# Clinical Practice Guideline on Perioperative Care in Major Abdominal Surgery

### NOTE:

It has been 5 years since the publication of this Clinical Practice Guideline and it is subject to updating.

The recommendations included should be considered with caution taking into account that it is pending evaluate its validity.

**CLINICAL PRACTICE GUIDELINES IN THE NHS** 

MINISTRY OF HEALTH, SOCIAL SERVICES, AND EQUALITY









# Clinical Practice Guideline on Perioperative Care in Major Abdominal Surgery

CLINICAL PRACTICE GUIDELINES IN THE NHS
MISTRY OF HEALTH, SOCIAL SERVICES, AND EQUALITY









This CPG is intended as an aid to decision-making in healthcare. The guidelines are not mandatory, nor do they take the place of the clinical judgement of healthcare staff.

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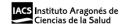
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# Introduction

Documenting the variability of clinical practices, analysing the causes, and adopting strategies aimed at eliminating it have been proven to be initiatives that encourage healthcare professionals to make decisions that are effective, safe, and focused on the patients. One of these strategies is the preparation of Clinical Practice Guidelines (CPGs), which are "sets of recommendations based on the systematic review of the evidence and the assessment of the risks and benefits of the different alternatives, in order to optimize the healthcare for patients".

The priorities of the Ministry of Health, Social Services, and Equality include the consolidation of the preparation of CPGs, coordinated by GuíaSalud, within the framework offered by the Spanish Network of Agencies for the Assessment of Health Technologies and Services of the National Health System (NHS).

These Clinical Practice Guidelines on Perioperative Care in Major Abdominal Surgery (MAS) have been prepared within this context.

Perioperative care refers to all of the strategies and actions related to patient care from the moment the decision to operate surgically is made until the patient leaves the hospital. It includes a wide range of procedures and practices that are aimed at reducing surgical stress, preventing complications, accelerating patient recovery, and improving the patient's experience.

The CPG on Perioperative Care in MAS answers clinical questions regarding some of these care interventions, in order to offer a series of common directives based on the best scientific knowledge available.

This CPG is the result of the concerled effort by a group of professionals from different health fields and disciplines, belonging to different specializations and representatives of several different Scientific Societies.

The Directorate-General for Public Health, Quality, and Innovation would like to thank all of these people for their work, and we hope that it will assist professionals and patients in decision making, improving the tailoring of care and quality of life of people who undergo elective major abdominal surgery.

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Spanish Society for Parenteral and Enteral Nutrition (SENPE)

Members of these societies participated in the authorship, expert collaboration, and external review of the CPG.

**Declaration of interests:** All members of the Work Group, as well as those who have participated in the expert comboration and external review, have made a declaration of interest which is presented in Annex 4.

# Key questions

### Preoperative Measures

### *Information for patients*

1. In patients who are going to undergo abdominal surgery, does information on the process (via clinic) help reduce the length of hospital stays?

### Nutritional screening

2. In patients who are going to undergo abdominal surgery, does the study of the state of the patient's nutritional state reduce postoperative complications (morbi-mortality)?

### Carbohydrate drinks

3. In patients who are going to undergo elective major abdominal surgery, does the administration of carbohydrate drinks (two hours before surgery), versus not administering anything, reduce postoperative complications? Does it shorten hospital stays?

### Anaesthetic premedication

4. In patients who are going to undergo elective major abdominal surgery, is the any evidence to support that not giving preanaesthetic medication can reduce or prevent postoperative ileus?

# Intraoperative Measures

ERAS and laparoscopic surgery

- 5. In patients who undergo elective major abdominal surgery, do the following interventions reduce morbi-mortality and hospital stays when compared with the use of laparoscopy and conventional perioperative care?
  - Laparoscopy + ERAS
  - Laparotomy + ERAS

### Perioperative measures

### Fluid therapy

6. In patients who undergo elective major abdominal surgery, does the use of a goal directed fluid therapy algorithm, versus restrictive fluid therapy, reduce postoperative complications? Does it shorten postoperative ileus? Does it shorten hospital stays?

### Analgesia

In patients who undergo elective major abdominal surgery, is transversus abdominis plane (TAP) block more effective and safer than epidural analgesia?

perative measures

### Postoperative measures

Early reinitiation of oral feeding

In patients who undergo elective major abdominal surgery, does the early administration of oral nutrition versus not administration anything shorten postoperative ileus?

Early mobilization

In patients who undergo elective major abdominal surgery, does early mobilization (getting out of bed within the first 6 hours) versus remaining in bed shorten

# Levels of evidence and recommendation grades

Table 1. SIGN Levels of evidence and grades of recommendation<sup>1</sup>

	Levels of evidence		
1++	High quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very low risk of bias.		
1+	Well-conducted meta-analyses, systematic reviews of clinical trials, or well-conducted clinical trials with little 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 or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.		
2+	High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.		
2-	Cohort or case-control studies with a high risk of bias and a significant risk that the relationship is not causal.		
3	Non-analytical studies such as case reports and case series.		
4	Expert opinion.		
	Grades of recommendation		
Α	At least one meta-analysis, systematic review or clinical trial rated as 1++ directly applicable to the target population of the guide; or a body of evidence consisting of studies rated as 1+ and showing overall consistency of results.		
В	A body of evidence consisting of studies rated as 2++, directly applicable to the target population of the guide and showing overall consistency of results; or evidence extrapolated from studies rated as 1++ or 1 +.		
С	A body of evidence consisting of studies rated as 2+ directly applicable to the target population of the guide and showing overall consistency of results; or evidence extrapolated from studies rated as 2++.		
D	Evidence level 3 or 4 or evidence extrapolated from studies rated as 2+.		

Studies classified as 1- and 2-must not be used in the preparation of recommendations due to their high potential for bias.

Good clinical practice

 $\sqrt{\phantom{a}}$  Recommended practice based on clinical experience and consensus of the editorial team.

<sup>\*</sup> Sometimes the development group wishes to highlight an important practical aspect for which there is probably no supporting evidence. In general, these cases are related to an aspect of treatment generally accepted to be good clinical practice and that would not normally be questioned by anyone. These aspects are evaluated as a point of good clinical practice. These messages are not an alternative to the recommendations based on evidence, but should be considered only when there is no other way of highlighting that aspect.

# Recommendations of the CPG

# 4. Preoperative measures

# 4.1. Information for patients

$\sqrt{}$	Oral and written information should be given to patients who are going to undergo major abdominal surgery, describing what will take place during the entire hospital stay, resolving any doubts and making the patient a participant in the surgical process.

It is recommended that the information that is communicated to the patient who is going to undergo major abdominal surgery be agreed upon previously by a multi-disciplinary team to promote a comprehensive understanding of the surgical process.

### 4.2. Nutritional screening

D	Nutritional screening of all patients who are going to undergo major abdominal surgery is recommended.
<b>V</b>	The assessment of the patient's nutritional state should be done during the preoperative visit to allow sufficient time for the nutritional support teams present in each centre to take the necessary measures based on the results of the assessment.

It is recommended that nutritional treatment be initiated during the preoperative period in all patients identified as being at risk of malnutrition during the nutritional screening.

### 4.3. Carbohydrate drinks

In non-diabetic patients who are going to undergo elective major abdominal surgery, the administration of 200 to 400 ml of a carbohydrate drink that contains at least 50 g of glucose, up to 2 hours prior to the surgical procedure, is recommended.

In non-diabetic patients who are going to undergo elective major abdominal surgery, it must be taken into account that the administration, up to 2 hours prior to surgery, of clear carbohydrate liquids is safe, not associated with any harmful effects for patients, such as vomiting or aspiration pneumonitis.

# 4.4. Anaesthetic premedication

The use of intermediate or long-acting sedative and/or anxiolytic premedication in patients who undergo major abdominal surgery is not recommended.

In cases in which the administration of anxiolytic premedication is deemed necessary, short-acting BDZs are recommended.

# 5. Intraoperative measures

### 5.1. ERAS and laparoscopic surgery

In patients who are going to undergo elective colorectal surgery, the laparoscopic approach is recommended, in combination with the application of an intensified abdominal surgery recovery program.

# 6. Perioperative measures

### 6.1. Fluid therapy

- Colorectal surgery that falls within the scope of a program of enhanced recovery after abdominal surgery (ERAS) should include a personalized fluid therapy plan for each patient.
- Abdominal surgery that falls within the scope of an ERAS program should include a personalized fluid therapy plan for each patient.
- In patients who undergo colorectal surgery, the use of a haemodynamic goal-directed fluid therapy algorithm is suggested when the necessary human and technical resources are available.
- In patients with low surgical risk (ASA I or II) who undergo colorectal surgery within the scope of an ERAS program, evaluate the possibility of applying an intraoperative fluid handling strategy with a balance close to zero.

### 6.2. Analgesia

Scientific evidence is insufficient to support a recommendation in favour of or against the use of transversus abdominis plane block for postoperative analgesia in major abdominal surgery.

If the TAP technique is used for postoperative analgesia, it should be applied via catheter with continuous perfusion.

# 7. Postoperative measures

### 7.1. Early rejuitiation of oral feeding

In patients who have undergone colorectal surgery, surgery of the small intestine, or gynaecological abdomiral surgery, it is recommended that oral ingestion of liquids and solids begin as soon as possible, based on the tolerance of the patient, preferably within the first 24 hours after the surgical procedure, with the possibility of resuming oral feeding starting 4 hours after surgery.

### 7.2. Early mobilization

The implementation of a plan of perioperative care that promotes early and progressive mobilization of the patient, getting the patient out of bed on the same day of the surgery, and starting to walk within the first 24 hours following the surgery.

В

# 1. Introduction

Perioperative care beings when the surgical treatment of the patient is decided and ends when the patient is discharged from the hospital. It includes a wide variety of procedures and practices aimed at preparing the patient and the patient's family physically and emotionally, favouring the success of the operation, preventing complications, and reducing convalescence time and the length of the stay in the hospital. This care is multi-disciplinary in nature and requires the coordination between different specializations and levels of health care.

Until several years ago, perioperative treatment of patients undergoing elective abdominal surgery consisted of a series of habits acquired through practice, rather than based on scientifically proven facts. This approach adopts an expectant attitude, waiting for the body to recover from the surgicaland pharmacological aggression, for example, by keeping the patient on an absolute diet until intestinal motility is restored. Practices such as the systematic use of tubes and drains, the prolonging of fluid therapy until the appearance of per staltism, or the use of analgesia with intravenous narcotics to control pain keep patients without postoperative complications in bed longer than necessary and draw out their convalescence<sup>2,2</sup>. In addition to all of this, we must also add the strategies that result in patients arriving at the operating room in sub-optimum conditions, such as preoperative fasting and dehydration caused by intensive preparation of the colon. In early 2000, the average postoperative hospital stay in Spain with this treatment regimen, following colorectal surgery, was 11.8 days (CI95% 11.21 to 12.7)<sup>4</sup>.

There is a large degree of variability in the perioperative handling of surgical patients in our area. A study published in 2014 suggests that key aspects such as restriction of perioperative fluids or early reinitiation of oral feeding are procedures with moderate to low application in normal clinical practice<sup>5</sup>. The reason for this praxis is probably due to a classic focus in which the preferences and experience of the different Surgical and Anaesthesia Departments play an important role and that is not based on scientific evidence.

Enhanced recovery or multimodal rehabilitation programs (MMRH), also known as *fast-track* or ERAS (which stands for *enhanced recovery after surgery*), revise traditional care interventions in order to rationalize perioperative treatment and thus improve the postoperative course of the patient. These programs are supported on three main pillars: the application of a package of perioperative measures and strategies; interdisciplinarity, understood as the joint and structured participation of the different healthcare professionals involved; and the active participation of the patient throughout the process.

It was professor Henrik Kehlet at the Hvidovre university hospital in Denmark who, at the end of the 1990s, promulgated the idea of reducing surgical stress by applying multimodal treatment with programs that conformed to the available scientific data, taking advantage of advances in anaesthesia techniques, minimally-invasive surgery, and perioperative care<sup>6,7</sup>.

Just over a decade ago, MMRH protocols began to become more widespread, mainly in patients programmed for colon and rectal surgery<sup>7</sup>. In 2001, the ERAS group (*Enhanced Recovery After Surgery*), was formed, with colorectal surgery departments from Scotland, Sweden, Denmark, Norway, and the Netherlands participating, with the goal of further developing the principles of MMRH. In 2005, this group agreed upon an MMRH program for patients undergoing colorectal surgery<sup>8</sup>, which was later updated<sup>9</sup>, and which was followed by the publication of guadelines on other surgical procedures<sup>10-13</sup>.

Table 2. Measures of ERAS protocols in colorectal surgery

### **PREOPERATIVE**

Preoperative information

No/selective preparation of the colon

Shorten preoperative fasting period

Preoperative ingestion of glucose

Avoid long-acting anaesthetic premedication

Antibiotic and pulmonary thromboembolism prophylaxis

### **INTRAOPERATIVE**

Anaesthesia with minimal postoperative residual effect

Epidural anaesthesia/analgesia

Optimization of fluid therapy

Minimally-invasive surgery

Maintenance of normothermia

Removal of drains

### **POSTOPERATIVE**

Epidural analgesia

Oral analgesia without opioids/NSAID

Removal of feeding tubes

Pharmacological prevention of postoperative ileus

Avoid fluid overload

Early reinitiation of oral ingestion

Prevention of post-surgical vomiting and nausea

Early mobilization

Adapted from Gustafsson et al.9

The application of the perioperative measures of the MMRH programs (table 2) appears to lead to an improvement in the surgical process. Most of the scientific evidence is drawn from colon and rectal protocols, although the practices of MMRH has spread progressively to other surgical specializations<sup>14,15</sup>. The meta-analyses suggest that MMRH protocols are effective and safe, reduce hospital stays of patients who underwent colorectal surgery by an average of -2.44 days (CI95% -3.06 to -1.83), and are associated with almost 30% fewer total complications, without increasing the readmittance rate<sup>16</sup>. This translates into a reduction in healthcare costs<sup>17</sup>.

A key factor in the success of multimodal treatment is the degree of compliance with the program. Gustafsson et *al.*<sup>9</sup> showed the existence of a dose-response relationship and suggest the need to comply with more than 70% of the items. The protocols of the published studies are heterogeneous; none contains the more than 20 proposed items<sup>9</sup>. However, it has been demonstrated that the more items that are implemented, the better the postoperative evolution of the patient<sup>5,18,19</sup>. Each one of the individual strategies has an additive effect and they should be applied together to maximize the benefit. Having consistent clinical methods with a high degree of protocolization also appears to have an effect on the success of MMRH programs<sup>20</sup>.

Enhanced recovery is currently considered to be the treatment of reference in elective major surgery<sup>21</sup>. In the United Kingdom, in 2009, the Ministry of Health added the *Enhanced Recovery Partnership Programme* to the National Health System, in collaboration with different entities, in order to implement enhanced recovery at the national scale in the clinical processes of elective major colorectal, orthopaedic, gynaecological, and urological surgery<sup>20</sup>.

In Spain, since 2008, the Spanish Multimodal Rehabilitation Group (GERM) has been preparing consensus protocols for different surgical specializations that are adapted to the specific characteristics of our healthcare system<sup>22</sup>. The principal objective of the GERM is the dissemination, implementation, and maintenance of MMRH programs in different surgical areas. Since early 2013, the GERM and the Ministry of Health, Social Services, and Equality have been collaborating on the development of a care plan aimed at reducing clinical variability in perioperative handling in elective major surgery<sup>23</sup>.

The scientific evidence suggests that this multidisciplinary focus is beneficial to patients<sup>24-28</sup>; however, there is some uncertainty in regard to the contribution of some individual items or strategies. In fact, studies of the effectiveness and safety of ERAS show a certain degree of variability, since none of them adopt all of the proposed measures<sup>9-13</sup>, which complicates the assessment of the impact of these programs. Here, the key aspects on which ERAS is based have been selected and evaluated individually to determine what role they play in the postoperative recovery of the patient.

The preparation of these Clinical Practice Guidelines (CPG) is justified by the need to promote a change in chinical practice that reduces the variability in the perioperative handling of patients in the area of major abdominal surgery, by addressing the uncertainty regarding some of the essential components of ERAS. Some hospitals have implemented ERAS programs<sup>5,29-34</sup> but effort and close collaboration with institutions and professionals will be needed to support the dissemination, adoption, and integration of a series of optimized perioperative care interventions throughout the National Health System.

# 2. Scope and Objectives

The purpose of these Clinical Practice Guidelines (CPG) is to serve as an instrument to improve the care of patients who undergo an elective major surgical procedure with abdominal involvement. It offers a set of recommendations related to the handling of patients before, during, and after the procedure, in order to improve the quality of care and thus optimize postoperative recovery and rehabilitation. The guidelines are also intended to unify the many different interventions related to perioperative care and reduce unjustified variability in clinical practice.

The target population of the guidelines is all patients older than 18 years of age with pathological intra-abdominal processes that require non-urgent (elective) major surgery. This indication includes some of the following procedures: colorectal surgery, gastrectomy, gastric bypass, hysterectomy, prostatectomy, cystectomy, other oncological, gynaecological, and urological surgery, etc. In this sense, the guidelines cover patients from different surgical specializations, such as general surgery, urological, and gynaecological surgery.

The scope of these CPG does not cover emergency surgery, outpatient surgery, and vascular surgery.

These CPG are aimed at all healthcare professionals involved in attending patients who are candidates for elective major abdominal surgery, mainly doctors specializing in surgery, anaesthesia, nutrition, urology, gynaecology, and nursing. The CPG are also of interest to administrators, clinic managers, and quality coordinators. Lastly, keeping in mind that the involvement and collaboration of the patient is necessary in the treatment process, the guidelines are also aimed at patients, and their family members and caregivers.

# 3. Methodology

The methodology used in the preparation of these CPG is covered in the *Methodology Manual for* the Preparation of CPGs in the National Health System<sup>1</sup>.

The principal stages involved in the preparation process are described below:

- Creation of a guideline working group made up of 11 healthcare professionals from different disciplines in the area of hospital care, from different regions and different specializations (general surgery, nursing, anaesthesiology, endocrinology and nutrition, urology) and 2 specialists in methodology from the Institute of Health Sciences of Aragon (IACS). To prepare the material aimed at patients, family members, and caregivers, the Work Group was assisted by a patient who had undergone MAS and had participated in an ERAS program. Also, the information aimed at patients, family members, and caregivers was revised by three non-medical persons to ensure that it was suitable and understandable.
- Preparation of the clinical questions, following the PICO format (Patient/Intervention/ Comparison/Outcome).
- Bibliography search, with de *novo* preparation of strategies for all questions. The sources consulted were MEDLINE (access via Pub- med), EMBASE (Elsevier.com), *Centre for Reviews and Dissemination* (CRD) *Databases, The Cochrane Library*, Índice Bibliográfico Español en Ciencias de la Salud (IBECs), and Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACs). The searches were limited to the types of studies that were most suitable based on the characteristics of the question and the languages of Spanish, French, and English. The search period covered from 2000 to 2014, through the months between May and July. Also, automatic email alerts were configured for new articles added to MEDLINE, EMBASE and *The Cochrane Library* after July 2014. A reverse search was done in the references of the articles identified and included in the guidelines. A non-systematic search of grey literature was also done.
- Initially, the studies that were returned were screened by title and abstract. In a second screening, the discarded studies were recorded and the causes for exclusion were specified.
- Evaluation of the quality of the studies and summary of the evidence for each question using the critical reading tool of the Agency for Healthcare Technology Assessment of the Basque Country (OSTEBA).
- Formulation of recommendations based on the "formal evaluation" or "justified opinion" of SIGN. The classification of the evidence and the grading of the recommendations were done using the system proposed by the *Scottish Intercollegiate Guidelines Network* (SIGN). In addition to the volume and quality of the evidence, the GWG had to consider the applicability of the results found, the concordance of the results,

concordance of the results, and the relevance of their application to the National Health System, or their clinical impact. Recommendations that were controversial or that lacked evidence were resolved by consensus in two meetings of the working group.

- The external reviewers reviewed the first draft of the CPG. The expert collaborators participated in the review of the recommendations. The review resulted in the introduction of minor changes in one recommendation, aimed at improving its feasibility.
- The scientific societies involved in the development of these guidelines, represented by members of the working group, expert collaborators, and external reviewers were the Spanish Society of Anaesthesiology, Reanimation, and Pain Therapy (SEDAR), the Spanish Multimodal Rehabilitation Group (GERM), the Spanish Association of Surgeons (AEC), the Spanish Association of Coloproctology (AECP), the Spanish Association of Surgical Nursing (AEEQ), the Spanish Society of Gynaecology and Obstetrics (SEGO), and the Spanish Society of Parenteral and Enteral Nutrition (SENPE).
- Material is available at www.guiasalud.es that presents detailed information with the
  methodology of the CPG (search strategies for each clinical question, critical reading
  sheets of the selected studies, tables synthesizing the evidence, and formal evaluation
  tables)
- An update of the guidelines is planned every three to five years, or sooner if new scientific evidence appears that could modify some of the recommendations in this guide. Updates will be made to the electronic version of the guidelines, available at the URL: http://www.guiasalud.es.

# 4. Preoperative measures

# 4.1. Information for patients

### **Ouestion to be answered:**

• In patients who are going to undergo abdominal surgery, does information on the process (via clinic) help reduce the length of hospital stays?

The exhaustive oral and written information for patients, highlighting the importance of their active collaboration in the process, is an essential component of the clinical method of enhanced recovery after abdominal surgery (ERAS). Counselling of surgical patients was evaluated as part of these programs in different randomized and controlled clinical trials and meta-analyses, especially in the area of colorectal surgery<sup>24,35</sup> Since it is considered to be a key element in the surgical process, it seems necessary to try to identify whether the information about the process, evaluated independently, plays any role in the postoperative recovery of the patient.

A systematic review that investigated the effectiveness of preoperative educational interventions to prevent complications and shorten hospital stays in patients undergoing colostomies or ilcostomies found inconsistent results for both outcomes. According to one RCT (64 patients) and 2 observational studies (443 patients), preoperative education shortened hospitals stays by a statistically significant amount, while two studies, one RCT (52 patients) and one observational study (86 patients) showed no differences between the two groups (experimental and control). The rate of stoma complications decreased in the group that received the educational intervention, but this difference was not statistically significant in two studies (RCT and observational)<sup>36</sup>.

RS of RCT and observational studies 1-/ 2-

A study done in the Republic of Singapore compared anxiety measured with the *State-Trait Anxiety Inventory* (STAI) before and after receiving information on the process, in 122 patients slated to undergo abdominal surgery, 49% of whom had cancer. The experimental group used a question prompt list (QPL) to consult with professionals in the immediate preoperative meeting. The average score on the STAI (adjusted for age, sex, and educational level) measured the day before surgery, after receiving the information, dropped significantly with respect to the average score obtained upon admittance, in the QPL group (mean difference 3.7; CI95% 1.2 to 6.2, p=0.005) and the control group (mean difference 2.6; CI95% 0.4 to 4.8, p=0.019). No statistically significant differences were observed in the average STAI scores when comparing the patients who used QPL with those who did not use it<sup>37</sup>.

RCT 1-

No suitably-designed studies with good methodology quality, with an appropriate study population and relevant result variables to provide an answer to the question posed in this section were found. In the review of Phatak et al.36 preoperative education is aimed at a very concrete aspect, care of the stoma. The differences in terms of format and content of the different educational interventions could explain the inconsistent results among the studies included in this review.

In addition to the studies described here, another seven studies were identified that were excluded from the volume of evidence because they were studies that evaluated the influence of the format in which the information was provided <sup>38,39</sup>, video<sup>40-42</sup>, multimed; a<sup>43,44</sup>).

### Summary of evidence

The 5 studies included in a systematic review showed inconsistent results and the data was too scarce to determine whether preoperative educational interventions reduce hospital stays in ostomized patients 36.

Patients (abdominal surgery) who received specific information on the surgical process in the immediate preoperative period day before the procedure) showed anxiety levels, according to the State-Trait Anxiety Inventory (STAI) that were significantly lower than before being informed (mean difference 2.6; CI95% 0.4 to 4.8, p=0.019)37.

### Recommendations

1-

Oral and written information should be given to patients who are going to undergo major abdominal surgery, describing what will take place during the entire hospital stay, resolving any doubts and making the patient a participant in the surgical process.

It is recommended that the information that is communicated to the patient who is going to undergo major abdominal surgery be agreed upon proviously by a multi-disciplinary.

It is recommended that the information that is communicated to the patient who is going to undergo major abdominal surgery be agreed upon previously by a multi-disciplinary team to promote a comprehensive understanding of the surgical process.

# 4.2. Nutritional screening

### Question to be answered:

In patients who are going to undergo abdominal surgery, does the study of the state of the patient's nutritional state reduce postoperative complications (morbi-mortality)?

The Spanish multi-centre study of Prevalence of Hospital Malnutrition and Associated Costs (PREDyCES) demonstrated that in Spain, one in four patients presents malnutrition or risk of malnutrition at the time of admittance, according to the *Nutritional Risk Screening* 2002 (NRS 2002)

test; however, less than one third of these patients follow a nutritional treatment during the time they are admitted<sup>45</sup>. The prevalence of preoperative malnutrition of surgical patients in the study was calculated at 17%. This data shows the existence of variability in care practices with respect to nutritional assessment of patients admitted to the hospital. Ideally, patients at nutritional risk who are going to undergo major surgery should be identified by a preoperative assessment and treatment should be instated before the surgical procedure.

With the exception of the study by Jie et *al.*<sup>46</sup>, which is described below no proof was found in the scientific literature that was directly applicable to this clinical question. For this reason, eleven observational studies<sup>47-57</sup> that investigate the relationship between preoperative nutritional state and the appearance of postoperative complications were reviewed and included as a source of indirect evidence.

A prospective cohort study done in China evaluated the results of application of a nutritional treatment on the appearance of short-term postoperative complications (hospital discharge) in 512 patients programmed for abdominal surgery, and on nutritional risk based on the NRS 2002 test<sup>(a)</sup>. Patients received nutritional treatment before the surgical procedure (parenteral or enteral nutrition for at least 7 days), in the opinion of the physician, who did not know the score obtained on the NRS 2002. In the group of patients with a score  $\geq 5$ , 35.8% (43/120) received nutritional treatment; in the group with scores of 3 or 4, the proportion was 5.3% (21/392). In the first group, the rate of total complications (25.6% versus 50.6%, p=0.008), infective complications (16.3% versus 33.8%, p=0.04), and non-infective complications (18.6% versus 36.4%, p=0.042) was significantly lower in the group that received nutritional support. No significant differences were found between the two groups in regard to rates of severe complications (7.0% versus 9.0%, p=0.53) and mortality (0% versus 2.6%, p=0.536). In the group of patients with scores of 3 or 4 on the NRS 2002 test, there were no significant differences in the rate of total complications (23.8% versus 23.2%, p=1.0), infective complications (p=0.50) and non-infective complications (p=0.75) between the patients who received preoperative nutrition and those who did not<sup>46</sup>.

(a)NRS 2002: *Nutritional Risk Screening* 2002, evaluates the following parameters: nutritional status, severity of the underlying disease, and age of the patient. It classifies results into two groups, based on the score: at nutritional risk (NRS≥3) and not at nutritional risk (NRS <3).

Cohort study

One prospective cohort study done in Switzerland found that a score of ≥3 on the NRS 2002 test is an independent predictor of short-term postoperative complications (<30 days) in patients who underwent major urological surgery (OR 3.27; CI95% 1.33 to 8.02)<sup>47</sup>. For ethical reasons, the study was interrupted when half of the expected number of patients (110 of 220) had been recruited, which could have caused the observed effect to be overestimated.

Cohort study

Based on a retrospective sample of 369 patients, and for a median monitoring period of 22 months, a study done in the U.S. investigates the effect of preoperative malnutrition (at least one of the following parameters: BMI<18,5 kg/m², albumi <3,5 gr/dL, weight loss>5% in the previous 6 months) on survival following partial or total nephrectomy due to renal cell carcinoma. Overall 3-year survival in malnourished and normo-nourished patients was 58.5% (CI95% 43 8 to 70.5%) and 85.5% (CI95%, 78.8 to 90.2%), respectively (p<0.001). Cancer-specific 3-year survival was 80.4% (CI95%, 68.8 to 88.1%) in malnourished patients versus 94.7% (CI95%, 93.5 to 98.3%) in normo-nourished patients (p<0.001). The study carried out a multivariate analysis that included the following parameters: age, comorbidity (Charlson index) anaemia, T stage, grade, malnutrition, and found that malnutrition was an independent predictor of overall mortality (HR 2.41; CI95% 1.40 to 4.18) and cancer-specific mortality (HR 2.76; CI95% 1.17 to 6.50). The authors did not monitor the nutritional status of the patients during the monitoring period after the operation<sup>49</sup>.

Cohort study 2+

A prospective cohort study carried on in Brazil, with the participation of 75 patients who had undergone major digestive surgery, hepatectomy, and pancreatectomy found that malnourished patients had a rate of postoperative pulmonary complications that was significantly higher than the rate observed in normo-nourished patients (31% versus 11%, p<0.05). Atelectasis was the most frequent complication in both groups (18% and 8.3%, respectively). Malnutrition was defined based on anthropometric parameters (IMC<20 kg/m², weight loss>10% in the previous six months) and biochemical parameters (albumin <35gr/L)<sup>48</sup>.

Cohort study 2-

One prospective cohort study used the SGA test( $^{b}$ ) to classify 38 patients who were candidates for liver transplants into two groups based on nutritional status: normo-nourished (SGA-A) and malnourished or at risk of malnutrition (SGA-B or -C). Preoperative malnutrition (SGA-B or -C) was associated statistically significantly with more episodes of post-transplant infection (85 versus 11, p<0.001), more episodes of infection per patient (mean 4.5  $\pm$  3.1 versus 0.6  $\pm$  0.9, p<0.001) and longer hospital stay (mean 41  $\pm$  19 days versus 18  $\pm$  19 days, p<0.001). In the regression analysis, malnutrition maintained a significant association with risk of postoperative infection and duration of hospital stay (confidence intervals were not shown)<sup>50</sup>.

(b) SGA: Subjective Global Nutritional Assessment, evaluates weight loss, ingestion, digestive symptoms of disease, functional capacity, metabolic stress, loss of subcutaneous fat or muscle mass, oedema, and ascites. It classifies the results into three g oups: A (good nutritional status), B (mild or suspected malnutrition) and C (severe malnutrition).

A retrospective cohort study done in the United States investigated the effect of malnutrition on short-term postoperative morbidity (<30 days) in 313 patients with chronic pancreatitis who had undergone a pancreatic oduodenectomy (PD), or lateral pancreaticojejunostomy (PYL), or distal pancreatectomy (PDI). For each type of surgery, patients were classified into four groups, based on the averaging of the scores of the three methods of nutritional screening (SGA, NRI(°) and INA(d)): adequate nutritional status (32%), mild malnutrition (29%), moderate malnutrition (30%), and severe malnutrition (9%). When comparing patients with and without malnutrition, the rate of complications of patients with moderate malnutrition was higher, although the difference was only statistically significant in the PYL group (14% versus 31%, p<0.05); severe malnutrition was associated with a statistically significant increase in the rate of complications of PD, PYL and PDI. Nutritional status did not affect mortality<sup>51</sup>.

- (c) NRI: Nutritional Risk Index, celculated using the following formula:  $(1.519 \times \text{serum albumin g/dl}) + (41,7 \times \text{current weight (kg)/ideal weight (kg)})$ .
- (d) INA: Instant Nutritional Assessment, takes into account the serum albumin concentration and the lymphocyte count. An albumin concentration  $< 3.5\,$  g/dl and lymphocyte count  $< 1500\,$  mm³ indicate a high risk of complications.

The studies cited below had a more general objective that consisted of identifying possible factors to forecast mortality and short-term postoperative complications in series of patients who had undergone major abdominal surgery. The number of factors studied varied between 3<sup>56</sup> and 35<sup>57</sup>, although most of the studies analysed between 10 and 15<sup>52,54,55</sup>. The data shown here are those that refer to the screening tools, anthropometric parameters, and biochemical parameters aimed at identifying malnutrition or nutritional risk.

Cohort study

Cohort study

In a prospective series of 352 patients who had undergone surgery for colorectal cancer, with a median age of 62.9 (range 20 to 92 years), done in South Korea, the following factors were associated with a higher rate of postoperative complications: decrease of recent oral ingestion (more than 25% in 3 months) (p=0.004), weight loss >5% in 3 months (p=0.003) and score on the NRS 2002 test  $\geq 3$  (p=0.006). The study found the following to be independent factors associated with the risk of postoperative complications: weight loss (OR 2.31; CI95% 1.36 to 3.91) and NRS 2002  $\geq 3$  (OR 3.05; CI95% 1 to 9.49). In turn, malnutrition based on NRS 2002 (score  $\geq 3$ ) was an independent risk factor of anastomotic dehiscence (OR 3.06; CI95% 1.15 to 8.18) and surgical wound infection (OR 3.51; CI95% 1.28 to 9.71)<sup>52</sup>.

Cohort study

The analysis of a retrospective series of 300 patients who underwent surgery for gynaecological cancer in the U.S. showed an average value of serum albumin concentration of 4.1 g/dl in patients who did not experience short-term postoperative complications (<30 days) (62.4%), a value of 3.7 g/dl in patients who experienced a complication (20%) and a value of 3.4 g/dl in patients who experienced two or more complications (17.6%) (p<0.031). The multivariate logistic regression found a significant association between albumin concentration (>3.9 g/dl versus <3.89 g/dl) and the risk of developing pestoperative complications (OR 0.29; CI95% 0.11 to 0.78)<sup>53</sup>.

Cohort study

The study done in China on a series of 314 patients with gastric cancer who underwent a gastrectomy, found that malnourished patients or patients at risk of malnutrition based on the NRS 2002 questionnaire (score  $\geq$ 3) had a higher rate of postoperative complications (39.8% versus 26.2%, p=0.039) and longer hospital stays (mean 19.06  $\pm$  11.79 days versus 13.6  $\pm$  7.24 days, p<0.001). By means of multivariate logistic regression, the authors showed that an NRS 2002 test score  $\geq$ 3 (OR 2.36; CI95% 1.32 to 4.94) increases the probability of suffering postoperative complications<sup>54</sup>.

Cohort study 3

A prospective study carried out in Japan investigated the relationship between preoperative nutritional assessment and postoperative clinical evolution in 50 living donor liver transplants (LDLT). The body composition or body cell mass (BCM) was used as the indicator of nutritional status. The BCM was measured with a multifrequency bioimpedance device (InBo- dy 720; Biospace, Tokyo, Japan). At the physician's discretion, preoperative nutritional therapy was administered: supplements enriched with branched-chain amino acids (BCAA): BCAA formula, or nothing. The rate of severe postoperative infection (requiring admittance to the ICU or death) and post-transplant sepsis (up to 30 days after the procedure) in patients with low BCM (38%, 19 patients) was significantly higher than in the case of patients with normal/high BCM. 42.1% versus 6.9% (p=0.003) and 84.2% versus 44.8% (p=0.002), respectively. Giving BCAA-enriched supplements versus not giving them reduced the rate of post-transplant sepsis (31.3% versus 70.6%, p=0.008). Using multivariable regression, the study found low BCM (OR 7.29; CI95% 1.63 to 44.52) or not giving BCAA-enriched supplements before the procedure (OR 5.4; CI95% 1.29 to 27.57) as risk factors for post-transplant sepsis<sup>55</sup>.

Cohort study

In a retrospective series of 196 patients with gastric cancer who underwent gastrectomy, the anthropometric and biochemical parameters studied (BMI, weight loss, and serum albumin) did not show a significant statistical association with the appearance of postoperative infective complications up to 30 days after the surgical procedure<sup>56</sup>.

Cohort study

A retrospective study done in Poland observed that the risk of malnutrition in patients who underwent distal pancreatectomy, based on the INA and NRI tests, is associated with a significantly higher rate of pancreatic fistulae. The multivariate analysis found that malnutrition based on INA (score ≤100) is an independent variable associated with the appearance of pancreatic fistula during the postoperative period (OR 8.12 CI95% 1.06 to 22.30). None of the tests showed a statistically significant relation to total complications or abdominal complications<sup>57</sup>.

Cohort study

No studies with robust methodological designs were found that compare the differences, in terms of morbidity and mortality, between surgical patients whose risk of malnutrition was systematically analysed, and other for whom the analysis or screening was not carried out. Only the study by Jie et al.46 investigates the effectiveness of treatment of malnutrition in the context of preoperative assessment of the nutritional status of the patient. Since it is the only study available to answer this question, the GWG felt that it was relevant to include the results of the studies that were found on the impact of malnutrition and the risk of malnutrition on the evolution of patients who have undergone major abdominal surgery.

Although the different diagnostic criteria used to define nutritional status complicate the comparison between the studies, the results found suggest that malnutrition is associated with increased postoperative morbidity and mortality. The GWG considers that propperative nutritional screening of all patients who are going to undergo surgery is fundamental and necessary to identify the patients who are at risk of malnutrition and who, without adequate preoperative nutritional intervention, will have a higher risk of unfavourable clinical evolution. There is currently no universally accepted nutritional assessment method, so the GWG does not suggest any one in particular.

The study Nozoe et al.58 was excluded because it assessed nutritional status with a tool, the Prognostic Nutritional Index or Onodera index, that is used widely in Japan and Chine, but for which no data in the west is available. Also, no reference is made to the study by De La Torre et al.59 in the volume of evidence due to the serious methodological limitations that it presents and the inadequate statistical analysis of the data by the authors.

### Summary of evidence

	<u> </u>
2+	In patients who have undergone major abdominal surgery (MAS) at risk of moderate or severe malnutrition (NRS $2002 \ge 5$ ), failure to administer preoperative nutritional treatment is associated with a statistically significant increase in the rate of total postoperative complications (25.6% versus 30.6%, p=0.008), infective complications (16.3% versus 33.8%, p=0.04) and non-infective complications (18.6% versus 36.4%, p=0.042). In patients with lower risk (NRS $2002 = 3$ or 4), there were no statistically significant differences <sup>46</sup> .
2+	The risk of malnutrition (NRS $2002 \ge 3$ ) is an independent predictor of short-term postoperative complications ( $\le 30$ days) in patients who underwent major urological surgery (OR 3.27; CI95% 1.33 to 8.02) <sup>47</sup> .
2+	In patients who underwent partial or total nephrectomy due to renal cancer, preoperative malnutrition (IMC<18.5 kg/m² and/or albumin<3.5 gr/dL and/or weight loss>5%) is an independent predictor of overall mortality (HR 2.41; CI95% 1.40 to 4.18) and cancerspecific mortality (HR 2.76; CI95% 1.17 to 6.50)49.
2-	In patients who have undergone major abdominal surgery, preoperative malnutrition (IMC<20 kg/m², albumin<35 gr/L, weight loss>10%) there is a statistically significant association with a higher rate of respiratory complications (31% versus 11%, p<0.05)48.
2- <sup>50</sup> 3 <sup>55</sup>	In patients who received liver transplants, preoperative malnutrition (SGA test B or C50 or body cell mass below 55) shows a statistically significant association with higher risk of postoperative infection50 and post-transplant sepsis (OR 7.29; CI95% 1.63 to 44.52)55.
2- <sup>51</sup>	In patients who have undergone surgery for chronic pancreatitis, severe malnutrition (average of three tests: SGA, NRI and INA) is associated with higher frequency of complications, regardless of the type of surgery51. In distal pancreatectomy, malnutrition (INA $\leq$ 100) is an independent variable associated with the appearance of pancreatic fistulae during the postoperative period (OR 8.12; CI95% 1.06 to 22.30)57.

3	In patients who have undergone colorectal surgery, weight loss >25% in 3 months (OR 2.31; CI95% 1.36 to 3.91) and an NRS 2002 test $\geq$ 3 (OR 3.05; CI95% 1 to 9.49) is associated with an increased risk of developing postoperative complications <sup>52</sup> .
3	In patients who have undergone surgery for gynaecological cancer a preoperative concentration of albumin <3.89 g/dL with an increase in the risk of postoperative complications (OR 0.29; CI95% 0.11 to 0.78) <sup>53</sup> .
3 <sup>54,56</sup>	In patients with gastric cancer who undergo gastrectomy, an NRS 2002 test ≥3 increases the probability of suffering postoperative complications (OR 2.36; CI95% 1.32 to 4.94)54. In another study, the anthropometric and biochemical parameters analysed did not show a statistically significant association with the appearance of infective complications <sup>56</sup> .

#### Recommendations

D	Nutritional screening of all patients who are soing to undergo major abdominal surgery is recommended.
1	The assessment of the patient's nutritional state should be done during the preoperative visit to allow sufficient time for the nutritional support teams present in each centre to take the necessary measures based on the results of the assessment.
1	It is recommended that nutritional treatment be initiated during the preoperative period in all patients identified as being at risk of malnutrition during the nutritional screening.

# 4.3. Carbohydrate drinks

### Question to be answered:

• In patients who are going to undergo elective major abdominal surgery, does the administration of earbohydrate drinks (two hours before surgery), versus not administering anything, reduce postoperative complications? Does it shorten hospital stays?

The administration of oral carbohydrates (OCH) prior to the surgical procedure is intended to reduce the body's catabolic response to surgical stress and preoperative fasting. This response is characterized by the presence to a greater or lesser degree of peripheral resistance to insulin, hyperglycaemia, muscular atrophy, and immunological depression. The preoperative use of OCH was proposed with the idea of triggering the normal diurnal metabolic rhythm of the body, with the activation of insulin before surgery<sup>60</sup>. Ingest 50 g of OCH stimulates an insulin release similar

to what is produced after a mixed meal. This reduces postoperative insulin resistance and protein consumption is reduced and its synthesis is improved, which generates a clinical benefit, to improve tissue repair in the immediate postoperative period. Also, administration of carbohydrate drinks can contribute to improving the patient's feeling of well-being (thirst, hungry, anxiety) in the preoperative period<sup>61</sup>. For this reason, many multimodal rehabilitation programs include the administration of 50 g of OCH 2 hours prior to surgery<sup>62</sup>. OCH does not delay gastric emptying or increase gastric acidity, so they are considered safe in patients programmed for elective surgery<sup>63</sup>. The objective of the question is to determine whether this intervention is associated with a lower probability of postoperative complications, and consequently, shorter hospital stays.

A Cochrane systematic review of quality examines the data from 27 RCTs that include a total of 1,976 patients with different elective surgical procedures. The meta-analysis by subgroups, done according to type of surgical procedure and the control group (placebo drink and preoperative fasting), showed a reduction in the average hospital stay of patients who have undergone MAS who received ≥ 45g of OCH within the four hours prior to the surgical procedure. This effect on length of hospital stay is limited to the meta-analysis that includes the data on all of the MAS studies, without taking into account whether the controls had received preoperative fasting or a placebo (10 studies, 213 participants), estimating an average hospital stay of 1.66 days less (CI95%-2.97 days to -0.34 days). No benefits were observed in the meta-analyses that compared OCH versus preoperative fasting (5 studies, 276 participants; mean difference -2.02 days, CI95% -4.13 days to 0.08 days) or in comparison with a placebo (7 studies, 464 participants, mean difference -1.23 days CI95% -2.79 days to 0.33 days). According to the authors, the evidence that preoperative use of carbohydrate drinks in MAS shortens hospital stays must be interpreted with caution due to the methodological limitations of the RCTs and the fact that the average stay in the different studies covers a very wide range. The degree of statistical heterogeneity between the original studies was high (I<sup>2</sup> ≥70%). The administration of OCH does not appear to influence the rate of postoperative complications after elective surgery, according to the meta-analyses that compare OCH against preoperative fasting or placebo (14 studies, 913 participants; RR 0.98, CI95% 0.86 to 1.11), OCH versus a placebo (10 studies, 594 participants; RR 0.92, CI95% 0.73 to 1.16) and OCH versus preoperative fasting (6 studies, 386 participants; RR 1.00, CI95% 0.87 to 1.16). PI 80.7% (184 of 228), 99.3% (156 de 157) y 41.1% (30 of 73) of the adverse events, respectively, from studies on MAS. Statistical heterogeneity was low (I<sup>2</sup>=0%). According to the authors, the evidence on the association between OCH and risk of postoperative complications is low quality due to the methodological limitations of the original studies and the lack of precision of the results.

Cohort study

Lastly, the meta-analysis showed that the administration of OCH reduces the mean return time of intestinal function by -0.39 days (CI95% -0.70 days to -0.07 days) (1st fl (2 studies, 86 participants), but does not significantly reduce the mean time to recovery of intestinal motility (1st intestinal movement) (2 studies, 54 participants; mean difference -0.48 days, CI95% -1.62 days to 0.66 days, I²=0%). The only study on MAS (142 participants) that analyses postoperative nausea in the first 24 hours, fatigue, and patient well-being, did not find a significant difference when comparing OCH versus a placebo. No cases of aspiration pneumonitis related to preoperative use of carbohydrate drinks was recorded (4 studies on MAS)64.

A study done in Australia investigated preoperative use of OCH in a sample of 44 patients programmed for colorectal surgery who were randomized to ingest OCH (800 ml the night before and 200 ml the following morning) or fasting before surgery, of which 26 (59%) were oncological patients and 37 (34%) underwent laparoscopic surgery. Both groups were allowed to drink clear liquids(1) until 5AM of the day of the surgery. The results adjusted for the duration of the operation and interval between the last ingestion of clear houids and the surgery showed that there were no differences for the analysed values. The average time to fulfil the criteria for discharge was 4.1 days (CI95\%\) 3.2 to 5.3) in the OCH group, versus 4.4 days (CI95% 3.3 to 5.7) for the control group (p=0.746). The average time until the appearance of the first flatus was 34.5 hours (CI95% 24.7 to 48.2) in OCH, versus 50.1 hours (CI95% 35.5 to 70.5) in controls (p=0.124), and the average until the appearance of the first intestinal movement was 46.2 hours (CI95% 33.7 to 63.4) versus 68.8 hours (CI95% 50.6 to 93.6) (p=0.075). Lastly, 4 patients (18.1%) in the control group, and 2 patients (9.1%) in the OCH group presented postoperative complications (p=0.376). No adverse effects were observed in association with preoperative administration of OCH65.

(1) Clear liquids: including, but not united to: water, herbal tea, light tea, black coffee, strained juices without pulp, carbonated beverages, and carbohydrate drinks<sup>66</sup>.

A systematic review and meta-analysis calculated, based on 7 RCTs (762 participants), a mean reduction of -1.08 days (CI95% -1.87 to -0.29) in duration of hospital stay among patients who received OCH before open abdominal surgery, when compared with controls (placebo or fasting). No statistically significant differences were observed between the OCH and control groups with respect to the rate of postoperative complications (9 studies, 878 participants; RR 0.88, CI95% 0.50 to 1.53). 99.2% (127 of 128) of the adverse events were generated in the 5 studies on MAS. No pulmonary complications related to OCH ingestion were observed67. The results showed a high degree of heterogeneity (I²=60%), which may have been partially due to the fact that two very different treatments (fasting and placebo) were used as the control group.

ECA 1+

RS de ECA

During the process to formulate recommendations ad in regard to their applicability and possible generalization, the GWG took into account that all of the studies exclude patients with diabetes mellitus, so the results are only applicable to patients without this disease.

Preoperative administration of carbohydrates, either orally or parenterally, during the 24 hours prior to the surgical procedure has shown beneficial effects on postoperative metabolic aspects when compared with traditional fasting during the night before the surgical procedure; it may also improve the preoperative well-being of the parient<sup>61,64</sup>. However, according to the evidence collected here, when relevant outcomes such as postoperative complications and duration of hospital stay are considered, the clinical benefit is inconclusive. There is no proof that administration of OCH in the immediate preoperative period has an effect on postoperative complications, and the evidence that the intervention is able to reduce the hospital stay to around one day is inconsistent and low quality. Nevertheless, when preparing the recommendations, the GWG took into account the favourable trend towards OCH in the reduction of hospital stay duration in all of the individual studies, and the fact that preoperative administration of OCH is safe for patients. The heterogeneity of the dosage(47.5 gr., 50 gr., 50.4 gr. or 67 gr.) and the treatment regimen for the administration of OCH were also taken into consideration, although most of the studies administered 50 g of OCH two or three hours before the surgery.

The inclusion of the SR and meta-analysis by Awad et al.<sup>67</sup>, prior to the Cochrane review<sup>64</sup> was considered to be pertinent because it contains data from two RCTs that are not included in Smith et al.<sup>64</sup>

#### **Summary of evidence**

1+64.65	When the administration of $\geq$ 45 gr. of OCH in the 4 hours prior to surgery is compared with preoperative fasting, in patients who underwent MAS, no statistically significant differences were observed in the mean duration of the hospital stay: mean difference -2.02 days (CI95% -4.13 days to 0.08 days)64 or 4.1 days (CI95% 3.2 to 5.3) versus 4.4 days (CI95% 3.3 to 5.7) (p=0.746) <sup>65</sup> .
1+	When the administration of $\geq$ 45 gr. of OCH in the 4 hours prior to surgery is compared with a piecebo, in patients who underwent MAS, no statistically significant differences were observed in the mean duration of the hospital stay: mean difference -1.23 days (CI95% -2.79 days to 0.33 days) <sup>64</sup> .
1+ <sup>64.65</sup>	When the results of all of the studies on MAS are combined, regardless of whether the control is a placebo or fasting, the administration of $\geq$ 45 gr. of OCH in the 4 hours prior to surgery reduces mean hospital stay by -1.66 days (CI95% -2.97 to -0.34)64 or -1.08 days (CI95% -1.87 to -0.29) <sup>67</sup> .
1+ <sup>64.65</sup>	The administration of $\geq$ 45 gr. of OCH in the 4 hours prior to MAS did not significantly influence the rate of postoperative complications <sup>64,65,67</sup> .

1+64.0	Preoperative administration of carbohydrate drinks does not significantly reduce time to restoration of intestinal motility after surgery <sup>64,65</sup> . There is some inconsistency in the results related to the recovery of intestinal function (1st flatus); one RCT showed that there were no differences <sup>65</sup> , while a meta-analysis of two RCTs showed that OCH reduce the average time until the appearance of first flatus by -0.39 days (CI95% -0.70 days to -0.07 days) <sup>64</sup> .
1+	Preoperative administration of carbohydrate drinks does not significantly affect postoperative nausea, fatigue, or postoperative well-being of the patient <sup>64</sup> .
1+ <sup>64.6</sup>	with harmful effects for patients such as comiting or aspiration

#### Recommendations

В	In non-diabetic patients who are going to undergo elective major abdominal surgery, the administration of 200 to 400 ml of a carbohydrate drink that contains at least 50 g of glucose, up to 2 hours prior to the surgical procedure, is recommended.
В	In non-diabetic patients who are going to undergo elective major abdominal surgery, it must be taken into account that the administration, up to 2 hours prior to surgery, of clear carbohydrate liquids is safe, not associated with any harmful effects for patients, such as vomiting or aspiration pneumonitis.

# 4.4. Anaesthetic premedication

## Question to be answered.

• In patients who are going to undergo elective major abdominal surgery, is there any evidence to support that not giving preanaesthetic medication can reduce or prevent postoperative iteus?

The preanaesthetic medication to which the question refers is that which could interfere with the recovery of patients in the immediate postoperative period.

Benzodiazepines (BDZs) are the drugs most commonly used as premedication to reduce anxiety and the response to the stress generated during the period prior to the surgical procedure. It also has a sedative, hypnotic, anxiolytic, and myorelaxing effect, in addition to inducing acterograde amnesia; but they can also cause excessive sedation, increased post-anaesthesia

recovery times, and delay the recovery of psycho-motor function<sup>68,69</sup>. The appearance of these undesirable effects has a negative effect on the patient's capacity to move and ingest beverages and food soon after the surgical procedure, which are key elements in the enhanced recovery after abdominal surgery (ERAS).

In general, there is no consensus among anaesthesiologists regarding the need for pharmacological premedication 70,71. The objective of the question is to investigate whether the systematic use of preanaesthetic medication is justified by scientific evidence.

No studies were found that had been done on representative samples of the target population of the CPG, or studies with relevant result variables. In the absence of empirical data that directly answers the question posed, two randomized controlled clinical trials (RCTs) done on patients with different elective surgical procedures who received premedication with benzodiazepines were taken into account as indirect sources of evidence<sup>72,73</sup>.

One multi-centre RCT (5 hospitals) done in France evaluated the effectiveness of sedating premedication in regard to the perioperative experience of the patient, in elective surgery with general anaesthesia. A total of 1,050 participants were randomized for premedication with lorazepam (2.5 lng 2 hours prior to the intervention), placebo, or nothing. 87.3% of the study sample was ≤65 years of age, 88% with physical status of ASA I or II, and 65% underwent orthopaedic or ear, nose and throat surgery. The overall satisfaction 24 hours after surgery (EVAN-G questionnaire)(a) of patients premedicated with lorazepam (mean score 72, CI95% 70 a 73) Was not higher than that of non-premedicated patients (mean score 73, CI95% 71 to 74), or those who received a placebo (mean score 71, CI95% 70 to 73), p=0.38. Extubation time was 17 minutes (CI95% 14 to 20) in the lorazepam group, 12 minutes (CI95% 11 to 13) in the non-premedicated group, and 13 minutes (CI95% 12 to 14) in the placebo group (p<0.001). The rate of patients with early cognitive recovery, 40 minutes after anaesthesia was ended, was significantly lower in the lorazepam group (51%, CI95% 45% to 56%) compared with the non-premedicated group (71%, CI95% 66% a 76%) or placebo (64%, CI95% 59% a 69%), p<0.001<sup>72</sup>.

(a) EVAN-G: Evaluation de Vécu de l'Anesthésie Generale, contains 6 different domains of satisfaction and one overall satisfaction index (score 0-100; higher scores indicating greater satisfaction).

An RCT done in France in non-outpatient general surgery (30% orthopaedic, 24% visceral, 15% ure ogical), did not find any statistically significant differences in anxiety or comfort levels perceived by patients in the operating room immediately prior to surgery, when premedication with 0.5 mg of alprazolam was compared with a placebo. All patients were given the treatment at 7 AM on the day of the procedure<sup>73</sup>.

RTC 1+

RTC 1-

The studies include a wide variety of surgical procedures, which makes it difficult to draw conclusions for the target population of this CPG. The analysis of a single drug was another limitation. According to Maurice-Szamburski et al.72 it is possible to assume a class effect for all BDZs, but although they all exercise an anxiolytic action that is quite similar69, the negative effects in the immediate postoperative period will be more frequent with long or prolonged-action BDZs such as diazepam (half-life from 20 to 40 hours). Lorazepam and alprazolam have a relatively prolonged half-life of 10 to 24 hours<sup>71</sup>.

Although there is no solid scientific evidence, the GWG understands that the expected benefit does not justify the routine use of sedative and/or anxiolytic premedication in major abdominal surgery, specifically long-acting BDZs that could hinder the rapid recovery of the patient in the immediate postoperative period.

#### Summary of evidence

In elective surgery with general anaesthesia, sedative premedication with lorazepam 2 hours before surgery, compared with no premedication or premedication with a placebo, not only did not improve the perioperative experience of the patient, evaluated the day after surgery, but was also significantly associated with longer extubation times (17 minutes versus 12 and 13 minutes, p<0.001) and with a lower post-anaesthesia cognitive recovery rate after 40 minutes (51% versus 71% and 64%, p<0.001)<sup>72</sup>.

Premedication with alprazolam, at 7 AM the day of the surgery, did not show significant differences versus a placebo in regard to the level of comfort and anxiety of patients measured in the operating room<sup>73</sup>.

#### Recommendations

The use of intermediate or long-acting sedative and/or anxiolytic premedication in patients who undergo major abdominal surgery is not recommended.

In cases in which the administration of anxiolytic premedication is deemed necessary, short-aring BDZs are recommended.

# 5. Intraoperative measures

# 5.1. ERAS and laparoscopic surgery

### **Ouestion to be answered:**

- In patients who undergo elective major abdominal surgery, do the following interventions
  reduce morbi-mortality and hospital stays when compared with the use of laparoscopy and
  conventional perioperative care?
  - Laparoscopy + ERAS
  - Laparotomy + ERAS

Laparoscopy is a minimally invasive surgical technique that reduces postoperative pain and at the same time preserves intestinal peristaltism, reduces postoperative complications, and shortens the length of hospital stays, without increasing mortality of patients who undergo major abdominal surgery (MAS). It even presents oncological results that are equivalent to those obtained with open abdominal surgery of colorectal cancer. Patients who require major abdominal surgery benefit greatly from this surgical technique<sup>74</sup>.

As commented earlier, enhanced recovery after abdominal surgery (ERAS) consists of a series of measures for the handling of the surgical patient before and during the procedure and in the immediate postoperative period, aimed at reducing the response to surgical stress in order to achieve faster and more satisfactory recovery after the surgery<sup>9-13</sup>.

In theory, the combination of both procedures, laparoscopic surgery and enhanced recovery programs would generate better short-term clinical results for patients. In the case of conventional colorectal surgery, ERAS programs have been proven to be effective and safe<sup>75</sup>. However, the need for ERAS programs in laparoscopic surgery has been questioned because this approach is already associated with shorter hospital stays and lower morbidity than open surgery. The objective of the question is to determine the best course of action for patients who undergo MAS.

The volume of evidence for the two comparisons posed by the question varied; most of the studies analysed patients who underwent laparoscopic surgery who received ERAS or conventional perioperative care<sup>74,76-80</sup>. Only one RCT with a 2×2 factorial design also compared standard care in laparoscopic surgery with the practice of open surgery as part of an ERAS program<sup>26</sup>.

A systematic review compared the effect of ERAS programs versus conventional perioperative care in laparoscopic colorectal surgery. The meta-analysis showed that ERAS generated a statistically significant reduction in both post-surgical hospital stays (3 studies, 387 participants; weighted mean difference -1.22 days, CI95% -1.57 to -0.87 days, I²=0%), as well as total length of stay or LOS (post-surgical stay plus readmittance within 30 days following discharge) (3 studies, 408 participants; weighted mean difference -1.00 day; CI95% -1.48 a -0.52 days, I²=0%). ERAS did not have a significant impact on readmittance rate (3 studies, 408 participants; OR 0.85 CI95% 0.33 to 2.21, I²=0%) or postoperative complications rate (4 studies, 486 participants; OR 0.68 CI95% 0.44 to 1.04, I²=38%)<sup>74</sup>.

SR of RCT 1+

An RCT done in China and including 116 patients who underwent laparoscopic surgery for rectal cancer compared conventional perioperative care with the strategies of an enhanced recovery program. Patients were between 40 and 70 years of age, ASA I or II physical status, and had not received preoperative chemotherapy or radiotherapy. ERAS was found to have a statistically significant association with shorter hospital stays (mean  $5.05 \pm 1.38$  days versus  $6.98 \pm 2.26$  days, p<0.001) and fewer postoperative complications (3.5% versus 16.9%, p=0.03). Also, recovery of intestinal function as significantly faster in the ERAS group, with an average elapsed time until first postoperative flatus of  $53.44 \pm 23,64$  hours versus  $67.85 \pm 20,12$  hours (p<0.001), and until first defecation of  $65.23 \pm 22,24$  hours versus  $86.98 \pm 24,85$  hours (p<0.001). The study did not provide information on readmittance or adverse effects<sup>77</sup>. RCT 1+

A multi-centre RCT (9 hospitals) done in the Low Countries (LAFA study, Laparoscopy and/or Fast track multimodal management versus standard care) randomized 400 patients to receive laparoscopic (Lap) or open (Open) surgery, and enhanced recovery (ERAS) or conventional care (CC), generating 4 treatment branches: Lap/ERAS (100 patients), Open/ERAS (93 patients), Lap/ CC (109 patients) and Open/CC (98 patients). Participants had adenocarcinoma of the colon without metastatic disease, were between 40 and 80 years of age, and physical status ASA I, II or III. In the Lap/ERAS group, an average of 11.2  $\pm$  2.2 of the 15 procedures of the ERAS protocol were applied successfully; in the Open/ERAS group, the average was  $11.1 \pm 2.2$  elements. In the Lap/ERAS branch, total length of say (TLOS) (median 5 days [IQR 4 to 8]) and post-surgical stay (PSS) (median 5 days [IQR 4 to 7]) was a median of 1 day shorter than the other three branches (p<0.001). When comparing Open/FT and Lap/CC, the length of stay did not vary significantly. The RCT did not find significant differences between the four groups with respect to the following variables: readmittance, re-operating, morbidity (overall, severe and minor) and mortality.

RCT 1+

According to the multiple regression analysis, laparoscopic is the only independent factor that influences TLOS, shortening it by 21% (CI95% -9% to -31%, p=0.001); ERAS only showed a non-significant trend towards shorter TLOS (-12% CI95% -23% a 10%, p=0.07), and the combination of both did not show any additional benefit. Likewise, only laparoscopy was shown to significantly reduce overall morbidity (OR 1.53 CI95% 1.02 to 2.29, p=0.041) and severe morbidity (OR 1.76 CI95% 1.01 to 2.95, p=0.045). Logistic regression did not find any significant association with mild morbidity, readmittance rate, or re-operation rate<sup>26</sup>.

A sub-study that was part of the LAFA study carried out the objective measurement of colonic transit by gammagraphy in 71 patients randomly distributed into the four branches of the main study. Isotope concentration in the colon on the third day after surgery was significantly higher in the Lap/ERAS branch in comparison with the other three branches. Laparoscopic surgery and enhanced recovery were independent predictors of faster recovery of intestinal function; the combination of both did not show an additional significant effect. There were no significant differences between the 4 branches in regard to readmittance or complications rates<sup>79</sup>.

An RCT done in New Zealand compared conventional care and an ERAS program on 78 patients who had undergone laparoscopic vertical gastrectomy or gastric sleeve. Participants were between 37 and 50 years of age, with a physical status of ASA II (62%) or III (38%), and body mass index of  $42.6 \pm 6.1$  kg/m² in the ERAS group, and  $46.1 \pm 6.3$  kg/m² in the control group. The median length of stay (principal variable) was 1 day in the ERAS group, which was shorter than for the control group (2 days), p<0.001. No statistically significant differences were observed in the short-term (<30 days) readmittance rate (20% versus 21%), or the rate of total complications (25% versus 21%) or severe complications (12.5% versus 13%). The overall level of compliance with the items of the ERAS protocol was 85%; perioperative care of both groups overlapped by 29%80.

A systematic review with meta-analysis that compared enhanced recovery programs ( $\geq$ 6 items) versus conventional perioperative care (CC) in gastric cancer surgery, found that patients who underwent laparoscopic surgery and followed an ERAS program had significantly shorter hospital stays (2 studies, 85 participants; weighted mean difference -1.19 days, CI95% -1.79 days to -0.60 days, I<sup>2</sup>=90.6%). ERAS also significantly reduced the time until the appearance of first flatus (2 studies, 85 participants; weighted mean difference -6.82 hours, CI95% -11,51 hours to -2.13 hours, I<sup>2</sup>=0%); however, no benefit was observed in regard to risk of postoperative complications (2 studies, 85 participants; RR 1.39 CI95% 0.77 to 2.51, I<sup>2</sup>=18.2%)<sup>76</sup>.

RCT 1+

RCT 1+

SR of RCT 1+ A study done in Italy evaluated the effectiveness of an ERAS program among patients who underwent laparoscopy for adenocarcinoma of the left colon (70%, 36 patients) or complicated diverticular disease (30%, 16 patients), by high anterior resection. The median age of the patients was 66 (range 29 to 83) and physical status ASA I or II. Compared with conventional perioperative care, ERAS significantly reduced the time the intestine takes to recover its unction: first intestinal movement (mean  $0.3 \pm 0.647$  days versus  $1.73 \pm 0.483$  days, p<0.005), first postoperative flatus ( $0.9 \pm 0.78$  days versus  $2.1 \pm 0.94$  days, p<0.005), first defecation ( $1.6 \pm 0.96$  days versus  $5 \pm 1.79$  days, p<0.005). The mean hospital stay in the ERAS group was  $4.7 \pm 2.4$  days, which was less than that of patients who received CC ( $7.65 \pm 2.4$  days) (p<0.005). No short ferm (<30 days) severe complications or readmittance were observed in either group. The surgeons referred to the presence of non-distended intestinal loops in patients who received preoperative maltodeytrin<sup>78</sup>

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Table 3 shows the items that were included in the ERAS protocols of each individual.

Table 3. Characteristics of ERAS protocols.

											ERAS								58
s	TUDY	Preoperative education	No preoperative fasting	Carbohydrates 2-3 h before surgery	No intestinal preparation	No premedication	Avoid fluid overload	Epidural anaesthesia	Prevent hypothermia	Minimally invasive surgery*	No routine use of nasogastric tube	No routine use of abdominal drains	Early postoperative mobility	Early postoperative feeding	No systematic use of opioids	Rouvine use of laxatives	Early remova o arinary catheter	Total n° of items	INTERVENTION
	Vlug (2011) <sup>26</sup>	✓	✓	✓	✓	✓	✓	✓	✓	•	✓	✓	<b>√</b>	48,0	√	✓	✓	15	Colon segment surgery
SRs Tan (2014) <sup>74</sup>	Wang Q (2012) <sup>81</sup>		✓		✓		✓	✓		•	✓	V:	100/5	✓	✓		✓	10	Colon segment surgery Anterior resection (32%)
SRs Tan	Wang G (2012) <sup>82</sup>		✓	<b>✓</b>	✓			✓		•	.X.	Ø √	✓	✓	✓			8	Colon segment surgery
	Lee (2011) <sup>83</sup>	✓								79/6g	<b>√</b>		✓	✓		✓		5	Colon segment surgery Anterior resection (47%)
	an Bree 2011) <sup>79</sup>	<b>√</b>	✓	✓	✓	✓	✓	V (	<u> </u>	•	✓	✓	✓	✓	<b>√</b>	✓	✓	15	Colon segment surgery
Feng	g (2014) <sup>77</sup>			✓	✓	~			✓	•	✓	✓	✓	✓	✓		✓	10	Anterior resection with total mesorectal excision
Mar	i (2014) <sup>78</sup>		✓	- 1	,C3×.	0/2	✓			•	✓		✓	✓	✓		✓	8	High anterior resection
	emanu 2013) <sup>80</sup>	✓	\ \ \	9/18/						•	✓	<b>√</b>	✓	✓	<b>√</b>			8	Gastric sleeve
SRs Chen (2014) <sup>76</sup>	Chen (2012) <sup>84</sup>	, 85/,	<b>√</b>	✓	✓		✓			•	✓	✓	✓	✓	✓	✓	✓	12	Distal gastrectomy
SRs Cher	Kim (2012) <sup>85</sup>	✓	✓		✓					•	✓	✓	✓	✓	✓			7	Distal gastrectomy
* All stu	idies compa	ared :	the l	aparos	сор	ic app	iroad	ch ve	ersu	s open	surge	ry.							

When formulating the recommendation, the GWG took the consistency between the different studies, applicability, and possibility of generalization of the results and their clinical relevance into account. It is difficult to compare studies to each other to determine whether the effects are consistent, due to the differences in ERAS protocols, the number of items, and how they were implemented, as well as the definition of the complications and the criteria for establishing discharge from the hospital. Nevertheless, a common pattern was observed: all of the studies refer to a significantly shorter hospital stay in patients who received ERAS, with no increase in morbidity or mortality. None of the studies evaluated delayed post-surgical complications, which constitutes a potential limitation.

The LAFA multi-centre study<sup>26</sup>, although it does have some limitations, had higher methodological quality than the other studies included in the volume of evidence, in aspects as relevant as, for example, the use of masking techniques. It can be considered to be robust enough to assume with a sufficient degree of confidence that the optimum results in surgery for colon cancer are achieved when an ERAS program associated with laparoscopic surgery is applied. ERAS and laparoscopic surgery work synergetically, with laparoscopic surgery being a determining factor in facilitating the postoperative recovery of the patient. Despite the fact that the regression analysis suggests that the impact of ERAS on patient evolution is very limited, it is likely that the real benefit that can be attributed to ERAS is greater, because, for ethical reasons, the standard care group received an average of 6 of the 15 procedures in the ERAS protocol, including key elements, such as epidural analgesia and the restriction of water overload. The application of the ERAS protocol did not reduce short-term (<30 days) morbidity, although it did not increase it either, which suggests that ERAS is safe.

The quality of the protocols used, in regard to the number and type of procedures or items, is an important question when determining the effectiveness of ERAS programs. It is commonly known that the more procedures that are successfully applied, the better the results of the program5,18,19. The studies included here apply approximately 35% to 75% of the key elements. In the opinion of the GWG, enhanced recovery programs in colorectal surgery should put into practice at least 70% of the items included in the protocols of the ERAS group<sup>9,10</sup>.

In a majority of the studies, the average age of the patients was between 55 and 65, more than 80% had a physical status of ASA I or II, did not present serious comorbidity or metastatic disease, and underwent colorectal surgery. In the opinion of the GWG, the evidence included cannot be generalized to other types of MAS and a recommendation for future research in this direction needs to be established (Chapter 10).

In addition to the two systematic reviews described, two other reviews<sup>86,87</sup> were also identified, which were excluded from the volume of evidence because they did not contribute new studies to respond to the question.

## **Summary of evidence**

1+	When laparoscopic or open surgery and enhanced recovery or conventional care are compared in patients with colon cancer, the laparoscopic approach as part of an ERAS program is the strategy that is associated with shorter PSS (median 5 days) and TLOS (median 5 days) (p<0.001). The logistic regression analysis suggests that laparoscopy is the only independent predictor of shorter hospital stays and reduced postoperative morbidity <sup>26</sup> .
1+	An ERAS program in laparoscopic surgery for rectal cancer achieved a significant reduction in length of stay (mean $5.05 \pm 1.38$ days versus $6.98 \pm 2.26$ days, p<0.001) and postoperative complications (3.5% versus 16.9%, p=0.03) <sup>77</sup> .
1+	The ERAS programs in laparoscopic colorectal surgery reduced mean PSS by -1.22 days (CI95% -1.57 to -0.87) and mean TLOS by -1 day (CI95% -1.48 to -0.52 days), when compared with traditional handling <sup>74</sup> .
1+	ERAS programs in patients who underwent gastric sleeve operations using laparoscopy reduced the median length of stay when compared with conventional care (1 day versus 2 days, p<0.001) <sup>80</sup> .
1-	Compared with conventional care, ERAS programs reduced average length of stay of patients who underwent laparoscopic gastrectomy for gastric cancer by -1.19 days (CI95% -1.79 to -0.60) <sup>76</sup> .
1+ <sup>26,74,80</sup> 1- <sup>76</sup>	No significant differences were found in the rate of short-term (<30 days) post-operative complications or readmittance when comparing ERAS programs with conventional care in patients who received laparoscopic surgery for stomach cancer <sup>76</sup> , colorectal cancer <sup>74</sup> , colon cancer <sup>26</sup> or gastric sleeve <sup>80</sup> .
1+ <sup>77,79</sup> 1- <sup>76,78</sup>	Enhanced recovery programs in laparoscopic surgery for stomach, colon, and rectal cancer significantly accelerated the recovery of intestinal function <sup>76-79</sup> .
1-	In patients who underwent high anterior resection using laparoscopy, the ERAS, compared with conventional care, was associated with a significantly shorter average length of stay $(4.7 \pm 2.4 \text{ days versus } 7.65 \pm 2.4 \text{ days, p} < 0.005)^{78}$ .

## Recommendations

B In patients who are going to undergo elective colorectal surgery, the laparoscopic approach is recommended, in combination with the application of an intensified abdominal surgery recovery program.

# 6. Perioperative measures

# 6.1. Fluid therapy

## Question to be answered:

• In patients who undergo elective major abdominal surgery, does the use of a goal-directed fluid therapy algorithm, versus restrictive fluid therapy, reduce postoperative complications? Does it shorten postoperative ileus? Does it shorten hospital stays?

Despite that fact that numerous studies have been done in this regard, uncertainty still persists with respect to the optimum handling of perioperative find therapy. Once of the points of debate is whether or not the administration of fluids should be guided by haemodynamic objectives.

Both deficient and excessive replacement of fluids are associated with the appearance of postoperative complications<sup>88-90</sup>. Taking into account that traditionally unmeasurable losses have been overestimated, resulting in an excess in the quantity of fluid therapy administered, there is a trend towards the use of "restrictive regimes" which is understood as the replacement of losses during surgery, avoiding overloading, in order to achieve a fluid balance close to zero, with no variations in the bodyweight of the patient.

Goal-directed fluid therapy (GDFT) allows the individualized adjustment of the quantity of fluid administered. It consists of the infusion of fluids as boluses, following a protocol, in order to achieve a specific haemodynamic of tissue perfusion goal.

The evidence shows that both restrictive fluid therapy (RFT) as well as GDFT generate benefits with respect to convertional fluid therapy in major abdominal surgery<sup>91-93</sup>, but it has not yet been determined which of the two strategies is more advantageous for the patient. There is no universally accepted definition of restrictive fluid therapy<sup>91,92,94</sup>. For this reason, the studies that explicitly indicate the use of fluid restriction in the methodology section were selected.

RCT 1++

A double-blind RCT done in New Zealand compared a goal-directed fluid therapy (GDFT) protocol and a restrictive fluid therapy (RFT) treatment in the framework of an enhanced recovery program in elective colon surgery (13 items). 85 patients with health status ASA I to III, 90.5% of whom had colon cancer and 14.8% of whom underwent laparoscopic surgery. The mean Surgical Recovery Score (SRS)(a) 7 days after the operation, the principal variable of the study. was 47 in the GDFT group versus 46 in the RF group (p=0.853). No significant differences were found between GDFT and RFT in regard to the number of patients with postoperative complications (26 in GDFT versus 27 in RFT, p=1 200); in the number of serious complications according to the Clavien – Dindo scale 95 (7 versus 9, p=0.782); or in median length of stay (p=0.570), which was 6 days (range 3 to 41) in the GDFT group, and 5 days (range 2 to 49) in the RFT group. The patients randomly selected to receive GDFT had a higher intraoperative aortic flow (TFc) (mean time  $374 \pm 33$  ms versus  $355 \pm 30$  ms p=0.018). The GDFT received significantly more colloids in the intraoperative period (mean  $591 \pm 471$  ml versus  $297 \pm 275$  ml, p=0.012) and total flow (1994 ± 590 ml versus  $1614 \pm 420$  ml, p=0.010) than the RFT group. Other result variables analysed were: intraoperative cardiac frequency, intraoperative cardiac index, weight (before surgery and 1, 2, and 3 days after surgery), urine production (intraoperative and 24 hours after surgery), concentration of brain natriuretic peptide, renin, and aldosterone (before surgery and 24 hours after), and sodium and creatinine concentration (before surgery and 1, 2 and 3 days after surgery). None of these result variables showed statistically significant differences. In both groups, flow was administered in the postoperative period according to clinical criteria<sup>96</sup>.

(a) SRS: Surgical Recovery Score, this postoperative recovery index (range 17 - 100) evaluates fatigue, vigour, mental function, and impact on physical activity and on the daily routine of the patient.

A double-blind multi-centre RCT done in Denmark investigated the frequency of postoperative complications and mortality when two intraoperative fluid therapy regimes in elective colorectal surgery, in the context of an ERAS program were compared(b). A sample of 150 patients, ASA I to III, 64% of whom had colon or rectal cancer, were randomized to receive GDFT (achieve a particular systolic volume), or RFT (achieve the equilibrium or "zero balance") between requirements and losses). The results showed that GDFT did not reduce postoperative mortality or complications with respect to RFT. In the group that received GDFT, 23 (32%) patients experienced complications, versus 24 (30%) in the RFT group (p=0.791). No significant differences were observed in the percentage of patients with serious complications (14% versus 10%, p=0.6%), minor complications (28% versus 28%, p=0.965), cardiopulmonary complications (7% versus 4%, p=0.744), or complications related to the surgical woun. Vanastomosis (11% versus 16%, p=0.481). On patient in each group died (p=1.00). The analysis by sub-groups based on the type of surgery, laparoscopic (n=70) or open (n=57), did not show any significant differences in terms of the percentage of patients with complications: 28% versus 26% (p=0.865) y 39% versus 34% (p=0.707), respectively. The median (range) of length of stay was 5 (2 to 42) days in the GDFT group versus 6 (2 to 61) days in the RFT group (p=0.620). After optimization, the systolic volume was significantly higher, during the entire operation, in patients who received GDFT (p<0.05). During the intraoperative period, more colloids were administered (mean 810 ± 543 ml versus 475 ± 598 ml, p < 0.005) and total fluids (1876 ml versus 1491 ml, p = 0.019) to patients in the GDFT group<sup>97</sup>.

(b) The ERAS program was not precisely described. Some of the items mentioned included no routine intestinal preparation, drinking fluids up to two hours before the operation, epidural analgesia, and early initiation of oral ingestion and mobilization in the postoperative period.

A systematic review evaluated the clinical benefit of GDFT guided by transoesophageal doppler, based on the data from 6 RCTs that included a total of 691 patients who underwent colorectal surgery. The meta-analysis of the sub-group of tests that compared GDFT versus RFT (2 studies96,97, 224 participants) did not find any statistically significant differences in the rate of postoperative complications (OR 1.02; CI95% 0.58 to 1.81;  $I^2=0\%$ ), or in the average length of stay 0.79 days, CI95% -1.38 days to 2.96 days;  $I^2=0\%$ )<sup>98</sup>.

SR of RCT

A study done in Australia with 100 patients classified as ASA I to III and who underwent colorectal surgery within an ERAS program<sup>(c)</sup>, did not find differences in length of stay or in the number of patients with postoperative complications when an intraoperative GDFT protocol, based on optimization of the systolic volume index (SVI) and corrected flow time (TFc) with transoesophagealdoppler, was compared with an intraoperative restrictive fluid therapy (RFT) protocol, despite the fact that the haemodynamic goals of the GDFT were achieved, with a significant increase in SVI and TFc, between the start and the end of the operation. 63% of the patients had colon or rectal cancer and 59% underwent laparoscopic surgery. The length of stay (principal variable) was a median of 6.5 days (IQR 5 to 9) in the GDFT group, versus a median of 6 days (IQR 4 to 9) in the RFT group (p=0.421). The number of patients who experienced postoperative complications was 30 (60%) in the GDFT group versus 26 (52%) in the RFT group (p=0.420). No significant difference were observed between the two groups in the proportion of patients with serious complications (grade 3 to 5 according to Clavien-Dindo (2% versus 8%, p=0.362). One patient in the RFT group died. The GDFT group received significantly more fluids during the intraoperative period than the RFT group (median 2190 ml [IQR 1350 to 2560] versus 1500 ml [IQR 1200 to 2000],  $p=0.008)^{99}$ .

(c) The ERAS program was not described precisely. Some of the items mentioned were administration of 400 ml of carbohydrate reverage the day before and 2 hours before the surgery, non-routine use of nasogast ic tube, and initiation of oral ingestion of liquids 4 hours after the operation and of solids the first day of the postoperative period.

A three-branch RCT done in China evaluated the effectiveness of two GDFT protocols, with colloids (hydroxyethyl starch 6%: 130/0.4) or with crystalloids (Ringer's Lactate), and an RFT protocol with crystalloids (Ringer's Lactate) in a sample of 60 low-risk patients (ASA I or II and  $\leq$  64 years of age) who underwent a gastrectomy (n=20). The goal-defined therapy was based on the optimization of pulse pressure variation (PPV). Both the average length of stay as well as mean time of return of intestinal function (1st flatus) were significantly shorter in the GDFT group that received colloids  $(9.1 \pm 1.4 \text{ days and } 86.2 \pm 7.2 \text{ hours, respectively)}$ , in comparison with the RFT group (length of stay:  $10.9 \pm 1.2$  days, p < 0.001; 1st fl  $92.1 \pm 9.7$  hours, p = 0.03), and with the GDFT group that received crystalloids (length of stay:  $11.9 \pm 1.2$ days, p < 0.015; 1st flatus 95.4 ± 9.1 hours, p = 0.002). The patients presented the following postoperative complications: vomiting (n=12 events, 70.6%), infection of surgical site (n=2), arrhythmia (n=1), pulmonary infection (n=1), intestinal obstruction (=1). There were no significant differences in the incidence of complications between the different groups (p>0.05). None of the patients died while admitted to the hospital<sup>100</sup>.

RCT 1₫

RCT 1-

Table 4 shows the goal-directed fluid therapy and restrictive fluid therapy protocols of the individual studies included here.

Table 4. Characteristics of the GDFT and RFT protocols.

			2	
STUDY	GDFT GROUP	RFT GROUP	TOTAL INTRAOPERATIVE FLUIDS	ERAS
Phan et al. <sup>99</sup>	250 ml colloid boluses* in 2 min. according to systolic volume index (if SVI>10%) and corrected flow time (if TFc <350 ms)  Baseline: 5 ml/kg/h Ringer's lactate.	Colloid boluses only to replace blood loss or hypotension that does not respond to vasopressor treatment.  Baseline: 5 ml/kg/h Ringer's lactate.	GDFT: 2190 (1350 to 2560) ml (median, JQR#) RFT: 1590 (1200 to 2000) ml (median, JQR)	YES
Srinivasa et al. <sup>96</sup>	Gelofusine® in boluses (7 ml/kg, continue with 3 ml/kg) according to corrected flow time (if TFc <350 ms) and systolic volume (if SV >10%)  Basal: limit of 1500 ml of Plasmalyte®	Gelofusine®, maximum 500 ml, adjusted based on blood loss, heart rate, blood pressure, urine production.  Basal: limit of 1509 ml of Plasmalyte®	GDFT: 1994 ± 590 ml (mean) RFT: 1614 ± 420 ml (mean)	YES
Brand- strup et al. <sup>97</sup>	Boluses of 200 ml of Voluven® until systolic volume increase <10%.  Baseline: Replacement volume by blood loss volume (Voluven®). An extra infusion of 500 ml (Voluven®) is allowed to maintain ABP>60 mmHg	In the case of hypotension with suspected hypovolemia, test effect of 200 ml of colloids.  Baseline: Replacement volume by blood loss volume (Voluven®). An extra infusion of 500 ml (Voluven®) is allowed to maintain ABP>60 mmHg	GDFT: 1876 (mean) RFT: 1491 (mean)	YES
Zhang et al. <sup>100</sup>	GDFT-colloids: Bolus 250 ml colloids (HF 6%: 130/0.4) in 15 min if PPV¶>11%  GDFT-crystalloids: Bolus 250 ml of Ringer's lactate in 15 min. if PPV>11%  Baseline: Infusion of 4 ml/kg/h of Ringer's lactate during the strigical procedure.	Bolus 250 ml of Ringer's lactate if urine production <0.5 ml/kg/h for 2 hours or central venous pressure (CVP) <4 mmHg  Baseline: Infusion of 4 ml/kg/h of Ringer's lactate during the surgical procedure.	GDFT-colloids: 1742.5 ± 333.01 ml (mean) GDFT-crystalloids: 2109.5 ± 474.25 ml (mean) RFT: 1260.00 ± 269.44 ml (mean)	NO

<sup>\*</sup> The choice of the type of colloid was made based on the opinion of the anaesthetist. 4% hydroxyethyl starch (Voluven® or Volulyte®), 4% Gelofusine® or 4% human serum albumin were used. The use of hydroxyethyl starches in the institution was suspended in July 2013.

<sup>#</sup> IQR, imerquartile range

<sup>¶</sup> PPV Pulse pressure variation.

When preparing the recommendations, the GWG took the applicability and consistency of the volume of the evidence, and its relevance and impact, into account. The evidence found is applicable to patients with low or moderate surgical risk, who undergo open or laparoscopic colorectal surgery with the scope of an ERAS program. The studies by Brandstrup et al. 97, Zhang et al. 100 and Phan et al. 99 optimize preloading with colloidal solutions that contain hydroxyethyl starch (HES). The European Medicines Agency (EMA) recommends avoiding the use of HES in patients with sepsis and renal insufficiency because an increase in renal damage has been demonstrated when they are used in the post-resuscitation phase of critical patients in the ICU<sup>101-103</sup>. But in the context of perioperative treatment of surgical patients, there is some uncertainty regarding the long-term safety of HESs<sup>104</sup>. The GWG does not consider HESs to be contraindicated in the treatment of surgical patients, provided that the precautions for their use are respected, which means that the applicability of the results of these studies is not compromised.

The results of Phan et al.<sup>99</sup> Srinivasa et al.<sup>96</sup> y Brandstrup & al.<sup>97</sup> suggest that within the framework of ERAS, and in patients with low surgical risk, neither strategy for intraoperative administration of fluids is better than the other. The consistency of this result is difficult to demonstrate due to the small number of studies found, and the fact that they evaluate different primary effectiveness variables, as well as different GDFT (haemodynamic parameters and fluid administration algorithms) and restrictive fluid therapy parameters. The study by Zhang et al.<sup>100</sup> is the only one that shows a greater benefit of GDFT with colloids versus restrictive fluid therapy with crystalloids, although the authors themselves acknowledge that the type of fluid may have contributed to shorter length of stay and earlier recovery of intestinal function in the patients treated with GDFT. In this study, unlike the previous ones, perioperative measures aimed at accelerating recovery of the patients were not applied.

The studies with the highest methodological quality did not show a significant effect of GDFT or RFT on the principal effectiveness variables, in this case, length of stay<sup>99</sup>, postoperative complications<sup>97</sup>, and Surgical Recovery Score on the 7th day after surgery<sup>96</sup>. This result suggests that in patients with low surgical risk and as part of an ERAS program, achieving a zero balance of intraoperative fluids is sufficient. In fact, no significant differences were observed between GDFT and RFT in regard to cardiac output at the end of the procedure<sup>96,97</sup>.

ERAS programs have increased the threshold required for GDFT to show a significant benefit, as observed in the studies within the framework of conventional perioperative care<sup>91,93</sup>. Measures such as avoiding occhanical preparation of the intestine, oral ingestion of clear liquids up to two hours prior to surgery, and preoperative administration of carbohydrate drinks may reduce the risk of volume depletion during surgery, because these practices as a group help patients reach the operating room in a normovolaemic state. In addition to this, ERAS programs in the three studies include restriction of fluid therapy<sup>96,97,99</sup>; for example, in the study by Srinivasa et al.<sup>96</sup> both groups received a maximum of 1,500 ml of crystalloid during surgery.

The GWG took into account the fact that the scientific evidence is scarce, heterogeneous, as well as the fact that the studies were not designed to detect more modest effects of GDFT. Also, it is less likely that a single intervention will result in a significant reduction in length of stay or postoperative complications in a context of optimized perioperative care.

Lastly, it is important to note that no studies that use inotropes and/or vasoconstrictors as part of the GDFT protocol were found. Also, no studies that extend the intervention into the postoperative period were found. According to the GWG, goal-directed therapy should ideally be done during the intra and postoperative periods in the post-anaesthesia recovery unit, and 3 or 4 hours after the patient is transferred to the ward. For this reason, the GWG proposes a recommendation for future investigation (Chapter 10).

### **Summary of evidence**

	S
	When protocols for haemodynamic goal-directed intraoperative fluid therapy (SV and
	TFc) are compared with RFT protocols (balance close to zero), in patients included
1++96,97	in enhanced recovery programs for colorectal surgery no statistically significant
1+98,99	differences were observed for the duration of the hospital stay 96-99, or in the mean
•	Surgical Recovery Score (7th day after surgery) <sup>96</sup> , or in the number of patients with
	postoperative complications <sup>96-99</sup> .
	In patients who underwent gastric surgery (66.7%) or colon surgery (33.3%),
	intraoperative GDFT with colloids compared with RFT with crystalloids produced
1-	a statistically significant reduction in the average length of stay and mean time until
	the appearance of first flatus. No significant differences were found in the rate of
	postoperative complications <sup>100</sup> .
	A*U

### Recommendations

	<u>.                                      </u>
A	Colorectal surgery that falls within the scope of a program of enhanced recovery after abdominal surgery (ERAS) should include a personalized fluid therapy plan for each patient.
1	Abdominal surgery that fails within the scope of an ERAS program should include a personalized fluid therapy plan for each patient.
В	In patients who undergo colorectal surgery, the use of a haemodynamic goal-directed fluid therapy algorithm is suggested when the necessary human and technical resources are available.
В	In patients with low surgical risk (ASA I or II) who undergo colorectal surgery within the scope of an TRAS program, evaluate the possibility of applying an intraoperative fluid handling strategy with a balance close to zero.

# 6.2. Analgesia

### Question to be answered:

In patients who undergo elective major abdominal surgery, is transversus abdominis plane (TAP) block more effective and safer than epidural analgesia?

Adequate control of pain the postoperative period allows early mobilization of the patient, which facilitates their recovery. Insufficient analgesia is associated with reduced comfort and a significant increase in morbidity, mortality, and costs<sup>105</sup>. The most notable characteristic of postoperative pain is that its peak intensity is during the first 24 hours, and that it decreases progressively after that<sup>106</sup>.

Transversus abdominis plane block (TAP) is a peripheral nerve block that produces postoperative analgesia of the abdominal wall. By means of an ultrasound guided puncture, local anaesthetic (LA) is administered to the plane known as the TAP, located between the transverse and internal oblique muscle of the abdomen, where the anterior branches of the spinal nerves that provide the nerve connections to the skin and abdominal muscles. There are two basic types of blocks, posterior and subcostal. The posterior approach provides analgesia to the lower abdominal wall, mainly the skin, muscles, and parietal peritoneum of T10 to L1. The subcostal approach supplies analgesia to the incisions that extend above the navel. The LA can be administered unilaterally or bilaterally, and before, during, or after surgery. At this time, the type, volume, and concentration of LA that provides optimum analgesia in TAP block is not known<sup>107-116</sup>.

Thoracic epidural analgesia is considered to be the "gold standard" in open abdominal surgery in terms of quality of the dynamic analgesia and reduction of extubation time, mechanical ventilation, and respiratory complications <sup>105,111</sup>; nevertheless, its role in laparoscopic abdominal surgery has been questioned due to the fact that laparoscopic techniques generate less postoperative pain. According to some authors, the risk/benefit ration in this context is high<sup>111,112</sup>. The TAP block technique does not present the same risk profile as epidural analgesia. It does not cause haemodynamic alterations, preserves motor and sensory function of the lower limbs, and may be use with patients receiving anticoagulant treatment. However, it tacks an effect on visceral pain, so it must necessarily form part of a multimodal analgesia protocol that combines analgesic drugs and techniques with different mechanisms of action <sup>106</sup>.

The objective of the question is to determine whether TAP block improves postoperative analgesia, reduces medication requirements to relieve pain, and is able to diminish adverse effects when compared with postoperative epidural analgesia.

There is insufficient quality scientific evidence to respond to this question. The four clinical trials identified compare different techniques of epidural analgesia with preoperative<sup>113</sup> or postoperative<sup>109,112,114</sup> TAP block, with subcostal bilateral <sup>112,113</sup>, posterior<sup>114</sup> or subcostal and posterior<sup>109</sup> application, and injection of a single dose of local anaesthetic, in three trials, administration in boluses<sup>112</sup> or in continuous infusion via catheter<sup>109,114</sup> (table 5).

Once RCT done in Australia, with the participation of 41 patients who underwent abdominal laparotomy (colorectal or urological surgery, or surgery of the upper gastrointestinal tract) did not find any statistically significant differences in the intensity of postoperative pain during the first 72 hours when compared with epidural analgesia initiated after surgery (catheter in T7–T9) with postoperative continuous TAP block via posterior or subcostal catheter (20 ml bolus of ropivacaine 0.375%, followed by continuous infusion of ropivacaine 0.2% at 8 ml/h for 72 hours). Approximately two-thirds of the patients underwent colorectal surgery. In the TAP block group, the median dynamic pain scores (numerical scale 0 to 10) in the PACU (0 and 1 hour) and in the ward (1st, 2nd, and 3rd day) were 3 (range 0 to 8), 3 (range 0 to 8), 6 (range 1 to 9), 5 (range 1 to 10) and 4.5 (range 0 to 8), respectively; while in the group that received epidural analgesia, the median scores were 2 (range 0 to 10), 2 (range 0 to 8), 5 (range 0 to 10), 5 (range 0 to 10) and 2.5 (range 0 to 8) ( $p \ge 0.1$ ). No differences were found between the two techniques in terms of cumulative mean total dose of fentanyl after one day (PCA, patient-controlled analgesia) or after 72 hours (2922  $\mu g \pm 1528 \mu g$  in epidural versus 2771  $\mu g \pm 1851 \mu g$  in TAP) (p=0.99). No serious adverse effects were recorded; on patient in the TAP group presented temporary sensory deficit and 4 patients in the epidural analgesia group suffered hypotension that responded to treatment. The therapeutic failure rate was similar in both groups, 22.7% (5/22) in TAP versus 26.3% (5/19) in epidural analgesia. No differences were observed in the level of satisfaction with the technique  $(p=0.47)^{114}$ .

One RCT done in China that included 82 patients who underwent radical gastrectomy compared subcostal bilateral TAP with thoracic epidural analgesia and with non-intervention (general anaesthesia). Continuous thoracic epidural analgesia during the first 72 hours was more effective than the 20 ml preoperative injection of ropivacaine 0.375% via subcostal TAP, with epidural better than TAP in consumption of morphine derivatives (patient-controlled analgesia) in the first 24 hours (mean difference -14 mg.; IC98.75% -23 to -4, p<0.001), but not in scores on the AVS pain scale (analogue visual scale) measured 1, 3, 6, 24, 48, and 72 hours after surgery. In the noninferiority analysis, TAP was comparable to epidural in both outcomes, consumption of morphine derivatives and VAS score. No significant differences were found in the rate of postoperative complications (hypotension, hypertension, cough and/or expectoration). The study did not analyse clinical or technical failures<sup>113</sup>.

RCT 1+

RCT 1+

An RCT done in the United Kingdom compared the analgesic effectiveness of subcostal TAP block with bupivacaine 0.375% administered in the form of intermittent boluses through a catheter (1 mg/kg every 8 hours for 72 hours) with patient-controlled epidural analgesia (PCEA), in 58 patients who underwent major open hepatobiliar or renal surgery. The results noted by patients on the VAS pain scale in the first 72 hours after the operation did not differ significantly between the group that received TAP block and the group that received PCEA. The medians (IQR) of the EVA scores during coughing of the PCEA group with respect to the TAP group in the first 8h, 24h, 48h and 72h were, respectively. 4.0 (2.5 to 5.3) versus 4.0 (2.3 to 6.0), p=0.21; 4.0 (1.8 to 4.6) versus 3.5 (1.8 to 5.5), p=0.29; 3.0 (1.0 to 4.5) versus 3.0 (0.3 to 4.3), p=0.63; 0.5 (1.0 to 5.0) versus 2.0 (0.8 to 4.0), p=0.15. Consumption of tramadol (50 - 100 mg/6h if pain) after 72 hours of the TAP group (median 400 mg., IQR 300 to 500) was significantly higher than in the PCEA group (median 200 mg., IQR 100 to 350), p=0.002. Therapeutic failure was defined as the addition of morphine (PCA) to the enalgesic regime. The PCEA group recorded a therapeutic failure rate of 22.6% n=7) versus 29.6% (n=8) in the TAP group. In the latter, the rate of catheter dislocation within the first 24 hours after surgery was 44.4% (n=12) in the TAP group and 7% (n=2) in the PCEA group. The authors did not record the adverse effects of epidural fentanyl. The patient satisfaction scores were similar  $(p=0.74)^{112}$ .

A noninferiority RCT done in the United Kingdom compared PCEA with a TAP block technique in 70 patients who underwent laparoscopic colorectal surgery. The block technique consists of the postoperative injection of 0.375% levobupivacaine via posterior and subcostal bilateral TAP (2.5 mg/kg in total for the 4 quadrants), followed by continuous infusion of levobupivacaine 0.25% via posterior bilateral TAP catheter for the first 48 hours after surgery. The intensity of dynamic pain (when coughing) and at rest was measured after 30 min., 6h, 12h, 24h, 36h, and 48h using the VAS scale. Analgesia (VAS). Postoperative analgesia after 24 hours resulting from the continuous infusion of local anaesthetic via posterior TAP catheter was comparable to the effect achieved by thoracic epidural infusion (catheter in T9 – T11). There were no differences in the cumulative consumption of tramadol after 48h (median, IQR), 100 mg. (0 to 250) vs. 125 mg. (0 to 200), p=0.48. Therapeutic failure was defined as the addition of morphine (patient-controlled analgesia) to the analgesic regime. The TAP group had a therapeutic failure rate of 7% (2/32), less than the 13% (4/31) of the epidural group. One patient assigned to TAP presented a unilateral abdominal haematoma of undetermined cause (trauma during insertion of the TAP catheter or laparoscopy (cocar). The percentage of patients who scored their satisfaction with the technique as excellent was significantly higher in the TAP group (32%) versus 59%,  $p=0.03)^{109}$ .

RCT 14

RCT 1-

Table 5.Characteristics of epidural analgesia and TAP block.

ST	TUDY	ANALGESIA DURING THE SURGICAL PROCEDURE	POSTOPERATIVE ANALGESIA	APPROACH	ADDITIONAL ANALGESIA	
Niraj et al. <sup>109</sup>	Epidural	Bupivacaine 0.25%, 20 ml	Single dose Levobupivacaine 0.375% 2.5 mg/kg (total 4 quadrants)  Catheters: Levobupivacaine 0.25% (infusion for 48 hours, rate of infusion not specified).  If analgesia is not effective in PACU* catheters are put back in place.  Rescue bolus of 10 ml bupivacaine 0.25% in the corresponding catheter if the patient indicates pain after being returned to the ward.  PCEA# with baseline infusion of bupivacaine 0.125% + fentanyl 2 g/ml. Bolus of 2 ml, closure in 30 min.  Infusion initiated at 8 ml/h increase 2 ml/h to 12 ml/h depending on the elevation of the block.  If analgesia is not effective in PACU catheters are put back in place.	Single dose: TAP block by puncture in 4 quadrants.  Catheters. posterior  Thoracic catheter T9–T11	g/6 h Diclofenac 150 mg/day Tramadol iv 100 mg /6 h	
<b>Rao</b> et al. 114	TAP  Epidural	No No	Bolus of 20 ml of ropivacaine 0.375% followed by continuous infusion 0.2% at 8 ml/h for 3 days.  Bolus of 8-15 ml of ropivacaine 0.2% followed by continuous infusion 5 - 15	Posterior subcostal if upper GI tract Thoracic catheter	Acetaminophen Fentanyl bolus 10 to 40 □g (ACP§, block interval of 5 min, without	
<b>Wu et</b> al. <sup>113</sup>	TAP	Single bilateral dose of 20 ml of ropivacaine 0.375%	ml/h for 3 days.	T7–T9 Bilateral subcostal	baseline infusio Morphine bolus 1mg, (PCA, block interval of 5 min, withou maximum	
	Epidural	Ropivacaine 0.25%, 8 ml before inducing anaesthesia, and 5 ml/h during the operation.	Bolus of 5 ml of ropivacaine 0.375% if pain after coming out of anaesthesia. For 72h: bupivacaine 0.125% with morphine (8□g/ml) at 5ml/h.	Thoracic catheter T8–T9	dose)	
Niraj et al. <sup>112</sup>	TAP	Bapivacaine 0.25%, 20 ml (via epidural catheter)	Single dose: bupivacaine 0.375% 1 mg/kg on each side. Catheters: bupivacaine 0.375% bolus every 8 hours of 1 mg/kg for 72 h	Bilateral subcostal	Acetaminophen 1 g/h (6 times) Tramadol 50 – 100 mg/h (times)	
_	Exclural	Bupivacaine 0.25%, 20ml	PCEA with baseline infusion of bupivacaine 0.125% + fentanyl 2□g/ml. Bolus of 2 ml, closure in 30 min. Infusion initiated at 6 ml/h increase 2 ml/h to 12 ml/h depending	Thoracic catheter T7–T9		

The studies included are heterogeneous, with variations between them in regard to the type of surgery (open<sup>112-114</sup> or laparoscopic<sup>109</sup>), the type of TAP block, the epidural analgesia technique, and the type of additional analgesia, which makes it difficult to draw valid conclusions. In addition to this, due to the small number of studies found, the decision was made to include a noninferiority clinical trial<sup>109</sup>, despite the fact that the correct design to answer the question is superiority design.

When preparing the recommendations, the GWG took the lack of statistical significance in regard to the principal variables of effectiveness or efficacy into account. Only one study 113 found that one of the techniques (EA) is more effective than the other (TAP) because it was associated with a significant and clinically relevant reduction in consumption of morphine derivatives, but conclusions cannot be drawn based on its results because it compares continuous epidural infusion versus a single preoperative injection via TAP. In fact, the GWG considers TAP block without continuous infusion not to be a suitable practice and took this into account when formulating its recommendations.

There is also insufficient data to make it possible to precisely determine the safety of the TAP block technique with regard to epidural analysis because the studies were not properly designed to detect significant differences in the rate of adverse events and therapeutic failure. Based on the experience of the experts in the GWG, control of the TAP catheter in continuous perfusion is complex, as suggested in the study by Niraj et al. Which showed a rate of catheter dislocations of 44.4% within the first 24 hours after surgery. It is important to note that no clinical trial recorded serious complications associated with TAP block or with epidural analgesia.

Lastly, the GWG considered, given the low number of studies, their moderate to low quality, and the inconsistency of the data that the scientific evidence is insufficient to support a recommendation in favour of or against the use of TAP block, making it necessary to establish a research recommendation (Chapter 10). New studies with higher methodology quality that precisely define the indications for TAP block are needed. In multimodal rehabilitation programs in MAS, TAP block may provide an additional benefit with respect to epidural because it preserves motor function of the lower limbs and does not affect the cardiovascular system. These characteristics may favour patient ambulation and speed up recovery.

# **Summary of evidence**

1+	In patients who underwent open abdominal surgery, continuous bilateral TAP block via catheter (posterior or subcostal) did not show any statistically significant differences in intensity of pain during the first 72 hours, or in total average cumulative dose of fentanyl daily or after 72 hours (2922 $\mu$ g $\pm$ 1528 $\mu$ g in epidural versus 2771 $\mu$ g $\pm$ 1851 $\mu$ g in TAP, p=0.99), when compared with epidural analgesia initiated after surgery <sup>114</sup> .
1+	In patients who underwent radical gastrectomy, thoracic epidural analgesia is more effective than bilateral subcostal TAP (a single preoperative injection of LA) in the treatment of acute postoperative pain, with epidural being superior to TAP in regard to consumption of morphine derivatives (PCA) (mean difference -14 mg.; IC98.75% -23 to -4, p<0.001), but not in the VAS score <sup>113</sup> .
1+	In patients who underwent major open hepatobiliar or renal surgery, no significant differences were observed in the intensity of pain measured with VAS when compared with bilateral subcostal TAP block (intermittent boluses of LA via catheter) with PCEA. The cumulative consumption of tramadol after 72 hours was significantly higher in the TAP group (median, IQR): 400 mg. (300 to 500) versus 200 mg. (100 to 350), p=0.002 <sup>112</sup> .
1-	In patients who underwent laparoscopic colorectal surgery, posterior and subcostal bilateral TAP block (single dose in 4 quadrants and continuous infusion via bilateral posterior catheter) was not lower than PCEA in regard to pain intensity measured after 24 hours with VAS. There are no statistically significant differences between TAP and EA in the cumulative consumption of tramadol after 48 hours (median, IQR): 100 mg. (0 to 250) versus 125 mg. (0 to 200), p=0.48 <sup>109</sup> .
1+ <sup>112-114</sup> 1- <sup>100</sup>	None of the studies was designed to evaluate the safety of the interventions. No severe adverse effects related to TAP or EA were recorded after 48 <sup>109</sup> or 72 hours <sup>112-114</sup> .  The rate of therapeutic failure in the TAP group was 7%109, 22.7%114, and 22.6% <sup>112</sup> ; the rate of therapeutic failure in the EA group was 13%109, 26.3%114 and 29.6% <sup>112</sup> .
1+ <sup>112-114</sup> 1- <sup>100</sup>	The results of the surveys done 72 hours after surgery did not show significant differences between TAP and epidural in regard to level of patient satisfaction <sup>112,114</sup> or were favourable to TAP <sup>109</sup> .

# Recommendations

	Scientific evidence is insufficient to support a recommendation in favour of or against the use of transversus abdominis plane block for postoperative analgesia in major abdominal surgery.
В -	If the TAP technique is used for postoperative analgesia, it should be applied via catheter with continuous perfusion.

# 7. Postoperative measures

# 7.1. Early reinitiation of oral feeding

### **Ouestion to be answered:**

• In patients who undergo elective major abdominal surgery, does the early administration of oral nutrition versus not administering anything shorten postoperative ileus?

Traditionally, absolute dieting until peristaltism resumes has been dogma in postoperative handling of abdominal surgery. The reasoning behind this practice is that the intestinal rest prevents nausea and vomiting, as well as dehiscence by preventing the passage of food by the anastomoses. But postoperative fasting is not supported by scientific evidence and there is no proof that delaying the start of oral feeding is beneficial for patient recovery 115,116. Despite this, there is a high degree of variability in the start of oral feeding in abdominal surgery. A survey done in five European countries, including Spain, showed that only between 5% and 50% of surgeons interviewed administered solid food early in order to minimize the risks generated by the delay in restoration of intestinal motility 117,118. The objective of the question is to determine whether resuming oral feeding in the immediate postoperative period is an effective and safe practice.

One good quality Cochrane systematic review included 5 studies (631 participants) done on open gynaecological abdominal surgery that compared the reinitiation of oral feeding within the first 24 hours after surgery versus absolute diet until resolution of postoperative ileus. Recovery of intestinal motility was faster in patients who received early nutrition. The meta-analyses showed a reduction in the time elapsed following the surgical procedure until the appearance of bowel sounds (2 studies, 338 patients; mean difference -0.32 days, CI95% -0.61 days to -0.03 days; I<sup>2</sup>=52%), the expulsion of flatus (3 studies 444 patients; mean difference -0.21 days, CI95% -0.40 days to -0.01 days; I<sup>2</sup>=23%), expulsion of faeces (2 studies, 249 patients; mean difference -0.25 days, CI95% -0.58 days to -0.09 days; I<sup>2</sup>=0%) and reinitiation of normal feeding 2 studies, 301 patients; mean difference -1.47 days, CI95% -2.26 days to 0.68 days; I<sup>2</sup>=92%). Early oral feeding was associated with a reduction in length of stay (4 studies, 484 patients), estimating an average stay of 0.92 days less (CI95% -1.53 days to -0.31 days; I<sup>2</sup>=68%). The data suggest that the intervention is safe because it did not increase the rate of gastrointestinal complications (nausea and/ or vomiting) (4 studies, 484 patients; RR 1.03, CI95% 0.64 to 1.67; I<sup>2</sup>=73%) of other postoperative complications<sup>119</sup>.

SR of RCT 1+

A systematic review and meta-analysis of 7 RCTs posed the question of whether early reinitiation of oral nutrition, within 24 hours following the surgical procedure, improved the results of patients who had undergone colorectal surgery. The length of stay of the group that began nutrition in the immediate postoperative period was significantly shorter than that of the group that was kept on absolute diet until the resolution of the postoperative ileus (5 studies, 507 participants; weighted mean difference -1.58 days, \$295\% -2.77 days to -0.39 days; I<sup>2</sup>= 78%). Early feeding was associated with a statistically significant reduction in the risk of total postoperative complications (7 studies, 587 participants; RR 0.70, CI95% 0.50 to 0.98;  $I^2 = 0\%$ ). However, when evaluated individually, early feeding did not have a significant effect on the risk of the following postoperative complications: anastomotic dehistence (6 studies, 558 patients; RR 0.47, CI95% 0.19 to 1.15;  $I^2 = 0\%$ ), pneumonia (6 studies, 559 patients; RR 0.71, CI95% 0.31 to 1.59; I<sup>2</sup>=0%), wound infection (4 studies, 449 patients; RR 0.69, CI95% 0.34 to 1.37; I<sup>2</sup>=0%). Nor were there significant differences in the rate of gastrointestinal complications, although an unfavourable trend was observed in early feeding: reinsertion of nasogastric feeding tube (5 studies, 508 patients; RR 1.31, CI95% 0.78 to 2.21; I<sup>2</sup>=0%), vomiting (4 studies, 308 patients; RR 1.08, CI95% 0.77 to 1.53; I<sup>2</sup>=35%)<sup>120</sup>.

SR of RCT 1+ One study done in India compared the results obtained by early reinitiation of oral feeding, 24 hours after ending anaesthesia, with those obtained with the traditional intervention, absolute diet until the resolution of postoperative ileus, in 120 patients who had undergone elective open intestinal surgery for neoplasia of the rectum, colon, and small intestine. The study showed that early reinitiation of oral feeding accelerated restoration of intestinal function measured by the expulsion of flatus (mean 2.6 days  $\pm$  0.9 versus 4.5 days  $\pm$  1.5; p<0.0001) and faeces (mean 3.8 days  $\pm$  1.3 versus 6.1 days  $\pm$  2.1; ,p<0.0001), and shortened the postoperative length of stay (mean 11.1 days  $\pm$  5.5 versus 14.4 days  $\pm$  8.5; p=0.011). No statistically significant differences were found between the two groups (p>0.05) in terms of the following complications, vomiting, and distension, wound infection, fever, anastomotic dehiscence, mortality <sup>121</sup>.

RCT [-

RCT 1+

One study done in South Korea, in which 54 patients (ASA  $\leq$  2) participated, investigated the safety and effectiveness of early oral feeding in surgery for gastric cancer. In the group of patients who received early feeding, sips of water on the day of surgical procedure and liquid diet the following day, recovery of intestinal motility (expulsion of gases, mean  $1.9 \pm 1.2$  days) was significantly faster than the time observed for the control group ( $2.9 \pm 0.8$  days, p=0.036), which was kept on absolute diet until the 3rd day after the surgery. The length of stay, the principal variable of the study, in patients who received early feeding was  $7.2 \pm 1.7$  days on average, versus  $8.5 \pm 2.9$  days on average of the controls (p=0.044). No differences were found between the groups in regard to postoperative morbidity rates (25% versus 3.1%, p=0.636), and the following postoperative symptoms: hunger, abdominal distension, vomiting, cramps, and diarrhoea (p>0.05). Two patients in the control group required reoperation due to dehiscence of the anastomosis<sup>122</sup>.

RCT 1-

According to a study done in Italy, early reinitiation of oral feeding (liquids on the day of the surgical procedure, bland diet on the next day, and gradual introduction of solids) did not accelerate the resolution of postoperative ileus in elective surgery for colorectal cancer. The median time for the recovery of intestinal activity of the group that received early feeding (50 patients) was 4 days (range 2 to 7), versus 4 days (range 2 to 8) in the control group (50 patients), who initiated oral feeding after the expulsion of flatus, and who were fitted with a nasogastric tube (NGT) for decompression in the immediate postoperative period (p>0.05). According to the authors of the study, the use of opiate analgesia in both groups and its effect on intestinal motility could mask possible differences due to early feeding. Nor was any benefit observed in the length of stay, which in the group of patients with early oral feeding was a median of 7 days (range 5 to 13) versus a median of 7 days (range 5 to 14) for the control group (p>0.05). 20% of the patients with early oral feeding required decompression with NGT, while in the control group, the rate of reinsertion of the NGT was 6% (p<0.05). Also, there were no statistically significant differences between the two groups with regard to the rate of postoperative complications (26% versus 24%, p>0.05)<sup>123</sup>.

When formulating the recommendation, the GWG took the applicability and possibility of generalization of the results, the consistency between the different studies, and their clinical relevance into account. The evidence on the effectiveness and safety of early initiation of oral feeding in the case of small intestine surgery is limited to the patients included in the study by Pragatheeswarane et al.<sup>121</sup>, done in India. Although the external validity may be compromised, the GWG decided to take this study into account because in the case of urological surgery, specifically after cystectomy, the small intestine is normally used for urinary diversion (Bricker ileal conduit or orthotopic intestinal neobladder). Also, in gastric surgery, most procedures also include the handling and anastomosis of the small intestine.

The GWG also took into account that the studies are heterogeneous, which makes it difficult to draw firm conclusions regarding the consistency of the effect. Some authors initiate oral tolerance in the first few hours after surgery<sup>120</sup>, others within the first 24 hours<sup>119,120,123</sup>, and two studies even consider the initiation of feeding 24 hours after surgery to be early feeding<sup>121,122</sup>. In some studies, intervention is more aggressive, in the sense that the normal diet is introduced in the first 24 or 48 hours<sup>119,120</sup>, while in others, patients make a gradual transition from a diet of clear liquids to a solid diet; however, resuming postoperative feeding with clear liquids<sup>123</sup> or sips of water<sup>122</sup> is not the same as with a normal diet<sup>119,120</sup> because the fasting time is extended, which could affect the patient recovery time.

Based on the scientific evidence found, there are not clear advantages to keeping patients on an absolute diet. In fact, the studies suggest a risk and benefit balance in favour of the intervention. Early oral feeding in colorectal and gynaecological surgery of the small intestine accelerated restoration of intestinal peristaltism, shortened length of stay, and was associated with fewer postoperative complications. In terms of individual clinical complications, these did not reach statistical significance but the direction of the effect indicates that early feeding could reduce the risk of anastomotic dehiscence, wound infection, or pneumonia. This data should be interpreted with caution because most of the studies do not define the diagnostic criteria used, and these effects are collected as a secondary data, within the framework of another principal objective that is proposed for the studies. In regar i to the risks, early feeding appears to increase the appearance of nausea and vomiting, although the result is not significant.

There are no studies that evaluate the potential benefits of early feeding with surgical techniques and perioperative care such as laparoscopic surgery and perioperative analgesia without opiates that reduce the response to surgical stress, promote mobilization of the patient, and accelerate the recovery of the patient. The GWG considers it likely that under these circumstances, tolerance to early initiation of oral feeding is even greater than was observed in the studies described here.

Three meta-analyses<sup>116,124,125</sup> that combined the results of different enteral feeding routes (oral, nasoduodenal, nasojejunal, etc.) were excluded from the body of evidence. They were not considered to be adequate because the morbidity associated with the use of tubes may modify the postoperative evolution of surgical patients, and consequently, the magnitude of the effect of the oral route that is the objective of the question.

# **Summary of evidence**

Summary of evidence		
1+	In patients who underwent colorectal surgery, early initiation of oral feeding during the first 24 hours after surgery reduced the risk of total postoperative complications (RR 0.70, CI95% 0.50 to 0.98), and was associated with 1,58 fewer days (CI95% -2.77 days to -0.39) of average length of stay <sup>120</sup> .	
1+	In patients who underwent colorectal and small intestine surgery, early initiation of oral feeding, after 24 hours had elapsed since the end of anaesthesia, accelerated the start of transit of gases (mean 2.6 days $\pm$ 0.9 versus 4.5 days $\pm$ 1.5; p<0.0001) and faeces (mean 3.8 days $\pm$ 1.3 versus 6.1 days $\pm$ 2.1; p<0.0001), and was associated with significantly shorter average length of stay (11.1 days $\pm$ 5.5 versus 14.4 days $\pm$ 8.5; p=0.011) <sup>121</sup> .	
1+120,121	In patients who underwent colorectal <sup>120,121</sup> and small untestine surgery <sup>121</sup> , early oral feeding in the first 24 hours after surgery <sup>120</sup> , or 24 hours after the end of anaesthesia <sup>121</sup> , did not significantly affect the rate of vomiting <sup>120,121</sup> , abdominal distension <sup>121</sup> , reinsertion of nasogastric tube <sup>120</sup> , anastomotic dehiscence <sup>120,121</sup> , and infection of the surgical wound <sup>120,121</sup> .	
1+	In gastric surgery, early initiation of oral feeding (sips of water on the day of the surgery, liquid diet the following day) resulted in a statistically significant acceleration of recovery of intestinal motility and shortened average length of stay $(7.2 \pm 1.7 \text{ days versus } 8.5 \pm 2.9 \text{ days, p=0.044})$ , without increasing postoperative morbidity or the rate of gastrointestinal complications (abdominal distension, vomiting, cramps, and diarrhoea) <sup>122</sup> .	
1+	In gynaecological abdominal surgery, early oral feeding, within the first 24 hours following surgery, accelerated the return of intestinal function and reduced average length of stay by -0.92 days (CI95% -1.53 days to -0.31 days) without increasing the rate of gastrointestinal complications (nausea and/or vomiting) or other postoperative complications <sup>119</sup> .	
1-	In surgery for colorectal cancer, early initiation of oral feeding (liquids on the day of surgery, bland diet the following day), when compared with initiation after the resolution of ileus combined with the use of NGT, did not accelerate recovery of intestinal function or shorten length of stay. Early oral feeding in these patients was not associated with a significant increase in the rate of postoperative complications, but the need for decompression with NGT is significantly higher (20% versus 6%, $p<0.05$ ) <sup>123</sup> .	

#### Recommendations

В

In patients who have undergone colorectal surgery, surgery of the small intestine, or gynaecological abdominal surgery, it is recommended that oral ingestion of liquids and solids begin as soon as possible, based on the tolerance of the patient preferably within the first 24 hours after the surgical procedure, with the possibility of resuming oral feeding starting 4 hours after surgery.

# 7.2. Early mobilization

### Question to be answered:

• In patients who undergo elective major abdominal surgery, does early mobilization (getting out of bed within the first 6 hours) versus remaining in bed shorten postoperative ileus?

Bed rest increases insulin resistance, increases loss of muscle mass and strength, and alters pulmonary function. Early mobilization after surgery has been proposed as a possible way to counteract insulin resistance due to immobilization and reducing respiratory complications<sup>2,126</sup>. The goal of the question is to determine the role that early mobilization may play in patient recovery during the postoperative period of major abdominal surgery.

No studies were found in the scientific literature that were specifically aimed at evaluating the influence of early rising, the day after abdominal surgery, on resolution time of postoperative ileus were not found. For this reason, the GWG felt it was pertinent to include the results of the studies on the initiation of ambulation after the first 24 hours following surgery, and its effect on other outcomes related to the evolution of the patient. One experimental study and another observational study were the only scientific evidence that was found.

One RCT with three branches done in Australia evaluated the effectiveness of early mobilization (starting the 1st day after surgery) (group A), early mobilization plus deep-breathing exercises (group B) and delayed mobilization (starting on the 3rd day) plus deep-breathing exercises (group C) in a sample of 86 patients with high risk of developing postoperative pulmonary complications (PPC) after abdominal surgery. The average age of patients was  $71.1 \pm 7.3$  years (group A),  $73.1 \pm 8.2$  years (group B) and  $72.1 \pm 9.3$  years (group C), 50% were catalogued with physical status of ASA III or IV and 16.3% required admittance to the ICU. The incidence of PPC in groups A, B and C was 6 (21%), 7 (25%) and 3 (10%), respectively (p=0.20). There were no significant differences in the average distance walked by patients on the 3rd day when comparing group A with Group C (mean difference: 39,11 metres, CI95% -8,1 to 86,3), or group B with group C (mean difference: 33 metres, CI95% -44,5 to 56,7). The mean distance that patients walked on the 5th day also showed no significant differences between group A and group C (mean difference: 21,3 metres, CI95%49,8 to 62,5), or group B with group C (mean difference: 6,38 metros CI95% 36,8 to 49,6). The average length of stay of group A was significantly shorter than that of group C (mean difference: - 4.4 days, CI95% -8,8 to -0.3); no significant differences were observed when groups B and C were compared (mean difference: 1.5 days, CI95% -3,9 to 7.0). Compared with group (early mobilization plus breathing exercises), group C (delayed mobilization plus breathing activities) had significantly fewer smokers and patients with COPD than group B (early mobilization plus breathing exercises)127.

One observational study done in Australia investigated the influence of different factors on the appearance of PPC in high-risk abdominal surgery. Patients (n=72) had an average age of 66,1 $\pm$  12.4 years, physical status ASA II (30%), III (60%) or IV (10%) and one-third required admittance to the ICU. The time elapsed until patients were able to sit out of bed in the group with PPC was a median of 19 hours (IQR 17 to 25) versus a median of 20 hours (IQR 16 to 31) in patients with PPC (p>0.05). The difference between the two groups in the time until the initiation of mobilization (walking a distance  $\geq$  10 metros) was not statistically significant (median difference 7.2 hours, CI95% -0.5 to 18,3). The study found that delaying postoperative mobilization is an independent factor associated with the risk of presenting pulmonary complications (OR 3.03; CI95% 1.16 to 7.96); but no relation was found between when patients were able to sit out of bed and the increased risk of complications (OR 0.46; CI95% 0.11 to 1.94). 22% of the patients had undergone emergency surgery 128.

Observational study 3

When formulating the recommendations, the GWG took into account that although the evidence on the effects of postoperative mobilization does not directly respond to the clinical question (resolution of postoperative ileus), is limited and non-conclusive, best rest is not advisable because it increases the risk of pneumonia and thromboembolism, insulin resistance, and muscle weakness<sup>129</sup>. For this reason, the GWG feels that mobilization of surgical patients should be done as soon as possible.

Another aspect that was taken into account was related to the need for patients to be in a care setting that facilitates early mobilization. This requires optimum analysia, limited use of catheters and drains, and coordination of healthcare personnel. In one recent qualitative study, patients who participated in an enhanced recovery program in gynaecological surgery were found to be especially concerned with early mobilization due to pain, presence of drains, and the possibility of damaging the tissue of the surgical wound. The intervention of a physical therapist was vital to allay these fears, and even more importantly, once patients were out of bed, they indicated that moving was not as difficult as they had expected.

### Summary of evidence

1+	When comparing early mobilization (1st day after surgery) with and without deep-breathing exercises, versus delayed mobilization (3rd day after surgery) with deep-breathing exercises, no significant differences were observed in the rate of PPC, or in the mean difference that patients walked 3 and 5 days after surgery <sup>127</sup> .
1+	The average length of stay of the early mobilization group was -4.4 days (CI95% -8,8 to -0.3) shorter than for the delayed mobilization plus deep-breathing exercises group; there were no significant differences between the latter group and the early mobilization plus deep-breathing exercises group <sup>127</sup> .
3	In patients who underwent abdominal surgery, delaying ambulation (walking a distance ≥10 metros) after surgery increased the risk of appearance of PPC (OR 3.03; CI95% 1.16 to 7.96); there was no relation between PPC risk and the time it took patients to sit out of bed (p=0,29) <sup>128</sup> .

### Recommendations

D The implementation of a plan of perioperative care that promotes early and progressive mobilization of the patient, getting the patient out of bed on the same day of the surgery, and starting to walk within the first 24 hours following the surgery.

# 8. Diffusion and implementation

The CPG is a tool to assist professionals and users to make decisions regarding the most appropriate health care. The introduction and implementation of the recommendations in these guidelines in the healthcare sectors in which their application is pertinent is therefore necessary. The following strategies are recommended to do this:

- Presentation of the CPG by the healthcare authorities to the communication mean.
- Presentation of the guidelines to the directorates and deputy directorates of Specialized Care of the different regional health services.
- Institutional presentation of the guidelines to the different scientific societies and associations involved.
- Collaboration with the scientific societies and associations that participated in the review of the CPG, to promote dissemination.
- Sending the CPG to the different databases that collect information on CPGs, for evaluation and inclusion.
- Free access to the different versions of the GPC at the GuíaSalud website, http://www.guiasalud.es>.
- Dissemination and information on the CPG at scientific activities related to enhanced recovery in abdominal surgery, general surgery, and surgery of the digestive tract, anaesthesiology and reanimation, urology, gynaecology, and nursing.
- Publication of the guidelines in raedical magazines.
- Translation of the complete version into English.

For the implementation of the recommendations of the guidelines, the methodology included in the *Methodological Methodological Methodologica* 

# 9. Lines of future investigation

The following proposals for future investigation were identified during the process of preparing the CPG:

# 6.1. ERAS and laparoscopic surgery

The execution of rigorous, well-designed studies to determine the effectiveness and safety of laparoscopic surgery in combination with enhanced recovery in other types of major elective abdominal surgery, apart from colorectal surgery is recommended.

# 7.1. Fluid therapy

Studies with designs that extend the analysis of fluid therapy (RFT and GDFT) to the perioperative period (up to 24 hours after surgery) are needed.

# 7.2. Analgesia

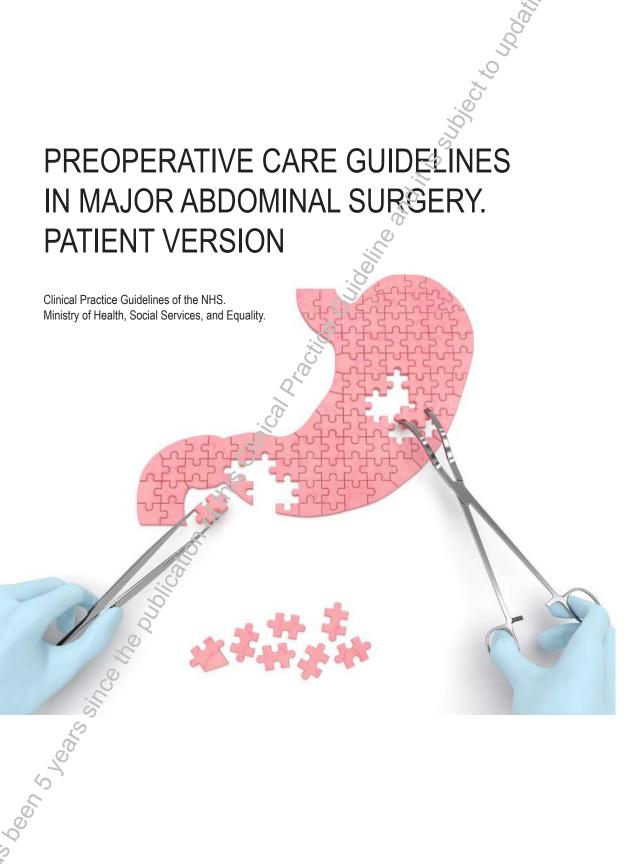
The execution of rigorous, well-designed studies on patients who are going to undergo major abdominal surgery, both open and laparoscopic surgery, that make it possible to determine the effectiveness and safety of transversus abdominis plane block versus postoperative epidural analgesia in terms of analgesia, length of stay, and postoperative complications is recommended.

## 8.2. Early mobilization

Studies with good methodological quality that assess the impact of early mobilization on patient recovery are needed.

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# Annex 1. Information for patients



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This information is also available in in electronic format at the GuíaSalud website (www.guiasalud.es). At this website, you can also consult the complete and summarized versions of the Clinical Practice Guidelines on Perioperative Care in Major Abdominal Surgery. All of the documents are planned to be updated every five years, with the possibility of updating the electronic version more frequently if necessary.

The declaration of interests of all of the members who participated in the preparation of the information for patients is presented in Annex 4 of the complete version of the Clinical Practice Guidelines on Perioperative Care in Major Abdominal Surgery.

Work Group of the Clinical Practice Guidelines on Perioperative Care in Major Abdominal Surgery. Patient version

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# **SUMMARY** What is Major Abdominal Surgery? What is perioperative care? ..... Who will inform you? When? What information will be given?..... What is preoperative nutritional screening? Wity is it recommended?..... Why is drinking carbohydrate drinks before the operation recommended?..... 7. Why do I not have to feel pain?.... 9. When can I start to eat again after the operation?..... When can I get out of bed after the operation? 11. How can farolly members and/or caregivers help with recovery?...... pag. 22

# 1. INTRODUCTION

This material has been prepared to help patients who are going to undergo non-emergency major abdominal surgery. It may also be useful to their family members and caregivers, or to any other person interested in the subject. It contains explanations on the care before, during, and after the operation that is recommended in the Clinical Practice Guidelines on Perioperative Care in Major Abdominal Surgery\*. This information will help you to prepare for the operation that you will undergo and in your recovery afterwards.

(\*) Patient information, nutritional screening, carbohydrate beverages before the operation, minimally invasive surgery, premedication, treatment of postoperative pain, early initiation of oral feeding, early initiation of mobilization.

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# 2. WHAT IS MAJOR ABDOMINAL SURGERY? WHAT IS PREOPERATIVE CARE?

Major surgery refers to the most complex operations with the most risk of complications. They normally require general anaesthesia and recovery may take several days or weeks. In major abdominal surgery, the surgeon accesses the abdominal cavity to operate on the organs there (colon, liver, kidney, bladder, uterus, etc.).

From the time it is decided that you need surgery until you are released from the hospital, the team of professionals that cares for you will program a series of care actions to help you to recover from the operation.



If you are going to undergo major surgery, the prior preparation and care during and after the operation are very important.

These actions will prepare you both physically and emotionally for the operation, and they will prevent complications and reduce the length of your hospital stay.

# 3. WHO WILL INFORM YOU? WHEN? WHAT INFORMATION WILL BE GIVEN?

During the first visit, the surgeon will explain the purpose, characteristics, potential risks, and expected results of your specific surgical procedure and will answer all of your questions.

As a patient, you have the right to decide what will be done to you after receiving information on the different treatment options. Only after making this decision will you be asked to sign a written consent form for the operation.

At the appointment with anaesthesia, several days before surgery, you will be informed of the anaesthesia plan, the types, and potential risks based on your pathology, and all of your questions will be answered.

You will receive information describing what will happen throughout your hospital stay, all of the steps that will be followed on the day of surgery, in the operating room, and after the surgery in the hospital ward. You will receive instructions about what you can do at each step to accelerate your recovery. Do not hesitate to consult the professionals who are caring for you at any time if you have questions or concerns.

The information on the process is aimed at reducing the fear that causes anxiety and making you an active participant in the care.

You will also be given a brochure with the same information and instructions in writing. The elements described will vary depending on the type of surgery.

For example, some of the instructions from a brothure for patients who are going to undergo a colon resection:



### SECOND DAY AFTER THE OPERATION

If you have a catheter to urina it, it will probably be removed today.

If you have a drain, it will probably be removed today.

If you are tolerating liquids well, you may start with a puréed diet. Only eat and drink what you can tolerate.

You will be given or all analgesics (pills) for the pain. You should

continue your breathing exercises and walking

The nursing staff will give you this information orally and in writing at the first surgical visit, when they worm you about the type of operation that they are going to perform.

Remember that it is important that you answer all of your questions and doubts with the surgeon, especially in regard to the expected results of the operation (curing the disease, etc.). This information will help make you less nervous and anxious while you wait for the day of the surgery. The time between the diagnosis of your disease and the operation will be as short as possible.

# 4. WHAT IS PREOPERATIVE NUTRITIONAL SCREENING? WHY IS IT RECOMMENDED?



Before the operation, you will be asked to visit the hospital so that the medical team that will work with you can evaluate your health status. This "preoperative evaluation" visit often takes place more or less one week before the operation, but this may vary. You will be asked to give your consent to run different tests on you.

There are some tests that are done even on people with no evident health problems, in order to determine whether they may have any disorders that could have a negative effect on the treatment. Other tests are more specific and are only carried out for specific operations, or because the patient has a known health issue.

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Nutritional screening is one of the tests that should be done on all patients who are going to undergo major abdominal surgery. It is a simple, fast test that detects patients who are malnourished. It identifies the problem so that it can be treated before the surgery. Well-nourished patients have fewer complications related to the operation.

There are different screening methods. The most commonly used methods take into account weight, height, weight changes, changes in eating habits, duration and evolution of the disease, and/or data from the blood analysis (for example, quantity of albumin protein).



If necessary, nutritional treatment will be started before the operation, in order to arrive at the operation in the best physical conditions.

Nutritional screening can be done by the nursing staff. If the result is unfavourable, the doctor will run a complete "nutritional assessment" and administer the corresponding nutritional treatment.

# 5. WHY IS DRINKING CARBOHYDRATE DRINKS BEFORE THE OPERATION RECOMMENDED?

Most people can drink liquids (carbohydrate-enriched drinks, water, herbal teas, tea, coffee, strained juice with no pulp, etc.) without risk until two hours before the operation.

Several hours before the surgery, you will be given between 200 and 400 ml of a drink that contains carbohydrates. This measure is recommended to avoid the undesirable effects that could be caused by preoperative fasting, such as discomment and the feeling of hunger or thirst.

If you have diabetes (increased glucose in the blood), the surgeon will inform you how you should proceed. Remember that before the operation, you must track your blood sugar levels as closely as possible. Your general practitioner or nurse will help you to do this.



# 10 40 dalling.

### 6. MINIMALLY INVASIVE SURGERY

This type of surgery avoids opening the body cavities it makes it possible to operate through small incisions (wounds). In conventional (crean) surgery, larger incisions are made, which can cause more pain and prolong recovery.

Laparoscopic surgery consists of inserting a laparoscope (a long, thin tube that is connected to a video camera) and special instruments into the abdominal cavity (into which gas has been introduced), through small incisions around the navel; the surgeon receives an image of the organ in the cavity and can operate on them by manipulating the instruments externally.

Most of the operation is done through small incisions, but sometimes a slightly larger incision must be made to remove all or part of an organ.

The gas that is pumped into the abdomen could cause abdominal discomfort for one or two days after the procedure. As the gas is absorbed, the pain will disappear.

Your doctor will inform you of the different surgical treatment options, and will tell you which technique is best suited for treating your disease.

# 7. WHAT IS PREMEDICATION? WHEN IS IT ADMINISTERED?

All surgical procedures cause some type of emotional reaction (anxiety, depression, fear, apprehension, etc.). Ideally, the information provided by the team that is treating you will help you to better handle the fear and anxiety before the operation. However, each person's ability to handle situations of tension is different. Inform the team that is treating you of any need or feelings of discomfort that you may have in this regard.

If there is a high degree of anxiety and fear, they will give you medication to make you more comfortable and help ensure that you are relaxed when you reach the operating room.

- One pill the night before surgery (sleeping pill).
- One pill 1 or 2 hours before the operation.

Remember that you can express any doubts and concerns that you have at any time to the team of professionals treating you.



It is possible that after the operation, you will feel very drowsy and may not clearly remember some moments due to the effect of these medications.



# 8. WHY DO I NOT HAVE TO FEEL PAIN?

Controlling pain is important for your recovery. If you have pain, you shouldn't bear it thinking "it's normal for it to hurt after an operation". This attitude can lead to complications and delay your recovery.

If you feel less pain, you can start to waik and regain your strength and vigour faster.

After surgery, you will be transferred to the Post-Anaesthesia Recovery Unit. Pain is a personal sensation for each patient and the anaesthesiologist who is responsible for your care will prescribe a treatment for the pain that is adapted to your individual needs and the type of surgery.

You should be aware that the intensity of postoperative pain is greatest during the first 24 hours and that it diminishes progressively.





# How is postoperative pain treated?

With a series of pain killers that are administered at a fixed rate every 6 or 8 hours, and a pain killer called a "rescue" pain killer that will kee given to you when you request it. These medications will be administered intravenously (drip) in the first 24 to 48 hours, and then orally (pills).

For some surgery, the anaesthesiologist may also connect a series of special devices to control pain better. For example, a patient-controlled analgesia (PCA) pump. This is a device that administers pain killers at a tixed rate. It has a handset with a button so that you can increase the dosage. Everything is programmed so that there is no danger of giving yourself too much.

The healthcare staff are available 24 hours a day to control your pain and resolve any concerns in this regard.

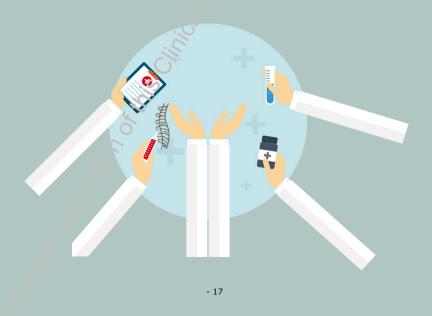
The nursing staff will monitor your level of pain and will adjust the prescribed treatment accordinaly.

- 16

# What is epidural analgesia?

For certain types of surgery, the anaesthesiologist will connect an epidural catheter (a thin, flexible tube in the spinal column) in the operating room. After surgery, it is connected to a PCA pump that administers medications that block the nerves that send pain signals to your brain.

All drugs used to treat pain can cause unwanted effects. For example, epidural analgesia could cause you to feel vertigo or weakness in your legs, which could last for some time; the effect is temporary and does not require treatment.



# 9. WHEN CAN I RESUME EATING AFTER THE OPERATION?

After major abdominal surgery, intestinal movement stops temporarily due to the manipulation of the intestine during the operation. This condition is not serious. In most cases, it resolves itself spontaneously in the first few nours, although 3 to 5 days may be needed depending on the type of surgery.

In the past, keeping patients without food until intestinal transit started again was a normal practice.

Remember immobilization in bed works against you. You need to start walking again as soon as possible to stimulate muscle tone and avoid complications

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Today, it is recommended that patients begin to drink and eat as soon as possible, preferably within the first 24 hours after the operation.

This should be done progressively. First, you will be given a few sips of water in a semiupright position, the progressing to foods that are easy to digest, provided that there is no nausea or vomiting.

You should be aware that drinking and eating a few hours after the operation is safe. It does not increase the risk of opening the wound (sutures) even if they have operated on your digestive tract.

The first defecation normally takes place 2 or 3 days after feeding is resumed; it is not normal for this to cause pain or haemorrhage.

# 10. WHEN CAN I GET OUT OF BED AFTER THE OPERATION?

Before, it was customary for patients to lie in bed for the first few days after an operation, to avoid complications involving the wound as a result of the effort to get out of bed.

We now know that immobilization in bed poses a significant risk of blood clots in the veins of the legs and lungs, muscular weakness, and pneumonia, which is caused by the retention of bronchial secretions.

Remember immobilization in bed works against you. You need to start walking again as soon as possible to stimulate muscle tone and avoid complications



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The same day of the surgery, you can sit in a chair with the help of the healthcare staff or a family member. The next day you can get out of bed and take short walks around the room.

The professionals treating you will make sure to provide you with proper analgesia to prevent pain. The use of catheters and drains (tubes) will also be reduced to encourage you to begin to walk.

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# 11. HOW CAN FAMILY MEMBERS AND/OR CAREGIVERS HELP WITH THE RECOVERY?

The healthcare professionals will inform the family members and/or caregivers who participate in the patient's care. They need to understand the risks and benefits of the care that the patient is going to receive before, during, and after the operation, because:

- They will often help patients to make decisions regarding their treatment.
- They can provide support for care in which the patient's collaboration is essential (reinitiation of feeding and mobilization after the operation).





- Your collaboration is really important; you play a fundamental role in their recovery.

- Each one of the care actions described in this guide has a single goal: to obtain a favourable result from your surgical procedure and allow you to resume your normal routine as soon as possible.

Keep in mind...



### Annex 2. Glossary

**Patient-Controlled Analgesia or PCA:** consists of the on-demand administration of morphine derivatives by means of an electronic device (PCA pump).

**Epidural analgesia:** local-regional anaesthesia technique that consists of the continuous perfusion of local anaesthetic in the epidural space to provide the patient with postoperative analgesia by means of a neuroaxial block.

**Multifrequency bioimpedance:** a method developed to estimate body composition, the central axis for the assessment of nutritional status. It is based on the opposition of cells, tissues, and bodily liquids to the passage of electrical current. This method measures the total body water and makes it possible to estimate the fat-free body mass and fat mass.

**Transversus Abdominus Plane or TAP Block:** a local-regional anaesthetic technique related to the blocking of the conduction of the anterior branches of the spinal nerves located between the transversal and internal oblique muscle of the abdomen (peripheral nerve block), which produces postoperative analgesia of the abdominal wall.

**Elective surgery:** a surgical procedure that can be programmed ahead of time because it is not a medical emergency. Also called programmed surgery.

**Laparoscopic surgery:** surgical procedure that is carried out with minimal abdominal incisions, inserting an optical and surgical system through the openings.

**Major surgery:** any surgical procedure that is carried out in an operating room, with hospitalization of the patient before and after surgery, with the application of regional or general anaesthesia (by an anaesthesiologist) and with two or more assistants participating, in addition to the surgeon. It refers to more complex surgical procedures, which normally pose a certain degree of risk to the life of the patient or of serious disability, and in which the preparation for the surgery (except in the case of emergency surgery) as well as the recovery may take several days or weeks.

**Minimally invasive surgery:** refers to all surgical procedures carried out through small incisions. From the surgical point of view, this is characterized as being technologically-dependant surgery.

**Colloids:** intravenous fluids that possess molecules that are large enough that they cannot pass through the cellular membrane, giving them osmotic power and the ability to retain intravascular liquids. Examples of colloid solutions: albumin, dextrans, gelatins.

**Colostomy:** externalization of the colon (ascending, transverse, or sigmoid) through the abdominal wall, exiting through the skin in order to create and artificial outlet for faecal content.

**Postoperative complication:** any event that occurs in the planned course of a surgical procedure with a local or systemic response that could delay recovery and endanger the patient's vital functions or life (for example, infection of the surgical wound or dehiscence of the anastomosis).

**Nutritional screening:** the use of assessment tools to identify patients with nutritional risk upon admittance and during their hospital stay. This is different from a complete nutritional assessment, because it is not intended to diagnose malnutrition, but simply to detect patients who are at risk and who require a complete assessment and possible treatment.

**Crystalloids:** these are inorganic solutions that possess water, ions and/or glucose in a proportion and osmolarity that is similar to that of plasma. They lack oncotic power because they are no proteins and their distribution in the body is a function of ionic concentration. Examples of crystalloid solutions: physiological saline, glucosaline.

**State-Trait Anxiety Inventory or STAI:** measures the anxiety trait or personality factor that predisposes a person to suffer or not suffer from anxiety, and the anxious state, in other words, the environmental factors that protect against or generate anxiety.

Adverse surgical effect: an unfavourable result that can be attributed to a surgical procedure. Adverse surgical effects are related to intraoperative surgical or anaesthetic accidents with immediate or delayed postoperative complications and the failure of the surgical procedure. Based on the severity of their consequences, they may be minor, moderate, life-threatening, or fatal if the patient dies. They have been classified into complications of the surgical wound (infection, haematoma, dehiscence and evisceration); complications of the surgical technique (haemorrhage, fistula, or anastomotic dehiscence, infection of the cavity, and intraoperative iatrogeny); systemic complications (respiratory infection, urinary tract infection, central line infection, myocardial infarct, deep vein thrombosis, pulmonary thromboembolism, and organ failure), surgical failure due to persistence or relapse of the disease or its symptoms, and anaesthetic accidents.

Randomized clinical trial: an experimental study in which participants are assigned randomly to receive a treatment or intervention from among two or more possible options. One of the groups usually receives the conventional treatment (control group), which serves as the reference for comparison, while the other group receives the treatment that is being studied (experimental group).

Visual Analogue Scale (VAS): used to measure the intensity of pain described by a patient with the maximum reproduceability among observers. It consists of a horizontal line 10 centimetres long with the extreme expressions of a symptom at the ends. The absence or lower intensity is on the left and greater intensity on the right. The patient is asked to mark the point on the line that indicates the intensity and it is measured with a ruler with millimetre precision. The intensity is expressed in millimetres or centimetres.

ASA physical status (American Society of Anaesthesiologists): classification that describes the preoperative status of patients based on the presence of certain diseases. Although it was not initially intended for the establishment of risk groups, a positive correlation was found between this classification and mortality related to the anaesthesia action.

Physical status classification (ASA)

- I. Healthy patient, with a localized process without systemic affectation.
- II. Patient with mild systemic disease.
- III. Patient with severe but not incapacitating systemic disease.
- IV. Patient with severe and incapacitating systemic disease that constitutes a constant threat to the patient's life.
- V. Moribund patient, whose life expectancy is less than 24 hours, regardless of whether or not the surgical procedure is carried out.

**Stoma:** artificial opening in an internal organ to connect it to the surface of the body. The surgical operation to create the stoma has different names depending on the organ affected: colostomy (colon), ileostomy (ileon), urostomy (bladder), etc. May be temporary or permanent.

**Cohort study:** consists of following one or more cohorts of healthy individuals who present different degrees of exposure to a risk factor and in whom the appearance of the disease or condition being studied is measured.

**Observational study:** a set of epidemiological studies in which there is no intervention by the researcher, who is limited to measuring the variables defined in the study.

**Indirect evidence:** the information that is available is indirect in situations in which there are no direct comparisons between the interventions considered, or there are important differences between the available studies and the population, the interventions, or the outcomes proposed in the question of interest.

**Fluid therapy:** a therapeutic method aimed at maintaining or restoring the normal volume and composition of bodily fluid intravenously. The principal objective of perioperative fluid therapy is to maintain tissue perfusion and oxidative metabolism during the surgery.

**Goal-directed fluid therapy:** consists of the infusion of fluids as boluses, following a protocol, in order to achieve a specific haemodynamic or tissue perfusion goal. Allows the individualized adjustment of the quantity of fluid administered.

**Restrictive fluid therapy:** although there is no universally accepted definition, this term usually refers to the replacement of losses during surgery, avoiding overload, in order to achieve a fluid balance close to zero, without variations in the body weight of the patient.

**Heterogeneity:** In meta-analyses, heterogeneity refers to the variability or differences in the estimates of the effects between studies. A distinction must be made between "statistical heterogeneity" or differences in the declared effects, and "clinical heterogeneity", or differences between studies in terms of fundamental characteristics of the participants, interventions, or measurements of the results. The statistical tests of heterogeneity are used to evaluate whether the variability observed in the results of the studies is greater than what would be expected at random

**Postoperative ileus:** the cessation of gastrointestinal motility during a certain period of time that is normally observed after major abdominal surgery as a result of intestinal manipulation to a greater or lesser extent.

**Ileostomy:** externalization of the ileum to the abdominal wall, normally in the lower right quadrant of the abdomen.

**Charlson Comorbidity Index:** this is a system for assessing ten-year life expectancy, depending on the age at which the subject is assessed and their comorbidities. In addition to age, it consists of 19 items that if present, have been proven to have a concrete influence on the life expectancy of the individual.

**Confidence interval:** this is the range within which the true magnitude of the effect (which is never known exactly) lies with a pre-established degree of security or confidence interval. The term "95% confidence interval" is often used. This means that the true value of the effect of the study would be found in that interval in 95% of the cases measured.

**Systolic volume index:** this is the systolic volume divided by the total body surface area. It is used in non-invasive haemodynamic monitoring of cardiac output. It predicts the response to fluids in GDFT.

**Clear liquids:** these include, among others, water, herbal teas, light tea, black coffee, strained juices without pulp, carbonated beverages, and carbohydrate-enriched beverages.

**Meta-analysis:** a statistical method that combines the results of different studies to evaluate heterogeneity and generate overall results.

**Intraoperative period:** the time elapsed between when the patient is received in the operating room until he or she is transferred to the recovery room.

**Perioperative period:** the time elapsed between the decision to surgically treat the patient until the patient is discharged from the hospital.

**Postoperative period:** the time elapsed between the end of the surgical procedure and complete or partial recovery, with after-effects, of the patient. If the treatment fails, this could end with the death of the patient.

**Preoperative period:** the time elapsed between the decision to surgically treat the patient until the patient enters the operating room.

**Placebo:** an inactive substance or procedure that is administered to a participant, to compare its effects with those of the intervention being studied. Placebos are used in clinical trials to blind subjects to their assignment to treatment. The placebo must not be distinguishable from the intervention in order to ensure adequate blinding.

Anaesthetic premedication: comprises the set of drugs that are administered prior to general or local-regional anaesthesia, before the patient enters the operating room. The objectives of anaesthetic premedication are anxiolysis and/or sedation, analgesia in certain situations, and prevention of postoperative nausea and vomiting.

**Enhanced recovery from abdominal surgery:** consists of a series of measures for the handling of the surgical patient before and during the procedure and in the immediate postoperative period, aimed at reducing the response to surgical stress in order to achieve faster and more sansfactory recovery after the surgery. Also known as multimodal rehabilitation or ERAS (Enhanced Recovery After Surgery).

**Systematic review:** an investigation method that provides a summary of the existing studies on a particular question, using explicit and systematic methods for the identification, critical evaluation, and synthesis of the scientific literature.

**Nutritional risk:** the risk of suffering complications as a result of the patient's nutritional status. Certain situations, pathologies, and treatments (for example, major surgery) increase nutritional risk due to an increase in energy requirements and nitrogenates (caused by the base pathology or treatment) or malabsorption and/or use of them.

**SIGN** (Scottish Intercollegiate Guidelines Network): the Scottish agency that has been preparing clinical practice guidelines since 1993 with recommendations based on the best available scientific evidence, as well as methodological documents on the design of clinical practice guidelines.

**Nutritional support:** the administration of nutrients and other necessary coadjuvant therapeutic substances, orally or directly in the stomach or intestine, and/or intravenously, in order to improve or maintain the nutritional status of a patient.

**Corrected flow time:** ejection time of the left ventricle, adjusted to the duration of the cardiac cycle according to Bazett's formula. The typical values for a healthy adult are 330 to 360 milliseconds (ms). The most common cause of short TFc (<330 ms) is hypovolaemia.

**Pulse pressure variation:** variable obtained from the analysis of the arterial pressure curve during ventilation with positive pressure, which predicts the response to volume in GDFT.

Clinical pathway: an instrument aimed at structuring actions in response to clinical situations that present a predictable evolution. It describes the steps that should be followed, defines the sequences over time of each step, and defines the responsibilities of the different professionals who are going to participate.

## Annex 3. Abbreviations

BCAA branched-chain amino acids
PCA patient-controlled analgesia

PCEA patient-controlled epidural analgesia

LA local anaesthetic
BCM body cell mass
BDZs benzodiazepines
OCH oral carbohydrates

MAS major abdominal surgery

**PPC** postoperative pulmonary complications

**RCT** randomized controlled clinical trial

TLOS total length of stay

PSS post-surgical stay

VAS Visual analogue scale

GDFT goal-directed fluid therapy

RF restrictive fluid therapy

GWG guideline working group

**CPG** clinical practice guidelines

**HR** hazard ratio

BMI Body mass index
SVI systolic volume index

**OR** Odds ratio

MMRH multimodal rehabilitation

**IQR** interquartile range

**ERAS** enhanced recovery after abdominal surgery

RR relative risk

SR systematic review

**SRS** surgical recovery score

**TAP** transversus abdominis plane

TFc corrected flow time ICU intensive care unit

**PACU** post-anaesthesia care unit pulse pressure variation

**SV** systolic volume

## Annex 4. Declaration of interests

The following members of the preparation group have declared that they have no conflicts of interests:

Antonio Arroyo Sebastián, José María Calvo Vecino, Patricia Gavín Benavent, Javier Martínez Ubieto, Carmen Gloria Nogueiras Quintas, Pablo Royo Dachary, Jorge Subira Ríos.

Rubén Casans Francés, has been paid professional fees by Merck Saharp & Dohme (MSD) for presentations.

Emilio Del Valle Hernández, has received funding from MSD to attend meetings, congresses, and courses.

M<sup>a</sup> Jesús Gil Sanz, has received financing from Astellas and Ipsen to attend meetings, congresses, and courses, and has received professional fees from Abbvie y Janssen for presentations. Juan Ignacio Martín Sánchez has received funding from MSD to attend meetings, congresses, and courses.

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Francisco Faus Gabandé, has received financing from the Universidad de Valencia to attend meetings, congresses, and courses.

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