplate the following strategies:

- Use behaviour modification techniques: positive reinforcement, token economy systems, modelling, extinction, response cost, time-out technique, overcorrection, etc.
- Teach the child or adolescent training techniques in self-control, problem-solving, social skills training or relaxation techniques.
- Clearly define, together with the child or adolescent, the short and long-term goals, both referring to curricular contents and to their behaviour at school.
- Adapt the environment and control the level of distracting elements in the classroom, situating the child or adolescent in a place where they can easily be supervised and at a distance from any stimuli that might distract them.
- Adapt the tasks and expectations to the child's or adolescent's traits,reducing or simplifying the instructions given to them to carry out the tasks, using short, simple and clear instructions.
- Adapt the assessment method, modifying the way of administering and assessing the tests and examinations.
- Complement the oral instructions with visual instructions and reminders by the teacher.
- Offer the child or adolescent aid system to control their tasks every day, and complete short and long-term work (control of agenda, reminders, etc.).
- Achieve an adequate level of motivation in students, offering frequent feedback about their improvements in behaviour and effort.

11. Addresses and reference bibliography

11.1. Associations in Spain

To find out the updated list of all the ADHD associations, refer to the Spanish Federation of Association of Aid to Attention Deficit and Hyperactivity:

F.E.A.A.D.A.H.
President: Fulgencio Madrid Conesa.
Address: Colegio San Carlos. C/Del Romeral, 8 Tentegorra 30205 Cartagena
Tel.: 663 086 184 Fax: 968 316 150
Email: adahimurcia@hotmail.com
URL: www.feaadah.org

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11.3. Websites of interest

AACAP: www.aacap.org/cs/root/facts_for_families/informacion_para_la_familia

AIAQS: www.aiaqs.net

Fundación ADANA: www.fundacionadana.org

Guía Salud: www.guiasalud.es

Barkley: www.russellbarkley.orgCADDRA: www.caddra.caCHADD: www.chadd.org

Fundación ADANA: www.fundacionadana.org

Guía Salud. www.guiasalud.es

Hospital Sant Joan de Déu: www.hsjdbcn.org

NICE: www.nice.org.uk/cg072

NIMH:www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml

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Appendix 4. Glossary

AGREE: Instrument that assesses the quality of the clinical practice guidelines.

Bias: A systematic deviation or error in the results or inferences of a study.In studies on the effects of healthcare, biases may arise from systematic differences in the characteristics of the groups that are compared (selection bias), in the care given or the exposure to other factors, apart from the intervention of interest (execution bias), in the abandonment or exclusions of people initially included in the study (wear bias) or in the assessment of the outcome variables (detection bias).The biases do not necessarily represent an imputation of prejudice, as they could also be the researchers' preferences for some specific results, which is different to the traditional use of this word to refer to a partisan point of view. Many varieties of biases have been described. See, too, methodological quality, validity.

Case and control study (synonyms: Case control study, case reference study):A study that starts by identifying the people who present the diseases or outcome of interest (cases) and an appropriate control group without the disease or outcome of interest (controls).The relationship between a factor (intervention, exposure or risk factor) and the outcome of interest is examined by comparing the frequency or level of this factor in the cases and in the controls. For example, to determine if thalidomide was the cause of birth defects, a group of children with these malformations (cases) was able to be compared with a group of children without those defects (controls). Then, both groups were compared with respect to the proportion of those exposed to thalidomide in each one of them by their mothers taking that medication.The case and control studies are retrospective, as they are always developed looking backward in time.

Case series: A non-controlled observational study that includes an intervention and an outcome for more than one person.

Case study (synonyms: anecdote, case history, information of an individual case): A non-controlled observational study that includes an intervention and an outcome in an individual person.

Clinical trial (synonyms: therapeutic trial, intervention study): A study or trial that tests a medicine or another intervention to evaluate its efficacy and safety. This general term includes randomised controlled clinical trials and controlled clinical trials.

Clinician: Health professional.

Cohorts study (synonyms: follow-up, incidence, longitudinal study): An observational study where a defined group of people (the cohort) is followed in time and where the results or outcome are compared between the subgroups of the cohort that were or were not exposed (or exposed to different levels) to an intervention or another factor of interest.The cohorts can be formed at that moment and followed prospectively (a concurrent cohort study) or identified based on historical records and followed in time forwards from that moment to now (a historical cohort study). As a random distribution is not used, a pairing or a statistical adjustment must be used to guarantee that the comparison groups are as similar as possible.

Confidence Interval (CI): The interval in which the "true" value (e.g. the effect size of an intervention) is estimated may have a certain degree of certainty (e.g. 95% or 98%). Note: the confidence intervals represent the probability of committing random errors, but not committing systematic errors (biases).

Control: In clinical trials that compare two or more interventions, a control is a person from the comparison group that receives a placebo, no intervention, traditional care or some other type of service.

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In case and control studies, a control is a person in the comparison group without the disease or outcome of interest.

In statistics, controlling means adjusting or bearing in mind the external influences or observations.

Controlled clinical trial: This refers to a study that compares one or more intervention groups with one or more comparison groups (control). Although not all the controlled studies have a random distribution, all the clinical trials are controlled.

Cranial MRI: This is a non-invasive method to create detailed images of the brain and the surrounding nervous tissues.

Unlike radiographies and computerised tomographies that use radiation, the magnetic resonance uses radio waves and powerful magnets.

Cross-sectionalstudy or prevalence study: A study that examines the relationship between the diseases (or other health characteristics) and other variables of interest that might exist in a defined population at a specific moment in time:the temporary cause-effect sequence cannot necessarily be established in a cross-sectionalstudy.

Double blind double masked: Neither the participants in the clinical trial nor the researchers (those who evaluate the outcome) are aware of which intervention has been administered to the participants.The purpose of "blinding" the participants (both receivers and suppliers of the care) is to prevent performance bias.The objective of "blinding" the researchers (the assessors of the outcome, who may be the suppliers of the care) is to prevent detection bias.

EEG-biofeedback: Also known as encephalogram biofeedback, neurofeedback or neurotherapy, it is a series of experimental procedures, whose studystarted in the 1940s in the United States, when an external instrument was used to provide the organisation with immediate information about the state of biological conditions such as muscletone, skin temperature, brain waves, blood pressure, heart rate, etc., in order to be able to make use of this information.

Effect estimation (synonym: Therapeutic effect): In studies on the effects of the healthcare, the relationship observed between an intervention and an outcome, expressed, for example, as the number of patients that need to be treated (NNT), odds ratio, risk difference, relative risk, standardised mean difference or weighted mean difference.

Effectiveness: The extent to which a specific intervention, when used under normal circumstances, achieves what it is supposed to do.Clinical trials that evaluate the effectiveness are sometimes called management trials.

Efficacy: The extent to which an intervention produces a beneficial outcome under ideal circumstances.Clinical trials that evaluate efficacy are sometimes called explanatory trials and their participation is restricted to people who cooperate fully.

Electroencephalogram (EEG): Neurophysiological examination that is based on recording the bioelectric brain activity in basal conditions of rest, wakefulness or sleep, and during different activations.

Encephalopathy: Generic term that groups together all the diseases that affect the encephalon and especially the brain.

Evoked potentials: Neurophysiological examination that assesses the function of the acoustic, visual and somatosensory sensory system and its pathways by means of provoked responses to a known and normalised stimulus.

Executive functions: The concept of executive functions defines a series of cognitive skills that permit anticipating and establishing goals, forming plans and programmes, starting activities

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and mental operations, self-regulating tasks and the skill to carry them out efficiently.This concept defines the activity of a series of cognitive processes associated with the functioning of the front brain lobes of the human being.

Functional image studies: The neuroimage is a minimally invasive technique that permits exploring the human brain, intact, and at the same time, analyse the variations of the functional activity of areas of the brain in specific mental processes of the human being.Thus, not only are the brain areas involved in mental functions explored, but they can also be related to the brain activity of the conscious individual.The end product of these techniques is a map of the brain based on direct or indirect data of the neuronal activity.

GuiaSalud CPG Library of the SNS: GuiaSalud, is a body pertaining to the SNS, which the 17 autonomous communities participate in to promote the development and use of CPGs and other tools, as well as scientific evidence-based products.Its mission is to foster the offer of resources, services and products based on scientific evidence, to support the decision-making of professionals and patients in the SNS, as well as to promote the creation of networks of collaborators and the cooperation between entities related to the CPGs and evidence-based medicine.

Hepatotoxicity: Also called drug-induced toxic hepatic disease, it entails damage, either functional or anatomic, to the liver induced by the intake of chemical or organic compounds.

Institute for Clinical Systems Improvement (ICSI): This institute groups together different health organisations and its main aim is to protect the quality of healthcare and help its members identify and accelerate the implementation of the best clinical practices for their patients. It is a non-profit and independent North American institution.

Likert type evaluation: The Likert type scale is a psychometric scale commonly used in questionnaires and the most widely used in surveys for research.When we respond to an element of a questionnaire developed with the Likert technique, we do so by specifying the level of agreement or disagreement with a statement (element, item or reagent).

Medline/PubMed: Medline/Pubmed is a service of the National Library of Medicine that includes quotes of biomedical articles taken from the Medline database and additional, free access, scientific journals.

Meta-analysis (MA): The use of statistical techniques in a systematic review to integrate the outcome of the studies included.It is also used to refer to systematic reviews that use meta-analyses.

Methodological quality (synonyms: validity, internal validity): The extent to which the design and development of a clinical trial have avoided probable systematic errors (bias).A variation in the quality of the studies may explain the variation of the results of the clinical trials included in a systematic review. The more rigorously designed clinical trials (with better quality) probably provide results that are closer to the "truth". See, too: external validity, validity

National Guidelines Clearinghouse (NGC): This is a public resource on scientific evidence-based CPGs created by the Agency for Healthcare Research and Quality (AHRQ) of the U.S. Department of Health and Human Services.

Neurophysiologic studies: Effective research and diagnostic means to determine the anatomical and functional state of the neuromuscular apparatus.

New Zealand Guidelines Group (NZGG): This is a group that leads a movement of change towards quality socio-health and healthcare based on scientific evidence-based medicine and on effectiveness.

Nonmaleficence: Intentionally abstain from carrying out actions that might cause harm.

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Observational study (synonym: non-experimental study): A study in which nature is allowed to take its course. The changes or differences in a characteristic (e.g. if the population did or did not receive the intervention of interest) are studied in connection with the changes or differences in other(s) (e.g. if they passed away or not), without the intervention of the researcher.They represent a greater risk of selection bias than the experimental studies (randomised controlled clinical trials).

Odds Ratio (OR): The odds quotient of an episode in an experimental group (intervention group) and the odds of the episode in the control group.An odds ratio of 1 indicates that there is no difference between the comparison groups.For undesirable results, an OR of less than 1 indicates that the intervention is effective in reducing the risk of that outcome.When the rate of the episode is small, the odds ratios are very similar to the relative risks.

Open-ended clinical trial: There are three possible meanings for this term:

1. A clinical trial where the researcher and participant are aware of the intervention that will be used in each participant (that is, it is not double blind).Random assignment may or may not be used in these trials.

2. A clinical trial where the researcher decides which intervention is going to be administered (non-random assignment).

It is also known at times as an open label (although some trials called "open labels" are randomised).

3. A clinical trial that uses a sequential open label.

Pellets: Granulated tablets.

PET: The positron emission tomography is a non-invasive diagnostic and imaging research technique that is able to measure the metabolic activity of the different tissues of the human body, especially of the central nervous system.

Phenotype classification: Grouping of visible genetic characteristics.

Placebo: A substance or inactive procedure administered to a patient, usually to compare its effects with those of a real medication or with another intervention, but sometimes for the psychological benefit of the patient who believes that he or she is receiving an active treatment. Placebos are used in clinical trials to "blind" participants with respect to the assignment of the treatment they receive.The placebos should be indistinguishable from the active intervention in order to guarantee adequate blinding.

Plateau effect: The plateau effect means that the drug has reached its maximum power.

Prima facie: These principles are considered as prima facie principles, in other words, morally compulsory if there is no conflict between them, but that they must be hierarchised for those situations where, because they enter into conflict, not all of them can be preserved.

Prospective study: In the assessments of the effects of the health interventions, a study in which the people are divided into two groups that are or are not exposed to the intervention or interventions of interest before the outcome has occurred.Controlled clinical trials are always prospective studies and case and control studies never are.Concurrent cohort studies are prospective studies, whilst the historical cohort studies are not (see, also cohort study), despite the fact that in epidemiology a prospective study is sometimes used as a synonym for cohort studies. See retrospective study.

Randomised Control Trial (RCT) (synonym: Randomised clinical trial): An experiment where researchers randomly assign a randomised clinical trial to eligible people in several groups (e.g. treatment and control group) for them to receive or not receive one or more of the interven-

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tions that are to be compared.The results are evaluated by comparing the results in one group and in the other. NOTE: When MEDLINE is used, the word must be consulted spelt with an "s" and not a "z", namely randomised and randomized.

Rebound effect: The rebound effect consists in a state of nervousness and irritability with the subsequent worsening of the behaviour, which is sometimes observed when the effect of the stimulant drug disappears.

Relative risk (RR) (synonym: risk quotient): The risk quotient in the intervention group divided by the risk in the control group.The risk (proportion, probability or rate) is the quotient of the number of people with a characteristic in a group divided by the total number of members in the group.A relative risk of one indicates that there is no difference between the groups that are compared. For undesirable results, a relative risk f less than 1 indicates that the intervention was efficient to reduce the risk of that event.

Retrospective study: A study where the events or outcome have occurred to the participants before the study began.Case and control studies are always retrospective, whilst cohort studies sometimes are and controlled clinical trials never are. See prospective study.

Risk factor: A characteristic or lifestyle of a person, or of his or her environment, that increases the probability of a disease occurring.

Scottish Intercollegiate Guidelines Network (SIGN): This is a Scottish institution whose aims are to improve the quality of healthcare for Scottish patients in order to reduce variability in normal clinical practice and in the results, based on the development and dissemination of national CPGs that contain recommendations for effective practice based on current scientific evidence.

Screening: Identification of people within a population who have a specific pathology.

Sluggish Cognitive Tempo: The term sluggish cognitive tempo arose as a construct to group together characteristics that reflected an irregular state of alert and orientation associated with some children with ADHD, such as: sluggish, forgetful, sleepy, apathetic, with tendency to daydream, lost in their own thoughts, unmotivated, in the clouds, confused, together with a low performance in some neuropsychological or visual search tests.

SPECT: This is a diagnostic technique that permits visualising the three-dimensional distribution of a radioactive contrast located in a body or organ of interest, in this case the brain.With the brain SPECT we obtain images ("cuts or sections"), in any spatial plane, which, depending on the radiodrug used, represent the regional perfusion, concentration of neuroreceptors or the metabolic activity of a known or suspected injury.

Statistical significance: An estimation of the probability that an effect, which is as broad as or broader than the effect observed in a study, has occurred because of chance.Normally it is expressed as the P value, for example a P value of 0.049 for a bias difference of 10% means that there is less than 1 out of 20 probabilities (0.05) that such a large or larger effect or association like this has occurred by chance, and therefore, it could be said that the results are statistically significant at the level of P = 0.05. The cut-off point for statistical significance usually lies at 0.05, but sometimes at 0.01 or 0.10. These cut-off points are arbitrary and have no specific importance. Although this is often done, it is not appropriate to interpret the results of a study in a different way depending on the P value; if this P value is, for example 0.055 or 0.045 (which are very similar but not opposing values).

Suicidalideation: Persistent presence in the individual of thoughts or ideas aimed at committing suicide.

Systematic review (SR): A review of a clearly formulated questions, which uses systematic and explicit methods to identify, select and critically assess the relevant research, as well as to

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obtain and analyse the data of the studies included in the review.Statistical methods (meta-analyses) may or may not be used to analyse and sum up the results of the studies included. See also Cochrane review.

The Cochrane Library: A series of databases, published on floppy and CD-ROM and updated every three months, which contain the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Register, the Database of Abstracts of Reviews of Effectiveness, the Cochrane Review Methodology Database and information about the Cochrane Collaboration.

The Health Technology Assessment (HTA) Database. The Database of Abstracts of Reviews of Effectiveness (DARE): These are two databases offered by the Centre for Reviews and Dissemination (CRD) of York University, whose mission is to provide science-based information about the effects of the interventions used in health and social care.It contains information about HTA and about medical technology assessment.DARE contains systematic review abstracts that satisfy strict quality criteria and whose aim is to evaluate the effects of the interventions.

Therapeutic holidays: Scheduled rest periods from the pharmacological treatment.

Validity (synonym: internal validity): Validity is the extent to which a result (or a measure or a study) probably comes near the truth and is free from bias (systematic errors). Validity has some other meanings. It is normally accompanied by a word or a sentence that qualifies it; for example, in the context of making a measurement, expressions such as construction validity, content validity and criterion validity are used.The expression, internal validity, is sometimes used to distinguish this type of validity (the degree to which the observed effects are true for the people of the study) from the external validity or generability (the degree to which the observed effects in a study really reflect what is expected to be found in a broader target population than the people included in the study). See, too, methodological quality.

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Appendix 5. Abbreviations

AACAP	*American Academy of Child and Adolescence Psychiatry*
AAP	*American Academy of Pediatrics*
ADHD	Attention deficit hyperactivity disorder
ADHD-C:	Attention deficit hyperactivity disorder, Combined subtype
ADHD-HI	Attention deficit hyperactivity disorder, predominantly hyperactive-impulsive subtype
ADHD-I	Attention deficit hyperactivity disorder, predominantly Innatentive subtype
AGREE	*Appraisal of Guidelines Research and Evaluation*
AHA	*American Heart Association*
AHRQ	*Agency for Healthcare Research and Quality*
AIAQS	*Agència d'Informació, Avaluació i Qualitat de Cataluña*
AMA	*American Medical Association*
APA	*American Psychiatric Association*
BASC	*Behavior Assessment System for Children-Parent Rating Scales*
BOE	Official State Gazette
BP	Blood pressure:
BT	Behavioural therapy
CAM	*Complementary and Alternative Medicine*
CBCL	*Child Behavior Check-List*
CBT	Cognitive behaviour therapy
CCT	Craniocerebral trauma
CD	Conduct disorder
CDC	Centers for Disease Control and Prevention
CDC	Developmental coordination disorder
CHTE	Study habits and techniques questionnaire
CI	Confidence Interval
CMA Infobase	*Canadian Medical Association*
Cmax	Maximum plasmatic concentration

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CNS	Central Nervous System
CPG	Clinical Practice Guideline
CPRS	*Conners Parents Rating Scale*
CPT II	*Conners Performance Test II*
Cranial MRI:	Cranial magnetic resonance
CRD	*Centre for Reviews and Dissemination*
CSAT	*Children Sustained Attention Task*
CTRS	*Conners Teachers Rating Scale*
D2	D2 (Attention test)
DICA-IV	*Diagnostic Interview for Children and Adolescents-IV*
DIE	Integrated study diagnosis
DISC	*Diagnostic Interview Schedule for Children*
DSM –IV-TR	Diagnostic and StatisticalManual for Mental Disorders, 4th edition, revised text
DSM-II	Diagnostic and StatisticalManual for Mental Disorders, 2nd edition
DSM-III	Diagnostic and StatisticalManual for Mental Disorders, 3rd edition
EDAH	Scales for evaluating the attention deficit hyperactivity disorder
EEG	Electroencephalogram
FDA	*US Food and Drug Administration*
FSJD	Sant Joan de Déu Foundation
H.R	Heart rate
ICD-10	International Classification of Diseases, 10th version
ICSI	*Institute for Clinical System Improvement*
IHE	Study habits inventory
IQ	Intellectual quotient
K ABC	Kaufman assessment battery for children
K BIT	Kaufman brief intelligence test
kg	kilograms
K-SADS	*Schedule for Affective Disorders and Schizophrenia in School-Age Children*

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MA	Meta-analysis
MFF_20	Matching familiar figure test-20
mg	milligrams
MHS	*Multi-Health Systems Inc*.
MSCA	McCarthy Scale of Children's Abilities
MTA Study	*The Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder*
NICE	*National Institute for Healthand Clinical Excellence*
NIMH	*National Institute of Mental Health*
NLM	*U.S. National Library ofMedicine*
NNTB	*Number needed to benefit*
NNTH	*Number needed to harm*
NZGG	*New Zealand Guidelines Group*
ODD	Oppositional defiantdisorder
OMC	Collegiate Medical Organisation of Spain
PET	*Positron emission tomography*
PICO	Patient / Intervention / Comparison / Outcome or result.
PROESC	Writing process assessment series
PROLEC-R	Revised reading process assessment series
PROLEC-SE	Reading process assessment in third cycle students of primary and secondary education
RCF	Complex Rey Figure
RCT	Randomised controlled trial
RR	Relative risk
SDQ	Skills and Difficulties Questionnaire
SIGN	*Scottish Intercollegiate Guidelines Network*
SMD	Standardised mean difference
SNRI	Selective Noradrenaline Reuptake Inhibitors
SNS	National Health System
SPECT	*Single Photon Emission Computed Tomography*

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SR	Systematic review
SS	Social skills
SSRI	Selective Serotonin Reuptake Inhibitors
STROOP	Stroop Colour and word test
SUD	Substance use disorder
TAD	Tricyclic antidepressants
TALE	Reading and writing analysis test
TALEC	Reading and writing analysis test in Catalan
TP	*Toulouse-Pieron*
TRF	*Teacher Report Form*
UAB	Autonomous University of Barcelona
UN	United Nations Organisation
WAIS-III	*Weschler Adult Intelligence Scale, version III*
WHO	World Health Organisation
WISC – IV	*Weschler Intelligence Scale for Children, version IV*
YSR	*Youth Self Report Form*

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Appendix 6. Declaration of interest

Development Group of the CPG on ADHD

Mónica Fernández Anguiano and Beatriz MENA Pujol have stated there is no conflict of interest.

Jose Ángel Alda Diez has received aid from Janssen-Cilag, Lilly and Juste to attend meetings and congresses, he has received fees as a speaker and has carried out consultancy activities for Janssen-Cilag and Illy.

Cristina Boix Lluch has received aid from Janssen-Cilag and Juste to attend congresses and courses, and she has received fees from Janssen-Cilag as a speaker.

Roser Colomé Roura has received aid from Janssen-Cilag to attend congresses and meetings.

Rosa Gassió Subirachs has received aid from Janssen-Cilag to attend congresses, she has received fees as a speaker and has received funding to participate in a research project.

Jon Izaguirre Eguren has received aid from Janssen-Cilag and Novartis to attend courses and congresses, he has received fees from Janssen-Cilag as a speaker and has received funding from Lilly and Novartis to participate in a research project.

Juan Ortiz Guerra has received aid from Janssen-Cilag and Lilly Novartis to attend congresses, he has received fees from Janssen-Cilag as a speaker and has received funding from Lilly to participate in a research project.

Anna Sans Fitó has received aid from Janssen-Cilag and Lilly to attend meetings and congresses, she has received fees from Janssen-Cilag as a speaker and has carried out consultancy activities for Janssen-Cilag, Juste and Lilly.

Eduardo Serrano Troncoso has received aid from Janssen-Cilag to attend a congress.

Anna Torres Giménez has received fees from Janssen-Cilag to attend a course.

Methodological advice from the Agència d'Informació, Avaluació i Qualitat (AIAQS)

Maria Dolors Estrada Sabadell has stated there is no conflict of interest.

Ethical and legal aspects chapter

Sabel GabaldónFraile and Núria Terribas Sala have stated there is no conflict of interest.

Other collaborations

Antoni Parada Martinez has stated there is no conflict of interest.

Expert collaborators

Juan Antonio Amador Campos has stated there is no conflict of interest.

Josefina Castro Fornieles has received aid from Lilly to attend a congress and has carried out consultancy activities for Lilly.

Lefa S. Eddy Ives has received fees from Janssen-Cilag as a speaker.

Jesús Eiris Puñal has received aid from Lilly to attend a congress, he has received fees from Janssen-Cilag and Lilly as a speaker, and he has received funding from Lilly, Janssen-Cilag, Rubio and Juste for educational programmes or courses.

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Marta Garcia Giral has received aid from Janssen-Cilag, Lilly and Juste to attend meetings and congresses, she has received fees from Janssen-Cilag, Lilly and Rubio as a speaker at different conferences and courses; she has carried out consultancy activities for Janssen-Cilag, Lilly, Rubio and Juste; she has stated there is no personal conflict of interest on behalf of Juste for providing stationery material as reinforcement for groups of patients and economic aid from Janssen-Cilag, Lilly and Rubio to fund research.

Oscar Herreros Rodríguez has received aid from Lilly, Janssen-Cilag, AstraZeneca, Novartis, Wyeth, GlaxoSmithKline, Almirall, Esteve, Juste to attend several national and international activities; he has received fees from Lilly, Janssen-Cilag, Wyeth and Juste as a speaker and he has received funding from Lilly, Janssen-Cilag, AstraZeneca, Novartis, Wyeth, Almirall, Esteve, Juste, GlaxoSmithKline and Pfizer for educational programmes or courses; he has received funding from Lilly to participate in a research project; he has carried out consultancy activities for Lilly, Janssen-Cilag Juste; he has also stated there is no personal conflict of interest on behalf of Lilly, Janssen-Cilag, AstraZeneca, Novartis, Wyeth, Almirall, Esteve, Juste, GlaxoSmithKline or Pfizer for funding educational programmes or courses for the unit.

Amaia Hervás Zúñiga has received aid from Janssen-Cilag and Lilly to attend courses and congresses, she has received fees from Lilly as a speaker and has carried out consultancy activities for Janssen-Cilag, Lilly and Bristol Myers Squibb; she has also stated there is no personal conflict of interest on behalf of Lilly for economic aid for a research project.

María Jesus Mardomingo Sanz has received aid from Janssen-Cilag and Lilly to attend meetings and congresses, she has received fees from Lilly, Janssen-Cilag and Rubio as a speaker, and has received funding from Janssen-Cilag and Lilly to finance education programmes or courses.

Rosa Nicolau Palou has received aid from Janssen-Cilag and Lilly to attend courses and congresses, she has received feed from Lilly and Rubio as a speaker, and she has economic interests in a private practice, is a participatory partner in Tekton, TeDeA, Attentia, Unidad TDAH per nens i adolescents people; she has also stated non-economic type conflict of interest as a member of the scientific-ethical advisory committee of the Adana Foundation.

Cesar Soutullo Esperón has received aid from Almirall-Prodesfarma, AstraZeneca, Lilly, Esteve, Bristol-Myers Squibb, Janssen-Cilag, Pfizer, Pharmacia Spain to attend courses and congresses, he has received fees from AstraZeneca, Lilly, GlaxoSmithKline, Janssen-Cilag, Novartis y Solvay as a speaker; he has received funding from

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Alicia Koplowitz Foundation, Janssen-Cilag, Juste, Lilly, Rubio and Shire for education programmes or courses; he has carried out consultancy activities for the Alicia Koplowitz Foundation, Lilly (Spain and Europe), Juste, EINAQ (European Interdisciplinary Network ADHD Quality Assurance), Janssen-Cilag (Spain and Europe), Pfizer (Global), Shire (Global), Otsuka (Europe), Bristol-Myers Squibb; he has economic interests as a clinical consultant (clinical head) and associated professor of the University Clinic, University of Navarre and non-economic type conflicts of interest due to copyright for publications in DOYMA, Editorial Médica Panamericana, Grupo Correo, EUNSA, Euro RSCG Life Medea; he has also declared non-personal conflicts of interest on behalf of the Alicia Koplowitz Foundation, Lilly and Shire for funding the creation of a unit or service.

Javier San Sebastián Cabasés has received aid from Janssen-Cilag to attend congresses.

External Review

Anna Bielsa Carrafa, Fulgencio Madrid Conesa and Mateu Servera Barceló have stated there is no conflict of interest.

Pedro Benjumea Pino has received aid from Lilly to attend a congress.

María Dolores Domínguez Santos has received aid from Lilly to attend a congress.

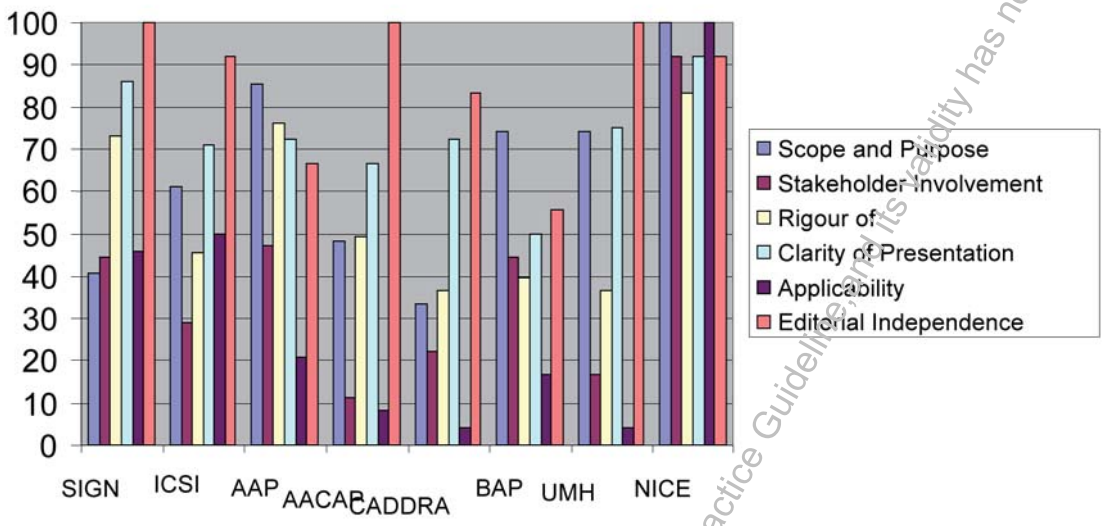
Joaquín Fuentes Biggi has received aid from Lilly, Janssen-Cilag and Shire to attend courses and congresses; he has received fees from Lilly, Janssen-Cilag and Shire as a speaker at non-promotional scientific activities; he has received funding from Lilly too participate in different research projects and he has carried out consultancy activities for Lilly, Janssen-Cilag and Shire.

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Appendix 7. Description of the CPG included

Eight international CPGs on ADHD have been included. Furthermore, the CPG on ADHD has also drawn inspiration from five guidelines on other disorders and international consensus.

The chart shows the quality according to the six dimensions of the AGREE instrument of the eight CPGs on ADHD assessed.



Attention Deficit and Hyperkinetic Disorders in Children and Adolescents. A National Clinical Guideline[1]

CPG Abbreviation:	SIGN 2005
Organisation:	Scottish Intercollegiate Guidelines Network
Date of publication:	August 2005
Population:	Children and adolescents with ADHD
Application context:	Scotland
Aimed at:	Health Professionals
Funding:	SIGN
Quality according to AGREE:	Recommended

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Health Care Guideline: Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Primary Care for School-Age Children and Adolescents[179]

CPG Abbreviation:	ICSI 2007
Organisation:	Institute for Clinical Systems Improvement
Date of publication:	March 2007
Population:	Children and adolescents with ADHD
Application context:	United States
Aimed at:	Primary Care physicians, organisations that provide or make decisions
Funding:	ICSI
Quality according to AGREE:	Recommended with modifications

Clinical Practice Guideline: Diagnosis and Evaluation of the Child with Attention Deficit/ Hyperactivity Disorder. Treatment of the School-Aged Child UIT Attention-Deficit/Hyper activity Disorder[196]

CPG Abbreviation:	AAP 2005
Organisation:	American Academy of Pediatrics
Date of publication:	June 2005
Population:	Children and adolescents with ADHD
Application context:	United States
Aimed at:	Paediatricians, Health Professionals
Funding:	AAP
Quality according to AGREE:	Recommended

Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder[72]

CPG Abbreviation:	AACAP 2007
Organisation:	American Academy of Child and Adolescent Psychiatry
Date of publication:	July 2007
Population:	Children and adolescents with ADHD
Application context:	United States
Aimed at:	Child psychiatrists, health professionals
Funding:	AACAP
Quality according to AGREE:	Recommended with modifications

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Canadian ADHD Practice Guidelines[359]

CPG Abbreviation:	CADDRA 2008
Organisation:	Canadian Attention Deficit Hyperactivity Disorder Resource Alliance
Date of publication:	2008
Population:	Children, adolescents and adults with ADHD
Application context:	Canada
Aimed at:	Health Professionals
Funding:	CADDRA
Quality according to AGREE:	Not recommended

Evidence-based guidelines for management of attention deficit hyperactivity disorder in adolescents in transition to adult services and in adults: recommendations from the British Association for Psychopharmacology[360]

CPG Abbreviation:	BAP 2006
Organisation:	British Association for Psychopharmacology
Date of publication:	2006
Population:	Adolescents in transition to adulthood and adults with ADHD
Application context:	Great Britain
Aimed at:	Health professionals
Funding:	BAP
Quality according to AGREE:	Not recommended

Guidelines for Clinical Care: Attention Deficit Hyperactivity Disorder[361]

CPG Abbreviation:	UMHS 2005
Organisation:	University of Michigan Health System
Date of publication:	August 2005
Population:	Children and adolescents with ADHD (6-18 years)
Application context:	United States
Aimed at:	Health Professionals
Funding:	UMHS
Quality according to AGREE:	Not recommended

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Attention deficit hyperactivity disorder. The NICE guideline on diagnosis and manage¬ment of ADHD in children, adolescents and adults[2]

CPG Abbreviation:	NICE 2009
Organisation:	National Institute for Health and Clinical Excellence
Date of publication:	2009
Population:	Children, adolescents and adults with ADHD
Application context:	Great Britain
Aimed at:	Health professionals, families, organisations that provide or make decisions
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Quality according to AGREE:	Highly recommended

Inspiration guidelines for specific sections of the CPG on ADHD

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