Clinical Practice Guideline for the Patient Safety at Surgery Settings

NOTE:

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

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

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

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

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This CPG is an aid for decision-making in healthcare. Its use is not compulsory, and it does not replace the clinical judgement of healthcare staff.

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Presentation

Clinical decisions that are appropriate, effective, and safe require professionals with up-to-date knowledge and skills.

Scientific information is more accessible than ever, but the large amount of information, the lack of time, and the need to grade the relevance of scientific evidence make it necessary to have certain tools aimed at supporting the clinical decision-making process. Clinical Practice Guidelines(CPG) answer the most relevant questions that may arise when dealing with a patient with a concrete pathology, and present scientific evidence in the form of recommendations graded on the basis of the studies on which they are based.

Realising that CPGs make thousands of clinical decisions easier every day, and that they are a tool to improve health outcomes, the Quality Agency supports their development, dissemination, and use, while ensuring that those prepared in Spain are of high quality.

In 2003, the Inter-Territorial Council of the Spanish National Health System (*Sistema Nacional de Salud* - SNS) set up the *GuíaSalud* (HealthGuide) project. *GuiaSalud* has as its ultimate goal to improve the clinical decision–making process based on scientific evidence, through training and by setting up a CPG register in the SNS. Since then, the *GuíaSalud* project has evaluated numerous CPGs in accordance with explicit criteria generated by its scientific committee, registered those CPGs, and disseminated them over the Internet. Early in 2006, the Directorate General of the SNS Quality Agency developed a Quality Plan for the Spanish National Healthcare System (SNS), which consists of twelve strategies. The aim of this Plan is to increase the cohesion of the SNS and to guarantee the highest quality in healthcare for all members of the public, regardless of where they live.

The tenth strategy of the Plan is designed to improve clinical practice. Its objectives include reducing variability in clinical practice and encouraging the preparation and use of the CPGs. *GuíaSalud* is meeting the objectives set out in the quality plan with regard to setting up a register, providing training and advice, and creating new guides through the CPG Drafting Programme.

In 2006, various agencies and groups of experts in prevalent disorders related to health strategies were assigned the task of developing eight CPGs. They were also asked to define a common methodology for developing CPGs within the SNS. The task resulted in a Methodological Manual for Drafting CPGs that has been available to all professionals since November 2007, and that, from a methodological point of view, is the reference work for the guides prepared in this Programme.

A further fourteen CPGs were subsequently prepared in collaboration with the same institutions and with the participation of the scientific societies involved. This CPG on the safety of surgical patients is part of that group of guides.

The *GuíaSalud* project was renewed in 2007 with the creation of the CPG Library, which has as its main objective to deepen the methodology used in the preparation of CPGs. It also includes services and products that are related to Evidence-Based Medicine and that aim to support the clinical decision-making process. The CPG Library places special emphasis on the diffusion, dissemination, and implementation of CPGs in order to encourage their use, as well as on the evaluation of outcomes for public health.

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In its classic work "To Err is Human: Building a Safer Health System", the Institute of Medicine determined the importance of clinical safety. Clinical procedures at all levels must be completed without complications, human shortcomings, or errors in the system. This fact is of special importance in the field of surgery, given all the professionals that take part in it and the complexity of all the procedures involved in the peri-operative process. Recent studies have highlighted the relevance to public health of the current volume of surgical procedures that are carried out. This fact takes on greater significance when the percentage of patients who will suffer surgery-related complications is estimated. These data have led to the rapid reaction of the World Health Organisation, which has set up its Second World Challenge for Patient Safety under the slogan "Safe Surgery Saves Lives".

The preparation of this CPG required the participation of a team of professionals from a range of disciplines. They made a significant effort to draw up a CPG based on evidence, as well as explicit recommendations to reduce peri-operative complications for the most common clinical situations. The process of external revision was also multidisciplinary, with the participation of healthcare system users who supplied their points of view.

We hope that this project may contribute effectively to improving the safety of patients who undergo surgery, which is key to improving the quality of assistance in the field.

PABLO RIVERO CORTE
General Director of the NHS Quality Agency

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Authorship and collaborations

Working group of the CPG for the Patient Safety at Surgery Settings

Pablo Alonso Coello, Family and Community Medicine Physician
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Rosa Jam Gatell, Nurse, Intensive-Care Unit
Hospital Parc Taulí. Sabadell (Barcelona)

Fernando Gilsanz Rodríguez, specialist physician, Anæsthesiology and Re-animation
Head of the Department of Anæsthesiology and Re-animation
La Paz University Hospital (Madrid)

Laura Martínez García, Preventative Medicine and Public Health Physician
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Carola Orrego, Nurse and Matron, Director of Projects – Research into Patient Safety
Instituto Universitario Avedis Donabedian (FAD) (Barcelona)

David Rigau Comas, specialist physician, Clinical Pharmacology
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Manuel Romero Simó, specialist physician, General and Digestive Surgery
Head of Section – General and Digestive Surgery
Hospital General Universitario de Alicante (Alicante)

Ángel Salvatierra Velázquez, specialist physician, Thoracic Surgery
Head of Department and Unit Director – Thoracic Surgery and Lung Transplants
Hospital Universitario Reina Sofía (Córdoba)

Raquel Sánchez Santos, specialist physician, General and Digestive Surgery
Area Specialist / Consultant, Bariatric and Œsophago-Gastric Surgery
Department of General and Digestive Surgery, Complejo Hospitalario de Pontevedra (Pontevedra)

Jesús Sastre Pérez, specialist physician, Oral and Maxillo-Facial Surgery
Department of Maxillo-facial Surgery, Hospital Universitario de la Princesa (Madrid)

Ivan Solà Arnau, Researcher
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Víctor Soria Aledo, specialist physician, General and Digestive Surgery
Research Co-ordinator, General Surgery and Digestive-Surgery Unit
Hospital General Universitario Morales Meseguer (Murcia)

Juan Torres Lanzas, specialist physician, Thoracic Surgery
Head of the Department of Thoracic Surgery
Hospital Universitario Virgen de la Arrixaca (Murcia)

Rafael José Toscano Méndez, specialist physician, General and Digestive Surgery
Director of Surgery
Benalmádena High-Resolution Hospital (Málaga)

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Sera Tort Donada, Family and Community Medicine Physician
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Diego Alejandro Utor Fernández, specialist physician, General and Digestive Surgery
Breast Pathology Clinical Unit
Hospital Universitario Puerta del Mar (Cádiz)

Co-ordination

Ivan Solà Arnau, Researcher
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

Pablo Alonso Coello, Family and Community Medicine Physician
Iberoamerican Cochrane Centre; Hospital de la Santa Creu i Sant Pau (Barcelona)

External revision

José Luis Aguayo-Albasini, specialist physician, General and Digestive Surgery
Head of the Department of General Surgery and Professor
Head of Quality Management of the Spanish Association of Surgeons
Hospital General Universitario Morales Meseguer (Murcia)

Jesús Aranaz Andrés, Preventative Medicine and Public Health Physician
Head of the Department of Preventative Medicine and Healthcare Quality and Professor
Universidad Miguel Hernández, Hospital Universitari Sant Joan d'Alacant (Alicante)

María José Castro Ruiz, Nurse, Clinical Quality and Documentation Service
Hospital Universitario Reina Sofía (Córdoba)

Sergio Minué Lorenzo, Family and Community Medicine Physician
Director of the Management Area of Healthcare Practice
Escuela Andaluza de Salud Pública yUniversidad de Granada (Granada)

Joaquín Morís de la Tassa, Internal Medicine Physician
Co-ordinator of the Patient Safety Programme in the Principality of Asturias
Hospital de Cabueñes (Gijón)

Rosa María Muñoz Albarracín, Nurse, Head of Surgical Nursing
Hospital de la Santa Creu i Sant Pau (Barcelona)

Anna Oller Castells, Nurse, Head of the Sterilisation Centre
Hospital de Sabadell, Corporació Sanitària del Parc Taulí (Sabadell)

Pedro Ruiz López, specialist physician, General and Digestive Surgery
Health Co-ordinator, 12 October University Hospital (Madrid)

Sergi Sabaté Tenas, specialist physician, Anæsthesiology and Re-animation
Catalan Society for Anæsthesiology, Re-animation, and Pain Therapy
Department of Anæsthesiology, Puigvert Foundation (IUNA) (Barcelona)

Vicente Santana López, Director of the Observatory for Patient Safety
Andalusia Agency for Health Quality (Seville)

Antonio José Torres García, Professor of Surgery, Complutensian University of Madrid
Head of the Department General and Thoracic Surgery
Saint Charles Clinical Hospital (Madrid)

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Pere Vila Caral, specialist physician, Anæsthesiology and Re-animation
Department of Anæsthesiology and Re-animation
Germans Trias i Pujol University Hospital (Badalona)

Expert partnership

Arturo Martí Carvajal, specialist physician, Hæmatology and Hæmotherapy
Universidad de Carabobo (Bárbula, Carabobo, Venezuela)

Collaborating Societies

Spanish Association of Surgeons

Avedis Donabedian University Institute

Spanish Society for the Quality of Care

Spanish Society for Bariatric Surgery

Spanish Society for Oral and Maxillo-Facial Surgery

Spanish Society for Intensive Nursing and Coronary Units

Spanish Society for Pneumology and Thoracic Surgery

Members of those societies are part of the authorship of the CPG

Declaration of Interest: The declaration of interest by all members of the Working Group, as well as by the persons who took part in expert collaboration and external revision, can be found at **Appendix 4**.

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Questions to be answered

PREVENTING SURGICAL SITE INFECTIONS

1. What are the principal measures for reducing the risk of post-operative infection?
2. What is the effectiveness of irrigating wounds as a means of reducing surgical site infections?
3. Is it effective to administer additional oxygen to reduce the incidence of surgical site infections?
4. What are the best methods for wound closure in order to favour healing?

USING ANTIBIOTIC PROPHYLAXIS

5. Is antibiotic prophylaxis indicated in patients undergoing a surgical procedure?
6. What are the antibiotics of choice for antibiotic prophylaxis in various surgical procedures?
7. When is it appropriate to administer antibiotics intravenously?
8. What is the optimum duration of antibiotic prophylaxis?

PREVENTING CARDIOVASCULAR EVENTS

9. Do beta-blockers, statins, acetylsalicylic acid, alpha-2 agonists, calcium antagonists, or coronary revascularisation prevent cardiovascular events in patients undergoing non-cardiac surgery?
10. What are the risk factors of suffering cardiac arrhythmia after surgery?
11. What treatments can prevent auricular fibrillation in patients undergoing non-cardiac surgery?

PREVENTING VENOUS THROMBO-EMBOLISM

12. For antibiotic prophylaxis in surgical patients, what is the effectiveness of available antithrombotic treatments?
13. In patients who undergo general surgery, are different prophylactic measures recommended depending on risk?
14. In antithrombotic prophylaxis for surgical patents, when should prophylaxis begin?
15. In antithrombotic prophylaxis for surgical patients, what should be the duration and dose of the prophylaxis?

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PREVENTING PROBLEMS DERIVED FROM BLOOD TRANSFUSIONS

16. What are the main risk factors in surgery that favour blood transfusion?
17. In patients undergoing cardiac surgery, what factors can be used to predict blood transfusion?
18. What characteristics should patients undergoing surgery display in order to receive allogenic red blood cell transfusions?
19. What is the effectiveness of cell savers and autotransfusion in the peri-operative context?
20. Before surgery, what interventions reduce the need for blood transfusions during the peri-operative period?

MAINTAINING NORMOTHERMIA

21. What is the optimum patient body temperature at the time of the intervention?
22. What is the target temperature in patients that receive some form of active heating before the intervention?
23. Are heat insulation or active heating before the intervention preferable to the usual care in preventing hypothermia?
24. In patients who undergo surgery, does convective hot air have any effect on controlling body temperature?
25. Are the different devices for active heating (forced-air heaters, electrically-heated blankets, or electrically-heated pillows) used in interventions effective in preventing inadvertent hypothermia?
26. Does the infusion of nutrient solutions reduce the incidence of inadvertent hypothermia in patients with some form of active heating during the intervention?

ASPECTS DERIVED FROM ANÆSTHESIA

27. What pre-surgical interventions are effective at preventing problems derived from anæsthesia?
28. What in-surgery interventions are effective at preventing problems derived from anæsthesia?
29. What patients have a risk of presenting with post-operative nausea and vomiting?
30. What factors are related to reducing the risk of presenting with post-operative nausea and vomiting?
31. What anti-emetic drugs are effective at preventing post-operative nausea and vomiting?

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CPG recommendations

4. Safe interventions in surgery

4.1. Preventing surgical site infections

4.1.1. Pre-operative prevention

Strong	It is recommended that patients take a shower or a bath with soap at least on the night before surgery.
Strong	When it is convenient to shave, it is recommended that this be done on the day of surgery with electric clippers fitted with a single-use head. It is not recommended that blades be used for shaving, because they increase the risk of SSI.
	The patient must be given clothing that is suitable for the operating room, appropriate for the surgical procedure, and that allows access to the surgery site and the positioning of other devices, e.g. intravenous lines.
	All surgical staff must use clothing that is specifically intended for use in an operating room, and do so in all areas where surgery is performed.
	Surgical staff who wear non-sterile clothing should minimise their entries to and exits from the surgical area.
Strong	It is not recommended that nasal decontamination be used with topical antimicrobial agents to eliminate *S. aureus* on a routine basis to reduce the risk of SSI.
Strong	It is not recommended that mechanical preparation of the intestine not be routinely used to prevent SSI.
Strong	Hands should be washed before and after each episode of direct contact with the patient, and after gloves have been removed. Hands that are visibly dirty or potentially contaminated with dirt or organic material should be washed with soap and water. For the sake of convenience and efficiency, if the hands are not visibly dirty, an alcohol-based gel should be preferred. Hands should be washed with soap and water after several successive applications of alcohol-based gel.
	Surgical staff must remove rings, nail polish, and artificial nails before operations.

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4.1.2. Prevention during surgery

	Surgical staff must wash their hands before the first intervention on the list, using an antiseptic surgical solution, with a single-use nail brush. Between operations, hands must be washed using an alcoholic or antiseptic solution.
Strong	It is recommended that self-adhesive surgical fields should not be routinely used, since they can increase the risk of SSI.
	Surgical staff must wear sterile gowns in the operating room during surgery. Surgical clothing must comply strictly with standard EN 13795.
	It is recommended that two pairs of sterile gloves be used when there is a high risk of glove perforation and the consequences of contamination can be serious.
Weak	It is recommended that the skin be prepared in the operating room using chlorhexidine before making the incision. If chlorhexidine is not available, the use of iodised povidone can be considered.
Weak	It is not recommended that diathermia be used in the surgical incision to reduce the risk of SSI.
Weak	It is recommended that adequate perfusion be maintained during surgery.
Strong	It is not recommended that insulin be routinely administered in non-diabetic patients to optimise glycæmia in the post-operative phase to reduce the risk of SSI.
Weak	It is not recommended that the wound be irrigated to reduce the risk of SSI.
Weak	It is not recommended that an additional wash using antibiotics be used to reduce the risk of SSI.
Weak	It is not recommended that the skin be re-disinfected at the end of the operation to reduce the risk of SSI.
	It is recommended that surgical wounds be covered using an appropriate bandage at the end of the operation.

4.1.3. Post-operative prevention

	It is recommended that an aseptic technique be used to change or remove the bandage from the surgical wound.
	It is recommended that sterile saline serum be used to wash the wound in the first 48 hours after surgery. Patients can shower starting 48 hours after surgery.
Weak	It is recommended that antimicrobial agents not be used for surgical wounds that are healing by primary intention to prevent the risk of SSI.

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4.2. Use of antibiotic prophylaxis

4.2.2. Administering antibiotic prophylaxis (selection, duration, dose, and route of administration)

Weak	Antibiotics chosen for prophylaxis must target the pathogens that are expected in the surgery to be performed.
	Legislators working on antibiotics policies must have the experience and information needed to make recommendations on specific regimes of pharmaceuticals, based on evidence, local information on resistance, and costs.
	Narrow-spectrum and cheaper antibiotics must be the first choice for antibiotic prophylaxis in surgery.
	Before high-risk surgery, eradicator treatment should be started in patients who are MRSA carriers.
Weak	Intranasal mupirocin must be used prophylactically in patients undergoing surgery with a high risk of morbidity and who are MRSA carriers.
Strong	Glucopeptides must be considered for antibiotic prophylaxis in patients undergoing high-risk surgery and who are MRSA carriers.
Strong	Endovenous prophylactic antibiotics must be given 30 to 60 minutes before surgical incision.
	A single standard dose of antibiotic is sufficient for prophylaxis in most circumstances, except if surgery that lasts longer than four hours or if loss of blood exceeds 1500 cc.
Weak	It is recommended that a single dose of antibiotic that has an average life that is sufficient to maintain activity during the whole operation be used. However, in the case of arthroplasty, it is recommended that antibiotic prophylaxis be administered for up to 24 hours.
	A further two doses of antibiotics may be needed in the case of lengthy operations (i.e. over four hours in length), or in the case of significant loss of blood (>1500 ml) during surgery.
	Antibiotic prophylaxis for surgery should be administered endovenously.
Weak	In addition to endovenous antibiotics, it is recommended that antibiotic-impregnated cement be used in the fitting of joint prostheses.
Strong	Intracameral antibiotic prophylaxis is recommended in cataract surgery.
Weak	Intravitreous antibiotic prophylaxis is recommended at the end of surgery following eye-penetrating wounds.
Weak	It is not recommended that LCR drainage valves impregnated with antibiotics be used routinely, although they may be considered if local rates of infection are high.

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4.3. Preventing cardiovascular complications in non-cardiac surgery

4.3.2. Coronary revascularistion

Weak	In patients undergoing surgery who need treatment with statins for medical reasons and regardless of the type of surgery, assess the pre-operative use of statins, e.g. patients with a high vascular risk, coronary disease, or high levels of LDL-cholesterol.
Weak	In patients who meet the criteria for treatment with statins, whether for primary or secondary prevention, use the peri-operative period to introduce the treatment.
Strong	In patients undergoing non-cardiac surgery, it is recommended not to use beta-blockers on a routine basis to prevent cardiovascular episodes.
Weak	In patients undergoing non-cardiac surgery, it is in principle not recommended that use be made of alpha-2 agonists to prevent cardiovascular events. For vascular surgery, assess its use on an individual basis.
Weak	In patients undergoing non-cardiac surgery and who are not being treated with acetylsalicylic acid, make a case-by-case assessment of its use in the peri-operative environment in patients with low risk of bleeding and high cardiovascular risk.
Weak	In patients undergoing non-cardiac surgery in treatment with acetylsalicylic acid, it is not recommended that the treatment be withdrawn except in individual situations where the risks outweigh the benefits.
Strong	In patients undergoing vascular surgery, coronary revascularisation is not recommended in patients who are subject to it, before surgery is carried out.

4.3.3. Prevention of arrhythmia

Weak	In patients undergoing non-cardiac surgery, consider the use of calcium antagonists in preventing auricular fibrillation on a case-by-case basis.
Strong	In patients undergoing non-cardiac surgery, it is recommended that beta-blockers should not be used routinely to prevent auricular fibrillation.
Strong	In patients undergoing non-cardiac surgery, it is recommended that digitalis should not be used to prevent auricular fibrillation.
Weak	In patients undergoing non-cardiac surgery, it is recommended that amiodarone, flecainide, and magnesium should not be used to prevent auricular fibrillation.

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4.4. Preventing venous thrombo-embolism

4.4.3. Pharmacological measures in patients receiving routine anticoagulant or anti-aggregating treatment

	An assessment must be made of the risk of thrombotic complications in any patient due to undergo surgery, considering the type of surgery and the characteristics of the patient.
Strong	All patients due to undergo surgery and who will remain in hospital after surgery must receive some effective method of preventing thrombotic complications.
Strong	For all patients who are due to undergo surgery and who will remain in hospital after surgery, it is recommended that compression stockings be used, preferably graduated to the hips or the thighs, if there is no contra-indication.
Weak	Intermittent pneumatic pressure mechanisms are an alternative to pharmacological treatment.
Strong	In patients with certain factors of risk of thrombosis, or who will undergo surgery with a high risk of thrombotic complications, treatment with low-molecular-weight heparin is recommended, in addition to mechanical measures.
Strong	In patients undergoing treatment with low-molecular-weight heparins, it is suggested that treatment be started between two and twelve hours before surgery, and that treatment be maintained for at least one week after discharge from hospital, or for a maximum of 30 days.
	It is advisable to carry out an individual assessment of the dosages of heparins based on surgical risk (for thrombosis and haemorrhaging) and the characteristics of the patient (age, weight, or renal alteration)
Weak	In patients who are due to undergo surgery with a high risk of thrombotic complications, unfractionated heparin, oral anticoagulants, or fondaparinux are alternatives to low-molecular-weight heparin.
Weak	In patients who are due to undergo orthopædic surgery of a lower extremity, an assessment can be made of treatment with dabigatran or rivaroxaban as alternatives to low-molecular-weight heparin.
Weak	In patients undergoing surgery with a very high risk of bleeding (neurosurgery or involving vascular malformations), it is recommended that mechanical measures be used to prevent thrombotic complications.
	The risk-benefit balance of the strategies for preventing thrombotic events must be individualised and based mainly on the clinical history of the patient, pharmacological interactions, type of anæsthesia, risk of thrombosis and bleeding associated with surgery.
Strong	In patients receiving anticoagulant or antiaggregant treatment and who are due to undergo surgery, an assessment of the peri-operative risk of venous thrombo-embolism must be carried out, as well as of the risk of maintaining treatment for certain specific procedures.
Strong	In patients from whom it is decided to withdraw anticoagulant treatment, this must be done five days before surgery in the case of warfarin and two or three days before surgery in the case of acenocoumarol.

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Weak	If the INR remains high, between 1 and 2 mg of oral vitamin K can be administered on the day of surgery.
Weak	In patients with indication of treatment using anticoagulant and high or medium risk of thrombo-embolism in the peri-operative period, substitution treatment should be carried out with therapeutic doses of low-molecular-weight heparin administered subcutaneously.
Strong	In patients with indication of anticoagulant treatment and low risk of thrombo-embolism in the peri-operative period, either low doses of low-molecular-weight heparin should be administered subcutaneously, or nothing at all.
Strong	In patients receiving antiaggregant treatment, who have not had stents fitted recently, and who have a low risk of thrombo-embolism in the peri-operative period, treatment should be withdrawn before surgery.
Weak	In-patients receiving antiaggregant treatment and who have not recently been fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for non-cardiac surgery or percutaneous coronary intervention, treatment with aspirin must be continued before and after surgery.
Weak	In patients receiving antiaggregant treatment and who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative stage, and who have been scheduled for non-cardiac surgery, treatment with clopidogrel should be stopped at least five days in the ten days preceding surgery.
Strong	In patients receiving antiaggregant treatment and who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for a coronary bypass, treatment with aspiring should be continued before and after surgery. If that treatment is stopped, it should be restarted between 6 and 48 hours after surgery.
Strong	In patients receiving antiaggregant treatment, who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for coronary bypass surgery, treatment with clopidogrel should be stopped at least five days in the ten days before surgery.
Weak	In patients receiving antiaggregant treatment, who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for percutaneous coronary intervention, clopidogrel should be re-started with a load of between 300 and 600 mg.
Strong	In patients receiving antiaggregant treatment, who have a metallic coronary stent, and who need surgery in the six weeks after the stent was fitted, treatment with aspirin or clopidogrel should be continued in the peri-operative period.
Strong	In patients receiving antiaggregant treatment, who have been fitted with a drug-releasing coronary stent, and who need surgery within twelve months of the stent being fitted, antiaggregant treatment must be continued in the peri-operative period.

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4.5. Aspects derived from blood transfusion

4.5.6. Orthopædic surgery

Weak	Given the potential risks, each allogenic transfusion should have a valid, defined, and justifiable indication, which must appear in the clinical history.
Weak	The transfusion of leuco-depleted allogenic blood should not be limited by doubts over the increase in the recurrence of cancer or peri-operative infection.
	In a patient who is hæmodynamically stable, one unit of erythrocyte concentrate should be transfused once only, with a re-evaluation at 24 hours.
Strong	At the time of transfusion, it is essential to check the match between the patient's details and those contained in the request for the blood components to be transfused.
	A transfusion threshold should be defined as part of an overall strategy for optimum patient treatment.
	All patients undergoing major elective surgery must have a hæmogram before surgery, to avoid cancellations in the short term and to allow the appropriate treatment of anæmia.
Weak	Anæmia must be treated before major surgery to reduce exposure to allogenic transfusion.
Weak	In the post-operative period, a transfusion is required if hæmoglobin is s <70 g/l or <90 g/l in patients with cardiovascular disease.
Weak	All hospitals should use a programme for requesting blood so they can supply erythrocyte concentrates.
	For all patients undergoing surgery with major loss of blood, and who have signed a transfusion consent form, there must be a minimum supply of blood of their group in the blood bank.
Strong	Pre-operative autologous blood donation can be used to reduce exposure to allogenic blood, although it increases the total number of transfusions.
Weak	Pre-operative autologous blood donation must be aimed at men who present with Hb of between 110 and 145 g/l, and women who present with Hb of between 130 and 145 g/l.
Strong	Erythropoietin must be administered to patients under the age of 70 who are scheduled for surgery with major loss of blood and with Hb <130 g/l.
Strong	In healthy patients undergoing elective major surgery, erythropoietin can be used in combination with the autologous blood donation or to obtain multiple donations of erythrocytes and maintain adequate Hb on the day of surgery.
Weak	Acute normovolemic hæmodilution must be limited to patients with Hb levels that are sufficiently high to allow the extraction of 1000 ml of blood.
Strong	It is recommended that tranexamic acid be used in patients undergoing elective cardiac surgery with high risk of transfusion.

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Strong	Tranexamic acid can be used to reduce blood loss and transfusion requirements in patients scheduled for knee-prosthesis surgery, when other blood-conservation techniques are inappropriate and major loss of blood is foreseen.
Weak	The re-infusion of blood recovered from the mediastinal drain, drawn out, and washed can be used for reducing allogenic transfusion in cardiac surgery.
Weak	In orthopædic surgery, the recovery of unwashed cells using drains must be considered in patients expected to suffer an estimated post-operative blood loss of between 750 and 1500 ml.
Strong	In orthopædic surgery, the recovery of unwashed cells using drains must be considered in patients expected to suffer a predicted post-operative blood loss of between 750 and 1500 ml.

4.6. Maintaining normothermia

4.6.6 Pharmacological agents for preventing hypothermia

Recommendations – Maintaining normothermia in the pre-operative phase	
	An assessment should be made of the risk of hypothermia for each patient before surgery. Healthcare professionals must ensure that patients are not cold before going into the operating room. They should be covered with blankets or a comforter, especially if they have received medication.
Weak	Body temperature should be 36ºC or higher when the patient is taken to the operating theatre. If body temperature is <36ºC, warming using forced air should start before the patient is taken to the operating room, and should be maintained intraoperatively.
Recommendations – Maintaining normothermia during the operation	
	The patient's temperature should be taken and recorded before anæsthetic induction and every 30 minutes until the end of surgery.
	Anæsthetic induction should not be started until the patient's temperature is ≥36ºC.
	The patient must be adequately covered during the intervention in order to conserve heat.
Weak	Patients at risk of hypothermia and who are given anæsthetic < 30 minutes must be warmed during the operation using a forced-air device.
Weak	All patients given anæsthesia > 30 minutes must be warmed from anæsthetic induction using a forced-air warming device.
	The temperature of the convective hot air devices must be set to maximum and then adjusted to maintain a minimum temperature in the patient of 36.5ºC.
	Endovenous liquids for irrigation must be warmed to a temperature of 38ºC-40ºC.
Recommendations – Maintaining normothermia in the post-operative phase	
	Erythropoietin must be administered to patients under the age of 70 who are scheduled for surgery with major loss of blood and with Hb <130 g/l.
	If the patient's temperature is less than 36ºC, convective hot air should be started until the patient is discharged from the reanimation area or feels comfortable.

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4.7. Aspects derived from anæsthesia

4.7.2 Preventing nausea and vomiting

Strong	Identify risk factors associated with PONV in each patient who is due to undergo surgery.
Strong	Prophylaxis using antiemetics should be considered in patients with a moderate to high risk of presenting with PONV.
Weak	If patients are allowed to choose on anæsthesia, they must be advised that the risk of PONV decreases with the use of regional rather than general anæsthesia.
Weak	Regional anæsthesia should be considered in patients with high risk of presenting PONV. If general anæsthesia is used, risk factors should be reduced whenever possible.
Weak	The use of opioids should be minimised in interventions. Professionals should evaluate the balance between risks and benefits of administering opioids in relation to the risk of PONV.
Strong	The prevention of PONV through the administration of dexamethasone, ondansetron, or droperidol should be taken into consideration.
Weak	Patients with high risk of presenting with PONV should receive combination therapy for preventing PONV.

4.7.3. Implications of the World Health Organisation check list

Strong	The "Surgical Safety Checklist" must be implemented in all surgical procedures to improve the safety of surgical interventions and to reduce avoidable complications.

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1. Introduction

1.1. Magnitude of the problem

A recent study highlights the fact that each year, one in every 25 persons undergoes an operation (Weiser 2008). This study estimated that 2004 saw a global volume of between 187 and 281 million cases of major surgery, a figure that in Spain stood at some three million procedures, equivalent to a rate of 7027 surgical interventions for every 100000 people.

About 16% of those surgical procedures lead to complications relating to the morbidity of the patients or to adverse events, with serious consequences in nearly 1% of cases. Along the same lines, a systematic review of the incidence of adverse events related to hospital care showed that almost 40% of adverse events identified in the various studies on the topic were directly related to surgical procedures (de Vries 2008). Those data appear to show that each year, up to seven million patients appear to suffer a serious complication during or immediately after surgery, with death occurring in one million cases (Weiser 2008).

In Spain, the *Estudio Nacional sobre los Efectos Adversos ligados a la Hospitalización* (National Study on Adverse Effects linked to Hospitalisation) (ENEAS 2006, Aranaz 2008) has shown a very similar incidence of adverse events between medical and surgical services (8.86% versus 8.07%). The data gathered in the ENEAS study showed a level of incidence of adverse events in general surgical services of 10.5% (Aranaz 2007) and 3% in ambulatory major surgery services (Aranaz 2008b). Of the adverse events identified in the study, 36% were assessed as being avoidable.

The fact that the majority of studies that estimate the level of adverse events arising from surgery agree that between one third and one half of those complications are avoidable (Kable 2002, Baker 2004, de Vries 2008) shows up the extent to which surgical safety must be a priority topic for public health. Given that surgical patients are more inclined to develop adverse events, this highlights the need to apply measures aimed at prevention, amongst which some authors have included the use of clinical practice guidelines to clinical practice (CPG), clinical pathways, and protocols (Aranaz 2008b).

The interest in standardising procedures associated with peri-operative care is not new (SIGN 2004), but the aforementioned epidemiological data have led to reaction and coordination on a worldwide scale to improve peri-operative safety, ensuring compliance with practices supported by scientific literature (World Alliance for Patient Safety 2008).

Given this context, justification is provided for developing a CPG that sets out the results of scientific research that evaluates a series of practices that are common in peri-operative care.

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2. Scope and objectives

This Clinical Practice Guideline(CPG) brings together recommendations on interventions to avoid complications and adverse events in patients undergoing surgery. For the definition of surgery this Guide has followed internationally-accepted criteria, taking surgery to be an intervention carried out in an operating room and that involves incision, excision, manipulation, or suturing of tissue, and that generally requires some form of anæsthesia (local, local-regional, sedative, and / or general) and analgæsia to manage pain arising from the intervention. The target population of this Guide includes any adult who is due to undergo surgery, excluding emergency surgical procedures. Recommendations included in the CPG include the most common clinical situations.

The target audience is all healthcare professionals who carry out their activities in an operating room, mainly surgeons, anæsthetists, and nursing staff, all of whom are involved in the post-operative care of patients undergoing surgery.

This Guide covers questions relating to interventions in order to reduce, in the entire peri-operative process, morbidity and mortality associated with surgical procedures, or strategies aimed at improving surgical safety and reduce avoidable adverse events.

The Guide does not contain any recommendations concerning the organisation of health services and teams; recommendations are directed at the clinical aspects of the peri-operative process. Some of the aspects covered in this Guide can be consulted in other, similar documents which, due to their high level of methodological rigour and clear presentation, have been listed in **Appendix 5**.

2.1. Objectives

The "Clinical Practice Guidelinefor the Safety of the Surgical Patient" brings together recommendations based on the results of scientific literature to encourage the use of interventions and strategies with the aim of reducing complications in surgery. On those points for which there is insufficient literature on which to make recommendations, some points of best practice have been set out.

The intention of this GPC is to offer recommendations that enable improving or avoiding adverse events in surgery, and fostering a culture of surgical safety. This is achieved by covering very common aspects in the peri-operative process with a special emphasis on preventing complications. In this way, the Guide deals with the prevention of infections of surgical wounds, the use of antibiotic prophylaxis, and the prevention of cardiovascular adverse events and of thromboembolic disease. There is also a discussion of aspects related to blood transfusion, maintaining normothermia, and some aspects related to anæsthesia.

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3. Methodology

The methodology used is set out in detail in the *Servicio Nacional de Salud* Methodological Manual for drawing up Clinical Practice Guidelines (2007 CPG Working Group). The *GuiaSalud* web site (www.guiasalud.es) contains material that sets out the information in detail, together with the methodological process followed in drawing up the CPG.

The steps followed are:

Constituting the guide preparation group

This is made up of professionals contacted through the various Scientific Societies that relate to the topic of the Guide.

The Working Group was made up of physicians specialising in anæsthesiology and reanimation, preventive medicine and preventive health, general surgery, thoracic surgery, digestive surgery, bariatric and œsophago-gastric surgery, as well as surgical nurses and healthcare-quality co-ordinators.

Users and patients were not include in the Working Group for this Clinical Practice Guideline (GPC).

Formulating clinical questions

An initial meeting with members of the Working Group defined the clinical questions to needed to be answered by the Guide. All the questions follow the PICO format: Patient, Intervention, Comparison, and Outcome or result variable.

Bibliographic search

Give the scope of the topics cove red by the Guide, a search of other CPGs that provided similar coverage of the topics defined was carried out. To this end, CPGs were identified in the following resources:

- TRIP database
- Clinical Excellence
- NHS National Library of Guidelines
- AHRQ National Guideline Clearinghouse

Likewise, a search the web pages of the main international producers of CPGs (NICE, SIGN, NHMRC) and relevant Scientific Societies in the field of interest (e.g. American Heart Association, Hospital Infection Society) was carried out.

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Each of the CPGs identified was evaluated using the AGREE tool (AGREE Collaboration 2003) in order to assess the possible adaptation of its recommendations (Etxeberría 2005). The main systematic revisions on which their recommendations were based were checked.

Systematic reviews and reports on health technologies published after the date of the search for the CPGs were also identified. This stage included a consultation of the following electronic databases:

- Cochrane Database of Systematic Reviews (The Cochrane Library) – Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment (HTA) Database
- NHS Economic Evaluation Database (NHS EED)
- MEDLINE (accessed through PubMed)
- EMBASE (accessed through Ovid)

A second phase included a wider search of individual studies to update the systematic reviews relevant to answer the various questions of the CPG. Primarily, there was an attempt to identify randomised clinical trials (RCTs) and observational studies. Wherever possible, the original search strategy for the relevant systematic revisions was respected. When they were not available, specific strategies were designed for each of the questions; validated filters were added in each case in order to identify RCTs or observational studies. This phase included a search of the following electronic databases: The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library), MEDLINE, and EMBASE (accessed through Ovid).

There were no language limits set upon the searches carried out, but most studies were in Spanish, English, and French. Searches were carried out until December 2008, although relevant studies were identified in the biomedical publications of greatest impact during the entire process of preparation of the CPG.

Formulating recommendations using the GRADE system

As part of the process of formulating recommendations, the Working group must ask itself to what point there is confidence that following a recommendation will bring more benefits than damages. This decision is not a simple one, and it is influenced by multiple factors that turn this stage into one of the most complex in the process of preparing a guide.

For most of the topics covered in this Guide, the first phase of the search included the identification of other good-quality CPGs. They were used to draw up evidence summaries for the various questions posed. These summaries were updated when the reference CPGs were of outdated, with an evaluation of the quality of studies considered to be relevant, in a process of adaptation (Etxeberría 2005).

This Guide followed the guidelines of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) working group to classify the quality of evidence and rate the strength of recommendations. It is considered that GRADE offers some advantages over the rest of the systems available to formulate recommendations, given that it sets out an easy-to-use methodology that aims at being transparent and explicit in its process. Furthermore, it GRADE overcomes the shortcomings of other systems for formulating recommendations since,

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for example, it does not base the classification of the quality of evidence solely on the design of the studies considered (Schunemann 2006, Guyatt 2008a, Guyatt 2008b). The main stages in developing the GRADE system are:

a) Classification of the relative importance of the variables of the result

In this stage, it is recommended that the Working Group set out explicitly the result variables that are of interest for the questions, and classify their relative importance. This process must be determined by consensus at the initial stage of formulating the clinical questions. Variables are ranked in importance according to the following nine-point scale:

- 1 to 3: result variables that are not important for decision-making and that do not play an important role in formulating recommendations.
- 4 to 6: result variables that are important, but do not have a key role in decision-making.
- 7 to 9: result variables that have a key role in decision-making.

b) Evaluating the quality of scientific evidence

When evaluating scientific literature for a CPG, the degree of validity of the results must be considered. This can be done based on a series of aspects that determine the degree of confidence of the estimate of the effect of the intervention in the studies.

The GRADE system sets out a series of factors that can lessen the quality of clinical trials (that are considered to be of high quality), and other factors that can increase the quality of observational studies (that are considered to be of low quality). The quality of evidence is classified for each variable of interest, and is rated as high, moderate, low, or very low (**Appendix 1**). The aspects that can reduce the quality of an RCT are:

Limitations on design and execution: Lack of concealment of the randomising sequence, inadequate masking, significant losses, a lack of analysis by intention to treat, finalising the study ahead of time for reasons of benefit, among others.

Inconsistent results: very different estimates of the effect of a treatment in the available studies suggest real differences between those estimates. The differences can be due to differences in population, intervention, result variables, or quality of the studies. Heterogeneity that is not explained in a reasonable manner reduces the level of confidence in the results of a study.

Lack of direct scientific evidence: occasionally, there is a lack of direct comparisons between two types of treatment (comparing treatments with a placebo, but not comparing them with each other). At other times, the results of a study with a specific medication are extrapolated to other medications of the same family, in the absence of a demonstrated class effect. Frequently, there are significant differences between the population to which the recommendations will be applied and the population included in the studies evaluated. Finally, an assessment must also be made of the aspects of the potential applicability in a given environment, or the external validity of the scientific evidence available.

Imprecision: when the studies available include relatively few events and few patients, and, therefore, wide confidence intervals, the scientific evidence can be considered to be of lesser quality.

Publication bias: quality and confidence of evidence can be diminished if there is reasonable doubt as to whether the authors have or have not included all the studies (e.g. publication bias in the context of a systematic review), or if the authors have or have not included all the relevant result variables (reporting bias).

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On the other hand, the aspects that may increase the quality of observational studies are:

Significant magnitude of effect: it is improbable that observed effects that show a consistent and strong (RR >2 or <0.5) or very strong (RR >5 or <0.2) association based on studies without any confusion factors are due solely to the weakest design of the study. In such cases, the quality can be considered to be moderate or even high.

The presence of a *dose-response gradient*.

Situations in which all *the possible confusion factors may have reduced the association observed*. In cases where patients receiving the intervention of interest have a worse prognosis, and yet present better results than the control group, it is probable that the real observed effect is greater.

c) Grading the strength of recommendations

The GRADE system offers a simple system for grading the strength of recommendations as *strong* or *weak*. A strong recommendation is made *in favour* of an intervention when there is confidence that the beneficial effects of an intervention outweigh the risks. It can also be *strongly against*, where the harm outweighs the advantages. *Weak* recommendations, whether for or against an intervention, are made when there is no conclusive proof of the effects of an intervention. In the process of grading the strength of the recommendations, the following factors were taken into account (**Appendix 1**):

Balance between benefits and risks: in order to carry out an adequate assessment of the balance between benefits and risks, it is necessary to take into account the basal risk of the population at which the recommendation is aimed, and the effect in both relative and absolute terms.

Quality of scientific evidence: before carrying through a recommendation, it is necessary to know the degree of certainty of the estimate of the effect observed. If the quality of the scientific evidence is not high, even if the magnitude is significant, the confidence level, and thus the strength of a recommendation, should be reduced.

Values and preferences: uncertainty concerning the values and preferences of the target population at which the Guide is aimed is a factor that must be taken into account. The values and preferences of healthcare staff, patients, and society in general must be reflected in the grading of recommendations.

Costs: unlike other result variables, costs are much more variable over time, in various geographical areas, and based on various types of involvement. Thus, although a high cost reduces the probability of a recommendation being graded as strong, context is essential for the final assessment.

Finally, the Guide is intended for a type of recommendations in cases where, in spite of not having conclusive scientific proof, putting those recommendations into practice is considered to be a form of best practice. Such recommendations are identified with the following mark: .

External revision

Member of the Drafting Group suggested a multidisciplinary group of external revisers made up of professionals with experience in the field of quality of assistance and the field of surgery, which appears in the section entitled "Authorship and partnerships". The final version of the text of the guide was revised and approved by the group of authors.

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Updating

The scientific literature available recommends updating the recommendations of the CPG every three years (Shekelle 2001, CPG update working group 2008). This period of time has been taken as a reference for this Guide. Where necessary, the electronic version of the guide will be updated more frequently.

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4. Safe Interventions in Surgery

4.1. Preventing surgical site infections

Question to be answered

- What are the main measures for reducing the risk of post-operative infection?
- What is the effectiveness of irrigating wounds as a measure to reduce the risk of surgical site infections?
- Is the administration of additional oxygen effective in reducing the incidence of surgical site infections?
- What are the best methods of closing wounds so as to encourage healing?

4.1.1. Pre-operative prevention

4.1.1.1. Pre-operative shower

When an incision is performed on the skin, microorganisms that colonise the surface can contaminate the exposed tissues, proliferate, and cause a surgical site infection (SSI). Thus, interventions that reduce the number of skin microorganisms around the incision can reduce the risk of SSI. This section reviews the effectiveness of the pre-operative bath or shower using antiseptics to prevent SSI.

A systematic review (SR) was identified (six RCTs, 10 007 participants), in which the primary result variable was the incidence of SSI, although the definitions of the same differed between the studies (Webster 07). The only antiseptic used was chlorhexidine. Meta-analysis of five RCTs (8445 participants) showed that there are no statistically significant differences in the incidence of SQI between the groups who showered with clorhexidine or with soap or detergent (RR 0.90; 95% CI: 0.79 to 1.02).

High quality

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4.1.1.2. Shaving

Shaving can be necessary to allow adequate access to the surgical incision site. However, small micro-abrasions created on the skin by using a blade can encourage bacterial growth, leading to contamination of the wound and the subsequent development of SSI. This section reviews the effectiveness of shaving the intervention site in order to prevent SSI.

A SR (eleven RCTs, 4627 participants) examined the evidence of pre-operative shaving to prevent SSI (Tanner 06). Methods for hair removal included the use of a blade, clipping, and the use of a depilatory cream. A subsequent RCT compared the effect of using a blade with not shaving in spinal surgery (Celik 07) and there were no statistically significant differences between the two groups. Meta-analysis of two studies of the SR showed no statistically significant differences in the incidence of SSI using blades or not shaving (RR 1.82; 95% CI: 0.93 to 3.59). High quality

One of the RCTs of the SR compared the incidence of SSI in two groups randomly allocated to either remove hair using a depilatory cream or no hair removal. There were no statistically significant differences between the two groups. No study compared the use of a clipper against no hair removal.

Three RCTs (3193 participants) compared the effects of using blades or clippers on the incidence of SSI: 2.8% (46/1627) of people who were shaved using blades developed SSI compared with 1.3% (21/1566) who were shaved using clippers (RR 2.02; 95% CI: 1.21 to 3.36).

Seven RCTs of the SR (1213 participants) compared the relative effects of using blades or depilatory creams to remove hair. Meta-analysis showed higher SSI (with statistically significant differences) in people who were shaved (65/670) compared with those who used a depilatory cream (38/ 543) (RR 1.54; 95% CI: 1.05 to 2.24).

No studies were identified that compared the use of clippers with a depilatory cream.

The same SR (eleven RCTs, 4627 participants) examined the evidence relating to the time of pre-operative shaving in order to prevent SSI (Tanner 06). One of the RCTs included compared shaving the night before surgery with shaving on the day of surgery. There were no no statistically significant differences between groups with respect to incidence of SSI, measured 15 days and 30 days after the interventions, or with respect to the the use of blades or clippers.

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4.1.1.3. Surgical clothing for the patient

It is traditional for patients to put on clean clothes before being taken to the operating room. The risk of infection from airborne transmission of microorganisms from clean clothing is unlikely to be high. Compared with the surgical team, the movement of patients during interventions is very limited, thus reducing the dispersal of microorganisms from the skin and from clothing.

No RCT was identified that examined surgical clothing for patients and the rates of post-operative SSI.

4.1.1.4. Clothing for surgical staff

Surgical staff usually put on clean rather than sterile surgical clothing before an operation. The clothing is usually changed only if it becomes dirty from blood or other body fluids. This section reviews the clinical effectiveness of the use of non-sterile surgical clothing (surgical scrubs, masks, caps, overshoes) in preventing SSI.

The use of masks that cover the mouth and nose, caps that cover the hair, sterile surgical clothing, and sterile and waterproof gloves are standard practices amongst surgical staff. Some elements correspond to basic principles of aseptic techniques, and their use is based on laboratory studies, microbiological studies, or common sense. However, the scientific evidence concerning their impact on preventing infection of surgical wounds has not been evaluated or is the subject of debate (WHO 2009). High quality

No studies were identified that evaluated the use of surgical scrubs, caps, or overshoes.

The use of masks significantly reduces contamination of the surgical area, but there is no clear association between the use of masks and surgical infection (Alwitry 2002, McLure 1988). An SR (1453 patients) that included two quasi-randomised studies (Lipp 02, Lipp 05), compared the effectiveness of using disposable masks against not using them in preventing post-operative SSI. Evidence exists to show that the use of masks offers protection against splashes of blood or other body fluids from patients during surgery, but their use in preventing the transmission of microorganisms is not clear (Aisien 2006, Collins 2000, Sharma 2003).

One of the studies included in the SR (Lipp 02, Lipp 05) included 3088 patients who underwent breast, vascular, or acute surgery. Data were presented on 1429 patients who underwent clean surgery: 13/706 (1.8%) of the SSIs occurred in the masked group, and 10/723 (1.4%) in the unmasked group (the differences are not statistically significant). When the results for elective surgery (clean and dirty) were combined (2394 participants), the difference in incidence of SSI between the two groups was not significant.

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The other SR study, with 41 patients who underwent gynæcological surgery, was suspended because 30% of SSI cases occurred in the unmasked group, although it could not be proven that infection was caused by the absence of masks. There were no SSIs in the masked group, but the difference between groups was not statistically significant.

4.1.1.5. Entry and exit of surgical staff

Surgical staff usually change from surgical clothing to conventional clothing when they leave the operating room, and change back into clean surgical clothing when they enter the operating room.

No studies have been identified that examine the effect of entries and exits of surgical staff on the incidence of SSI.

4.1.1.6. Nasal decontamination

The nasal area is the main breeding reservoir for *Staphylococcus aureus* in the body. This microorganism is the commonest cause of SSI in all types of surgery, with patients themselves often being carriers. Various measures were looked at with the aim of eliminating *S. aureus* from the nasal area before surgery; those measures were evaluated to see if they reduced SSI. The measures involved the use of topical antiseptics or antibiotics against *S. aureus*.

Five RCTs were identified that examined the effects of nasal decontamination in preventing SSI (Kalmeijer 02, Perl 02, Konvalinka 06, Suzuki 03, Segers 06). High quality

Two RCTs (4478 participants) showed no statistically significant differences in the incidence of SSI after decontamination using mupirocin or placebo (Kalmeijer 02, Perl 02).

Two RCTs (Perl 02, Konvalinka 06) evaluated the effectiveness of mupirocin versus placebo only in patients who were carriers of *S. aureus*. Heterogeneity between the studies did not enable a meta-analysis, and the individual results with respect to the incidence of SSI were not statistically significant in any study.

One RCT (395 participants) compared the incidence of SSI after nasal decontamination with mupirocin against no nasal decontamination, in patients who underwent abdominal surgery (Suzuki 03). There were no statistically significant differences in the rates of SSI between the two groups.

Another RCT (954 participants) compared the effect of chlorhexidine with a placebo, and found no statistically significant differences in the rates of SSI between the groups.

No RCT was identified that compared various times for carrying out nasal decontamination to prevent SSI.

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4.1.1.7. Mechanical preparation of the intestine

Most SSI is acquired intra-operatively from the bacterial flora that colonise the patient's skin, gastro-intestinal tract, and mucous membranes. Currently, the best method for preventing SSI after colorectal surgery is a matter of debate. Traditional surgical practice suggests that the elimination of fæcal matter from the colon and the rectum before elective colorectal surgery provided an advantage, and the mechanical preparation of the intestine has become a fundament al component of intestinal surgery. Mechanical preparation of the intestine has been considered to be an advantage for several reasons, including the time taken for the operation, ease of manipulating the intestine, rate of stoma formation, and the ability to palpate lesions on the intestinal wall.

12 RCTs (5383 participants) were identified that evaluated the effectiveness of mechanical preparation of the intestine in preventing SSI in patients who underwent colorectal surgery: nine RCTs (1592 participants) were obtained from one SR (Guenaga 05), while the remaining three (Jung 07, Pena-Soria 07, Contant 08) were not part of any SR. There were no significant differences in the incidence of SSI between the treatment groups and the control groups of the nine RCTs included in the SR. — High quality

4.1.1.8. General hand hygiene

The commonest way through which microorganisms are transferred to patients are the hands of staff members. Pathogens are frequently acquired through the hands by contact with patients and their environment. In order to prevent infections, such contacts must be eliminated, especially before contact with vulnerable sites such as wounds, or with invasive instruments. Microorganisms acquired by contact can be SSIfly eliminated using soap and water as well as alcohol-based gels, although alcohol should not be used when hands are visibly dirty.

A CPG on the infections associated with healthcare (Pratt 07) established a series of recommendations on hand washing, from preparation at the preoperative stage to the time of patient discharge (those recommendations can be consulted at the end of the section). The difficulties (including ethical ones) of adequately designing clinical trials to evaluate the impact of hand hygiene mean that some of those recommendations are based on the results of non-randomised studies or quasi-experimental studies. However, the beneficial effects of hand washing are beyond dispute, which justifies strong recommendations in the matter. — Moderate quality

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4.1.1.9. Rings, artificial nails, and nail polish

The usual practice is for surgical staff not to wear rings during surgical procedures. However, some people do not agree with not wearing wedding rings, nail polish, or nail extensions.

One SR (one RCT, 102 participants) evaluated the effect of having surgical staff remove rings and nail polish on the rates of post-operative SSI (Arrowsmith 01). This SR did not show any statistically significant differences in the bacterial load of nails before or after surgical washing (measured using the number of colony-forming units). As there is insufficient evidence to establish a direct association between the number of colony-forming units and SSI, the SR could not determine if removing nail polish or rings may have an effect on SSI.

High quality

Summary of the evidence – Pre-operative prevention

High quality	A pre-operative shower with chlorhexidine is as effective as a shower with soap in preventing SSI (Webster 07). This should be done at least on the night before the intervention.
High quality	There is no difference in the incidence of SSI between pre-operative shaving (using a depilatory cream or blades) and not shaving (Tanner 06, Celik 07). Less SSIs occur after clipping or using a depilatory cream than after using a blade. There is insufficient evidence to determine if the timing of pre-operative shaving using a blade or clippers affects the incidence of SSI. It is proposed that shaving be done on the day of the intervention. There is a risk of coetaneous reactions when using depilatory creams. The use of a blade is associated with increased SSI, more so than any other shaving method.
	There is no information relating to the clothing that patients must use when going to the operating room.
	There is no information concerning the use of surgical scrubs, caps, or overshoes to prevent SSI.
Moderate quality	Two quasi-randomised studies show that there is no difference in the rate of SSI when using masks during clean or dirty surgery (Lipp 02).
	No information is available on the effect of entry and exit of surgical staff and clothe changing on the incidence of SSI.

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High quality	There is evidence to shows that nasal decontamination with mupirocin (Kalmeijer 02, Perl 02, Suzuki 03) or chlorhexidine (Segers 06) administered to all patients who undergo surgery does not affect the overall rate of SSI. Nasal decontamination with mupirocin applied to all bearers of *S. aureus* who undergo surgery does not reduce the incidence of SSI caused by *S. aureus*, or the incidence of SSI due to any cause (Perl 02, Konvalinka 06). No information is available on the right time to perform nasal decontamination.
High quality	In patients undergoing colorectal surgery, there is no difference in the rate of incidence of SSI between those who receive mechanical preparation of the intestine versus those who do not receive such preparation (Guenaga 05, Jung 07, Pena-Soria 07, Contant 08).
High quality	There is insufficient information to determine if the removal or non-removal of nail polish, rings, or nail extensions have an effect on the rate of SSI (Arrowsmith 01).

Recommendations – Pre-operative prevention

Strong	It is recommended that patients take a shower or a bath with soap at least on the night before surgery.
Strong	When it is convenient to shave, it is recommended that this be done on the day of surgery with electric clippers fitted with a single-use head. It is not recommended that blades be used for shaving, because they increase the risk of SSI.
	The patient must be given clothing that is suitable for the operating room, appropriate for the surgical procedure, and that allows access to the surgery site and the positioning of other devices, e.g. intravenous lines.
	All surgical staff must use clothing that is specifically intended for use in an operating room, and do so in all areas where surgery is performed.
	Surgical staff who wear non-sterile clothing should minimise their entries to and exits from the surgical area.
Strong	It is not recommended that nasal decontamination be used with topical antimicrobial agents to eliminate *S. aureus* on a routine basis to reduce the risk of SSI.
Strong	It is not recommended that mechanical preparation of the intestine not be routinely used to prevent SSI.
Strong	Hands should be washed before and after each episode of direct contact with the patient, and after gloves have been removed. Hands that are visibly dirty or potentially contaminated with dirt or organic material should be washed with soap and water. For the sake of convenience and efficiency, if the hands are not visibly dirty, an alcohol-based gel should be preferred. Hands should be washed with soap and water after several successive applications of alcohol-based gel.
	Surgical staff must remove rings, nail polish, and artificial nails before operations.

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4.1.2. Prevention during surgery

4.1.2.1. Surgical cleaning of hands

Hands must be decontaminated before surgery, so as to minimise the risk that the flora that normally colonise the skin, or microorganisms acquired by contact, may contaminate the surgical wound. Transitory microorganisms are easily eliminated using soap and water, but antiseptics like alcohol or detergent solutions like chlorhexidine or iodised povidone are needed to eliminate microorganisms that live in hair follicles and in cracks in the skin. Surgical staff must decontaminate their hands several times a day, but without damaging the skin.

An RCT was identified (4823 participants) that evaluated the incidence of SSI by comparing the surgical brushing of hands with an 75% aqueous alcohol solution, or with 4% iodised povidone, all used before surgery (Parienti 02). No significant differences were observed between the two decontamination techniques in the prevention of SSI. High quality

4.1.2.2. Self-adhesive surgical fields – incision cuts

Self-adhesive surgical fields are fine adhesive films used to cover the skin at the site of the incision, in order to minimise contamination of the surgical wound by microorganisms that colonise the skin around the wound.

One SR (Webster 07) and one RCT (Alexander 85) that evaluated the effectiveness of self-adhesive surgical fields to prevent SSI were identified. Meta-analysis of the five RCTs included in the SR showed a higher incidence of SSI in the group with self-adhesive surgical field than in the group without self-adhesive surgical field (RR 1,23; IC 95% 1,02 to 1,48). High quality

The RCT (Alexander 85) did not show significant effects, nor did it elicit substantial changes when the previous meta-analysis was added.

Meta-analysis with all the RCTs showed a statistically significant difference in favour of not using self-adhesive surgical fields (RR 1.20; 95% CI: 1.02 to 1.43).

4.1.2.3. The use of sterile gowns

No studies were identified that evaluated the effectiveness of using sterile gowns to prevent SSI.

4.1.2.4. Single-use or reusable operating room linen (sheets, cloths, towels, and gowns)

Operating room linen acts as a barrier between the surgical field and potential sources of microorganisms that exist in the environment, the patient's skin, and the members of staff involved in the intervention. It also has an additional function of protecting the surgeon from exposure to blood or other body fluids.

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Two RCTs (1001 patients) that compared the use of single-use towels and gowns against reusable towels and gowns on the incidence of SSI found no significant differences between groups (Garibaldi 86, Bellchambers 99). High quality

The origin of microorganisms that could give rise to SSI can be internal, but external sources (the environment, members of staff, or the patient) are also important. Surgical clothing (gowns, cloths, and clean-air suits) aim to avoid the risk of transmission of microorganisms from the surgical team to the surgical wound, and should meet minimum quality requirements that guarantee such a barrier.

European Standard 13795, drawn up by the European Committee for Standardisation CEN/TC 205 (EN 13795-1:2002) under the title "Cloths, gowns, and clean-air suits for surgical use as sanitary products for patients, clinical staff, and equipment" is available to all healthcare professionals. It aims to homogenise the processes of evaluating and selecting surgical clothing, and offer guidance on the requirements that must be met by these sanitary products.

The Standard establishes some minimum criteria regarding information that manufacturers should provide to know how they have tested their products and their main characteristics: i) information about the safe reuse of reusable sterile products; ii) information about the sterilisation of non-sterilised products supplied; iii) identification of possible critical areas of the product. Low quality

The Standard determines that surgical clothing must meet the following criteria to contribute to the reduction of SSI:

- resistance to microbial penetration: surgical must create a sterile field around the surgical field so as to avoid contamination, and whether wet or dry, it must show a low penetration of colony-forming organisms;
- cleanliness: surgical clothing should have a low bacterial load before sterilisation, and contain very little particulate material that could come away from the product;
- low particle shedding or loosening of fibres during handling;
- resistance to liquid penetration: by water-proofing the product or by chemical treatment to improve fabric tension;
- resistance to breaking, whether wet or dry;
- resistance to traction, whether wet or dry
- in addition, cloths must adhesive in order to insulate the skin.

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4.1.2.5. Gloves

Gloves are currently made of latex; they are single-use, sterile, and disposable. Other varieties exist for people who have an allergy to latex. The use of gloves is part of the ritual of aseptic surgery in order to reduce the risk of introducing infection. Gloves protect the hands of surgical staff, and also offer protection against viral transmission (hepatitis and HIV) from the patient's body fluids during surgery. It has also been suggested that the use of two pairs of gloves reduces the risk of perforation, thus reducing the risk of the surgical wound possibly being contaminated by microorganisms from the surgeon's skin.

No studies were identified that investigated the use of two pairs of gloves in comparison with one pair regarding the prevention of SSI. — Moderate quality

Two RCTs examined the correlation between various techniques of using two pairs of gloves, the rates of perforation, and the incidence of SSI (Sanders 90, Sebold 93). There were no cases of SSI in any of the RCTs.

4.1.2.6. Antiseptic preparation of the skin

When an incision is performed on the skin, microorganisms that colonise the surface can contaminate the exposed tissue and cause SSI. Skin antiseptics are used to reduce the number of microorganisms on the skin around the incision. Flora living in skin fissures cannot be removed using soap and water, but their numbers can be reduced with antiseptics like Chlorhexidine or iodised povidone.

An SR (six RCTs, 2850 participants) and four subsequent RCTs examined the effects of skin antiseptics on the prevention of SSI in clean surgery. The antiseptics evaluated were: iodine/iodophors (including iodised povidone), alcohol in various concentrations, and chlorhexidine. — High quality

A quasi-randomised study evaluated the effects of a shower with soap and saline irrigation on the operation site against a shower with soap and iodised povidone (Kalantar 05). Neither arm of the study showed signs of SSI. — High quality

Two RCTs compared Chlorhexidine with iodine, and found no significant differences between the two groups (Alexander 85, Brown 84). In addition, no differences were seen between various comparisons: alcohol and chlorhexidine (Alexander 85), an iodine/alcohol mixture at various concentrations (Alexander 85), aqueous iodine compared with iodine in alcohol (Kothius 81), and alcohol compared with iodine in alcohol (Alexander 85). A comparison was also made between an iodophor film and an aqueous iodophor tincture; there were no significant differences in the incidence of SSI between groups. The results of a recent trial (849 participants) showed that there is a clear reduction in SSI associated with the use of Chlorhexidine when compared with iodised povidone (RR 0.59; 95% CI: 0.41 to 1.85) (NCT00290290). — Moderate quality

Two studies compared the single or multiple application of iodised povidone (Segal 02, Ellenhorn 05); meta-analysis showed that there was a small but not significant difference between groups (RR 1.05; 95% CI: 0.58 to 1.91). — High quality

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4.1.2.7. Diathermy

Diathermy is a technique used to coagulate small vessels that are bleeding and to cut tissue. The use of diathermy to gain access through the incision, instead of using a scalpel or scissors, is controversial because it can cause further tissue damage, although it can reduce the incidence of post-operative hæmatoma.

Eight RCTs (1122 patients) were identified in which various types of cutting instruments were used.

Six RCTs (1002 participants) compared the effect of using diathermy or scalpel/scissors on the rate of SSI (Groot 94, Hata 05, Johnson 90, Kearns 01, Pearlman 91, Rodd 07). Meta-analysis did not show significant differences between groups. High quality

Two RCTs showed no difference in the incidence of SSI after the incision was performed using diathermy or laser (Pearlman 91, Steger 88). Two others did not show differences either in the use of diathermy or ultrasound laser (Hata 05, Tsimoyiannis 02).

4.1.2.8. Maintaining patient homœostasis

During surgery, and especially when general anæsthesia is used, patient homœostasis must be maintained. All tissues heal more easily under optimum conditions of oxygenation, perfusion, and body temperature.

The effects of maintaining normothermia on the prevention of SSI are reviewed in the corresponding chapter (4.6 Maintaining normothermia). This section reviews the maintenance of oxygenation, perfusion, and blood glycæmia for reducing SSI.

4.1.2.8.1. Oxygenation

All tissues need an adequate level of oxygenation to heal effectively without risk of SSI. The purpose of this section is to evaluate if the peri-operative administration of higher or supplementary concentrations of oxygen are effective against SSI.

Four RCTs compared high and low concentrations of peri-operative oxygen (Greif 00, Belda 05, Pryor 04, Mayzler 05). Two of them (Greif 00, Belda 05) showed a statistically significant difference favouring the administration of high concentrations of oxygen (OR 0.43; 95% CI: 0.22 to 0.86 and OR 0.54; 95% CI: 0.30 to 0.97, respectively). The following RCT showed a significant difference favouring the group of low concentrations of oxygen (OR 2.63; 95% CI: 1.11 to 6.20) (Pryor 04), and the last one showed no significant differences. Meta-analysis of three of those RCTs (the fourth was very heterogeneous) showed a statistically significant difference favouring the administration of high concentrations of oxygen (OR 0.50; 95% CI: 0.32 to 0.77). However, consideration must be given to the risk of atelectasis by re-absorption associated with oxygenation using high fractions of oxygen. Moderate quality

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A single RCT (24 participants) compared the effects of oxygen administered post-operatively with no administration of oxygen; no differences were identified between groups (Whitney 01).

4.1.2.8.2. Perfusion

Patients must be kept well hydrated, especially before general anæsthesia.

One RCT (256 participants) evaluated the effects of peri-operative administration of supplementary endovenous serum on the rates of SSI, with no significant differences being shown between groups (Kabon 05). Moderate quality

4.1.2.8.3. Peri-operative glycæmic control

Insulin-resistant hyperglycæmia is part of a metabolic response to surgery. Strict glycæmic control has not been adapted as a habitual surgical practice, although some authors suggest that is it a method to reduce SSI.

One RCT (61 patients) examined the effects of strict post-operative glycæmic control (glycæmia <120 mg/dl) against standard glycæmia control on rates of SSI. It found a statistically significant reduction of rates of SSI associated with strict post-opertative control (OR 0.15; 95% CI: 0.03 to 0.77) (Grey 04). Moderate quality

Another RCT (78 participants) compared the effect of intensive glycæmic control (glycæmia between 80 and 120 mg/dl) and insulin therapy versus conventional glycæmia control (< 220 mg/dl) and insulin therapy. There was one case of SSI in the first group and two in the second (OR 0.46; 95% CI: 0.04 to 5.31) (Bilotta 07).

In spite of these results, a recent SR (twenty-nine RCTs, 8432 participants) issued a benefits-versus-risks warning that was very unfavourable to this intervention. The results of studies with surgical patients (7 RCTs, 2264 participants) showed that even though strict glycæmic control had no effect on short-term mortality when compared with routine care (RR 0.88; 95% CI: 0.63 to 1.22), while reducing the rate of septicæmia (five RCTs, 2 049 patients, RR 0.54; 95% CI: 0.38 to 0.76), there is a considerable increase in the risk of hypoglycæmia (four RCTs, RR 5.37; 95% CI: 2.64 to 10.93). However, for each case of septicæmia avoided, three cases of hypoglycæmia arose. High quality

4.1.2.9. Irrigating the wound and intracavitary washing

Irrigation and intracavitary cleansing of the wound are widely practised as methods for reducing SSI. Hypothetically, organisms that have appeared on the edges of the skin during surgery, or that have contaminated the wound, can disappear with irrigation or washing.

4.1.2.9.1. Irrigating the wound

Three RCTs (2423 participants) compared saline serum with antibiotics (ampycillin in one and tinidazole in the other two) to irrigate the wound. No differences were seen in the incidence of SSI between groups (Al-Shehri 94, Eklund 87, Farnell 86). High quality

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An RCT (500 participants) showed a greater number of SSIs associated with irrigation of the wound with saline serum as opposed to subcutaneous irrigation using iodised povidone (OR 5.98; 95% CI: 2.62 to 13.65) (Sindelar 128). Moderate quality

An RCT (1 979 participants) showed no statistically significant differences in the incidence of SSI between subcutaneous irrigation of the wound and drainage without irrigation (Eklund 87).

In an RCT (283 participants), irrigation of the muscles and of the subcutaneous tissue of the wound (using a syringe to apply saline under pressure) was associated with a reduction of the incidence of SSI compared with no irrigation (OR 0.28; 95% CI: 0.14 to 0.58) (Cervantes 00).

4.1.2.9.2. Additional intracavitary washing

Four RCTs (360 participants) did not find differences in the incidence of SSI between intracavitary washing using antibiotics and saline serum (Greig 87, Rambo 72, Schein 90, Sherman 76). However, another RCT compared peritoneal washing using tetracycline and saline serum with the same procedure using saline serum alone, and showed a statistically significant reduction in the incidence of SSI, favouring the washing procedure with tetracycline (OR 0.29; 95% CI: 0.13 to 0.65) (Silverman 86). High quality

Two RCTs that compared intracavitary washing using antiseptics against the same procedure using saline serum showed no differences in the incidence of SSI (Baker 94, Sindelar 85). Another RCT showed a lower incidence of SSI associated with washing with iodised povidone rather than saline serum (OR 0.19; 95% CI: 0.06 to 0.59) (Johnson 85).

In another RCT, there were no differences between washing with oxygenated water as compared with saline serum in the rate of SSI (Kubota 99). Moderate quality

An RCT (431 participants) compared the effects of 1g of endovenous latamoxef with washing using tetracycline, and showed a statistically significant reduction in the incidence of SSI in the group undergoing endovenous treatment (OR 0.44; 95% CI: 0.24 to 0.82) (Sauven 86).

An RCT (356 participants) with patients who had undergone hemi-arthroplasty, found a lower incidence of SSI after washing with a mechanical irrigation system using saline serum as compared with washing using serum administered using a syringe (15.6% in the control group 5.6% in the group that underwent pulse washing, for the overall incidence of SSI global) (Hargrove 06). Moderate quality

Another RCT (83 patients) showed a statistically significant decrease in the incidence of SSI among patients randomized to no treatment, as compared with the patients randomized to saline peritoneal washing (RO 6.30; 95% CI: 1.27 to 31.27) (Buanes 91).

An RCT (88 participants) did not find any differences in the rates of SSI between endovenous cephamandole, washing and irrigating with cephamandole, or washing, irrigating, and endovenous cephamandole (Freischlag 84).

There were no differences in the rate of SSI between washing and irrigating the wound using saline serum or cephalozine (Magann 93).

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4.1.2.10. Antiseptic and antimicrobial agents before the wound is closed

It is a general belief that the application of topical antiseptics and antimicrobial agents in surgical incisions before the wound is closed reduces the risk of SSI. This is a usual practice as a method of intra-operative decontamination after dirty surgical procedures, or operations that involve the insertion of orthopædic or vascular prostheses.

An RCT (1340 participants) assessed the effect of re-disinfecting the skin using iodine with or without incise drapes before the wound was closed. No significant differences were shown between groups regarding the rate of SSI (Cordtz 89). — Moderate quality

An RCT (107 participants) looked into the effect of iodised povidone applied at the site of the incision before the wound was closed, and did not show significant differences between groups (Harihara 06).

Three RCTs (855 participants) showed that topical iodised povidone in spray form on the superficial cove rings of the wound before the wound was closed reduces the incidence of SSI (Gray 81, Sherlock 84, Walsh 81). The meta-analysis of the three RCTs showed a significant difference in favour of using iodised povidone in spray form (OR 0.54; 95% CI: 0.36 to 0.81). — High quality

The topical application of iodine in dirty surgery favoured the prevention of SSI in two RCTs (Sherlock 84, Walsh 81), although statistically significant differences only arose in one of them (OR 0.17; 95% CI: 0.06 to 0.50) (Sherlock 84).

Two RCTs (2492 participants) showed that the insertion of a collagen-gentamicin implant before sternal closure in conjunction with systemic antibiotic prophylaxis reduces the rate of sternal SSI in patients who have undergone cardiac surgery (OR 0.49; 95% CI: 0.64 to 0.68) (Eklund 05, Friberg 05).

One RCT (177 participants) examined the effects of cephotaxime applied to the subcutaneous layer during wound closure in contaminated surgery, and showed no differences between the two groups (Mœsgaard 89). — Moderate quality

4.1.2.11. Methods of closure

There is no clear definition of the role of materials and of the methods of suture in SSI. It is believed that silk and catgut, which are both being eliminated from clinical practice, may cause excessive tissue reaction that may be related to an increased risk of SSI. This section offers a review of the materials and methods of closure that may have an effect on the incidence of SSI.

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4.1.2.11.1. Closure of the skin

Two RCTs that included 185 participants (Murphy 04, Leaper 85) compared non-absorbable monofilament sutures with absorbable monofilament sutures. There was one case of SSI in each of the groups, but without statistically significant differences. Moderate quality

An RCT with 135 patients compared the effects of triclosan-coated polyglactin sutures with traditionally-coated polyglactin sutures with respect to the incidence of SSI (Ford 05). Although two infections occurred in the group in which triclosan-coated sutures were used, the difference between groups was not statistically significant.

An RCT with 60 patients randomised wounds to continuous or interrupted wound closing (Murphy 95). There was one infection in the group in which continuous sutures were used, and two infections in the group in which interrupted sutures were used. The confidence interval of this RCT is too wide to draw conclusions (RR 0.58; 95% CI: 0.05 to 6.67).

An RCT showed 3/50 SSIs in patients whose wounds were closed using the bilayer method, as compared with 2/50 in patients whose wounds were closed using a vertical mattress stitch (Sadick 94). Both groups used the same suture material. The difference between groups was not statistically significant (RR 1.53; 95% CI: 0.24 to 9.59).

Eleven RCTs compared cutaneous sutures against staples (Harvey 86, Johnson 97, Mullen 99, Bathia 02, Wolterbeek 02, Beresford 93, Ranaboldo 92, Chughtai 00, Kumar 89, Murphy 04, Grgić 02). None of these RCTs found statistically significant differences between groups in the incidence of SSI after closure. Moderate quality

Four RCTs that compared closure using butyl cyanoacrylate glue against closure with suture showed a greater incidence of SSI in the group in which sutures were used (13/197) as compared with the group in which glue was used (10/166), but without statistically significant differences (Van den Ende 04, Ozturan 01, Dowson 06, Keng 89).

Five RCTs compared closure using octyl cyanoacrylate glue with suture closure, and identified 6/185 SSI in the glue-based group as compared with 3/189 SSI in the suture-based group. Three RCTs showed no SSI in any group (Ong 02, Gislason 95, Sebesta 03). One RCT showed 5/48 SSIs in the glue-based group as compared with 3/50 in the suture-based group (Maartense 02). Another RCT found a single case of SSI in the glue-based group (Sebesta 03). None of the results was statistically significant.

One RCT compared the effect of using tissue adhesive against that of using plaster to close wounds on the incidence of SSI (Maartense 02), with no significant differences being observed between groups.

Finally, one RCT (48 patients) randomised patients by leaving wounds open and filled with compresses impregnated with saline serum, or closed using staples (Velmahos 02). Increased SSI was observed in the group in which wounds were closed using staples (17/26) compared with the group in which wounds were left open (8/22) (RR 0.30; 95% CI: 0.09 to 0.99).

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4.1.2.11.2. Closure of subcutaneous and muscle layers

Two RCTs compared polyamide monofilament against polyglyconate monofilament on the incidence of SSI (Carlson 95, Gys 89). No statistically significant differences were observed between groups of either RCT, or in their meta-analysis (Peto RR 1.55; 95% CI: 0.71 to 3.36). High quality

Two RCTs compared polypropylene monofilament (non-absorbable) with polydioxanone (absorbable) (Krukowski 87, Cameron 87). The meta-analysis of these RCTs showed a statistically significant effect in favour of polyoxidanone sutures to close all layers (Peto RR 1.94; 95% CI: 1.20 to 3.13).

Another RCT compares polyamide sutures with polyoxidanone sutures (Wynne 04) It did not find, statistically significant differences between groups.

The meta-analysis of these five RCTs showed that the use of absorbable sutures, compared with non-absorbable sutures, has a statistically significant protective effect on the incidence of SSI in closing all tissue layers (Peto RR 1.70; 95% CI: 1.14 to 2.52).

An RCT evaluated the closure method for internal tissue layers using mass closure with continuous or interrupted polyglactin sutures (Gislason 95). No statistically significant differences were observed between groups with regard to the incidence of SSI.

Another RCT compared the effects of the fascia closure technique using continuous or interrupted polyglyconate monofilament on SSI. Once again, no statistically significant differences were observed (Orr 90).

No statistically significant differences were observed between mass double-loop sutures as compared with polypropylene sutures (Nasir 01), or between continuous sutures and polydioxanone sutures (Niggebrugge 99).

The comparison between closing and not closing subcutaneous tissue was evaluated in a systematic review (Anderson 04) and four subsequent RCTs (Cardosi 06, Paral 07, Stenvik 06, Yigit 05). The meta-analysis of all the RCTs showed no statistically significant differences in the incidence of SSI between groups.

Another two RCTs that compared the non-closure or the suturing of subcutaneous fat with the insertion a drain also failed to find statistically significant difference in the rate of SSI between groups (Cardosi 06, Magann 02).

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4.1.2.12. Covering the wound

The main purpose of a surgical dressing is to allow appropriate evaluation of a wound in the post-operative phase, absorb exudate, ease pain, and protect recently formed tissue. A dressing maintains an optimum humid environment without causing maceration of the surrounding skin, given that it must be permeable to humidity and gas. This section contains an evaluation of the effectiveness of dressings in the immediate post-operative phase on the prevention of SSI.

An RCT (207 participants) compared the use of a dressing with dry gas for five days against applying Vaseline without a dressing. No significant differences were identified between groups with regard to the rate of SSI (Phan 93). — Moderate quality

Two RCTs (670 participants) compared the use of a hydrocolloid dressing with the use of a dry absorbent dressing. There were no statistically significant differences between groups (Wynne 04, Vogt 07).

No significant differences were observed between groups in two RCTs and one quasi-randomised study (1 879 participants) that compared the use of a hydroactive dressing with the use of a dry absorbent dressing (Wynne 04, Cosker 05, Segers 07).

One RCT (494 participants) compared the use of a hydroactive dressing with the use of a hydrocolloid dressing for preventing SSI. There were no significant differences between groups (Wynne 04).

One RCT (300 participants) looked into the effect of various types of dressings (polyurethane-membrane dressing, absorbent dressing, and hydroactive dressing) on the incidence of SSI. No differences were shown between groups (Cosker 05). — Moderate quality

One RCT (250 participants) compared the use of absorbent dressings with the use of hydroactive and hydrocolloid dressings. A significant difference was found that favoured the use of hydroactive and hydrocolloid dressings as compared with absorbent dressings (RR 5.15; 95% CI: 1.06 to 25.00) (Wikblad 95).

One RCT (857 participants) compared removing the bandage and leaving the wound to air in the 12 hours after surgery, with keeping the wound dry and covered for 48 hours. No significant differences were observed between groups (Heal 06).

A quasi-randomised study (1202 participants) examined the effect on the incidence of SSI of leaving the post-surgical wound uncovered for the first 24 hours, as compared with keeping the wound covered until suture removal (Chrintz 89). No significant differences were observed between groups. — Low quality

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Summary of evidence – Prevention during surgery

High quality	There is no difference on the incidence of SSI if a 75% aqueous solution of alcohol is used as opposed to a 4% aqueous solution of iodised povidone, or a 4% aqueous solution of chlorhexidine, for surgical hand-washing (Parien-ti 02).
High quality	The use of self-adhesive surgical fields increases the risk of SSI (Webster 07, Alexander 85).
High quality	There is insufficient information to determine if the use of sterile gowns is clinically effective in preventing SSI.
	There is no difference in the incidence of SSI arising from the use of re-usable surgical clothing (drapes and gowns) as opposed to single-use drapes and gowns (Garibaldi 86, Bellchambers 99).
High quality	European Standard EN 13795 sets out the basic criteria required for surgical clothing in order to contribute to a reduction of SSI: (i) resistance to microbial penetration; (ii) cleanliness; (iii) reduced particle emission or undoing of fibres during handling; (iv) resistance to liquid penetration; (v) resistance to breaking and pulling when dry and when wet; and for cloths, (vi) ensuring adhesion by fixing in order to isolate skin.
Moderate quality	There is insufficient information to determine if there is a difference between using one pair or two pairs of gloves with regard to the rates of SSI. It is also unknown if there is a correlation between the degree of perforation of the gloves and the rate of SSI.
Moderate quality	Although the results of studies that have evaluated antiseptic preparations have given varying results (Kalantar 05, Alexander 85, Brown 84, Kothius 81, Edwards 04, Segal 02, Ellenhorn 05), a recent trial showed a greater reduction in SSI with the use of chlorhexidine than with iodised povidone.
High quality	There is no difference in the incidence of SSI following an incision with a scalpel or with diathermy (Grisot 94, Hata 05, Johnson 90, Kearns 01, Pearlman 91, Rodd 07). There is insufficient evidence to show if the use of diathermy compared with a laser (Pearlman 91, Steger 88) or an electronic scalpel (Hata 05, Tsimoyiannis 02) has an effect on the incidence of SSI.
High quality	Information available concerning the effectiveness of oxygen on the peri-operative phase to prevent SSI is inconsistent: two RCTs showed positive results (Greif 00, Belda 05), one RCTS showed a significant difference in favour of using low concentrations (Pryor 04), and another showed no differences (Mayzler 05).
Moderate quality	There is insufficient evidence to establish if there is a difference in the rates of SSI when additional oxygen is administered in the post-operative phase (Whitney 01).
High quality	There is insufficient evidence to suggest that the additional administration of endovenous fluids reduces the rates of SSI, as compared with standard practice (Kabon 05).
High quality	There is insufficient evidence as to whether strict glycæmia control in the post-operative phase can affect the incidence of SSI (Grey 04, Bilotta 07). Furthermore, consideration must be given to the high risk of hypoglycæmia associated with this intervention.

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High quality	During the operation, subcutaneous irrigation of the wound using iodised povidone (Sindelar 128) or saline under pressure (Cervantes 00) reduces the incidence of SSI. No differences have been observed between saline irrigation or antibiotic irrigation (Al-Shehri 94, Eklund 87, Farnell 86), or between irrigation and drainage (Eklund 87).
High quality	There is no evidence that additional intracavitary washing with antibiotics reduces the incidence of SSI (Greig 87, Rambo 72, Schein 90, Sherman 76), although in one RCT, the use of tetracycline for washing reduced the incidence of SSI (Silverman 86).
Moderate quality	An RCT stated objectively that washing with iodised povidone reduced the incidence of SSI (Johnson 85). An RCT on arthroplasty surgery showed that washing with pulsed saline could reduce the incidence of SSI (Hargrove 06).
High quality	Iodised povidone in spray form on the upper layers of the wound before closure can reduce the incidence of SSI (Gray 81, Sherlock 84, Walsh 81). Disinfecting the skin beside the wound with iodine before closure does not have an effect on the incidence of SSI (Cordtz 89). Inserting a collagen-gentamicin implant before sternal closure after cardiac surgery and adjuvant to systemic antibiotic prophylaxis may reduce the rate of sternal SSI (Sherlock 84, Walsh 81). In addition to systemic antibiotic prophylaxis, applying topic cefotaxime has no effect on the incidence of SSI (Moesgaard 89).
Moderate quality	For skin closure, there is no information to determine if the incidence of SSI is affected by differences in using absorbable and non-absorbable monofilament sutures (Murphy 04, Leaper 85), or by differences in using continuous or interrupted non-absorbable sutures (Murphy 95). There is also insufficient evidence to determine if there are differences between the bilayer technique and the vertical mattress sutures in the incidence of SSI (Sadick 94). An RCT did not show any significant difference on the incidence of SSI between the use of polyglactin sutures coated with triclosan and the use of polyglactin sutures with traditional coating (Ford 05). There are no differences in the incidence of SSI between the use of staples or sutures (Harvey 86, Johnson 97, Mullen 99, Bathia 02, Wolterbeek 02, Beresford 93, Ranaboldo 92, Chughtai 00, Kumar 89, Murphy 04, Grgić 02). There is no evidence available to determine if there is a difference on the incidence of SSI arising from the use of sutures versus the use of glue (Van den Ende 04, Ozturan 01, Dowson 06, Keng 89, Maartense 02, Ong 02, Gislason 95, Sebesta 03), or between the use of glue versus the use of plaster (Maartense 02). An RCT showed that delayed closure of the wound using compresses impregnated with saline serum reduced the rate of SSI in relation to primary closure using clamps (Vermahos 02).

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High quality	Regarding closure of subcutaneous and muscle layers, absorbable sutures have shown a protective effect in relation to the incidence of SSI in comparison with non-absorbable sutures (Peto RR 1.71; 95% CI: 1.14 to 2.52) (Carlson 95, Gys 89, Krukowski 87, Cameron 87, Wynne 04). There is insufficient evidence on which one is the best method of closure to prevent SSI: no differences were observed between mass closure using continuous or interrupted polyglactin sutures (Gislason 95), between the continuous or interrupted closure of fascias using polyglyconate monofilament (Orr 90), or between closure using continuous loops, continuous mass closure (Nasar 01), or continuous stitching using polydioxanone sutures (Niggebrugge 99). No significant differences were observed SSIth regard to the incidence of SSI between the closure and non-closure of subcutaneous tissue (Anderson 04, Cardosi 06, Paral 07, Stenvik 06, Yigit 05), or between the non-closure and the suturing of subcutaneous fat with the insertion of a drain (Cardosi 06, Magann 02).
High quality	There is insufficient evidence on the best bandage to prevent SSI in the immediate post-operative period: the studies evaluated did not show significant differences between the various types of bandage in relation to the incidence of SSI (Phan 93, Wynne 04, Vogt 07, Cosker 05, Segers 07, Wikblad 95, Heal 06, Chrintz 89).

Recommendations – Prevention during surgery

	Surgical staff must wash their hands before the first intervention on the list, using an antiseptic surgical solutions with a single-use nail brush. Between operations, hands must be washed using an alcoholic or antiseptic solution.
Strong	It is recommended that self-adhesive surgical fields should not be routinely used, since they can increase the risk of SSI.
	Surgical staff must wear sterile gowns in the operating room during surgery. Surgical clothing must comply strictly with standard EN 13795.
	It is recommended that two pairs of sterile gloves be used when there is a high risk of glove perforation and the consequences of contamination can be serious.
Weak	It is recommended that the skin be prepared in the operating room using chlorhexidine before making the incision. If chlorhexidine is not available, the use of iodised povidone can be considered.
Weak	It is not recommended that diathermia be used in the surgical incision to reduce the risk of SSI.
Weak	It is recommended that adequate perfusion be maintained during surgery.
Strong	It is not recommended that insulin be routinely administered in non-diabetic patients to optimise glycæmia in the post-operative phase to reduce the risk of SSI.
Weak	It is not recommended that the wound be irrigated to reduce the risk of SSI.

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Weak	It is not recommended that an additional intracavitary wash using antibiotics be used to reduce the risk of SSI.
Weak	It is not recommended that the skin be re-disinfected at the end of the operation to reduce the risk of SSI.
	It is recommended that surgical wounds be covered using an appropriate bandage at the end of the operation.

4.1.3. Post-operative prevention

4.1.3.1. Changing the bandage

The aseptic bandage technique is a habitual practice. It is assumed that the practice promotes healing and prevents SSI. For that reason, it is the standard technique when dealing with post-operative surgical wounds. It is not known if there is a difference between this bandage technique and others that are less costly, in relation to the incidence of SSI.

No studies have been identified that assessed the risk of infection, although a small RCT (30 participants) has been identified that compared the application of a clean bandage with the antiseptic bandage technique in dealing with wounds that heal on second intention. No significant differences were identified between groups (Stotts 97). Low quality

4.1.3.2. Post-operative cleanliness

Washing the surgical wound using a sterile solution is a habitual practice amongst health professionals. Apart from improving the patient's wellbeing, the practice is used to remove excess exudate from the wound, as well as crusts or remains.

One RS (fourteen RCTs) was identified that examined the evidence relating to post-operative washing of the wound and the solutions used (Fernández 04). It only included two quasi-randomised studies that assessed the incidence of SSI. In the first one (121 participants), patients were randomised and showered on the first day of the post-operative period, or they kept the wound dry for fourteen days. No SSI was observed in any group. Low quality

In the other quasi-randomised study (82 participants), patients were randomised to either showering (on the second day of the post-operative period) or not showering. Two cases of SSI arose in the first group, and four in the second group (a difference that was not statistically significant).

No other RCTs have been identified that assess the relationship between washing the wound and incidence of SSI.

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4.1.3.3. Topical antimicrobial agents in wound healing by primary intention

The use of topical antibiotics in wound healing by primary intention is open to discussion, given the risks of possible absorption and toxicity, allergy, and antimicrobial resistance.

An RCT (92 participants) was identified that assessed the effect of applying a topical antimicrobial agent to the surgical wound and the presence of SSI. Chloramphenicol cream was applied to the incision site at the end of the procedure and on the third day of the post-operative period (Kamath 05). No significant differences were observed between groups. High quality

Summary of the evidence – Post-operative prevention

Low quality	No information is available that compares the aseptic bandage technique with other bandages and the incidence of SSI. There is no evidence available on the effects of washing the wound and preventing SSI. There is insufficient information on having patients shower in the immediate post-operative period and the incidence of SSI (Fernández 04).
High quality	There is insufficient information on the topical use of antibiotics in preventing SSI (Kamath 05).

Recommendations – Post-operative prevention

	It is recommended that an aseptic technique be used to change or remove the bandage from the surgical wound.
	It is recommended that sterile saline serum be used to wash the wound in the first 48 hours after surgery. Patients can shower starting 48 hours after surgery.
Weak	It is recommended that antimicrobial agents not be used for surgical wounds that are healing by primary intention to prevent the risk of SSI.

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4.2. Using antibiotic prophylaxis

Question to be answered

- Is antibiotic prophylaxis indicated in patients who have undergone surgery?
- What are the antibiotics of choice for antibiotic prophylaxis in various surgical procedures?
- When is the right time to administer antibiotics endovenously?
- What is the optimum duration of antibiotic prophylaxis?

4.2.1. Indications for antibiotic prophylaxis

The prophylactic administration of antibiotics in surgery inhibits the growth of contaminating bacteria, thus reducing the risk of SSI (Cars 93, Lorian 75, Tornqvist 90). SSI increases the time spent in hospital, and antibiotic prophylaxis can help in reducing that time.

However, the administration of antibiotics also increases the prevalence of bacteria that are resistant to antibiotics (Goldmann 96), and predisposes the patient to infection by organisms such as *Clostridium difficile*, a cause of colitis associated with antibiotics (Jobe 95). For that reason, antibiotic prophylaxis should be used if there is evidence of its benefit. It should not be considered if there is evidence of a lack of effectiveness. High quality

Another of the aspects to be considered before assessing the use of antibiotic prophylaxis is the risk of allergy, especially to penicillin and to cephalosporins. Patients with a history of allergy to penicillin must be assessed to rule out non-immunological adverse reactions (Park 05).

It is important to take account of the classification of surgical wounds developed by the *National Academy of Sciences* in 1960, which distinguishes four levels of risk:

– **clean surgery**: surgical wound with no inflammation, with no interruption of sterile technique, and in which there is no penetration of the respiratory, digestive, or genito-urinary tracts
– **clean-contaminated surgery**: surgical wound in which there is penetration of the respiratory, digestive, or genito-urinary tracts under controlled conditions and with no contamination High quality
– **contaminated surgery**: surgical wound that meets the following criteria: i) failure in sterile technique or leakage of gastro-intestinal liquid, ii) signs of acute non-purulent inflammation, iii) traumatic wound that has been opened between 12 and 24 hours

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– **dirty or infected surgery**: surgical wound that meets the following criteria: i) wound in an operation involving perforated viscera; ii) detection of acute inflammation with pus during the intervention, iii) traumatic wound where the treatment is delayed and there is fæcal contamination or devitalised tissue.

Various studies have shown the association between classification of the surgical wound and the incidence of infection of the surgical wound (Cluver 1991, Neumayer 2007, Kaye 2005). Moderate quality

In a retrospective analysis of a large database of vigilance over infection, the ratio of incidence of infection of the surgical wound per 100 operations was 2.1; 3.3; 6.4; 7.1 for clean, clean-contaminated, contaminated, and dirty wounds, respectively (Cluver 1991). Low quality

In a study on vascular operations, it was stated that the type of surgical wound was a an independent factor in predicting infection of the surgical wound (if infection of the surgical wound in clean surgery has an OR of 1, infection of the surgical wound in clean-contaminated, contaminated, or dirty surgery was had ORs of 1.04, 1.7, and 1.5, respectively, $p < 0.0001$) (Neumayer 2007). In a third prospective study, a statistically significant increase of SSI was found in contaminated and dirty wounds (type of wound >2; OR 2.3; 95% CI: 2.0 to 2.7) (Kaye 2005).

The main risk factors of SSI to indicate the need for antibiotic prophylaxis in a surgical procedure are (NICE 2008 SSI): Moderate quality

– **age**: the patient's age is a significant risk factor for SSI (Scott 2001), which shows a rising trend with increasing age (Cruse 1973, Kaye 2005)
– **co-morbidity**: patients with an ASA score that is equal to or greater than 3 have a greater risk (Kaye 2005, Neumayer 2007, Ridgeway 2005); diabetes is associated with a greater incidence of SSI (Neumayer 2007), as is malnutrition (Cruse 1973). Treatments involving radiotherapy or steroids are independent factors for predicting the risk of SSI (Neumayer 2007)
– **obesity**: obesity is strongly associated with an increase in the risk of SSI (Abboud 2004, Cruse 1973, Friedman 2007, Latham 2001, Ridderstolpe 2001, Russo 2002, Olsen 2003, Olsen 2008)
– **smoking**: smoking is a an independent risk factor for SSI (Abbound 2004, Neumayer 2007), as well as the the number of cigarettes smoked per day or the time when the habit was started (Gravante 2008)
– **classification of the surgical wound**: in relation to its level of contamination (Cluver 1991, Neumayer 2007, Kaye 2005).

This section contains a description of the indications that are recommended for surgical antibiotic prophylaxis, adapted from a recent CPG (SIGN 104). Recommendations are based on the evidence of clinical effectiveness of antibiotics in reducing the incidence of SSI. Four levels of recommendation have been established:

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- **highly recommended**: prophylaxis undoubtedly reduces greater morbidity and hospital costs, and it is probable that is may reduce the overall consumption of antibiotics
- **recommended**: prophylaxis reduces morbidity in the short term, reduce hospital costs, and may reduce the overall consumption of antibiotics
- **to be taken into consideration**: prophylaxis should be considered for all patients, although politicians seek to identify exceptions, since prophylaxis may not reduce costs and may increase the consumption of antibiotics
- **not recommended**: it has not been proven that prophylaxis is clinically effective. Given that the consequences of infection produce morbidity in the short term, it is possible that prophylaxis may increase hospital consumption of antibiotics in exchange for a very small clinical benefit.

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**Recommended indications for surgical antibiotic prophylaxis.
Adapted from Scottish Intercollegiate Guidelines Network. SIGN 104:
Antibiotic Prophylaxis in Surgery. A national practical guideline. Edinburgh: SIGN; 2008**

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.1. HEAD AND NECK			
4.2.1.1.1. Intracraneal			
Craniotomy	Recommended	SSI	High quality (Barker 94)
Cephalorachidian fluid derivation	Recommended	SSI Infection derivation	High quality (Haines 94, Langley 93)
Spinal surgery	Recommended	SSI	High quality (Barker 02)
4.2.1.1.2. Ophthalmic			
Cataract surgery	Highly recommended	Endophthalmitis	High quality (Endophthalmitis Study Group 07)
Glaucoma or corneal graft	Recommended	Effectiveness inferred from evidence from cataract surgery	High quality (Endophthalmitis Study Group 07)
Tear duct surgery	Recommended	SSI	Low quality (Vardy 00)
Eye-penetrating wound	Recommended	Endophthalmitis	High quality (Narang 03, Soheilian 07)
4.2.1.1.3. Facial			
Mandibular fractures	Recommended (duration not > 24 hours)	SSI	High quality (Zallen 75, Abubaker 01, Andreasen 06)
Oral bone grafts	Recommended	There was no direct comparison between antiobiotic and non-antibiotic proiphylaxis	High quality (Lindeboom 06)
Orthognathic surgery	Recommended Duration of prophylaxis should not > 24 hours. Appropriate broad-spectrum antibiotics should be administered for oral flora.	SSI	High quality (Baqain 04, Bentley 99, Fridrich 94, Zijderveld 99)

Surgical intervention	Recommendation	Result variable	Quality
4.2.1.1. HEAD AND NECK (cont.)			
Facial surgery (clean)	Not recommended		
Facial plastic surgery	Must be considered	Effectiveness is inferred from evidence from other procedures that involve the insertion of a prosthesis	Very low quality (Dellinger 94)
4.2.1.1.4. Benign otorhinolaryngology			
Ear surgery (clean / clean-contaminated)	Not recommended	No subgroup analysis was done for clean and clean-contaminated surgery	High quality (Verschuur 04)
Nasal surgery, paransal sinus surgery, and endocopic sinus surgery	Not recommended		High quality (Annys 00)
Complex septorhinoplasty (including graft)	Prophylaxis should not last for > 24 hours		High quality (Andrews 06)
Tonsillectomy	Not recommended	No studies were identified that showed evidence of the effectiveness of prophylaxis	
Adenoidectomy (by curettage)	Not recommended		High quality (Sánchez-Carrión 06)
Insertting drainage tubes	Recommended	Otorrrhœa	High quality (Nawasreh 04, Zipfel 99)
4.2.1.1.5. Head and neck			
Head and neck surgery (clean, benign)	Not recommended		Very low quality (Johnson 87, Simo 06)
Head and neck surgery (clean, malign, neck dissection)	Must be considered	SSI	Low quality (Coskun 00, Seven 04)

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.1. HEAD AND NECK (cont.)			
Head and neck surgery (contaminated / clean-contaminated)	Recommended Prophylaxis time should not exceed 24 hours Give broad-spectrum antibiotics to cover ærobic and anærobic organisms	SSI	High quality (Becker 79, Dor 73, Johnson 84, Velanovich 91) Low quality (Avery 06, Coskun 00) Very low quality (Simo 06)
4.2.1.2. THORAX			
Breast-cancer surgery	Must be considered		High quality (Cunningham 07)
Mam moplasty	Must be considered	Infection after 6 weeks	Low quality (Ahmadi 06)
Breast surgery or implant (reconstructive or æsthetic)	Recommended	Effectiveness is inferred from evidence from breast-cancer surgery and other procedures that include the insertion of a prosthesis	High quality (Cunningham 07), Very low quality (Dellinger 94)
Inserting a pacemaker	Recommended	Any infection	High quality (Da Costa 98)
Open-heat surgery	Recommended Prophylaxis should not last for more than 24 hours	SSI	Low quality (Fong 79, Austin 80, Penketh 85) Low quality (Harbarth 00, Eagle 04, Zanetti 01)
Lung re-section	Recommended	Infection at the site of surgery	High quality (Ilves 81, Aznar 91)
4.2.1.3. UPPER GASTROINTESTINAL			
Œsophageal surgery	Recommended	Effectiveness is inferred from evidence from other clean-contaminated procedures	Very low quality (Bricard 94)
Gastric and duodenal surgery	Recommended	SSI	High quality (Evans 73, Lewis 79, Polk 69)
Gastric-bypass surgery	Recommended	Effectiveness is inferred from evidence from other clean-contaminated procedures	Very low quality (Dellinger 94)

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.3. UPPER GASTROINTESTINAL (cont.)			
Small-intestine surgery	Recommended	Effectiveness inferred from evidence from other clean-contaminated procedures	Very low quality (Dellinger 94)
4.2.1.4. HEPATOBILIARY			
Bile-duct surgery	Recommended	SSI	High quality (Meijer 90)
Pancreatic surgery	Recommended	Effectivness inferred from evidence from biliary surgery	High quality (Meijer 90)
Hepatic surgery	Recommended	Effectivness inferred from evidence from biliary surgery	High quality (Meijer 90)
Open cholecystectomy	Recommended	SSI	High quality (Meijer 90)
Laparoscopic cholecystectomy	Recommended		High quality (Meijer 90) High quality (Catarci 04)
4.2.1.5. LOWER GASTROINTESTINAL			
Appendectomy	Highly recommended	SSI Intra-abdominal abcesses	High quality (Andersen 05)
Colorectal surgery	Highly recommended	SSI Intra-abdominal abcesses	High quality (Song 98)
4.2.1.6. ABDOMEN			
Inguinal herniorrhaphy (inguinal / femoral, with or without mesh)	Not recommended		High quality (Aufenacker 06, Sanchez 04)
Laparoscopic inguinal herniorrahphy with or without mesh	Not recommended	Effectiveness inferred from evidence from repairing open inguinal / femoral hernias	High quality (Aufenacker 06, Sanchez 04)

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.6. ABDOMEN (cont.)			
Herniorraphy (incisional, with or without mesh)	Not recommended	Effectiveness inferred from evidence from repairing open inguinal / femoral hernias	High quality (Aufenacker 06, Sanchez 04)
Laparoscopic / open surgery with mesh (e.g. gastric band or rectopexy)	Not recommended except for high-risk patients	Effectiveness inferred from evidence from repairing open inguinal / femoral hernias	High quality (Aufenacker 06, Sanchez 04)
Endoscopic diagnositc procedures	Not recommended		Very low quality (British Society for Gastroenterology 01)
Therpeutic endoscopic procedures (endoscopic retrograde cholangiopancreatography and endoscpoic percutaneous gastrostomy)	Must be considered in high-risk patients		Very low quality (British Society for Gastroenterology 01)
Splenectomy	Not recommended except for high-risk patients		High quality (Meijer 90)
4.2.1.6.1. Gynæcology			
Abdominal hysterectomy	Recommended		
Vaginal hysterectomy	Recommended	Pelvic infection	High quality (Allen 72, Ledger 73)
Cæsarean	Highly recommended	SSI	High quality (Smaill 05)
Assisted birth	Not recommended		High quality (Liabsuetrakul 04)
Perineal tear	Recommended for 3rd- and 4th-degree tears that affect the anal sphincter or the rectal mucosa	SSI	Very low quality (RCOG 01)
Manual placenta removal	Recommended for patients with infection due to chlamnydia or gonorrhœa		Very low quality (WHO 00)

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.6. ABDOMEN (cont.)			
Induced abortion	Highly recommended	Infection of the upper genital tract	High quality (Sawaya 96)
Evacuating an incomplete abortion	Not recommended		High quality (May 05)
Inserting intra-uterine device	Not recommended		High quality (Grimes 99)
4.2.1.6.2. Urogenital			
Transrectal prostate biopsy	Recommended	Bacteriuria	Higfh quality (Crawford 82, Ruebush 79)
Shockwave lithotripsy	Recommended	Urinary-tract infection	High quality (Pearle 97)
Percutaneous nephrolithoto-my	Recommended for patients with calculi ≥20 mm, or with pyelocaliceal dilation	Urosepsis	High quality (Mariappan 06) High quality (Mariappan 06)
Endoscopic removal / frag-mentatio of ureteral calculus	Recommended	Bacteriuria Post-operative fever	High quality (Knopf 03) Calidad baja (Takahashi 05)
Transurethral resection of the prostate	Highly recommended	Bacteriuria Infectious complications	High quality (Berry 02)
Transurethral resection of bladder tumours	Not recommended		Very low quality (Delavierre 93)
Radical cystectomy	Recommended	SSI high after cyctectomy	Very low quality (Takeyama 05)
4.2.1.7. EXTREMITIES			
Arthroplasty	Highly recommended In addition to endovenous antibiotics, anti-biotic cement is recommended Consideration should be given to antibiotic prophylaxis for up to 24 hours	Hip infection Joint infection	High quality (Hill 81, Lidwell 82) Low quality (Block 05, Engesaeter 03) Low quality (Block 05, Engesaeter 03)
Open fracture	Highly recommended	SSI	High quality (Gosselin 04)

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Surgical intervention	Recommendation	Result variable	Quality
4.2.1.7. EXTREMIDADES (cont.)			
Open surgery to repair a closed fracture	Highly recommended	Deep infection of the surgical wound	High quality (Gillespie 00)
Hip fracture	Highly recommended	Deep infection of the surgical wound	High quality (Southwell 04)
Orthopædic surgery (without implants)	Not recommended	Effectiveness inferred from evidence from clean-contaminated procedures	Very low quality (Dellinger 94)
Amputation of lower limb	Recommended	SSI	High quality (Sonne 85)
Vascular surgery (abdominal arterial reconstruction and reconstruction of the lower extremities	Recommended	SSI	High quality (Stewart 07)
Surgery of soft tissues of the hand	Recommended	Effectiveness inferred from evidence from orthopædic and vascular surgery	High quality (Gosselin 04, Gillespie 00)
4.2.1.8. NON-SURGICAL INTERVENTIONS			
Intravascular catheter insertion: – non-tunnelled central venous catheter – tunnelled central venous catheter	Not recommended		Very low quality (O"Grady 02) High quality (van de Wetering 05)
4.2.1.9. GENERAL			
Clean-contamniated procedures when no specific evidence is available	Recommended		Very low quality (Dellinger 94)
Prosthesis insertion when no specific evidence is available	Recommended		Very low quality (Dellinger 94)

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4.2.2. Administration of antibiotic prophylaxis (selection, duration, dosage, and method of administration)

4.2.2.1. Selection

In spite of a wide variety of organisms that can cause infections in surgical patients, infection of surgical wounds (SSI) is usually due to a small group of common pathogens. Only those pathogens must be targetted with the antibiotic prescribed (Mangram 99). — Low quality

The antibiotics selected can be those used for active treatment of the infection. They must reflect local and specific information on usual pathogens and their antimicrobial susceptibility. Accordingly, in choosing antibiotics for each type of surgery, it is necessary to know the most frequent related microorganisms, their sensitivity to available antibiotics, and the main characteristics of the latter (e.g. antimicrobial spectrum or toxicity). — Moderate quality / High quality

In a meta-analysis of heterogeneous studies, the peri-operative administration of ceftriaxone showed a 30% reduction in the relative risk of SSI when compared with other cephalosporins (Dietrich 02), and a 22% reduction in comparison with other types of antibiotics (Esposito 04). Given the heterogeneousness of the studies, it cannot be concluded that ceftriaxone is better for a determined intervention. — Moderate

A meta-analysis on antibiotic prophylaxis for cardiac surgery did not show differences between beta-lactam antibiotics and glycopeptides regarding effectiveness in reducing the risk of SSI (Bolon 04).

Being a carrier of MRSA (Methicillin-Resitant *Staphylococcus aureus*) can be a risk factor for SSI, which can cause a high level of morbidity in patients who undergo high-risk surgery. — High quality

A meta-analysis of peri-operative prophylaxis with intranasal mupirocin in non-general surgery found a reduction in the incidence of SSI in two RCTs (RR 0.80; 95% CI: 0.58 to 1.10) and in three non-randomised controlled studies (RR 0.40, 0.29 to 0.56). There was no reduction in SSI in general surgery (Kallen 05).

A meta-analysis of antibiotic prophylaxis in cardiac surgery showed that glucopeptides are more effective than beta-lactam antibiotics in the prevention of MRSA-caused SSI (Bolon 04).

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4.2.2.2. Time of administration

The time required for an antibiotic to reach an effective level of concentration in a determined tissue reflects its pharmacokinetic profile and the method of administration (Martin 94). Antibiotic prophylaxis that is administered too late or too early reduces the effectiveness of the antibiotic, and can increase the risk of SSI (Baum 81, Donovan 79, Willis 76, Winslow 83). — High quality

Administering prophylaxis more than three hours after the start of the intervention reduces its effectiveness significantly (Classen 92).

A non-systematic review showed that endovenous antibiotics should be given at least 30 minutes before the operation for all types of surgery, except Cæsarean section (Mangram 99). The WHO Surgical Safety Checklist advocates the administration of antibiotic prophylaxis in the final hour before surgery (Haynes 2009). — Low quality

A systematic review concluded that the risks and benefits of giving antibiotics after clamping the cord in a Cæsarean section cannot be determined based on the evidence available (Berghella 05). — High quality

4.2.2.3. Dosage

It is generally accepted as best practice that the dosage of an antibiotic needed for prophylaxis is the same as for treating infection.

4.2.2.4. Duration

For most usual surgical interventions, there is consistent evidence that a single dose of antibiotic with an average life that is sufficient to maintain activity during the operation is adequate (Song 98, Velmahos 02, Mui 05). — High quality

Various studies on antibiotic prophylaxis during surgery show that a longer duration does not being an increase in benefit, although some studies are of better quality (Andreasen 06, Baqain 04, Fridrich 94, Andrews 06, Smaill 05) when compared with others that exhibit a greater risk of bias (Avery 06, Coskun 00, Ahmadi 05, Zanetti 01, Takahashi 05). — Moderate quality

A wide cohort study on arthroplasty showed that antibiotic prophylaxis for 24 hours was associated with lower rates of re-intervention than single-dose prophylaxis (Engesaeter 03). — Low quality

Another cohort study of cardiac operations showed that a single dose of cephazolin is as effective as two doses in short cardiac operations (<240 min), although an extra dose during the intervention in cases of operations of over four hours led to a 16% reduction in the overall rate of infection (Zanetti 01).

Antibiotic concentrations in serum are reduced with loss of blood and the administration of liquids, especially in the first hour of surgery, when pharmacological levels are high (Levy 90, Wollinsky 96, Dehne 01). The precise effects of loss of blood and of the administration of liquids are difficult to predict, and will depend on the antibiotic used, the time, the amount of blood lost, and the amount of liquids administered.

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4.2.2.5. Method of administration

Systemic antibiotic prophylaxis by the endovenous route has always been presented as an effective and efficient prophylaxis against SSI in all types of surgery.

With regard to oral administration, there is little evidence available on the effectiveness of that method for antibiotic prophylaxis. An additional problem is that, very often, it is not guaranteed that the antibiotic will be administered at the appropriate time (because the patient is outside the operating room, etc.).

Regarding the topical method, there is evidence that the topical application of antibiotics can minimise SSI after surgery (e.g. by placing a collagen tissue impregnated with absorbable gentamicin after the abdominoperineal excision) in rectal cancer (Gruessner 01), or a collagen-gentamicin implant in the sternum after cardiac surgery (Eklund 05, Friberg 06). — High quality

A combination of endovenous antibiotics and antibiotic-impregnated cement when joint prostheses are being implanted was found to be more effective than endovenous prophylaxis alone in the reduction of the risk of SSI (Engesaeter 03).

After cataract surgery, the intracameral application of cefuroxime reduces the risk of developing endophthalmitis to one fifth of the risk when antibiotics are not used (Seal 06).

Intravitreous antibiotic prophylaxis (vancomycin and ceftazidime) prevents serious eye infections after the open wound of the eyeball, in comparison with not administering antibiotics intravitreously (Soheilian 07).

An RCT using LCR-derived valves impregnated with antibiotics, compared with unimpregnated valves, showed a significant reduction in the rate of infection (Govender 03). Two cohort studies also showed lower rates of infection (Sciubba 05, Aryan 05), as well as an RCT with ventricular drains impregnated with antibiotics (Zabramski 03). — Moderate quality

A meta-analysis showed that the use of central venous catheters impregnated with antimicrobial agents or with heparin reduces blood infections by 2.32% (95% CI: 1.04% a 3.61%) (Marin 00). — High quality

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Summary of the evidence

Moderate quality	A description has been given of the following SSI risk factors to indicate the need for antibiotic prophylaxis in a surgical procedure: age of the patient, obesity, diabetes, smoking habit, level of contamination of the procedure, and some factors like an ASA score that is equal to or higher than 3, malnutrition, and treatment using radiotherapy or steroids.
Low quality	SSI is usually caused by a small group of common pathogens, which are the only ones that should be targetted with the antibiotic prophylaxis.
Moderate quality	Two heterogeneous meta-analyses showed greater effectiveness of ceftriaxone in reducing the risk of SSI when compared with other cephalosporins (Dietrich 02) and with other antibiotics (Esposito 04). A meta-analysis did not show differences between beta-lactam antibiotics and glucopeptides (Bolon 04).
High quality	A meta-analysis of peri-operative prophylaxis with intranasal mupirocin showed a reduction in the incidence of SSI in non-general surgery, but not in general surgery (Kallen 05). A meta-analysis on cardiac surgery showed that glucopeptides are more effective than beta-lactam antibiotics in preventing SSI caused by MRSA (Bolon 04).
High quality	Antibiotic prophylaxis that is administered too late (Classen 92) or too early is reduced in effectiveness, and can increase the risk of SSI (Baum 81, Donovan 79, Willis 76, Winslow 83).
High quality	A single dose of antibiotic with an average life that is sufficient to maintain activity during the operation is acceptable (Song 98, Velmahos 02, Mui 05).
Low quality	Antibiotic concentrations in serum are reduced with loss of blood and with the administration of liquids (Levy 90, Wollinsky 96, Dehne 01).
High quality	The topical application of antibiotics can minimise SSI after rectal cancer surgery (Gruessner 01), cardiac surgery (Eklund 05, Friberg 06), and the fitting of tympanic drains (Zipfel 99).
High quality	Cefuroxime applied intracamerally reduces the risk of developing endophthalmitis in cataract surgery (Seal 06), whilst intravitreous antibiotic prophylaxis (vancomycin and ceftazidime) prevents serious eye infections after an open wound to the eyeball (Soheilian 07).
Low quality	A combination of endovenous antibiotics and antibiotic-impregnated cement in fitting joint prostheses was found to be more effective than endovenous prophylaxis alone in reducing the risk of SSI (Engesaeter 03).
Moderate quality	The application of LCR drainage valves impregnated with antibiotics may be effective in reducing the rate of infection (Govender 03, Zabramski 03) (Sciubba 05, Aryan 05).

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Recommendations

Weak	Antibiotics chosen for prophylaxis must target the pathogens that are expected in the surgery to be performed.
	Legislators working on antibiotics policies must have the experience and information needed to make recommendations on specific regimes of pharmaceuticals, based on evidence, local information on resistance, and costs.
	Narrow-spectrum and cheaper antibiotics must be the first choice for antibiotic prophylaxis in surgery.
	Before high-risk surgery, eradicator treatment should be started in patients who are MRSA carriers.
Weak	Intranasal mupirocin must be used prophylactically in patients undergoing surgery with a high risk of morbidity and who are MRSA carriers.
Strong	Glucopeptides must be considered for antibiotic prophylaxis in patients undergoing high-risk surgery and who are MRSA carriers.
Strong	Endovenous prophylactic antibiotics must be given 30 to 60 minutes before surgical incision.
	A single standard dose of antibiotic is sufficient for prophylaxis in most circumstances, except if surgery that lasts longer than four hours or if loss of blood exceeds 1500 cc.
Weak	It is recommended that a single dose of antibiotic that has an average life that is sufficient to maintain activity during the whole operation be used. However, in the case of arthroplasty, it is recommended that antibiotic prophylaxis be administered for up to 24 hours.
	A further two doses of antibiotics may be needed in the case of lengthy operations (i.e. over four hours in length), or in the case of significant loss of blood (>1500 ml) during surgery.
	Antibiotic prophylaxis for surgery should be administered endovenously.
Weak	In addition to endovenous antibiotics, it is recommended that antibiotic-impregnated cement be used in the fitting of joint prostheses.
Strong	Intracameral antibiotic prophylaxis is recommended in cataract surgery.
Weak	Intravitreous antibiotic prophylaxis is recommended at the end of surgery following eye-penetrating wounds.
Weak	It is not recommended that LCR drainage valves impregnated with antibiotics be used routinely, although they may be considered if local rates of infection are high.

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4.3. Preventing cardiovascular complications in non-cardiac surgery

Question to be answered

- Beta-blockers, statins, acetylsalicylic acid, alpha-2 agonists, calcium antagonists, and coronary revascularisation: do they prevent cardiovascular events in patients undergoing non-cardiac surgery?
- What are the risk factors of suffering cardiac arrhythmia after surgery?
- What treatments can prevent auricular fibrillation in patients undergoing non-cardiac surgery?

Non-cardiac surgery is associated with significant morbidity and mortality, with peri-operative cardiac complications being frequent as well as giving rise to significant mortality, morbidity, and health costs (Devereaux 2005). For example, mortality due to in-hospital acute myocardial infarction (AMI) after non-cardiac surgery is in excess of 30%.

A recent study with surgical data from 56 countries around the world estimated at over two hundred and thirty million the total number of major surgical interventions that are carried out annually (Weiser 2008). If we take into account that cardiac surgery and pædiatric surgery represent just a small percentage of those operations, we can state that annually, over two hundred million adults undergo major non-cardiac surgery, and over two million will experience a serious cardiovascular episode (acute myocardial infarction, cardiac arrest, non-fatal ictus, or cardiovascular death) (Devereaux 2005). In spite of the magnitude of the problem, there are few studies that have looked at this topic and very few RCTs that have assessed interventions to reduce peri-operative cardiovascular risk.

4.3.1. Pharmacological prevention

4.3.1.1. Beta-blockers

Recently, the largest study carried out in peri-operative medicine (8351 patients) showed that metoprolol CR (slow-release metoprolol succinate), compared with a placebo in patients undergoing non-cardiac surgery with moderate or high vascular risk reduces the risk of suffering peri-operative infarction (415 events; HR=0.73; 95% CI: 0.60 to 0.89) (POISE 2008, Alonso-Coello 2009). However, the study showed that this medication increased the risk of death (226 events; HR=1.33, 95% CI: 1.03 to 1.74) and the risk of suffering disabling ictus (60 events; HR=2.17, 95% CI: 1.26 to 3.74).

High quality

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A greater proportion of patients that did not receive metoprolol compared with those who did receive it experienced clinically significant hypotension (1 029 events; HR=1.55; 95% CI: 1.38 to 1.74). Likewise, a greater proportion of patients who received metoprolol experienced clinically relevant bradycardia (378 events; HR=2.74; 95% CI: 2.19 to 3.43). The increase in clinically significant hypotension observed in the POISE study was consistent with the previous results of the meta-analysis, which included different doses of other peri-operative beta-blockers (RR=1.27; 95% CI: 1.04 to 1.56). Significant hypotension and bradycardia, as well as ictus caused by beta-blockers, are responsible for over half the deaths that occurred in the POISE study. This would explain the increase in the risk of death associated with the use of peri-operative beta-blockers.

The results of the POISE study suggests that for every 1000 patients with a similar risk profile undergoing non-cardiac surgery, metoprolol CR would avoid AMI in about 15 patients, revascularisation in three, and the appearance of clinically significant auricular fibrillation in seven. Similarly, for every 1000 patients treated with metoprolol peri-operatively, eight will die, five will suffer ictus, 53 will experience clinically significant hypotension, and 423 will experience significant bradycardia.

A subsequent SR that includes the POISE study showed similar results, with a reduction in AMI risk and an increase in the risk of ictus and possibly death (Bangalore 2008). The authors indicate that due to the risk of ictus, bradycardia, and hypotension (which was an independent predictor of death in POISE), beta-blockers should not be used routinely in patients undergoing non-cardiac surgery, except if the patient were already taking them (Bangalore 2008). The review recommends that guides should tone down their recommendations in favour of that intervention, and that peri-operative beta-blockers should not be used as a process indicator (Bangalore 2008). High quality

The POISE study has given rise to some criticism following its publication – specifically: the inclusion of high-risk patients, the beta-blocker chosen, and the dose. With respect to the inclusion of high-risk patients or patients with worse prognosis in the POISE study, both the latter as well as the subsequent systematic review that includes it show that the unfavourable risk/benefit balance is observed independently of basal patient risk (Bangalore 2008). That same SR shows how the quality of studies is a determining factor in the variability observed in the results. Specifically, low-quality studies give an excessively optimistic and inconsistent view of results.

As regards to dosage, it is plausible – although probable – that other dosages could have different results. The POISE study used a dosage of metoprolol that represents 50% of the maximum daily therapeutic dose. Recommendations made by Clinical Practice Guidelinesare based on studies that used dosages representing 25% to 50% of the maximum daily therapeutic dose (Fleisher 2007). The DIPOM study, the second largest study after POISE, used the same drug and a target dose of 25% of the maximum daily dose, also showing an increase in the risk of cardiovascular complications. Similarly, the SR prior to POISE showed an increase in the risk of death and ictus associated with various dosages and types of beta-blockers (Bangalore 2008).

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4.3.1.2. Statins

The logic that underlies the use of statins is that they have plaque-stabilising properties, so they may prevent cardiac events. Evidence available to date on this matter is basically observational.

The SR of higher quality, which included observational studies as well as RCTs available to date, concludes that available studies suggest that statins administered peri-operatively may reduce the risk of vascular events in patients undergoing high-risk surgery (Kapoor 2006). Reductions in the risk of death or of coronary syndromes vary between 30% and 42% with respect to patients who do not take them. However, only two small RCTs (177 patients) have been published, and they do not allow the drawing of definite conclusions to (13 events; OR 0.26; 95% CI: 0.07 to 0.99). The time when treatment is started, the duration, the dosages, and the LDL target figures LDL, as well as the indications, are not clear for the moment. Other SRs show similar results (Chan 2008, Hindler 2006). Moderate quality

4.3.1.3. Alpha-2 agonists

Alpha-2 andrenergic agonists suppress the release of catecholamines weakening the response to stress acting at central level, and inhibiting the release of noradrenalin.

A systematic review (23 RCTs, 3395 patients) assessed the effectiveness of alpha-2 agonists (clonidinea, dexmedetomidine, mivazerol) showing a significant reduction in mortality (39 events; RR 0.47; 95% CI: 0.25 to 0.90) and the incidence of MI (110 events; RR 0.66; 95% CI: 0.46 to 0.94) in patients undergoing vascular surgery (Wijeysundera 2003). The effect in the case of non-vascular and non-cardiac surgery was not significant (twelve RCTs, 2854 patients). Studies with information on the risk of hypotension did not show an increase of that factor in the case of non-cardiac surgery (RR 1.03; 95% CI: 0.89 to 1.21; P for heterogeneity 0.22). Moderate quality

A meta-analysis (two RCTs, 358 patients) (Nishina 2002) and a subsequent RCT (190 patients) (Wallace 2004) on the effectiveness of clonidine showed that this medication reduced the incidence of myocardial ischæmia in patients undergoing non-cardiac surgery, without significantly affecting hæmodynamic stability. That last RCT is the only one that followed patients beyond the post-surgery 30-day mark (Wallace 2004).

4.3.1.4. Calcium antagonists

An SR (11 RCTs, 1007 patients) that assessed the effectiveness of this pharmacological group did not observe significant differences for variables of myocardial infarction (five events) or death (17 events) (Wijeysundera 2003). However, an improvement was observed with respect to ischæmia and supraventricular arrhythmia. Currently, the small number of events reduces confidence in the results obtained. Moderate quality

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4.3.1.5. Acetylsalicylic acid (ASA)

A SR (ten RCTs, 1769 patients) on the effectiveness of antiplatelet drugs when compared with placebo in patients undergoing infra-inguinal bypass surgery showed favourable results (168 events; RR 0.76; 95% CI: 0.54 to 1.05) (Robles 2001). However, one of the trials suggested an increase in the risk of ischæmic cardiac events in patients who received ASA undergoing surgery due to a hip fracture (HR 1.33; 95% CI: 1.00 to 1.78) (PEP 2000). The PEP trial also showed a protective effect on pulmonary embolism (HR 0.43; 95% CI: 0.18 to 0.60), which is questionable due to the fact that only 25% of patients in the placebo group received low-molecular-weight heparin (LMWH). Because of this, Clinical Practice Guidelinesadvise LMWH and not ASA for preventing venous thrombo-embolism (GPC Chest 2008, GPC NICE 2007). A study of cohorts included in the POISE trial (POISE 2008) showed –by means of a multivariate analysis of death predictors at the 30-day mark– that the only drug that offered protection was ASA (HR 0.54; 95% CI: 0.39 to 0.75). Moderate quality

Furthermore, the use of ASA in patients undergoing non-cardiac surgery is associated with an increase in the risk of bleeding. In the most significant study carried out to date (PEP 2000), there was an increase in the number of episodes of bleeding that required a transfusion (1.24%; 95% CI: 1 to 53%). In the case of patients at high risk of atherosclerosis, outside the surgical environment, an SR (195 RCTs, 135,640 patients and 17,207 serious vascular events) showed a significant reduction in the risk of AMI, ictus, and vascular mortality (BMJ 2002). The same meta-analysis shows how low dosages (75-150 mg/day) are as effective as, and less gastro-erosive than, higher dosages.

A meta-analysis of three prospective studies of cohorts (34,344 patients) assessed the effects of interrupting ASA in patients outside the surgical environment (Biondi-Zocccai 2006). The study showed that this was associated with an increase of serious cardiac episodes (RR 3.14; 95% CI: 1.75 to 5.61).

4.3.2. Coronary revascularisation

Two RCTs assessed the effectiveness of prophylactic coronary revascularisation in non-cardiac surgery (McFalls 2004, Poldermnas 2007). One of them, the CARP trial (CARP: Coronary Artery Revascularization Prophylaxis), randomised 510 patients to coronary revascularisation surgery or to a group not receiving surgical treatment (follow-up lasting 2.7 years) in patients undergoing vascular surgery (abdominal aortic aneurysm or severe claudication). Patients were eligible for the study if they presented at least one coronary artery with over 70% stenosis subject to revascularisation. No long-term significant differences were observed for the mortality variable (137 events; RR 0.98, 95% CI: 0.70 to 1.37). A pilot RCT in patients undergoing vascular surgery who had extensive cardiac ischæmia showed similar results for the compound variable made up of death and acute myocardial infarction (38 events; HR 1.4, 95% CI: 0.7 to 2.8). Moderate quality

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Summary of the evidence

High quality	In patients undergoing non-cardiac surgery, beta-blockers reduce the risk of myocardial infarction, but increase the risk of disabling ictus, hypotension, and serious bradycardia (POISE 2008, Bangalore 2008).
Moderate quality	In patients undergoing vascular surgery, alpha-2 agonists showed a reduction in the risk of death and of myocardial infarction. In the case of non-vascular surgery and non-cardiac surgery, that effect was not observed. Similarly, there was no observed increase in the risk of hypotension (Wijeysundera 2003).
Moderate quality	Acetylsalicylic acid (ASA) showed contradictory results with respect to the prevention of experiencing cardiovascular events in patients undergoing non-cardiac surgery. The use of ASA in those patients is associated with a risk of bleeding (PEP 2000).
High quality	In the case of patients at high risk of atherosclerosis, outside the surgical environment, acetylsalicylic acid reduces the risk of AMI, ictus, and vascular mortality. Low dosages (75-150 mg/day) are as effective as, and less gastro-erosive than, higher dosages (BMJ 2002).
Moderate quality	In patients undergoing non-cardiac surgery, calcium antagonists reduce cardiac ischæmia, but did not show that they reduced the risk of experiencing acute myocardial infarction or death (Wijeysundera 2003).
Moderate quality	Statins reduce the risk of death and of coronary syndromes in patients undergoing high-risk surgery. There is insufficient information on when to start treatment with statins, or for how long to maintain it, in patients undergoing non-cardiac surgery. Likewise, there is no information on the dosage, type of statins, LDL target figures, or indications for their use (Kapoor 2006).
Moderate quality	For now, coronary revascularisation has not been found to be effective in patients undergoing non-cardiac (vascular) surgery, with respect to reducing cardiovascular morbimortality (McFalls 2004, Poldermnas 2007).

Recommendations

Weak	In patients undergoing surgery who need treatment with statins for medical reasons and regardless of the type of surgery, assess the pre-operative use of statins, e.g. patients with a high vascular risk, coronary disease, or high levels of LDL-cholesterol.
Weak	In patients who meet the criteria for treatment with statins, whether for primary or secondary prevention, use the peri-operative period to introduce the treatment.
Strong	In patients undergoing non-cardiac surgery, it is recommended not to use beta-blockers on a routine basis to prevent cardiovascular episodes.
Weak	In patients undergoing non-cardiac surgery, it is in principle not recommended that use be made of alpha-2 agonists to prevent cardiovascular events. For vascular surgery, assess its use on an individual basis.

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Strong	In patients undergoing non-cardiac surgery and who are not being treated with acetylsalicylic acid, make a case-by-case assessment of its use in the peri-operative environment in patients with low risk of bleeding and high cardiovascular risk.
Weak	In patients undergoing non-cardiac surgery in treatment with acetylsalicylic acid, it is not recommended that the treatment be withdrawn except in individual situations where the risks outweigh the benefits.
Strong	In patients undergoing vascular surgery, coronary revascularisation is not recommended in patients who are subject to it, before surgery is carried out.

4.3.3. Preventing arrhythmia

Amongst cardiovascular complications, arrhythmia is a frequent complication in non-cardiac surgery. In spite of the magnitude of the problem, its physiopathology is little known. In the case of cardiac surgery, it is plausible that the mechanism is a direct irritation of the myocardium that alters electrical activity. However, in the cases of non-cardiac surgery, that view is not applicable,, which suggests that the possible causes of arrhythmias are a general inflammatory response or a response to stress with an increase in sympathomimetic and hormonal activity. Some authors also suggests that arrhythmia may be due to underlying co-morbidity, sepsis, or other episodes like acute myocardial infarction, pulmonary embolism, or electrolytic alterations, amongst others.

4.3.3.1. Auricular fibrillation

Auricular fibrillation (AF) occurs 2 to 4 days after surgery, and is self-limiting in most cases. The incidence of AF is little known, due to the heterogeneity of the results from available studies, which estimate it at between 1% and over 20%. The incidence of supraventricular arrhythmia (SVT) has been estimated to lie between 4% and over 20%, with an average of about 7% (Walsh 2007). This variability is due to differences between the design of studies, the types of surgery included (low-risk surgery versus high-risk surgery, especially thoracic surgery), the use of cardiac monitoring, the non-inclusion of episodes of AF that do not require intervention, or the joint inclusion of SVT arrhythmia. Due to those limitations affecting some studies, it is reasonable to think that the true incidence of AF is currently under-estimated.

With regard to the prognostic value of post-surgical AF, available literature is equally inconclusive. Information on the independent association of AF after surgery with morbidity and/or mortality is scant, and a description has been given of an association with an increase in the length of hospital stay, sepsis, and pulmonary complications (Polanczyk 1998, Braithwaite 1998, Murthy 2003). Although the increase in mortality described in some studies is striking, that does not represent independent association, and can be influenced by confounding factors. On the other hand, some studies show a similar prognosis for patients with that type of arrhythmia (Cardinale 1999, Valentine 2001).

Post-surgical AF is a risk factor for ictus, and it is probable that it should be so in the context of non-cardiac surgery. The POISE trial identified the appearance of AF after non-cardiac surgery as a predictor of ictus in the first 30 days after surgery (60 events; RR=3.51; 95% CI: 1.45 to 8.52) (POISE Study Group 2008). However, the population included was only made up of patients with or at risk of atherosclerosis.

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4.3.3.1.1. Risk factors

Both pre-operative and intra-operative risk factors have been postulated as predictors of the appearance of new episodes of AF after non-cardiac surgery. However, the evidence available is inconsistent, and it is complex to identify high-risk patients.

Amongst pre-operative factors, advanced age is the most consistent predictor (Khan 1993, Murthy 2003, Vaporciyan 2004, Passman 2005). Other related factors –albeit always inconsistently so– were gender (more frequent in males), cardiac conditions, valve conditions, and previous history of supraventricular arrhythmia (Polanczyk 1998). Amongst intra-operatives, some high-risk surgery such as vascular surgery, non-vascular abdominal surgery, repairing abdominal aneurysms, and intrathoracic surgery have been independently associated with the appearance of SVT arrhythmia (Goldman 1978, Polanczyk 1998, Curtis 1998, Perzanowski 2004).

4.3.3.2. Prophylactic interventions

Given the unfavourable prognosis of the appearance of AF in the context of surgical patients (non-cardiac surgery), some pharmacological interventions are used preventively. However, although there are studies available in this regard, data is scant and more research is needed to obtain deeper knowledge of its potential role in preventing that type of episode. The drugs evaluated include calcium antagonists, beta-blockers, magnesium, amiodarone, digitalis, and statins, amongst others.

4.3.3.2.1. Calcium antagonists

Two SR assessed the role of calcium antagonists (Wijeysundera 2003, Sedrakyan 2005). The more recent of the two identified four RCTs that assessed the effect of calcium antagonists on preventing auricular tachycardia (AT) (Sedrakyan 2005). Specifically, these RCTs (668 patients) showed a reduction in the risk of AT (99 events; RR=0.50; 95% CI: 0.34 to 0.73).

Moderate quality

In a previous SR published in 2003, five RCTs were identified that assessed the effect of calcium antagonists on the risk of supraventricular tachycardia, all carried out on patients undergoing thoracic surgery (Wijeysundera 2003). The meta-analysis (682 patients) showed a protective effect (127 events; RR=0.52; 95% CI: 0.37 to 0.72) without statistical heterogeneity was observed. Diltiazem and verapmil both reduced the risk of SVT.

Both SRs showed an increase in the risk of bradycardia and hypotension.

4.3.3.2.2. Beta-blockers

One SR identified two RCTs (129 patients) showing that beta-blockers have a protective effect on the risk of AF (21 events; RR=0.40, 95% CI: 0.17 to 0.95) (Sedrakyan 2005). Afterwards, the POISE study (8351 patients) also showed a clinically significant protective effect through a reduction in the risk of AF (211 events; HR=0.76, 95% CI: 0.58 to 0.99) (POISE 2008). The SR and the POISE study show an increase in the risk of bradycardia and hypotension. Similarly, an SR on the effect of beta-blockers on cardiovascular events showed that those drugs, in spite of reducing the risk of AMI, increase the risk of ictus and probably the risk of death, in addition to increasing the risk of bradycardia and hypotension (Bangalore 2008).

Moderate quality

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4.3.3.2.3. Others

Low quality

The effect of digitalis in the prevention of peri-operative arrhythmia has been evaluated. In three trials (285 patients), digitalis compared with no treatment increased the risk of atrial tachycardia or arrhythmia (71 events; RR=1.51, 95% CI: 1.00 to 2.28) (Sedrakyan 2005). Similarly, in one trial (70 patients), digitalis was found to be inferior to diltiazem in patients undergoing pneumectomy (Amar 1997). In another small-scale trial (30 patients), digitalis was less effective than flecainide in patients undergoing non-cardiac thoracic surgery (Borgeat 1991).

Statins were evaluated in an observational study regarding their effect on the prevention of arrhythmia in non-cardiac surgery. In one study (Amar 2005) with 131 patients aged over 60 undergoing œsophageal resection, statins reduced the risk of AF (38 events; RR=0.26; 95% CI: 0.08 to 0.82).

In one study (194 patients), magnesium reduced the risk of AF (30 events; RR=0.40, 95% CI: 0.21 to 0.78) (Terzi 1996). Small-scale studies showed that amiodarone (62 patients) and flecainide (30 patients) had a protective effect with respect to the appearance of auricular tachycardia (RR=0.14, 95% CI: 0.02 to 1.10 and RR=0.16, 95% CI: 0.01 to 2.89) (Van Mieghem 1994, Borgeat 1989).

Summary of the evidence

Moderate quality	Administering calcium antagonists reduces the risk of arterial tachyarrhythmia, but increases the risk of hypotension and bradycardia (Wijeysundera 2003, Sedrakyan 2005).
Moderate quality	Administering beta-blockers reduces the risk of auricular fibrillation in patients undergoing non-cardiac surgery, but increases the risk of hypotension, bradycardia, and ictus (Sedrakyan 2005, POISE 2008, Bangalore 2008).
Low quality	Administering digitalis increases the risk of auricular tachyarrhythmia in patients undergoing non-cardiac surgery (Sedrakyan 2005).
Low quality	Statins, amiodarone, and flecainide may potentially reduce the risk of auricular fibrillation in patients undergoing non-cardiac surgery (Van Mieghem 1994, Terzi 1996, Borgeat 1989, Amar 2005).

Recommendations

Weak	In patients undergoing non-cardiac surgery, consider the use of calcium antagonists in preventing auricular fibrillation on a case-by-case basis.
Strong	In patients undergoing non-cardiac surgery, it is recommended that beta-blockers should not be used routinely to prevent auricular fibrillation.
Strong	In patients undergoing non-cardiac surgery, it is recommended that digitalis should not be used to prevent auricular fibrillation.
Weak	In patients undergoing non-cardiac surgery, it is recommended that amiodarone, flecainide, and magnesium should not be used to prevent auricular fibrillation.

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4.4. Preventing venous thrombo-embolism

Question to be answered

- In antithrombotic prophylaxis of surgical patients, what is the effectiveness of the available antithrombotic treatments?
- In patients undergoing general surgery, are different prophylactic measures recommended depending on risk?
- In antithrombotic prophylaxis of surgical patients, when should prophylaxis be started?
- In antithrombotic prophylaxis of surgical patients, what is the duration and dosage of prophylaxis?

Multiple interventions have been evaluated for antithrombotic prophylaxis in surgical patients. They can be grouped as follows:

Non-pharmacological measures: aimed at facilitating the venous return from the lower extremities by direct or induced compression using electrical stimulation. These measures are known as mechanical measures, so that they can be to distinguished from drugs (compression stockings, intermittent pneumatic pressure, electrical stimulation for muscular contraction).

Pharmacological measures: mainly heparins (unfractionated heparin and of low molecular weight), other drugs with anticoagulant action of a chemical structure, and various action mechanisms like oral anticoagulants, antiaggregants, fondaparinux, dabigatran, danaparoid, dextran, or rivaroxiban, which recently started to be commercialised.

These measures (individually or in combination) have been evaluated in randomised clinical trials and compared against placebo (or with no intervention) and against each other. In general, both interventions were effective in reducing thrombotic events in patients undergoing surgery.

In the clinical trials that evaluated these measures, which were generally carried out in higher-risk patients, the incidence of venous thrombosis without treatment was 29%, and the incidence of pulmonary embolism was 3%. Orthopædic surgery is of especial risk SSIth regard to thrombotic complications. The following table reflects certain characteristics in patients that lead to an increased risk of thrombotic complications.

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Table. Venous thrombo-embolism risk factors (NICE 2007)

– Active cancer or cancer treatment – Cardiac or respiratory insufficiency – Acute illness – Age: over 60 – Antiphospholipidic syndrome – Behçet's Disease – Central venous catheter *in situ* – Trips over 3 hours long, 4 weeks before or after the intervention – Immobility (or paralysis or plaster cast *in situ*) – Intestinal inflammatory disease – Myeloproliferative syndrome – Nephritic syndrome	– Obesity (BMI ≥ 30 kg / m^2) – Monoclonal gammopathy – Paroxysmal nocturnal hæmoglobinuria – Personal of family history of venous thrombo-embolism – Pregnancy or puerperium – Recent myocardial infarction or ictus – Serious infection – Use of oral contraceptives or hormone replacement therapy – Phlebitis or varicose veins – Hereditary thrombophilia (high levels of coagulation factors, hyperhæmocysteinæmia, low resistance to activated protein C, protein C, protein S, and antithrombin deficiency, prothrombin gene 2021 mutation)

It should be taken into consideration that in spite of abundant bibliography that evaluates oral anticoagulants as an antithrombotic strategy in surgical patients, most of the studies were conducted in the 1960s and 1970s. In addition, the most recent ones (from the 1990s) are comparative studies with low-molecular-weight heparin. The approved indication for acenocoumarol (the most widely used in our environment) is the treatment and prophylaxis for thrombo-embolic disease. Absolute contra-indications are considered to be those that have an increased risk of bleeding, including surgery. Accordingly, its use is restricted after surgery and after ensuring that the patient's hæmostasis is adequate.

Antiaggregants are not specifically indicated for the prevention of thrombotic events in surgery. Furthermore, given that there is no effective antidote to reverse bleeding should it occur, the usual recommendation is that antiaggregants be removed before an operation. In the separate section of the Guide, there is a discussion of the benefits of antiaggregants in reducing vascular events after surgery.

Other drugs, like danaparoid, are not on currently commercialised, while dextran, approved in Spain, is not indicated for the prevention of thrombotic events after surgery. The latter is used mainly as a plasma expander, and is administered endovenously during surgery.

A review by NICE and an assessment report on very recent technologies jointly evaluated the effectiveness of various interventions for antithrombotic prophylaxis in surgery. Both included studies involving various types of surgery, although many of them were surgery with a high level of thrombotic risk (NICE 2007, Roderick 2005). In addition, various SRs and RCTs have been localised that deal with the topic, although consideration has only been given to those references that provide a direct response to either of the questions, or that by their size or significance complement the information contributed by the two previous documents.

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4.4.1. Non-pharmacological measures

Several studies and SRs have evaluated various non-pharmacological or mechanical measures as a measure for thrombotic prophylaxis after surgery. They have been evaluated against each other and as an aid to pharmacological treatment. It should be pointed out that mechanical measures, when working by means of a pressure mechanism, should not be used in persons with peripheral vascular disease (regardless of cause).

The NICE SR carried out a combined analysis of the studies that evaluated a mechanical measure in comparison with no prophylaxis, and found 28 RCTs with a total of 3334 patients. The risk of deep vein thrombosis and of proximal deep vein thrombosis fell significantly by 54% and 48% respectively; no differences were found for pulmonary embolism. Also analysed were studies that evaluated a mechanical measure as an aid to other pharmacological or non-pharmacological measures (25 RCTs, 5 432 patients). Significant reductions were obtained with respect to venous thrombosis and proximal venous thrombosis when two mechanical measures were combined. In addition, upon combining a mechanical measure with a pharmacological measure, there was a significant reduction in the risk of venous thrombosis and pulmonary embolism. Finally, two RCTs were evaluated that compared electrical stimulation measures with no prophylaxis, where the former achieved a reduction of 59% in deep vein thrombosis (NICE 2007). Moderate quality

The greater volume of evidence comes from intermittent pneumatic compression mechanisms (28 RCTs) as well as compression stockings (19 RCTs). The analysis of these studies, based on the comparisons made, shows that the effectiveness of compression stockings in reducing venous thrombosis is greatest in long stockings that reach to the hips. Similarly, intermittent pneumatic pressure mechanisms, both those that reach the knee and those that cover the entire extremity, reduce the risk of venous thrombosis and of proximal venous thrombosis,. Lastly, in comparison with compression stockings, compression mechanisms were found to be better only when combined with pharmacological treatment. Electrical stimulation and pedis impulses have been assessed in few clinical trials carried out on a small scale. Their analysis is inconclusive because of the scant number of events recorded (NICE 2007). High quality

In spite of the effectiveness of compression stocking, a series of cases when they should not be used has been described (JBI Best Practice 2008): peripheral arterial disease, atherosclerosis, serious peripheral neuropathy, massive œdema in the lower extremities, pulmonary œdema, œdema caused by congestive cardiac failure, local diseases affecting the skin or soft tissue, gangrenous extremities, Doppler pressure reading <0.8, and excessive cellulitis.

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A recent SR that included six RCTs, as well as five non-randomised studies covering a total of 7431 patients, assessed the effectiveness of pneumatic compression in combination with pharmacological treatment. The combination strategy, when compared with pharmacological treatment, showed a significant reduction in deep vein thrombosis in four studies (RR 0.16; 95% CI: 0.07 to 0.34, 54 events), resulting in absolute difference of 3.6%. No estimate could be made of the effect on pulmonary embolism. The combination strategy also reduced the incidence of deep vein thrombosis (57%) and symptomatic pulmonary embolism (61%) as compared with mechanical measures as a sole intervention (Kakos 2008).

4.4.2. Pharmacological measures

4.4.2.1. Heparins and other comparable treatments

The effectiveness of unfractionated heparin when compared with a placebo (or with no prophylaxis) was evaluated in a NICE SR that had a total of 75 RCTs and 16,215 patients undergoing various types of surgery. Administration took place before or after surgery, with prophylaxis lasting for between two and sixteen days or until the patient could walk or until discharge from the hospital. Some studies also used other interventions to prevent thrombosis. Unfractionated heparins reduce the risk of venous thrombosis by about 56% (with varied results), of proximal venous thrombosis by 55%, and of pulmonary embolism by 30%. On the other hand, there was a significant risk of severe bleeding (NICE 2007).

Moderate quality

Similarly, the NICE SR jointly evaluated the results of studies on the effectiveness of low-molecular-weight heparin as opposed to a placebo (or no intervention) for a total of 28 RCTs and 8935 patients. In many studies, prophylaxis lasted for between one or two weeks and up to thirty days. Treatment with low-molecular-weight heparin reduced the risk of venous thrombosis, proximal venous thrombosis, and pulmonary embolism by 51%, 62%, and 64% respectively. The risk of bleeding increased by about 77% (NICE 2007).

Comparative effectiveness of unfractionated heparin and low-molecular-weight heparin was assessed in the NICE SR for a total of 76 RCTs and 22,574 patients undergoing various forms of surgery. Low-molecular-weight heparins reduced the risk of venous thrombosis (RR 0.87; 95% CI: 0.79 to 0.95; 67 RCTs, 1644 events), the risk of pulmonary embolism (RR 0.66; 95% CI: 0.46 to 0.95; 37 RCTs, 99 events), and the risk of proximal venous thrombosis (RR 0.62; 95% CI: 0.49 to 0.78; 19 RCTs, 282 events). Results were consistent across the various studies. In the subgroup of studies in which patients received mechanical prophylactic measures, no differences were found between the two forms of heparin for venous thrombosis or pulmonary embolism, and in the case of proximal venous thrombosis only, low-molecular-weight heparin showed effectiveness greater than that of unfractionated heparin.

High quality

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The analysis of serious hæmorrhagic events did not show differences between the two heparins in 47 RCTs and 678 events, even though the joint estimator favoured low-molecular-weight heparins, on the margin of significance (NICE 2007).

Only one RCT that directly compared the start of prophylaxis using low-molecular-weight heparins before (in the twelve hours preceding) or after hip-replacement surgery was found. No differences were found in the incidence of deep vein thrombosis (51 cases of thrombosis, ten of which were proximal) measured using venography at a follow-up session held after two weeks. Equally, there were no differences in adverse events (Paraleti G 1996). One analysis, using indirect comparisons in the NICE SR, assessed the effectiveness of low-molecular-weight heparins based on the start of treatment (before or after the operation) in a total of 26 RCTs. No significant differences were found between the two strategies for the principal variables analysed (venous thrombosis, proximal venous thrombosis, pulmonary embolism, and serious hæmorrhagic events) (NICE 2007). Moderate quality

The duration of prophylaxis using heparins (unfractionated or low-molecular-weight) was assessed in the NICE SR for a total of 12 RCTs (2809 patients) in orthopædic surgery. Comparisons were made between the usual heparin model (until discharge from hospital or up to fourteen days) and the models that continued heparin until one week after discharge or with a total duration of between 19 and 30 days. The results showed that extending the heparin model beyond discharge from hospital is associated with a significant reduction of deep vein thrombosis (52%), proximal deep vein thrombosis (66%), and pulmonary embolism (66%). Information on the incidence of serious hæmorrhagic events was obtained from a single study, without significant differences between the two strategies. Most of the studies were carried out using low-molecular-weight heparin (NICE 2007).

The NICE SR identified five RCTs of moderate quality that evaluated various dosages of low-molecular-weight heparin for the prophylaxis of venous thrombosis in surgery. Higher dosages ranged from 3500 IU to 5000 IU of dalteparin or 60 mg of enoxaparin, whereas lower dosages ranged from 2500 IU to 3000 IU of dalteparin or 40 mg of enoxaparin. The combined analysis of the results showed that higher dosages reduced the incidence of venous thrombosis by about 45%, but with a rise in cases of serious bleeding (NICE 2007).

The effectiveness of fondaparinux was assessed in a total of five RCTs, and was compared with low-molecular-weight heparins. Studies included patients undergoing orthopædic surgery or surgery with a high risk of thrombosis; in both cases, the dosage was 2.5 mg after the operation. All the studies allowed the use of elastic compression stockings. The NICE SR carried out a joint assessment of the results, showing a reduction of deep vein thrombosis with fondaparinux (RR 0.52; 95% CI: 0.44 to 0.60; five RCTs, 639 events), although it was associated with a 49% increase in cases of serious bleeding (five RCTs, 242 events) (NICE 2007). High quality

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The effectiveness of danaparoid was assessed in various trials, showing a reduction in deep vein thrombosis when compared with placebo, unfractionated heparin, and aspirin. There were no significant differences with unfractionated heparin or aspirin regarding the prevention of pulmonary embolism when compared, with a very limited number of events. The only trial that gave reliable results did not show differences between danaparoid and low-molecular-weight heparin (NICE 2007). Low quality

Low quality

In patients undergoing epidural or spinal anæsthesia for surgery, the administration of low-molecular-weight heparin for prophylaxis has on rare occasion been associated with the appearance of epidural or spinal hæmatomata, which causes prolonged or permanent paralysis. This risk is increased by the use of epidural or spinal catheters for anæsthesia, the concomitant administration of anticoagulants, and traumatic or repeated punctures.

If it is decided to perform a neuro-axial puncture, consideration must be given to the time until maximum effect of low-molecular-weight heparin, which is about four hours after administration. Plasma half-life is also four hours, but pharmacodynamic activity persists for between 16 and 24 hours after administration. Ideally, there should be less than ten hours between administering heparin and the puncture, or up to twenty-four hours if high dosages are used. Once the catheter has been inserted or removed, there should be at least two hours until the administration of a further dose of heparin, which should be delayed until the end of surgery.

4.4.2.2. Oral anticoagulants

One SR (29 RCTs) evaluated the effectiveness of oral anticoagulants (OACs) in the prophylaxis of thrombotic events in orthopædic surgery, compared with other prophylactic interventions (pharmacological or physical), placebo, or no intervention. In the great majority of RCTs, the anticoagulant used was warfarin. Also, coumarinic compounds (dicoumarol, acenocoumarol) was used in four studies, and phenindione, in two morecarried out in the 1960s. The results evaluated were deep vein thrombosis, pulmonary embolism, death, serious hæmorrhagic event, and hæmatoma in the surgical wound. Studies were of variable quality, with a blind or open design and a maximum follow-up period of six months. In eleven studies, treatment was started before surgery with variable duration, although in most studies, it was about three weeks or until discharge from hospital (Mismetti 2004).

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4.4.2.2.1. Deep vein thrombosis

Oral anticoagulants (OACs) with dosages adjusted according to the INR (International Normalised Ratio) reduced by about 44% the incidence of deep vein thrombosis when compared with placebo (or with no intervention). In relation to other interventions, OACs showed significantly lower effectiveness than low-molecular-weight heparins and danaparoid, whilst effectiveness was similar to that of dextran, unfractionated heparins, or intermittent pneumatic compression. All the results were consistent across the various trials included (Mismetti 2004). High quality

The results for the risk of deep vein thrombosis for the various comparisons were as follows:

OAC *versus* control: RR 0.56 (95% CI: 0.37 to 0.84) (8 RCTs, 224 events)

OAC *versus* dextran: RR 0.73 (95% CI: 0.37 to 1.43) (4 RCTs, 110 events)

OAC *versus* antiagreggants: RR 0.84 (95% CI: 0.55 to 1.28) (3 RCTs, 243 events)

OAC *versus* unfractionated heparins: RR 1.25 (95% CI: 0.87 to 1.81) (3 RCTs, 71 events)

OAC *versus* low-molecular-weight heparin: RR 1.51 (95% CI: 1.27 to 1.79) (10 RCTs, 1 480 events)

OAC *versus* danaparoid: RR 2.11 (95% CI: 1.51 to 2.95) (2 RCTs, 131 events)

OAC *versus* intermittent pneumatic compression: RR 1.21 (95% CI: 0.88 to 1.66) (4 RCTs, 121 events).

Absolute reduction of risk for OACs was about 25.8% with respect to the control. Absolute reductions of risk for low-molecular-weight heparins and danaparoid with respect to OACs was about 4.5% and 14.4% respectively.

Regarding proximal venous thrombosis, results of the comparison of OAC were only obtained from a further three interventions. OACs significantly reduced the risk of thrombosis with respect to intermittent pneumatic compression (54%, 46 events). No differences were found between OACs and antiaggregants. There was an increase of about 51% (293 events) in thrombosis with OACs in comparison with low-molecular-weight heparins.

4.4.2.2.2. Pulmonary embolism

Adjusted doses of OACs reduced by about 77% the risk of pulmonary embolism as compared with a placebo. No significant differences were found in comparison with other interventions (dextran or unfractionated heparins, or low-molecular-weight heparins), although the number of events analysed was very low. The absolute reduction of risk in comparison with a placebo was about 7.3% (4 RCTs, 32 events) (Mismetti 2004). High quality

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4.4.2.2.3. Mortality

OACs did not reduce the mortality compared to the interventions analysed, nor did they significantly reduce mortality with respect to the placebo (17.5% compared to 13.8% respectively) (Mismetti 2004). Moderate quality

4.4.2.2.4. Adverse effects

OACs showed a greater risk of bleeding from the surgical wound (RR 2.91; 95% CI: 1.09 to 7.75; 20 events) but not of serious bleeding, in comparison with placebo. There were no significant differences between OACs and the other interventions analysed for these two events although, once again, the number of events analysed was very small. With respect to heparins, OACs showed a non-significant tendency to present fewer hæmorrhage -related adverse effects (Mismetti 2004). Low quality

RCTs that evaluated the time when prophylaxis was started using OACs (between four and fourteen days before or just after the operation) (Francis 1996, Swierstra 1988), and the appropriate duration of treatment (until discharge from hospital or for four weeks after discharge) (Prandoni 2002) were found. All of them had a very limited number of events and no significant differences between the various strategies. Only the extended-OAC model (for four weeks after discharge) reduced the cases of proximal venous thrombosis (one event) when compared with finalisation following discharge (eight events).

One report on the assessment of technologies evaluated two RCTs (one in gynæcological surgery and the other in orthopædic surgery) that compared flexible or fixed models of OACs. The combined analysis showed a reduction of about 51% in venous thrombosis for flexible models (50 events) (Roderick 2005).

4.4.2.3. Antiaggregants

The NICE SR evaluated the effectiveness of antiaggregants (mainly aspirin) in preventing thrombosis in surgical patients through re-analysis of a review that also included non-surgical patients. Those trials were excluded, and a combined analysis of the results of a total of 44 events was made. High quality

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Antiaggregants as a group reduced the risk of deep vein thrombosis by about 24% in comparison with a placebo (or no prophylaxis) (RR 0.76; 95% CI: 0.65 to 0.87; 44 RCTs, 1 315 events). Results were very variable across studies. The benefit was independent of whether the drug used was aspirin or the antiaggregant alone, or aspirin in combination with another antiaggregant. Antiaggregants reduced the risk of proximal venous thrombosis by about 39% when compared with placebo (eleven RCTs, 157 events), although the analysis of the three trials that evaluated other antiaggregants did not show significant differences. In many of the studies, there were no serious hæmorrhagic events. Overall, there were no differences between antiaggregants and placebo in the analysis of nine RCTs covering a total of 33 events. In that same review, three RCTs of limited size compared high doses with low doses of aspirin. The range of doses was very wide, and no differences were found between the groups regarding deep vein thrombosis (NICE 2007).

A large study evaluated aspirin as an adjuvant treatment in other interventions for preventing the risk of thrombosis after surgery (unfractionated heparins or low-molecular-weight heparins, compression stockings, or techniques of non-general anæsthesia). The study included a total of 17,444 patients undergoing hip-fracture surgery or scheduled arthroplasty. The dosage of aspirin used was 160 mg per day, in most cases starting before the operation and maintained until discharge from hospital or for 35 days. The study mainly evaluated the risk of pulmonary embolism. Aspirin reduced the risk of pulmonary embolism (RR 0.57, 95% CI: 0.40 to 0.82; 127 events) after femur surgery; the absolute effect was 1.2% for the placebo and 0.7% for aspirin, with a reduction of 0.5%. The trial also showed a significant reduction of 29% in symptomatic venous thrombosis. In the subgroup of patients undergoing scheduled arthroplasty, aspirin did not reduce the risk of pulmonary embolism, probably because only nineteen events were recorded. In general, patients treated with aspirin presented more hæmorrhagic events, although there were no differences regarding serious hæmorrhagic events (PEP 2000).

According to the combined analysis of six RCTs with a total of 1 174 participants undergoing various types of surgery (NICE 2007), prophylaxis with aspirin prevents more events of deep vein thrombosis than low-molecular-weight heparins, (five RCTs, 70 events), without differences regarding pulmonary embolism or serious hæmorrhagic events.

4.4.2.4. Direct thrombin inhibitors (dabigatran)

Dabigatran is a direct thrombin inhibitor that was recently approved for the prophylaxis of venous thrombo-embolism in orthopædic surgery (scheduled knee and hip arthroplasty) in doses of 220 mg per day. Effectiveness and safety were evaluated in four RCTs that compared different dosages of dabigatran against enoxaparin. One joint analysis that covers the results of three RCTs for the currently marketed dose (220 mg) was found.

High quality

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The combined analysis of these RCTs was carried out with subgroups of patients that received the 220-mg dose (5450 participants), representing 66% of the total number of patients included in the original trials. Duration of prophylaxis varied between six and 35 days, starting with half the dose between one hour and two hours before surgery. Enoxaparin administered subcutaneously was started the night before surgery (40 mg) in two RCTs, and after between 12 and 24 hours following surgery (30 mg every twelve hours) in one RCT. Patients underwent scheduled knee surgery (two RCTs) or scheduled hip surgery (one RCT). The main variable for the three studies was the incidence of venous thrombo-embolism (clinical deep vein thrombosis, or diagnosed using venography and symptomatic pulmonary embolism) and death by any cause. For the main variable, there were no significant differences between dabigatran and enoxaparin (840 events), with inconsistent results across the studies. No differences were found regarding venous thrombo-embolism (excluding distal thrombosis) and related deaths, although for a total of only 131 events. The safety analysis also showed no differences for serious bleeding or clinically relevant bleeding (whether serious or not) (Wolowacz 2009).

The three RCTs included set up non-inferiority trials. In one of them, non-inferiority criteria were not met, and dabigatran (220 mg) showed an increase of about 5.8% in the absolute risk of thrombotic events (95% CI: 0.8 to 10.8) when compared with enoxaparin.

One RCT not included in the previous review explored the effectiveness of various doses of dabigatran (50 to 300 mg per day) compared against enoxaparin in 1973 patients undergoing hip of knee orthopædic surgery. The study showed that increasing doses of dabigatran were associated with a reduction in thrombo-embolic events (clinical or detected by venography). For the highest dose (300 mg), there was an excess of serious hæmorrhagic events in the dabigatran group (2.7%) on the margins of statistical significance (Eriksson 2005).

4.4.2.5. Direct factor Xa inhibitors (ribaroxaban)

Rivaroxaban is a direct Xa inhibitor that was recently approved for prophylaxis of venous thrombo-embolism in orthopædic surgery (scheduled knee and hip arthroplasty) at a dose of 10 mg per day. Effectiveness and security were evaluated in four RCTs that compared various doses of dabigatran with enoxaparin. One combined analysis that offered a combined evaluation of three RCTs was retrieved.

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This analysis included three RCTs (9349 participants) with patients undergoing orthopædic hip surgery (2 RCTs) and orthopædic knee surgery (one RCT). In all of them, the dose of rivaroxaban was 10 mg and the dose of enoxaparin administered subcutaneously was 40 mg per day. In two studies, the duration of treatment was the same in both interventions (two and five weeks), whilst in one study the duration of treatment with rivaroxaban was five weeks, while enoxaparin was used for two weeks. The first administration of enoxaparin was between six and eight hours after surgery, whilst enoxaparin was always administered before surgery. The main variable for the three studies was the combined incidence of deep vein thrombosis (distal or proximal), non-fatal pulmonary embolism, and death for any cause. Nonetheless, the combined analysis included only symptomatic cases of thrombo-embolism and mortality. The results show a significant relative reduction of 56% (56 events) and 62% (84 events) after two weeks and at the end of the study, respectively, favourable to rivaroxaban. Although the results were homogenous, the main benefit was seen only in a single study in patients undergoing knee surgery. The incidence of serious bleeding was similar in the two groups, at about 0.3% (Eriksson 2009).

Low quality

Individually, the three studies showed a significant reduction of the combined variable in the population that underwent surgery and that was correctly evaluated, which meant an overall loss to follow-up of over 30% (Mismetti 2004, NICE 2007, Wolowacz 2009).

A recently published RCT (3148 participants) involving patients undergoing knee surgery, compared rivaroxaban (10 mg per day) against enoxaparin (30 mg twice a day), both after surgery. The main variable was a combination identical to the one in the previous studies. The analysis was initially thought for non-inferiority, switching later on to superiority. The population analysed (patients who underwent surgery and who were correctly evaluated) suffered losses of almost 40%. At the seventeen-day mark, the study showed an absolute reduction for rivaroxaban, which was significant for the main variable (3.19%, 95% CI: 0.71 to 5.67) (164 events). There were no differences in the incidence of increased bleeding (0.7% for rivaroxaban; 0.3% for enoxaparin), although the evaluation was done during a very short time (Turpie 2009).

Moderate quality

In addition, four RCTs that included almost 3 000 patients who received doses of between 2.5 and 60 mg per day, or enoxaparin were found. The aim of these studies was to show a relationship of effectiveness or safety with the dosage. Overall, the studies showed that the dose with a better balance between benefits and risks was that of 10 mg per day (Eriksson 2007, Eriksson 2006a, Eriksson 2006b, Turpie 2005).

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4.4.2.6. Balance between risk and benefit

Moderate quality

Before setting up any type of treatment aimed at reducing the risk of thrombosis after surgery, the risks and benefits must be weighed carefully. Consideration should be given to the risk of thrombosis and bleeding depending on the type of surgery, the type of anæsthesia, the patient's characteristics, concomitant treatment, or other pathologies, habits, and lifestyles of the patient that presents a relevant increment of the risk of thrombosis. Some types of surgery, by their very location, carry a particular risk should bleeding occur in the surgical field, as is the case with neurosurgery or ophthalmologic surgery. The risk of bleeding must also be assessed on an individual basis, given that all pharmacological treatments for preventing thrombosis carry a certain inherent risk of hæmorrhage. In addition, consideration should be given to whether the patient is already receiving antiaggregant or anticoagulant treatment for any other indication. In addition, there are other risks and specific pharmacological interactions for each of the treatments set out (Mismetti 2004, NICE 2007, Wolowacr 2009).

Moreover, in general, oral anticoagulants and antiaggregants must be suspended before surgery, because if serious bleeding occurs, it will call for aggressive measures to stop it. In the case of antiaggregants, of which the effect on platelet aggregation is irreversible, treatment is usually suspended one week before surgery (if the surgery is elective). The effect of oral anticoagulants can be reversed with the administration of vitamin K, which has a non-immediate effect, and may also require the transfusion of rich plasma, which is coagulation factor. In patients already receiving treatment with oral anticoagulants for an existing medical condition, a change in therapy involving a move to low-molecular-weight heparin or unfractionated heparin before the operation is put in place. The effects of heparin can be countered by the administration of protamine.

Finally, strategies like unfractionated heparin or oral anticoagulants require strict patient monitoring to assess hæmostasis, whilst unfractionated heparins, dabigatran, and rivaroxaban do not require analytical controls after they have been started.

4.4.3. Pharmacological measures in patients receiving anticoagulant or antiaggregant treatment on a routine basis

In situations in which patients must undergo surgery and are also receiving anticoagulant or antiaggregant treatment on a routine basis, doubt arises as to whether treatment should be withdrawn, thus increasing the risk of a thrombo-embolic episode, or maintained, thus increase the risk of serious bleeding in the peri-operative phase. Caregivers must decide of the treatmentwithdrawn is substituted with another drug. The ACCP dealt with this casuistry in a chapter of its CPG on antithrombotic treatment (Douketis 2008), which was recently summarised and adapted (INFAC 2009).

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4.4.3.1. Evaluating thrombotic risk after ceasing antithrombotic treatment, and the risk of bleeding associated with surgery

Thrombotic risk in the peri-operative period depends on the indication for which the patient is receiving treatment and the presence of co-morbidity. Low quality

Patients who receive antiaggregants for the primary prevention of infarction or ictus are considered to be at low thrombotic risk, whilst those who recently had a stent fitted (between three and six months), or who suffered acute myocardial infarction during the previous three months, are considered to be at high risk (Douketis 2008). Some retrospective studies have shown that a thrombotic event after suspending treatment with aspirin can occur in 6% of patients, between three and twelve days after the suspension of treatment, with a risk that rises exponentially in patients with coronary stents (INFAC 2009). Although a classification of the peri-operative risk of thrombo-embolism has not been validated, there is one that can be used in the following table.

Patient stratification according to peri-operative risk of venous thrombo-embolism (VTE) or arterial thrombo-embolism

State of risk	Indication of antithrombotic therapy		
	Mechanical valve	**Auricular fibrillation**	**Venous thrombo-embolism**
High	Any mitral prosthesis Old aortic-valve prostheses Recent ictus or transitory ischæmic attack (TIA) (<6 months)	CHAD52 score of 5 or 6 Recent ictus or TIA (<3 months) Rheumatic valve disease	Recent VTE (< 3 months) Serious thrombophilia
Moderate	Bicuspid aortic valve prosthesis and one of the following: auricular fibrillation, previous ictus or TIA, hypertension, diabetes, congestive cardiac failure, age > 75 years	CHAD52 score of 3 or 4	VTE in the previous 3 to 12 months Non-serious thrombophilic conditions Recurrent VTE Active cancer
Low	Bicuspid aortic valve prosthesis without auricular fibrillation and with other risk factors for cerebrovascular accident	CHAD52 score of between 0 and 2 (and with no previous ictus or TIA)	Single VTE episode over 12 months ago and no other risk factors

Anticoagulant and antiaggregant treatments can increase the risk of bleeding during surgery, and consideration should be given to the risk inherent to some procedures in the case of maintaining treatment (INFAC 2009). Low quality

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Risk of bleeding associated with some surgical procedures

High risk of bleeding	Revascularisation of the coronary artery or of the cardiac valves Intracranial or spinal surgery Repairing an aortic aneurysm Peripheral artery bypass Other major vascular surgery Major orthopædic surgery, e.g. hip or knee Reconstructive plastic surgery Major cancer surgery Prostate and bladder surgery Tonsillectomy
Low risk of bleeding, but clinically important	Colon polyp resection, especially sessile polyps Prostate and kidney biopsy Fitting a pacemaker or cardiac defibrillators Retinal surgery
Low risk of bleeding with no clinical importance	Dental, dermatological, and ophthalmic procedures

4.4.3.2. Peri-operative handling of patients receiving anticoagulants

In cases in which treatment is interrupted, warfarin should be withdrawn five days before surgery, whereas acenocoumarol should be withdrawn two or three days before, so they can be eliminated from the organism, (INFAC 2009). — Moderate quality

In cases in which the INR remains high, between 1 and 2 mg of oral vitamin K may be administered, preferably on the day of the operation. — Low quality

Treatment should be resumed between 12 and 24 hours after surgery (INFAC 2009).

To assess a substitute treatment, the various risk groups must be stratified jointly with individual risk factors (Doukeris 2008).

ACCP recommendations for substitute treatment in the most common indications of anticoagulants (surgery in patients with a mechanical valve, auricular fibrillation, or venous thrombo-embolism)

Risk of thrombo-embolism	Change anticoagulant to
High	Therapeutic doses of LMWH sc or heparin iv. LMWH subcutaneously is preferable
Medium	Therapeutic doses of LMWH subcutaneously, therapeutic doses of heparin iv, or low doses of LMWH subcutaneously Therapeutic doses of LMWH subcutaneously are preferable
Low	Low doses of subcutaneous LMWH, or give nothing

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In cases in which substitute treatment is started, treatment must be interrupted 24 hours before surgery, administering half the total usual daily dose, and it should be re-started 24 hours after surgery (Douketis 2008). After major surgery or surgery with a high risk of bleeding, an individual assessment should be made of bleeding and of hæmostasis, so as to delay for 48 or 72 hours the start of treatment with low-molecular-weight heparin or intravenous heparin. Therefore, low doses of those drugs must be administered after surgery when hæmostasis is guaranteed, or else treatment must be avoided completely. (Douketis 2008).

Low quality

4.4.3.3. Peri-operative handling of patients receiving antiaggregants

Recommendations from the ACCP guide (Douketis 2008) make the decision to suspend antiaggregant treatment conditional upon whether the patient undergoing surgery has recently been fitted with a stent. A recent INFAC report summarizes the recommendations concerning the interruptions to treatment contained in the aforementioned guide (INFAC 2009):

Low quality

ACCP recommendations for patients receiving antiaggregant treatment and with no stent

Risk of cardiac event	Recommendation
High risk: none	Suspend the antiaggregant
High risk: patients scheduled for non-cardiac surgery	Continue with aspirin until surgery, and again after surgery. If the patient was taking clopidogrel, suspend for at least five days, and preferably within the 10 days preceding surgery
High risk: patients scheduled for coronary-bypass surgery	Continue with aspirin until surgery, and also after surgery. If aspirin is suspended, it is recommended that the drug be re-started between 6 and 48 hours after bypass surgery.
High risk: patients scheduled for percutaneous coronary intervention (PCI)	Continue with aspirin until the procedure, and also after surgery. If clopidogrel is suspended before the PCI, it is suggested that treatment be resumed with a load dose of between 300 and 600 mg.

ACCP recommendations for patients receiving treatment with antiaggregants and with a stent

Risk situation of cardiac event	Recommendation
Patients with a metallic coronary stent who require surgery within 6 weeks of the stent being fitted	Continue with aspirin and clopidogrel in the peri-operative period
Patients with a drug-releasing coronary stent who require surgery within twelve months of the stent being fitted	Continue with aspirin and clopidogrel in the peri-operative period

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Furthermore, in patients who have been recently fitted with stents, it is recommended that treatment be postponed whenever possible.	Low quality
The last doses before surgery must be administered between seven and ten days before surgery, with treatment being resumed 24 hours after surgery.	

Summary of the evidence

Moderate quality	The risk of thrombotic complications after surgery is high. Depending on the various clinical trials, as a general rule and in patients of greater risk, the incidence of venous thrombosis without treatment was 29%, and the incidence of pulmonary embolism was 3%. Orthopædic surgery is especially risky with regard to thrombotic complications (NICE 2007).
Low quality	Some patients' characteristics confer an increased risk of thrombotic complications (NICE 2007).
High quality	The effectiveness of graduated-compression stockings up to the thighs or the hips in reducing venous thrombosis has been shown. Intermittent pneumatic pressure mechanisms, both those going up to the knee and those covering the entire extremity, reduce the risk of venous thrombosis and proximal venous thrombosis. A description has been given of the following cases in which compression stockings should not be used: peripheral arterial disease, atherosclerosis, serious peripheral neuropathy, massive œdema in the lower extremities, pulmonary œdema, œdema caused by congestive cardiac arrest, local diseases of the skin or soft tissue, gangrenous extremities, Doppler pressure score <0.8, excessive cellulitis. In comparison with compression stockings, compression mechanisms were found to be superior only if they are combined with drug treatment. Electrical stimulation and pedis impulses have been evaluated in a few clinical trials of small size, the combined analysis of which proved to be inconclusive due to the small number of events recorded (NICE 2007, JBI Best Practice 2008).
Moderate quality	Studies carried out to date with high-risk patients have shown that the prevention of thrombotic complications with unfractionated heparin, low-molecular-weight heparin, oral anticoagulants, antiaggregants, or mechanical measures, is effective (NICE 2007).
Moderate quality	All pharmacological measures for reducing the risk of thrombotic complications present an increase in the risk of bleeding to a greater or lesser degree (NICE 2007).
Moderate quality	In general, the various clinical trials have shown that low-molecular-weight heparin presented benefits greater than those of unfractionated heparin, oral anticoagulants, and antiaggregants. (NICE 2007)
Moderate quality	The highest doses of low-molecular-weight heparin present a greater reduction of thrombotic complications in comparison with lower doses, with an increase in the risk of bleeding. Starting treatment before or after surgery has no effect on that risk (NICE 2007).

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Moderate quality	Prolonging the heparin model for at least one week after discharge from hospital (or a maximum of 30 days) reduces the risk of thrombo-embolism when compared with shorter models (until discharge from hospital or a maximum of fourteen days) (NICE 2007).
Moderate quality	Fondaparinux reduces the risk of deep vein thrombosis in comparison with low-molecular-weight heparin, although it is associated with a greater risk of serious bleeding (NICE 2007).
Low quality	Danaparoid, which is not marketed in Spain, is better at reducing the risk of deep vein thrombosis than low-molecular-weight heparin, with a similar risk of bleeding (NICE 2007).
Low quality	Dabigatran and rivaroxaban have shown effectiveness similar to that of enoxaparin in preventing thrombotic events after orthopædic surgery of the lower extremities. The risk of bleeding is also similar (NICE 2007, Wolowacz 2009).
Moderate quality	Mechanical measures associated with pharmacological treatment reduce the risk of thrombotic complications (NICE 2007).
Moderate quality	The mechanical measures with greater benefit are long compression stockings (up to the hip) and pneumatic-pressure mechanisms combined with pharmacological treatment (NICE 2007).
Low quality	The risk of thrombo-embolism in the peri-operative period depends on the condition for which the patient receives treatment and on the presence of co-morbidity. For that reason, a stratification of patients has been proposed on the basis of peri-operative risk of venous thrombo-embolism, and a classification of the risk that are contained in some procedures if treatment is maintained (NICE 2007).
Moderate quality	Warfarin should be withdrawn five days before surgery, and acenocoumarol should be withdrawn two to three days before surgery (NICE 2007).
Low quality	In cases in which the INR remains high, between 1 and 2 mg of oral vitamin K may be administered on the day of surgery (NICE 2007).
Low quality	Treatment involving the substitution of anticoagulants in patients with a mechanical valve, auricular fibrillation, or venous thrombo-embolism, should be done with therapeutic dosages of low-molecular-weight heparin administered subcutaneously, in patients at high or moderate risk of thrombo-embolism in the peri-operative period. For patients at low risk, either low-molecular-weight heparin administered subcutaneously or nothing at all can be given (NICE 2007).
Low quality	Patients receiving antiaggregant treatment who have not recently been fitted with stents can have treatment withdrawn before surgery if they are considered to be at low risk of thrombo-embolism in the peri-operative period. (Douketis 2008, INFAC 2009).

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Low quality	In patients receiving antiaggregant treatment and who have not recently been fitted with stents, treatment with aspirin must be continued before and after surgeryif they are considered to have a high risk of thrombo-embolism in the peri-operative period, and if they have been scheduled for non-cardiac surgery, or a coronary bypass,. If those patients receive clopidogrel, treatment must be stopped at least five days in the ten days before surgery (Douketis 2008, INFAC 2009).
Low quality	If treatment with aspirin is stopped in patients who take it routinely and who have not recently been fitted with stents, and they have been scheduled for a coronary bypass, treatment should be resumed in the 6 to 48 hours after surgery (Douketis 2008, INFAC 2009).
Low quality	In patients who receive antiaggregant treatment, who have been fitted with a metallic coronary stent, and who require surgery within six weeks of the stent being fitted, the antiaggregant treatment should be continued in the peri-operative period (Douketis 2008, INFAC 2009).
Low quality	In patients who receive antiaggregant treatment and who have been fitted with a drug-releasing coronary stent and who need surgery within twelve months of the stent being fitted, antiaggregant treatment must be continued in the peri-operative period (Douketis 2008, INFAC 2009).

Recommendations

	An assessment must be made of the risk of thrombotic complications in any patient due to undergo surgery, considering the type of surgery and the characteristics of the patient.
Strong	All patients due to undergo surgery and who will remain in hospital after surgery must receive some effective method of preventing thrombotic complications.
Strong	For all patients who are due to undergo surgery and who will remain in hospital after surgery, it is recommended that compression stockings be used, preferably graduated to the hips or the thighs, if there is no contra-indication.
Weak	Intermittent pneumatic pressure mechanisms are an alternative to pharmacological treatment.
Strong	In patients with certain factors of risk of thrombosis, or who will undergo surgery with a high risk of thrombotic complications, treatment with low-molecular-weigh heparin is recommended, in addition to mechanical measures.
Strong	In patients undergoing treatment with low-molecular-weight heparins, it is suggested that treatment be started between two and twelve hours before surgery, and that treatment be maintained for at least one week after discharge from hospital, or for a maximum of 30 days.
	It is advisable to carry out an individual assessment of the dosages of heparins based on surgical risk (for thrombosis and hæmorrhaging) and the characteristics of the patient (age, weight, or renal alteration)
Weak	In patients who are due to undergo surgery with a high risk of thrombotic complications, unfractionated heparin, oral anticoagulants, or fondaparinux are alternatives to low-molecular-weight heparin.

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Weak	In patients who are due to undergo orthopædic surgery of a lower extremity, an assessment can be made of treatment with dabigatran or rivaroxaban as alternatives to low-molecular-weight heparin.
Weak	In patients undergoing surgery with a very high risk of bleeding (neurosurgery or involving vascular malformations), it is recommended that mechanical measures be used to prevent thrombotic complications.
	The risk-benefit balance of the strategies for preventing thrombotic events must be individualised and based mainly on the clinical history of the patient, pharmacological interactions, type of anæsthesia, risk of thrombosis and bleeding associated with surgery.
Strong	In patients receiving anticoagulant or antiaggregant treatment and who are due to undergo surgery, an assessment of the peri-operative risk of venous thrombo-embolism must be carried out, as well as of the risk of maintaining treatment for certain specific procedures.
Strong	In patients from whom it is decided to withdraw anticoagulant treatment, this must be done five days before surgery in the case of warfarin and two or three days before surgery in the case of acenocoumarol.
Weak	If the INR remains high, between 1 and 2 mg of oral vitamin K can be administered on the day of surgery.
Weak	In patients with indication of treatment using anticoagulant and high or medium risk of thrombo-embolism in the peri-operative period, substitution treatment should be carried out with therapeutic doses of low-molecular-weight heparin administered subcutaneously.
Strong	In patients with indication of anticoagulant treatment and low risk of thrombo-embolism in the peri-operative period, either low doses of low-molecular-weight heparin should be administered subcutaneously, or nothing at all.
Strong	In patients receiving antiaggregant treatment, who have not had stents fitted recently, and who have a low risk of thrombo-embolism in the peri-operative period, treatment should be withdrawn before surgery.
Weak	In-patients receiving antiaggregant treatment and who have not recently been fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for non-cardiac surgery or percutaneous coronary intervention, treatment with aspirin must be continued before and after surgery.
Weak	In patients receiving antiaggregant treatment and who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative stage, and who have been scheduled for non-cardiac surgery, treatment with clopidogrel should be stopped at least five days in the ten days preceding surgery.
Strong	In patients receiving antiaggregant treatment and who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for a coronary bypass, treatment with aspiring should be continued before and after surgery. If that treatment is stopped, it should be restarted between 6 and 48 hours after surgery.

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Strong	In patients receiving antiaggregant treatment, who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for coronary bypass surgery, treatment with clopidogrel should be stopped at least five days in the ten days before surgery.
Weak	In patients receiving antiaggregant treatment, who have not been recently fitted with a stent, who have a high risk of thrombo-embolism in the peri-operative period, and who have been scheduled for percutaneous coronary intervention, clopidogrel should be re-started with a load of between 300 and 600 mg.
Strong	In patients receiving antiaggregant treatment, who have a metallic coronary stent, and who need surgery in the six weeks after the stent was fitted, treatment with aspirin or clopidogrel should be continued in the peri-operative period.
Strong	In patients receiving antiaggregant treatment, who have been fitted with a drug-releasing coronary stent, and who need surgery within twelve months of the stent being fitted, antiaggregant treatment must be continued in the peri-operative period.

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4.5. Aspects derived from blood transfusion

Question to be answered

- In surgery, what are the main factors that favour transfusion?
- In patients undergoing cardiac surgery, what are the predictor factors for blood transfusion?
- What characteristics must patients who undergo surgery have to receive a transfusion of allogenic erythrocyte concentrate?
- What is the effectiveness of cell savers and auto-transfusion in the peri-operative period?
- Before surgery, what interventions reduce the need for a blood transfusion during the peri-operative period?

The loss of a large volume of blood, especially the presence of hæmodynamic instability, has been clearly associated with a surgical result of worse prognosis (Gawande 07). Controlling hæmorrhaging and mitigating its clinical effects with the appropriate administration of hydroelectrolytic fluids are important components of intra-operative care. This section looks at the evidence available on the topic.

4.5.1. Risk of allogenic blood transfusion

The risk of a blood transfusion, in terms of morbidity and mortality, is unknown, mainly because the impact of a transfusion cannot be individualised in complex clinical circumstances. If a surgical intervention that may potentially save life can only be carried out with transfusion support, the benefits probably outweigh the risks. On the other hand, a post-operative transfusion with the aim of increasing the level of hæmoglobin (Hb) in a stable patient may offer no clinical benefit and carry a higher level of risk.

The risks of transfusion can be of the infectious type and the non-infectious type, and amongst the latter are to be found immune and non-immune risks (Hendrickson 2009).

4.5.1.1. Infections transmitted by transfusion and direct immunological damage

Current statistics show that the risk of HIV infection through transfusion is 1 per 2.3 million hæmoderivatives transfused. The riskof hepatitis C is 1 per 1.8 million, the risk of the T-cell lymphotropic virus is 1 per 2 million, and the risk of hepatitis B is 1 per 350,000 (Dood 2007).

Low quality

Hæmolytic and non-hæmolytic post-transfusion reactions are difficult to predict, although rapid identification and adequate treatment can reduce morbidity and mortality.

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4.5.1.2. Immunomodulation

Transfusion can cause modulation of the immune response (transfusion-induced immunomodulation), which can have benefits (Jakson 1997) and deleterious effects. The latter include a recurrence of cancer (Vamvakas 2007), or peri-operative infections (Hill 2003). Low quality

A meta-analysis (McAlister 98) of six RCTs and two studies of prospective cohorts, where participants in the control group received leuco-reduced transfusion (reduction in leucocytes) or autologous blood, did not show significant differences in the recurrence of cancer. However, the RCTs involved a small number of participants and the meta-analysis was not sufficiently powerful to detect a difference of less than 20% in the risk. The authors concluded that there was no evidence of an increase in the risk of adverse clinical sequels in patients with cancer who underwent allogenic transfusion. The studies are difficult to interpret, given the difficulties in comparing groups of transfused patients and non-transfused patients based on illness and treatment (Hendrickson 2009).

There is controversy in relation to the risk of post-operative infection and allogenic transfusion. One meta-analysis (Vamvakas 2002) of five RCTs that compared allogenic concentrates of leuco-depleted erythrocytes against whole blood in the control group with respect to the risk of post-operative infection, did not find any statistically significant differences. The update of this meta-analysis (Vamvakas 2007), which included twelve RCTs, ratified the absence of an increase in risk of post-operative infections following allogenic transfusion of allogenic concentrates of leuco-depleted erythrocytes (RR: 1.24; 95% CI: = 0.98 to 1.56). One meta-analysis (Hill 2003) of 20 RCTs detected an increase of 235% in the risk of post-operative infection (RR: 3.45; 95% CI: 1.43 to 15.15). High quality

4.5.1.3. Procedural errors

The blood-transfusion process is complex, and includes various disciplines and professionals. One study identified about 40 steps between the patient and the transfusion, each of the carrying the potential for human error (McClelland 96). When an error involves the incorrect administration of blood, the consequences can be fatal. During the 1990s in the USA, human error was recorded in about 1 in every 24,000 transfusions (Aubuchon 96). However, over the last few decades, the clinically significant incidence of illnesses transmitted by transfusion has been drastically reduced, which is based on the implementation of multiple strategies in the collection, processing, and administration of blood or hæmoderivatives (Luban 2005). Low quality

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4.5.1.4. Risk of not receiving a blood transfusion

As blood transfusions become safer, more consideration should be given to the risks of not performing a transfusion, e.g. the risk of peri-operative anæmia (Klein 07). Observational studies show that the elderly and people with cardiovascular diseases are worst able to handle peri-operative anæmia, so they need to receive transfusions with a higher level of hæmoglobin (Carson 02). Low quality

Only one RCT has been located that has directly compared the start of prophylaxis with low molecular weight heparins before (during the twelve preceding hours) or after hip replacement operation. No differences were found in the occurrence of deep vein thrombosis (51 thromboses, ten of them proximal) measured by venography in a follow-up after two weeks. There were no differences, either, in adverse events (Paraleti G 1996). An analysis performed through indirect comparisons in the NICE SR assessed the efficiency of molecular low weight heparins depending on whether treatment started before or after surgical intervention) in a total of 26 RCTs. No significant differences were found between the two strategies for the main variables analysed (vein thrombosis, proximal vein thrombosis, pulmonary embolism or severe haemorrhagic events) (NICE 2007). Moderate quality

The duration of the prophylaxis with heparins (unfractionated or low molecular weight) has been assessed in the NICE SR for a total of twelve RCTs (2809 patients) in orthopaedic surgery. The normal heparin regimes were compared (until discharge from the hospital or up to fourteen days) with the regimes that prolonged heparin until one week after discharge and with a total duration of nineteen to thirty days. Results showed that prolonging the heparin regime after hospital discharge is associated with a significant reduction of deep vein thrombosis (52%), proximal deep vein thrombosis (66%) and pulmonary embolism (66%). Information about the occurrence of severe haemorrhagic events was obtained from one single study, with no significant differences between the two strategies. The majority of the studies were performed with low molecular weight heparins (NICE 2007).

The NICE SR identified five moderate quality RCTs that assessed different doses of low molecular weight heparin for the prophylaxis of vein thrombosis in surgery. The higher doses were 3500 to 5000 IU of dalteparin or 60 mg of enoxaparin, whilst the lower ones were between 2500 and 3000 IU of dalteparin or 40 mg of enoxaparin. The joint analysis of the results of the studies showed that higher doses reduced the occurrence of vein thrombosis by about 45%, but with an increase in severe bleeding (NICE 2007).

The efficiency of fondaparinux has been assessed in a total of five RCTs and was compared with low molecular weight heparins. Studies included patients submitted to orthopaedic surgery or with high thrombotic risk and doses in all cases were 2.5 mg after intervention. All studies permitted the use of elastic compression stockings. The NICE SR assessed the results together, showing a reduction of deep vein thrombosis with fodaparinux (RR 0.52; 95% CI 0.44 to 0.60; five RCTs, 639 events) although it was associated with a 49% increase in severe bleeding (five RCTs, 242 events) (NICE 2007). High quality

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The efficiency of danaparoid has been assessed in different tests, showing a reduction of deep vein thrombosis compared with placebo, unfractionated heparin and compared with aspirin. There were no significant differences for the prevention of pulmonary embolism when compared with unfractionated heparin or aspirin, with a very limited number of events. The only trial that provided safety outcomes did not show any differences between danaparoid and low molecular weight heparin (NICE 2007). Low quality

In patients submitted to epidural or spinal anaesthesia for surgical intervention, the administration of low molecular weight heparin for prophylactic purposes has very rarely been associated with the appearance of epidural or spinal haematomas, with the final outcome of prolonged or permanent paralysis. This risk increases with the use of epidural or spinal catheters for anaesthesia, the concomitant administration of medication with effect on coagulation and due to traumatic or repeated punctures.

If a neuroaxial puncture is decided upon, the time at maximum effect of molecular low weight heparin must be taken into consideration, which is approximately four hours after administration. The plasma half-life is also about four hours but the pharmacodynamic activity persists until sixteen to twenty-four hours after administration. Ideally, at least ten to twelve hours must pass between the administration of heparin and the puncture or up to twenty-four hours if high doses are used. Once the catheter has been inserted or removed, at least two hours must elapse until the administration of a new dose of heparin, and this must be delayed until the surgical intervention has ended.

4.5.2. Hæmoglobin thresholds for initiating transfusion

The transfusion threshold is the level of hæmoglobin at which the transfusion is normally indicated, under stable conditions and in the absence of other clinical signs or symptoms of anæmia. The transfusion must be limited to the least amount of blood possible required to raise the patient above the transfusion threshold. It is usual for hospital laboratories to have their own definitions of anæmia, based on the normal level for the local population.

It is currently accepted that anæmic patients who are hæmodynamically stable should be transfused in the peri-operative period only when the level of Hb is <77 g / dl (Engelfriet 2002). The optimum level of Hb to indicate transfusion is unknown, and the facts that are known on this aspect are derived indirectly from other studies (Hebert 1999, Lieberman 2000, Weiskopf 2000). Low quality

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4.5.2.1. Pre-operative period

Pre-operative anæmia increases the probability of an allogenic transfusion, and should be investigated and –as far as possible– corrected before major surgery. In any case, there is limited evidence available on the appropriate concentrations of hæmoglobin in the pre-operative period (Spence 90). When a patient refuses a blood transfusion, pre-operative hæmoglobin is an important determinant of the result of the operation, especially in patients with myocardial ischæmia (Spence 90, Carson 96, Rawstron 70). Low quality

4.5.2.2. Intra-operative period

When there is loss of blood during the operation, the levels of hæmoglobin must be interpreted in the context of a clinical assessment with multiples aspects, which should include an assessment of blood volume. The use of an intra-operative transfusion must reflect the rate of continuous blood loss, hæmodynamic instability, and the forecast level of post-operative bleeding (Welch 92). Low quality

Two observational studies with patients who underwent cardiopulmonary bypass operations showed that post-operative mortality and serious ventricular dysfunction were related to low hæmatocrit during the bypass operation (Defoe 01, Fang 97). Although both studies showed an increase in risk when the hæmatocrit fell below 0.17, there was no agreement on the safe value of hæmatocrit that would indicate the need for a transfusion.

4.5.2.3. Post-operative period

Various declarations of consensus have recommended a transfusion threshold of between 70 and 100 g/l of hæmoglobin. Clinical indicators define the need for an allogenic transfusion between one value and another (Guidelines 96, Spence 95, Simon 98). Regarding the lower limits, it has been suggested that patients with cardiovascular problems should be transfused starting at 80 g/l (Hill 99). A retrospective study of surgical patients confirmed that there was no difference in mortality with a threshold of 80 or 100 g/l (Carson JAMA 98). It was not possible to draw conclusions with respect to a lower threshold, since 90% of patients were transfused with hæmoglobin <80 g/l. Two observational studies with patients who underwent cardiopulmonary bypass operations showed that post-operative mortality and serious ventricular dysfunction were related to low hæmatocrit during the bypass operation (Defoe 01, Fang 97). Although both studies showed an increase in risk when the hæmatocrit fell below 0.17, there was no agreement on the safe value of hæmatocrit that would indicate the need for a transfusion. Low quality

Regarding higher thresholds, one RCT randomised 800 patients admitted to intensive care to two thresholds of transfusion (70-90 g/l or 100-120 g/l), and found no difference in mortality at 30 or 60 days (Hebert 99). Another RCT also failed to find differences in mortality, post-operative myocardial infarction, or ventricular complications after randomising 428 patients who underwent coronary bypass surgery to transfusion thresholds of <80 g/l or >90 g/l (Bracey 99). High quality

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Two RCTs (with patients with fractured femurs and vascular reconstruction, respectively), did not find differences in mortality or morbidity when comparing transfusion thresholds from 80 to 100 g/l (Carson Transfusion 98, Bush 97). Moderate quality

A subgroup analysis of one RCT (Hebert 99) of a population of 357 patients with primary or secondary diagnosis of cardiovascular disease did not show a difference in mortality at 30 or 60 days, although the average levels of hæmoglobin were significantly different (85 g/l as against 103 g/l). However, the authors concluded that a careful watch had to be kept on patients with peripheral cardiovascular disease, recent myocardial infarction, or unstable angina.

4.5.3. Aids for making an effective request for blood

4.5.3.1. Risk factors

A series of studies with a heterogeneous population of over ten thousand patients who underwent a variety of surgical procedures (Transfus Med 94, Bierbaum 99, Churchill 98, Hatzidakis 00, Borghi 99) identified a series of nine risk factors that predict the need for an allogenic transfusion in a surgical intervention: Low quality

1. Low hæmoglobin or hæmatocrit before surgery or on the day of surgery.
2. Low weight.
3. Low height.
4. Female gender.
5. Age >65 years.
6. Availability of a pre-operative autologous blood donation.
7. Estimated surgical blood loss.
8. Type of surgery.
9. Primary or review surgery.

4.5.3.2. Equations for requesting blood

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The intention of the schemes for requesting blood is to link the request for blood with the probability that a transfusion may be required. Although this is linked to the type of surgery, individual risk factors must be taken into account. The link between the number of cross-matched units of erythrocytes for a determined intervention and the number of units transfused (the C:T ratio) should not exceed 2:1 (Murphy 95, Guidelines 90). Low quality

Using basic physiological principles, it is possible to derive simple equations that involve some of the risk factors for transfusion that can be changed for others (Brecher 97, Mercuriali 96):

Blood loss = Reduction in the volume of circulating erythrocytes (from the pre-operative period to the post-operative period) + erythrocytes transfused.

Mercuriali (Mercuriali 98) produced an algorithm based on a rigorous calculation of the volume of erythrocytes in the pre-operative period, taking height and weight into account:

Volume of pre-operative erythrocytes – Volume of post-operative erythrocytes = Loss of blood in operation – Extra transfusion request.

With those same data and a hæmatocrit threshold, it is possible to establish the minimum acceptable volume of erythrocytes for a determined intervention. Using that algorithm for ten years, Mercuriali showed that the allogenic transfusion of blood in patients who received a full hip replacement was restricted to less than 20% of patients, with just 10% using autologous units. Independent and specific patient risk factors can be added to this simple equation, as shown in the following table.

Factors linked to equations for requesting blood

Pre-operative volume of erythrocytes	Pre-operative volume of erythrocytes	Loss of blood during surgery	Extra request for transfusion
– Pre-operative hæmoglobin – Weight/height – Sex	– Level of post-operative hæmoglobin required – Weight /height – Sex – Age/clinical history	– Primary/review – Knee/hip – Local factors	– Cell saver – Pre-operative donation of autologous blood – Acute normovolemic hæmodilution

Nuttall also developed an equation for requesting surgical blood, taking into account the levels of hæmoglobin, and allowing for the supply of blood to be more closely tailored to the individual patient (Nuttall 00). Low quality

Those physiological relationships can be expressed in a simpler formula that assumes that a unit of blood lost or donated will increase or decrease the patient's hæmoglobin by 1 g /l:

No. of units of erythrocytes needed for an intervention = Estimated reduction of Hb – [pre-operative hæmoglobin – post-operative hæmoglobin threshold].

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Two SR of the allogenic transfusion of erythrocytes (Henry 99, Hebert 97) only identified two RCTs (Sumerai 93, Despotis 94) that evaluated methods for reducing variability in carrying out transfusions, using an algorithm or educational software. Although they showed significant reductions in the prescription of erythrocytes, the total number of interventions was small (63 and 103, respectively). Moderate quality

One systematic review of observational studies that evaluated the ability of education and of the initiatives to improve practice showed reductions in the determinants of transfusions (Henry 99). However, the methods used and the quality of the studies were very heterogeneous.

4.5.4. Blood-saving strategies

4.5.4.1. Pre-operative donation of autologous blood

Pre-operative transfusion of autologous blood is a safe and widely practiced form of transfusion. In several countries, it is usually carried out in most interventions with a high estimate of blood loss, with the aim of minimising exposure to allogenic blood.

Pre-operative transfusion of autologous blood cannot be done in all patients, since it requires time and hæmoglobin levels >110 g/l (Voak 93), which excludes most emergency surgery. It has the same risks inherent to collection of the blood, storage, identification, and administrative errors associated with allogenic transfusion, but it avoids the immunological and viral risks of the latter. Similarly, autologous blood transfusions are difficult to perform in persons of advanced age, with limited mobility, and medical and surgical conditions. Low quality

A meta-analysis with six RCTs and nine studies of cohorts of adequate quality (Forgie 98) evaluated the degree to which autologous donation reduces the patient's exposure to allogenic blood. Patients who pre-donated blood had a lower probability of receiving allogenic blood both in the RCTs (933 patients, RR 0.17; 95% CI: 0.08 to 0.32) and in the cohort studies (2 351 patients, RR 0.19; 95% CI: 0.14 to 0.26). However, donors had a higher probability of being transfused with allogenic or autologous blood (RR 3.03; 95% CI: 1.7 to 5.39). High quality

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Observational studies show that autologous donation is not necessary in primary joint surgery if hæmoglobin is higher than 145 g/l (Bierbaum 99, Churchill 98). Limiting the donation to two units in cases of total hip replacement and one unit in total knee replacement is sufficient to limit allogenic exposure without increasing the percentage of rejected blood (Bierbaum 99, Churchill 98). Low quality

When hæmoglobin is between 110 and 145 g/l in men and between 130 and 145 g/l in women, autologous donation is associated with reducing the expected number of patients exposed to allogenic donation to less than 20% of the total number of patients (Hatzidakis 00, Nuttall 00). Women who present with lower levels of hæmoglobin (110-130 g/l) may need additional transfusion support, e.g. erythropoietin, to achieve a similar rate of allogenic transfusion (Hatzidakis 00, Nuttall 00).

4.5.4.2. Erythropoietin

Human erythropoietin (EPO) is a glycoprotein hormone that regulates erythropoiesis, which is secreted at higher levels by the kidneys in cases of hypoxia or hæmorrhage. Erythropoietin is available as human recombinant erythropoietin (epoietin α and β), and has been widely used to treat anæmia in cases of chronic renal insufficiency.

The effect of erythropoietin in minimising exposure to allogenic blood in comparison with placebo has been studied in patients undergoing orthopædic surgery (Laupacis 98, Faris 98), cardiac surgery (Laupacis 98), and colon cancer surgery (Kettlehaek 98, Qvist 99). Except for one RCT (Kettlehaek 98), all showed a significant reduction in allogenic transfusion (RR 0.36; 95% CI: 0.24 to 0.56 in orthopædic patients, and RR 0.25; 95% CI: 0.06 to 1.04 in cardiac patients). The post-operative rate of transfusion changed from 40-60% in controls to 10-20% in patients treated with erythropoietin. High quality

One RCT classified 316 orthopædic patients into two groups; those who presented with Hb higher than 130 g/l and those with Hb lower than 130 g/l (de Andrade 96). In the group treated with erythropoietin, the rate of allogenic transfusion changed from 45% to 16% in those with Hb <130 g/l and from 13% to 9% in those with Hb >130 g/l (non-significant change).

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In patients with objections to allogenic transfusion (e.g. Jehovah's Witnesses), erythropoietin also has a significant role in surgery that involves significant loss of blood (Gaudiani 91). Low quality

The optimum dose of erythropoietin is unknown. The following regimes are widely used:

– 300 u/kg subcutaneously for fourteen days, starting ten days before surgery.

– 600 u/kg subcutaneously three times a day one week before surgery and on the day of surgery.

Both regimes were found to be effective and appear to be equal in terms of safety and effectiveness (Golberg 96).

There is little information available on the frequency and severity of the adverse effects of erythropoietin in the short term (Faught 98). In one study, the risk of deep vein thrombosis was higher in patients treated with erythropoietin who presented with Hb >130 g/l, but similar to controls when Hb is between 100 and 130 g/l (de Andrade 96). In one study of 126 cardiac patients treated with erythropoietin, there were seven deaths (four thrombotic), whereas tno deaths occurred in the control group (56 patients). That difference was not statistically significant, and it is comparable with the mortality rates for cardiac bypass surgery.

4.5.4.3. Erythropoietin and autologous transfusion

The effect of erythropoietin and auto-transfusion on the incidence of allogenic transfusion has been studied in orthopædic patients and cardiac patients. A meta-analysis of eleven RCTs (825 orthopædic patients) showed a statistically significant reduction in the proportion of patients transfused with allogenic blood (RR 0.42; 95% CI: 0.2 to 0.62) (Laupacis 97). In the five RCTs with cardiac patients included in that meta-analysis, a significant reduction was also observed in the proportion of patients transfused (RR 0.25; 95% CI: 0.08 to 0.82), but the total number of patients was small (224). High quality

Three RCTs with a small sample compared auto-transfusion aginst auto-transfusion plus erythropoietin (Mercuriali 98, Rau 98, Price 96). In the pre-operative period of three weeks, 80% of patients treated with erythropoietin were able to give more units of blood than the other group, and also presented with Hb levels significantly higher on the day of surgery, which has also been found in other studies (Cazenave 97, de Pree 97).

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4.5.4.4. Acute normovolemic hæmodilution

Low quality

Acute normovolemic hæmodilution consists of the withdrawal of whole blood and replacement of the blood volume with acellular fluid, shortly before the anticipated significant loss of blood. The maximum volume of blood than can be withdrawn during hæmodilution depends on pre-operative hæmoglobin, the minimum acceptable level of hæmoglobin during surgery, and the estimated volume of blood (Brecher 97, Kick 97, Cohen 95). Extraction of blood before the operation is always associated with autologous transfusion of blood in the immediate post-operative period, or during surgery in case of emergency.

Normovolemic hæmodilution is especially indicated in patients who meet the following criteria:

- substantial anticipated blood loss.
- target Hb level relatively low during surgery and in the post-operative period.
- Hb relatively high at the start of surgery.

Moderate quality

Mathematical models have been developed that allowed the identification of the point where those factors could save a unit of blood (Kick 97). One meta-analysis showed that the number of patients exposed to allogenic transfusion was reduced when more than one litre of blood was taken (Bryson 98). The RCTs in which the loss of blood was higher than 1000 ml were associated with a significant reduction in the average number of allogenic units transfused, but not in the number of patients exposed to allogenic blood.

In one RCT in which the loss of peri-operative blood was less than 1000 ml, hæmodilution was associated with a reduction in the total number of transfusions, but not with a reduction in the number of patients exposed to allogenic blood (Olsfanger 97). Another study compared hæmodilution with autologous donation, and did not find any differences in savings on erythrocytes or in exposure to allogenic transfusion (Monk 98).

4.5.5. Cardiac surgery

Cardiac surgery is associated with high consumption of blood and of hæmoderivatives. Any procedure with the aim of reducing the loss of blood or the need for transfusion will have a significant impact on the amount of blood available, in addition to reducing the risk of allogenic transfusion. Some drugs, such as aprotinin and other antifibrinolytic drugs (to reduce blood loss), have a negative or positive influence on the need for peri-operative transfusion in cardiac surgery.

4.5.5.1. Aprotinin and antifibrinolytic drugs

The *Agencia Española de Medicamentos y Productos Sanitarios* (Spanish Agency for Medicines and Health Products) suspended the marketing of aprotinin in Spain in November 2007, due to an increase in the risk of mortality related to its use (AEMPS 07, Mangano 2006, Mangano 2007).

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4.5.5.2. Aspirin

Aspirin increases loss of blood in patients undergoing myocardial revascularisation (Taggart 90, Kallis 94), and it must be stopped seven days before surgery. Although it increases post-operative bleeding, its use does not always imply a greater need for allogenic transfusion (Reich 94, Tuman 96). In patients who take aspirin in the pre-operative period, desmopressin can play a beneficial role. A reduction in the use of blood has been observed in patients who are given desmopressin peri-operatively, although there was a rise in the risk of myocardial infarction in the group treated (RR 2.39; 95% CI: 1.02 to 5.60) (Levi 99).

High quality

4.5.5.3. Cell saver

The cell saver has been used to minimise the need for allogenic transfusions in cardiac surgery. A suction pump returns the blood from the bypass reservoir, which is retransfused after filtration.

One meta-analysis that included 2061 patients in which one of the result variables was the proportion of patients receiving at least one unit of allogenic erythrocytes and the re-infusion of blood recovered from mediastinal drainage, showed lower allogenic exposure (RR 0.85; 95% CI: 0.79 to 0.92) (Huet 99). Cell recovery also reduced exposure to allogenic blood (RR 0.84; 95% CI: 0.77 to 0.93). This meta-analysis did not include any RCT with washed mediastinal blood, and may underestimate the value of re-infusion of blood recovered from mediastinal drainage, given that washed blood can prevent induced coagulopathy (Vertrees 96).

High quality

4.5.6. Orthopædic surgery

The orthopædic procedures that most frequently require blood transfusions are arthroplasties. The factors that can contribute to reducing allogenic transfusion are:

– the use of lower levels of Hb in transfusion protocols

– an increase in the use of recovery of erythrocytes in the peri-operative period

– the use of hypotensive techniques and regional anæsthesia.

4.5.6.1. Aprotinin and antifibrinolytic drugs

The *Agencia Española de Medicamentos y Productos Sanitarios* suspended the marketing of aprotinin in Spain in November 2007, due to an increase in the risk of mortality from its use (AEMPS 07, Mangano 2006, Mangano 2007).

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4.5.6.2. Tranexamic acid

Tranexamic acid is an antifibrinolytic (it inhibits fibrinolysis and reduces destruction of the coagulum). Its potential application in orthopædic patients is seen in patients with hip-prosthesis surgery, who are subject to tourniquet control. Removing the tourniquet can lead to post-operative bleeding (Klenerman 77, Petaja 87, Murphy 93).

Six RCTs showed a reduction in bleeding of between 43% and 54%, as well as a significant reduction in the number of units transfused and the number of patients exposed to allogenic blood (Jansen 99, Zohar 99, Hiippala 97, Benoni 96, Hiippala 95, Benoni 95). High quality

The greatest doubt arising from its use is the potential risk of thrombosis (Hiippala 97, Howes 96). None of these RCTs documented an increase in deep vein thrombosis detected clinically, although one RCT showed an upward trend (Benoni 96). An RCT with a greater number of orthopædic patients is needed before introducing tranexamic acid into practice.

4.5.6.3. Cell saver

The post-operative re-transfusion of blood from drains uses unwashed blood that is filtered to eliminate large concentrates of cells but not bacteria (Gannon 91, Kristensen 92, Martin 92). Some alterations in coagulation after the infusion of large volumes have been described (Rakower 73, Moore 80). Because of the risks of infectious colonisation, recovered blood should not be re-infused more than six hours after it has been recovered. Low quality

Some authors have questioned the use of this technique in unilateral arthroplasty, because of the relatively small amounts of blood obtained (Adalbert 98, Rizzi 98). Another technique consists of the intra-operative recovery of cells that are washed before being re-transfused (Elawad 91). In comparison with post-operative recuperation, large volumes can be re-transfused with significant risk to patients (Paravicina 83).

A meta-analysis of the effectiveness of the cell saver in minimising perioperative allogenic transfusion concluded that in orthopædic surgery, instruments that produced washed cells as well as unwashed cells reduce the frequency of exposure to allogenic blood to a degree similar to that of the control group (Huet 99).

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Summary of the evidence

Low quality	Blood transfusion carries risks of infection, immunological damage, and procedural error. It has been suggested that the transfusion of allogenic blood may increase the risk of cancer recurrence (Foster 85, Hyman 99, Tartter 85): One meta-analysis (McAlister 98) of three RCTs and two cohort studies, in which the control groups received blood with reduced leucocytes or autologous blood, did not show significant differences in cancer recurrence, although the RCTs covered a small number of participants. Other aspects that must be taken into consideration are the risks of non-transfusion (e.g. post-operative anæmia) (Klein 07)).
Low quality	Pre-operative anæmia increases the probability of an allogenic transfusion. It should be investigated and corrected before surgery. Limited evidence is available on the appropriate concentrations of Hb in the pre-operative period (Spence 90). The use of an intra-operative transfusion should reflect the rate of continuous loss of blood, hæmodynamic instability, and forecast post-operative bleeding (Welch 92). Various declarations of consensus have recommended a post-operative transfusion threshold of between 70 and 100 g/l of hæmoglobin (Guidelines 96, Spence 95, Simon 98). Regarding the lower limits, it has been suggested that patients with cardiovascular problems should receive a transfusion when Hb levels range from 80 to 100 g/l (Hill 02, Carson JAMA 98). Regarding the upper limits, no differences in mortality have been observed with levels of transfusion of between 70 and 120 g/l (Hebert 99), or between 80 and 100 g/l (Carson Transfusion 98, Bush 97).
Low quality	The following risk factors have been identified to estimate the need for transfusion during surgery: 1) a reduction in Hb or hematocryte before the intervention, 2) low weight, 3) low height, 4) female gender, 5) age >65 years, 6) availability of a pre-operative donation of autologous blood, 7) estimated blood loss, 8) type of surgery, and 9) primary surgery (Transfus Med 94, Bierbaum 99, Churchill 98, Hatzidakis 00, Borghi 99). The ratio of the number of cross-matched units of erythrocytes for a determined intervention to the number of units transfused (the C:T ratio) should not exceed 2:1 (Murphy 95, Guidelines 90). A simple equation for requesting blood is as follows (Brecher 97, Mercuriali 96): Blood loss = Reduction in the volume of erythrocytes in circulation (from pre-operative to post-operative) + Erythrocytes transfused. Two SRs that evaluated methods to reduce the variability in transfusion practice (using an algorithm or educational software) showed significant reductions in the prescription of erythrocytes (Henry 99, Hebert 97), although the total number of interventions was small.

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Low quality	Pre-operative donation of autologous blood requires time and Hb >110 g/l (Voak 93). One meta-analysis showed that patients who pre-donated blood had a lower probability of receiving allogenic blood both in the RCTs (933 patients, RR 0.17; 95% CI: 0.08 to 0.32) and in the cohort studies included therein (2 351 patients, RR 0.19; 95% CI: 0.14 to 0.26). These patients, however, had a higher probability of receiving a blood transfusion (RR 3.03; 95% CI: 1.7 to 5.39) (Forgie 98).
High quality	When HB levels lie between 110 and 145 g/l in men, and between 130 g/l and 145 g/l in women, autologous donation is associated with reducing the expected number of patients exposed to allogenic donation to less than 20% of the total number of patients (Hatzidakis 00, Nuttall 00).
High quality	Erythropoietin has been found to be effective in reducing allogenic transfusion (RR 0.36; 95% CI: 0.24 to 0.56 in orthopædic patients and RR 0.25; 95% CI: 0.06 to 1.04 in cardiac patients) (Laupacis 98, Faris 98, Qvist 99). One RCT showed a greater reduction in the rate of transfusion when Hb was <130 g/l (de Andrade 96). The simultaneous administration of erythropoietin and auto-transfusion has been found to be effective in reducing the proportion of patients receiving transfusions of allogenic blood (RR 0.42; 95% CI: 0.2 to 0.62 in orthopædic patients and 0.25; 95% CI: 0.08 to 0.82 in cardiac patients) (Laupacis 97).
Moderate quality	Acute normovolemic hæmodilution consists of removing whole blood and replacing the volume of blood with acellular fluid, shortly before an anticipated significant loss of blood. One meta-analysis showed that the number of patients exposed to allogenic transfusion was reduced when more than one litre of blood was recovered (Bryson 98), and was not reduced when the volume was lower than 1000 ml (Olsfanger 97), even though they reduced the total number of transfusions.
High quality	Aspirin increases blood loss in patients undergoing myocardial revascularisation, and should be stopped seven days before the operation.
High quality	One meta-analysis with 2061 patients showed a lower exposure to allogenic exposure (RR 0.85; 95% CI: 0.79 to 0.92) (Huet 99). Cell recovery also reduced exposure to allogenic blood (RR 0.84; 95% CI: 0.77 to 0.93).
High quality	Six RCTs showed a reduction in bleeding of between 43% and 54% with the use of tranexamic acid, as well as a significant reduction in the number of units transfused and the number of patients exposed to allogenic blood (Jansen 99, Zohar 99, Hiippala 97, Benoni 96, Hiippala 95, Benoni 95). There is a potential risk of thrombosis with the use of this medicine (Hiippala 97, Howes 96).
Low quality	Post-operative re-transfusion of blood obtained from drains uses blood that has not been washed but that has been filtered (Gannon 91, Kristensen 92, Martin 92). Some alterations were observed in coagulation after infusing large volumes of blood (Rakower 73, Moore 80). The intra-operative recovery of washed cells before re-transfusion permits the use of large volumes without significant risk to the patient (Paravicina 83). One meta-analysis showed that instruments with washed or unwashed cells reduce the frequency of exposure to allogenic blood to a degree similar to that of the control group (Huet 99).

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Recommendations

Weak	Given the potential risks, each allogenic transfusion should have a valid, defined, and justifiable indication, which must appear in the clinical history.
Weak	The transfusion of leuco-depleted allogenic blood should not be limited by doubts over the increase in the recurrence of cancer or peri-operative infection.
	In a patient who is hæmodynamically stable, one unit of erythrocyte concentrate should be transfused once only, with a re-evaluation at 24 hours.
Strong	At the time of transfusion, it is essential to check the match between the patient's details and those contained in the request for the blood components to be transfused.
	A transfusion threshold should be defined as part of an overall strategy for optimum patient treatment.
	All patients undergoing major elective surgery must have a hæmogram before surgery, to avoid cancellations in the short term and to allow the appropriate treatment of anæmia.
Weak	Anæmia must be treated before major surgery to reduce exposure to allogenic transfusion.
Weak	In the post-operative period, a transfusion is required if hæmoglobin is s <70 g/l or <90 g/l in patients with cardiovascular disease.
Weak	All hospitals should use a programme for requesting blood so they can supply erythrocyte concentrates.
	For all patients undergoing surgery with major loss of blood, and who have signed a transfusion consent form, there must be a minimum supply of blood of their group in the blood bank.
Strong	Pre-operative autologous blood donation can be used to reduce exposure to allogenic blood, although it increases the total number of transfusions.
Weak	Pre-operative autologous blood donation must be aimed at men who present with Hb of between 110 and 145 g/l, and women who present with Hb of between 130 and 145 g/l.
Strong	Erythropoietin must be administered to patients under the age of 70 who are scheduled for surgery with major loss of blood and with Hb <130 g/l.
Strong	In healthy patients undergoing elective major surgery, erythropoietin can be used in combination with the autologous blood donation or to obtain multiple donations of erythrocytes and maintain adequate Hb on the day of surgery.
Weak	Acute normovolemic hæmodilution must be limited to patients with Hb levels that are sufficiently high to allow the extraction of 1000 ml of blood.
Strong	It is recommended that tranexamic acid be used in patients undergoing elective cardiac surgery with high risk of transfusion.
Strong	Tranexamic acid can be used to reduce blood loss and transfusion requirements in patients scheduled for knee-prosthesis surgery, when other blood-conservation techniques are inappropriate and major loss of blood is foreseen.
Weak	The re-infusion of blood recovered from the mediastinal drain, drawn out, and washed can be used for reducing allogenic transfusion in cardiac surgery.

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Weak	In orthopædic surgery, the recovery of unwashed cells using drains must be considered in patients expected to suffer an estimated post-operative blood loss of between 750 and 1500 ml.
Strong	In orthopædic surgery, the recovery of unwashed cells using drains must be considered in patients expected to suffer a predicted post-operative blood loss of between 750 and 1500 ml.

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4.6. Maintaining normothermia

Question to be answered

- What is the best body temperature for the patient at the time of the intervention?
- What is the target temperature in patients with some form of active heating before the intervention?
- Is thermal insulation or active heating before surgery preferable to usual procedures in preventing hypothermia?
- In patients undergoing surgery, does convective hot air maintain control of body temperature?
- Are the various devices for active heating (like forced-air heating, electrically-heated mattresses, or electrically-heated pillows) used during surgery effective in preventing unobserved hypothermia?
- Does the infusion of nutrient solutions reduce the incidence of unobserved hypothermia in patients with some form of active heating during surgery?

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Unobserved peri-operative hypothermia is a frequent and preventable complication in surgery, which is associated with complications in patients and that is defined as body temperature below 36ºC. Patients run the risk of developing hypothermia in any phase of the surgical process: pre-operative (defined as one hour before anæsthesia), intra-operative (defined as the total time under anæsthetic), and post-operative (defined as the 24 hours after being moved to the reanimation area) (Guyton 00).

During the 30 or 40 minutes under anæsthetic, the patient's temperature may fall to below 35ºC. Reasons for this include the loss of behavioural response to cold, the failure of thermoregulator mechanisms due to general or regional anæsthesia, peripheral vasodilation induced by anæsthesia, and patient cooling whilst awaiting surgery (Sessler 00).

Patients with a higher risk of peri-operative hypothermia are those ranked according to an ASA (American Society of Anaesthesiologists Physical Status Classification System) >I (Kongsayreepong 03, Lau 01), and those who have a low temperature pre-operatively (Kongsayreepong 03, Abelha 05). Similarly, the duration of anæsthesia (Kongsayreepong 03) and major surgery have also been associated with the risk of hypothermia (Flores Maldonado 97). Low quality

Hypothermia in a surgical patient can include a greater peri-operative loss of blood (Bennett 94, Frank 97, Johansson 99, Kurz 96, Lenhardt 97, Schmied 96), morbid cardiac events like arrhythmia (Frank 93, Frank 97), an increase in the risk of surgical infection (Flores-Maldonado 01, Kurz 96, Walz 06), and possibly a longer stay in hospital (Casati 99, Fleisher 98).

4.6.1. Mechanisms for maintaining normothermia in the pre-operative period

Eight RCTs have been identified that reviewed various interventions to maintain normothermia before surgery (Bock 98, Buggy 94, Camus 95, Fossum 01, Just 93, Melling 01, Sheng 03). In three of them, convective hot air was used (Camus 95, Fossum 01, Melling 01). Other interventions included the use of an electric blanket at a temperature between 42ºC and 43ºC for at least 90 minutes before induction (Just 93), reflective caps and jackets (Sheng 03a), reflective caps (Sheng 03b), and reflective blankets (Buggy 94). Moderate quality

4.6.1.1. Thermal insulation

The meta-analysis of the three RCTs that compared thermal insulation (use of reflective caps, jackets, and blankets) the usual care did not show significant differences in the body temperature of the patient at the end of heating (Buggy 94, Sheng 03a, Sheng 03b). Moderate quality

Two RCTs that compared core temperatures thirty minutes after induction and upon arrival in the reanimation room showed a significant difference between thermal insulation and usual care (average difference 0.43; 95% CI: 0.21 to 0.64 y DM 0.27; 95% CI: 0.06 to 0.49, respectively) (Sheng 03a, Sheng 03b).

4.6.1.2. Active heating

Three RCTs that compared convective hot air (Bock 98, Camus 95) and the use of an electric blanket (Just 93) with usual care showed small significant differences at 30 and 70 minutes after induction in favour of active heating (with large confidence intervals and very small RCT sizes). Low quality

One RCT compared convective hot air over the whole body with a non-contact radiant heat dressing in 278 patients (Melling 01). The convective hot air was found to be more effective at the end of the heating period (standardised average difference 0.22; 95% CI: 0.08 to 0.36) and upon arrival in the reanimation room (standardised average difference 0.20; 95% CI: 0.07 to 0.33).

One RCT compared convective hot air and the electric blanket on the incidence of hypothermia in the reanimation room (Fossum 01), and showed a significant difference in favour of forced air (RR 0.61; 95% CI: 0.43 to 0.87). This corresponds to a number needed to treat of 4 (95% CI: 3 to 12).

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4.6.2. Mechanisms for maintaining normothermia during surgery

4.6.2.1. Active heating versus usual treatment

Moderate quality

One RCT with 22 patients compared the use of electric blankets with usual treatment. The average core temperature was significantly higher in the group using electric blankets (Camus 93a). Thirty minutes after the intervention, the average difference was 0.55 ºC (95% CI: 0.26 to 0.84); sixty minutes after, 0.63 ºC (0.14 a 0.12); and 120 minutes after, 1.23ºC (0.83 to 1.63).

Six RCTs compared convective hot air with usual treatment (Hynson 92, Camus 93, Ouellette 93, Matsukawa 94, Smith 94, Krenzischek 95). After 60 and 120 minutes, the meta-analysis of five and four RCTs respectively showed a higher average core temperature for the group using heating (average difference at 60minutes, 0.35 ºC; 95% CI: 0.21 to 0.49, average difference at 120 minutes, 0.77 ºC; 95% CI: 0.60 a 0.94).

Regarding the use of mattresses with circulating water, four RCTs were identified that compared its use against usual treatment (Tollofsrud 84, Joachimsson 87, Hynson 92). While after 60 minutes there were no differences in the temperature of the groups, the temperature was higher in the treatment group after two hours (weighted average difference 0.35ºC; 95% CI: 0.15 to 0.55), and after three hours (weighted average difference 0.33ºC; 95% CI: 0.07 to 0.59).

One RCT with thirty patients compared the use of caps and shirts using circulating water versus usual treatment (Radel 86). Patients in both groups received heated endovenous fluids (37ºC). After 30 and 60 minutes, small significant differences were observed in the average temperature for the treatment group.

In patients undergoing surgery with regional anæsthesia, two RCTs were identified that compared the use of convective hot air against usual treatment (Yamakage 95, Johansson 99). These RCTs showed small significant differences in the core temperature during and after the interventions. That same comparison was evaluated in an RCT with patients undergoing surgery with general and regional anæsthetia (Lindwall 98). Small significant differences were observed (with wide confidence intervals) in favour of the treatment group both intra-operatively and upon arrival in the reanimation area.

4.6.2.2. Thermal insulation versus usual treatment

Moderate quality

The meta-analysis of two RCTs (76 patients; general anæsthesia) that compared the use of reflective blankets against usual treatment (Ouellette 93, Sheng 03) showed an average temperature higher in the intervention group 30 minutes after the intervention (weighted average difference 0.32ºC; 95% CI: 0.24 to 0.40), but not after 60 or 90 minutes.

Another two RCTs that evaluated the same comparison in patients who were given regional anæsthesia (Ouellette 93, Sheng 03) did not report significant differences between groups with respect to core temperature.

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4.6.2.3. Active heating versus thermal insulation

Moderate quality

Two RCTs compared the effectiveness of convective hot air against reflective blankets (Ouellette 93, Borms 94), while another compared warm cotton blankets with reflective blankets (Whitney 1990). There were no significant differences in the core temperature after 30 or 60 minutes in any of the comparisons. Two hours after the intervention, one RCT showed a higher core temperature in the forced-air group (average difference 0.88ºC; 95% CI: 0.47 to 1.29) (Borms 94).

One RCT compared the effectiveness of convective hot air with reflective blankets in 50 patients who underwent hip arthroplasty with combined spinal and epidural anæsthesia (Casati 99). Both groups were given hot Lactated Ringer's Solution (37ºC). After 430 minutes, there were no differences between the groups, although there were clinically insignificant differences after 60 and 120 minutes. The incidence of hypothermia in the reanimation room was lower in the group with active heating (RR 0.44; 95% CI: 0.22 to 0.88).

One RCT with 30 patients who received combined epidural-general anæsthetia compared convective hot air against reflective blankets (Berti 97). There were only small significant differences after two hours and at the end of surgery in favour of the group with convective hot air (with wide confidence intervals).

4.6.2.4. Comparisons between methods of active heating

Moderate quality

Convective hot air was compared against warm cotton blankets in an RCT with 64 patients (Mason 98). Sixty minutes after the intervention, the average difference between groups in core temperature was not significant. After 120 minutes, the average temperature was significantly greater in the forced-air group (average difference 0.40ºC; 95% CI: 0.13 to 0.67). Upon arrival in the reanimation room, the incidence of hypothermia was lesser in the forced-air group (RR 0.14; 95% CI: 0.05 to 0.43). This corresponds to a number needed to treat of 2 (95% CI: 1 to 3) for a rate in the control group of 66% (21/32).

Convective hot air was also compared against electric blankets, and no difference was observed in the patient's temperature 30 or 60 minutes after the intervention (Matsuzaki 03, Hofer 05). After 120 minutes, one RCT (Hofer 05) showed an average temperature that was higher in the group using electric blankets (average difference –0.40ºC; 95% CI: –0.76 to –0.04), whilst the other RCT did not present any differences between groups at any point.

Three RCTs compared the effectiveness of convective hot air against electrical devices under the blankets (Russell 95, Baxendale 00, Harper 07). After two hours, two RCTs (Russell 95, Harper 07) showed significant differences in the average temperature of the forced-air group (average difference 1.50ºC; 95% CI: 1.26 to 1.74). After four hours and at the end of surgery, the average temperature was also significantly higher in the forced-air group (average difference 1.80ºC; 95% CI: 1.56 to 2.04 and 1.90ºC, 1.68 to 2.12, respectively).

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Another five RCTs compared convective hot air with circulating-water mattresses (Hynson 92, Kurz 93a, Kurz 3M, Matsuzaki 03, Negishi 03). After 60 minutes, the meta-analysis of two RCTs (Hynson 92, Matsuzaki 03) found an average temperature that was higher in the forced-air group (weighted average difference 0.28ºC; 95% CI: 0.17 to 0.40). At the end of surgery, a higher average temperature was also observed in the forced-air group (weighted average difference 0.64ºC; 95% CI: 0.33 to 0.95).

Convective hot air was also compared against radiant warming in three RCTs (Lee 04, Wong 04, Torrie 05) that used radiant warming on the hand, face, and the palm of the hand, respectively. After two hours, the meta-analysis of two RCTs (Lee 04, Wong 04) showed a significant difference in the average temperature of the forced–air group (not significant clinically). After 3 and 4 hours, there was also a significant difference in favour of the same group, but with a wide confidence interval.

One RCT compared the effectiveness of convective hot air with the use of water garments (Hofer 05). After 60 minutes, the average temperature was significantly higher in the water-garment group (average difference –0.80ºC; 95% CI: –1.08 to –0.52). After 2 hours and at the end of surgery, small significant differences in the temperature were also observed in favour of the same group (with wide confidence intervals).

Two RCTs compared the use of electric blankets with circulating-water mattresses (Matsuzaki 03, Negishi 03). The first of those RCTs, conducted with patients who had been given general anæsthesia, showed significant differences in the average temperature in favour of the electric-blanket group during the whole intervention (after 60 minutes: average difference 0.34ºC; 95% CI: 0.22 to 0.45). The second RCT, in patients who had been given regional anæsthesia (Negishi 03), also showed significant differences in temperature in favour of the electric-blanket group after 60 minutes (average difference 0.50ºC; 95% CI: 0.15 to 0.85) and after two hours (average difference 1.10ºC; 95% CI: 0.73 to 1.47).

The use of electric blankets was also compared with the use of water garments in one RCT (Hofer 05). The average difference was significantly higher in the water-garment group during the whole operating period (although with wide confidence intervals).

4.6.2.5. Comparison of convective hot air applied to various parts of the body

Two RCTs compared various sites of convective hot air (Yamakage 95, Motamed 00). One of them, which compared the effectiveness of warming the upper part of the body against warming the lower part only (Motamed 00) did not detect significant differences in temperature between groups. The second RCT made the same comparison in patients who had been given regional anæsthetia. During the operating period, there were significant differences in temperature in favour of the group with warming in the lower part of the body, but the small number participants (14) limited the validity of these results.

Moderate quality

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4.6.2.6. Comparison between different dosages of forced-air heating

Three RCTs compared different dosages of heating (Camus 93b, Kurz 96; Winkler 00). One of them (Camus 93b) compared the use of insulated warming of the lower body (with additional sheets over and above the forced-air blanket) against regular warming of the lower body. After two hours, the average temperature was significantly higher in the group with insulated warming (average difference 0.44ºC; 95% CI: 0.15 to 0.73). Moderate quality

Another RCT compared convective hot air and endovenous serums at 37ºC against convective hot air at ambient temperature (Kurz 96). During the whole operating period, the average temperature was higher in the first group (after 60 minutes: average difference 0.39ºC; 95% CI: 0.22 to 0.56, and after three hours: average difference 1.75ºC; 95% CI: 1.59 to 1.91).

One RCT in patients who underwent hip arthroplasty with epidural anæsthetic compared the effectiveness of convective hot air in maintaining a core temperature of 36.5ºC (aggressive warming) or 36ºC (conventional warming) (Winkler 00). The average difference in final temperature was clinically and statistically significant for the group with aggressive warming (0.50ºC; 95% CI: 0.36 to 0.64).

4.6.2.7. Active warming and thermal insulation versus usual treatment

One RCT with 43 patients who underwent abdominal surgery compared active warming (water mattress and humidifying heaters) and thermal insulation (reflective blankets) against usual treatment (Joachimsson 87). There was a lower incidence of hypothermia in the intervention group (RR 0.06; 95% CI: 0.01 to 0.28). This corresponds to a number needed to treat of 2 (95% CI: 1 to 2, for a 100% rate in the control group (18/18). Moderate quality

4.6.2.8. Thermal insulation of two areas versus thermal insulation of one area

One RCT with 44 patients who underwent abdominal surgery under general and regional anæsthetic compared the effectiveness of thermal insulation to the head and face, in addition to the extremities and the trunk. Patients in the control group only received thermal insulation to the extremities and the trunk (Kamitani 99). There were no differences in temperature between groups 30 and 60 minutes after intervention. The average final temperature was significantly higher in the intervention group (average difference 0.40ºC; 95% CI: 0.10 to 0.70). Moderate quality

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4.6.3. Mechanisms for maintaining normothermia in the pre-operative period and during surgery

4.6.3.1. Thermal insulation versus usual treatment

One RCT assessed the effect of a reflective blanket applied before induction in 68 patients. No differences were observed in core temperature 15, 30, and 45 minutes after the intervention (Buggy 94). Moderate quality

4.6.3.2. Thermal insulation versus usual treatment

Three RCTs compared active warming against usual treatment (Bock 98, Wong 07, Wongprasartsuk 98) from the pre-operative period onwards. Only small differences in temperature were observed at various timings after the start of the intervention, and only for some of the RCTs. After three hours, however, one RCT showed a clinically and statistically significant difference in the core temperature of the intervention group (average difference 0.92ºC; 95% CI: 0.56 to 1.28) (Bock 98). Moderate quality

4.6.3.3. Active warming plus warm serum versus usual treatment

One RCT of 336 patients compared the combination of convective hot air in the pre-operative and intra-operative periods and warming using endovenous serums versus usual treatment (Smith 07). The incidence of hypothermia at the end of the intervention was lower in the intervention group (RR 0.32; 95% CI: 0.22 to 0.47) for a rate of 53% in the control group. This corresponds to a number needing to be treated of 4 (95% CI: 3 to 5). The average temperature was also significantly higher in the intervention group upon arrival in the reanimation area (average difference 0.4ºC; 95% CI: 0.29 to 0.51). Moderate quality

4.6.4. Warming endovenous liquids

4.6.4.1. Active warming of endovenous liquids versus endovenous liquids at ambient temperature

Various RCTs compared the effectiveness of active warming with endovenous liquids versus endovenous liquids at ambient temperature (Cooper 94, Camus 96, Muth 96, Smith 98, Smith 98b, Hasankhani 05) in patients given general anæsthetic. The temperature of the endovenous liquids administered varied in the different studies (from 37.5ºC to 42ºC), as well as the volume infused (from 0.918 litres to 3.6 litres). Moderate quality

The meta-analysis of two RCTs with 88 patients showed a lower incidence of hypothermia for the group with active warming with endovenous liquids (Peto RR 0.10; 95% CI: 0.04 to 0.24). This corresponds to a number needing to be treated of 3 (95% CI: 2 to 4).

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After 30 minutes, the meta-analysis of four studies (Camus 96, Smith 98, Smith 98b, Hasankhani 05) in 186 patients showed an average temperature significantly higher in the group with warm endovenous liquids (weighted average difference 0.40ºC; 95% CI: 0.26 to 0.54) for a control-group temperature of 35.5ºC to 36.25ºC. After 60 minutes, the difference was also significant for the group with warm endovenous liquids (weighted average mean 0.38ºC; 95% CI: 0.21 to 0.54) for a control-group temperature of 35.8ºC to 36.2ºC. Two, three, and four hours later, significant sddifferences were also observed in the temperature of the group with active warming of endovenous liquids, but with large confidence intervals.

At the end of surgery, the meta-analysis of four studies (Camus 96, Muth 96, Smith 98, Hasankhani 05) showed an average temperature that was significantly greater for the group with warmed endovenous liquids (0.66ºC; 95% CI: 0.50 to 0.81) for a control-group temperature of 34.2ºC to 35.9ºC.

4.6.4.2. Active warming of the patient and active warming of endovenous liquids versus usual treatment

Five RCTs compared the combined effects of active warming of the patient and of the endovenous liquids in comparison with usual treatment (endovenous liquids not warmed) (Kurz 95, Schmied 96, Zhao 05, Steinbrook 97, Motamed 98). Moderate quality

After 60 minutes and two hours, the meta-analysis of two studies (Kurz 95, Zhao 05) with 114 patients showed average temperatures significantly higher for the group with active warming (weighted average difference 0.41ºC; 95% CI: 0.26 to 0.57 and weighted average difference 1.12ºC; 95% CI: 0.94 to 1.30, respectively), although significant heterogeneity was observed.

After three hours, one RCT (Kurz 95) showed a temperature significantly higher for the warmed group (weighted average difference 2.04ºC; 95% CI: 1.85 to 2.23) for a control-group temperature of 34.5ºC.

On arrival in the reanimation area, the meta-analysis of two RCTs (Kurz 95, Steinbrook 97) showed a temperature significantly higher for the actively-warmed group (weighted average difference 2.07ºC; 95% CI: 1.87 to 2.28). After two hours (Kurz 95, Schmeid 05) a significantly higher temperature was also observed in the same group (weighted average difference 1.17ºC; 95% CI: 0.99 to 1.35). Three, four and five hours after arriving in the reanimation area, only one RCT documented the temperature (Kurz 95), which remained significantly higher in the warmed group (although it fell gradually to leave no difference after six hours).

One RCT with patients who were given epidural anæsthetic compared active warming of endovenous liquids and blood with usual treatment (Motamed 98), and at the end of surgery, showed an average temperature that was higher for the warmed group (average difference 1.40ºC; 95% CI: 1.02 to 1.78).

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4.6.4.3. Warming endovenous liquids for irrigation versus no warming

Low quality

Three RCTs with regional anæsthesia compared the irrigation of warmed endovenous liquids with irrigation using endovenous liquids at ambient temperature. In the first RCT (Dyer 86), no significant differences were observed in average temperature after 30, 60, and 120 minutes. Another RCT showed that the change in average temperature (difference between temperature at the start and the lowest temperature) was significantly lower for the group with irrigation using actively warmed endovenous liquids (average difference 0.97ºC; 95% CI:, 0.51 to 1.43) (Pit 96). The third RCT presents a confidence interval that is too large to determine if there is a difference in the average temperature (Monga 96).

Two RCTs with general anæsthesia compared the effectiveness of irrigation using warmed endovenous liquids with irrigation using endovenous liquids at ambient temperature (Moore 96, Jaffe 01). In the two RCTs, the patients of both groups received active warming. There was no significant difference in temperature after 30 and 60 minutes. At the end of surgery, there were no significant differences in temperature (average difference 0.05; 95% CI: –0.14 to 0.24) in one RCT (Jaffe 01).

4.6.5. Warming gases

4.6.5.1. Insufflation of warmed gas versus insufflation of unwarmed gas

Moderate quality

Five RCTs compared the insufflation of warmed gas versus the insufflation of unwarmed gas (Nelskyla 99, Saad 00, Farley 04, Champion 06, Hamza 05).

In one of them, there were no significant differences in temperature after 30 or 60 minutes (Hamza 05). At the end of insufflation (about 90 minutes) the average temperature was significantly higher in the group with warmed gas (average difference 0.59ºC; 95% CI: 0.22 to 0.96) compared with the control group, for which the temperature was 35ºC.

Another RCT showed a significantly smaller change in the average intraoperative temperature in the intervention group (average difference 0.32ºC; 95% CI: 0.13 to 0.51), with a change in the control temperature of –0.03ºC (Farley 04).

At the end of surgery, one RCT showed no significant differences between groups regarding temperature (Nelskyla 99). The meta-analysis of two more RCTs (Hamza 05, Saad 00) with 65 patients showed a significantly higher temperature in the group with warmed gas (average difference 0.51ºC, (95% CI: 0.31 to 0.70) compared with the control group, which had a temperature ranging from 35.0ºC to 35.7ºC. The difference was clinically significant, and no heterogeneity was observed.

The meta-analysis of two RCTs (Farley 04, Champion 06) did not show any significant differences in temperature upon arrival in the reanimation area, or after 30 minutes, 60 minutes, or 4 hours.

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4.6.5.2. Inspiration of warmed gases versus usual treatment

Various RCTs compared the inspiration of warmed gases against usual treatment. One of them showed a significantly lower incidence of hypothermia in the warmed-gas group (RR 0.06; 95% CI: 0.01 to 0.28) with a number needed to treat of 2 (95% CI: 1 to 2) and a 100% rate of hypothermia in the control group (18/18) (Joachimsson 87). Moderate quality

Three RCTs showed a small significant difference in the treatment group 30 minutes after the start of the intervention (Conahan 87, Joachimsson 87, Ouellette 93) (average difference 0.19ºC; 95% CI: 0 to 0.38). After 60 minutes, the meta-analysis of eight RCTs (Tollofsrud 84a, Tollofsrud 84b, Joachimsson 87, Goldberg 92, Hynson 92, Ouellette 93, Johansson 03) showed an average temperature significantly higher for the warmed-gas group (weighted average difference 0.12ºC; 95% CI: 0.03 to 0.21), in comparison with a control-group temperature ranging from 35.5ºC to 36.6ºC. After two hours, a higher temperature was also observed in the warmed-gas group (weighted average difference 0.42ºC; 95% CI: 0.24 to 0.59) for a control-group temperature ranging from 35.2ºC to 35.8ºC, with significant heterogeneity.

At the end of surgery, the meta-analysis of two RCTs (Joachmisson 87, Ouellette 93) showed a higher temperature for the warmed-gas group (average difference 0.45ºC; 95% CI: 0.08 to 0.82) for a control-group temperature of 35.4ºC. The temperature was also higher in the intervention group upon arrival in the reanimation area (average difference 0.50ºC; 95% CI: 0.26 to 0.74) (Conahan 87, Goldberg 92).

One RCT that carried out the same comparison and that used thermal insulation in both groups (Eckerbom 90) showed that 20 minutes after the end of anæsthesia, a significantly higher temperature was observed for the warmed-gas group (average difference 0.60ºC; 95% CI: 0.12 to 1.08) for a control-group temperature of 36.6ºC.

4.6.6. Pharmacological agents for preventing hypothermia

4.6.6.1. Alpha-andrenergic agonists

One RCT compared the use of an infusion of phenylephrine 0.5 μg/kg/min from the start of anæsthesia versus no treatment in 18 patients (Ikeda 99). Endovenous liquids were warmed to 37ºC, the operating-theatre temperature was 25ºC to 26ºC, and the patients were covered with cotton blankets and surgical drapes. Average temperatures were significantly higher in the patients of the intervention group at 15, 30, 45, and 60 minutes, and at the end of surgery. Low quality

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4.6.6.2. Alpha-andrenergic antagonists

Two RCTs compared the use of endovenous urapidil at the end of surgery versus a placebo in 120 patients (Piper 00, Piper 01). The patients were covered with a cotton sheet. No significant differences appeared between the intervention regarding the average temperature 15 and 60 minutes after extubation.

Low quality

4.6.6.3. Infusion of nutrient solutions

One RCT evaluated the change in temperature in 16 patients after infusion of a solution of amino acids against infusion of a saline solution for two hours before anæsthesia (Selldén 96). The operating theatre temperature was between 21 and 23ºC, and the patients did not receive any type of warming, except one patient from the control group. A statistically significant difference was observed in the core temperature during the post-operative period in the treatment group (average difference 0.51ºC; 95% CI: 0.14 to 0.88), although the temperatures were taken at different times in the two groups.

Moderate quality

Two RCTs evaluated the effect of amino acids versus placebo in the intra-operative phase. One compared an amino-acid solution with anæsthesia using isoflurane against anæsthesia using isoflurane (Sahin 02). The same RCT also compared an amino-acid solution with anæsthesia using propofol against anæsthesia using propofol (Sahin 02). All the patients received crystalloids and colloids at ambient temperature, and the operating theatre was maintained at 21ºC. The second RCT compared an amino-acid solution against a saline solution. The operating room temperature was maintained between 21 and 23ºC, and no type of warming was used (Selldén 94).

The meta-analysis of these RCTs did not reveal significant differences intra-operatively between groups. At the end of surgery, the meta-analysis showed an average core temperature that was higher in the intervention group (weighted average difference 0.76ºC; 95% CI: –0.08 to 1.60).

Three RCTs evaluated the effect of amino acids in the pre- and intra-operative phases (Mohamed 05, Selldén 96a, Umenai 06). One RCT recorded core temperature at various points of the intervention in 40 patients with an amino-acid solution (one hour before induction and one hour after) versus no infusion (Mohamed 05). Both groups received warm saline serum. This RCT found statistically significant differences at all times in favour of the amino-acid group.

Moderate quality

One RCT compared the infusion of amino acids against the infusion of a saline solution two hours after anæsthesia, for six hours (Umenai 06). It found that temperatures were significantly higher in the aminoacid group during and at the end of surgery (average difference 0.50ºC; 95% CI: 0.18 to 0.82).

Another RCT recorded patients' temperatures upon awakening from anæsthetia and found that patients in the aminoacids group had temperatures significantly higher (average difference 1.16; 95% CI: 0.58 to 1.74) (Selldén 96a) than those in the group with the saline solution.

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One RCT compared the infusion of fructose against the infusion of saline serum, started three hours before surgery and maintained for one hour after induction (Mizobe 06). Temperature in the operating room was maintained at 24ºC, and patients were covered with a cotton blanket before surgery and with drapes during the intervention. The temperature was significantly higher in the fructose group for all measures. Three hours after anæsthesia, the average difference was 0.60ºC (95% CI: 0.25 to 0.95).

Summary of the evidence – Maintaining normothermia in the pre-operative period

Moderate quality	There were no significant differences in patient temperature associated with thermal insulation at the end of warming (Buggy 94, Sheng 03a, Sheng 03b), but 30 minutes after induction and upon arrival in the reanimation room, active insulation was more effective than usual treatment (Sheng 03a, Sheng 03b).
Moderate quality	Convective hot air (Bock 98, Camus 95) and the use of an electric blanket (Just 93) were not effective when compared with usual care, at30 and 60 minutes after induction. Convective hot air was more effective than electric blankets and the heat-irradiating garment regarding the incidence of hypothermia at the end of warming and in the reanimation room (Melling 01, Fossum 01).

Summary of the evidence – Maintaining normothermia during the operation

Moderate quality	In one RCT, use of the electric blanket was more effective than usual treatment for increasing temperature during the intervention (Camus 93a).
Moderate quality	Convective hot air was more effective than usual treatment in obtaining higher temperatures during the intervention (Hynson 92, Camus 93b, Ouellette 93, Matsukawa 94, Smith 94, Krenzischek 95). Convective hot air was moderately effective in patients who had been given regional anæsthetic (Yamakage 95, Johansson 99, Lindwall 98).
Moderate quality	The use of water-circulating mattresses was associated with higher temperatures. Compared with usual treatment, differences were significant 2 and 3 hours after the intervention (Tollofsrud 84a, Tollofsrud 84b, Joachimsson 87, Hynson 92).
Moderate quality	One RCT that compared the use of cap and shirt with water circulation versus usual treatment found higher temperatures with small but significant differences in the treatment group (Radel 86).
Moderate quality	In two RCTs, the use of reflective blankets was associated with higher temperatures after 30 minutes from the start of the intervention, but not after 60 or 90 minutes, whencompared against usual treatment (Ouellette 93, Sheng 03). In patients who had received regional anæsthetic, the use of reflective blankets was not effective (Ouellette 93, Sheng 03).

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Moderate quality	Convective hot air was discretely more effective than reflective blankets regarding the incidence of hypothermia and the presence of higher temperatures during the intervention (Ouellette 93, Borms 94, Whitney 90, Casati 99, Berti 97).
Moderate quality	Convective hot air was compared against warm cotton blankets (Mason 98), electric blankets (Matsuzaki 03, Hofer 05), electric underblankets (Russell 95, Baxendale 00, Harper 07), water-circulating mattresses (Hynson 92, Kurz 93a, Kurz 93b, Matsuzaki 03, Negishi 03), radiant warming (Lee 04, Wong 04, Torrie 05), and water garments (Hofer 05). In all comparisons, convective hot air was associated with discretely higher temperatures during the intervention.
Moderate quality	Various RCTs compared convective hot air in different places (upper part of the body versus the lower part) but failed to find significant differences (Yamakage 95, Motamed 00). Forced-air warming (Camus 93b), convective hot air and serums at 37ºC (Kurz 96), and aggressive convective hot air (Winkler 00), were more effective than conventional convective hot air. Active warming and thermal insulation together were more effective than usual treatment (Joachimsson 87a). Thermal insulation of two areas was somewhat more effective than thermal insulation of a single area (Kamitani 99).

Summary of the evidence – Maintaining normothermia in the pre-operative phase and during the operation

Moderate quality	The use of a reflective blanket before induction was effective maintaining normothermia (Buggy 94). Active warming started during the pre-operative phase was associated with small but statistically significant differences in temperature during the intervention (Bock 98, Wong 07, Wongprasartsuk 98, Bock 98). Convective hot air and the use of warm serums staretd during the pre-operative phase were effective reducing the incidence of hypothermia at the end of the intervention and maintaining a higher temperature during the intervention (Smith 07).

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Summary of the evidence – Warming endovenous liquids

Moderate quality	Warming endovenous liquids was associated with a lower incidence of hypothermia in patients who received warm endovenous liquids at the end of surgery when compared with liquids at ambient temperature (number needing to be treated 3; 95% CI: 2 to 4) (Smith 98, Muth 96). Warming endovenous liquids was moderately effective in maintaining significantly higher temperatures during the intervention and at the end of surgery (Cooper 94, Camus 96, Smith 98, Smith 98b, Hasankhani 05). No difference in temperature during surgery was assocaited with continuous warming of endovenous liquids or withthe use of prewarmed liquids (Ellis-Stoll 96). The combination of active warming of the patient and warming endovenous liquids was more effective than administering unwarmed endovenous liquids maintaining temperature during the intervention and in the reanimation area (Kurz 95, Schmied 96, Zhao 05, Steinbrook 97, Motamed 98). Irrigation using warm endovenous liquids was not associated with significant differences in average temperature during the intervention (Dyer 86, Monga 96, Moore 96, Jaffe 01).

Summary of the evidence – Warming gases

Moderate quality	Insufflating warmed gas was associated with discrete but significant differences in temperature at the end of insufflation (Hamza 05), in intra-operative temperature (Farley 04), and in temperature at the end of surgery (Hamza 05, Saad 00). One RCT found that a lower incidence of hypothermia was associated with the inspiration of warmed gas (number needing to be treated 2; 95% CI: 1 to 2) when compared against usual treatment (Joachimsson 87). Inspiration of warmed gases was moderately effective in maintaining higher average temperatures during the intervention (Tollofsrud 84a, Tollofsrud 84b, Joachimsson 87, Goldberg 92, Hynson 92, Ouellette 93, Johansson 03), at the end of surgery (Joachmisson 87, Ouellette 93), and upon arrival in the reanimation area (Canahan 87, Goldberg 92).

Summary of the evidence – Pharmacological agents

Low quality	One RCT that evaluated the use of a phenylephrine infusion (in addition to warming endovenous fluids and with the operating room at a temperature of 25 to 26ºC) found significantly higher average temperatures in the intervention group during and at the end of surgery (Ikeda 99). Endovenous urapidil was not effective in maintaining temperature after extubation (Piper 00, Piper 01).

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Moderate quality	The infusion of an amino-acid solution was discretely effective in maintaining temperature (Selldén 96b, Sahin 02a, Sahin 02b, Selldén 94, Mohamed 05, Selldén 96a, Umenai 06). In one RCT, the infusion of fructose was moderately effective in maintaining temperature (Mizobe 06).

Recommendation – Maintaining normothermia in the pre-operative phase

	An assessment should be made of the risk of hypothermia for each patient before surgery. Healthcare professionals must ensure that patients are not cold before going into the operating room. They should be covered with blankets or a comforter, especially if they have received medication.
Weak	Body temperature should be 36ºC or higher when the patient is taken to the operating theatre. If body temperature is <36ºC, warming using forced air should start before the patient is taken to the operating room, and should be maintained intraoperatively.

Recommendation – Maintaining normothermia during the operation

	The patient's temperature should be taken and recorded before anæsthetic induction and every 30 minutes until the end of surgery.
	Anæsthetic induction should not be started until the patient's temperature is ≥36ºC.
	The patient must be adequately covered during the intervention in order to conserve heat.
Weak	Patients at risk of hypothermia and who are given anæsthetic < 30 minutes must be warmed during the operation using a forced-air device.
Weak	All patients given anæsthesia > 30 minutes must be warmed from anæsthetic induction using a forced-air warming device.
	The temperature of the convective hot air devices must be set to maximum and then adjusted to maintain a minimum temperature in the patient of 36.5ºC.
	Endovenous liquids for irrigation must be warmed to a temperature of 38ºC-40ºC.

Recommendation – Maintaining normothermia in the post-operative phase

	The patient's temperature must be taken and recorded upon arrival in the reanimation area and subsequently every 15 minutes.
	If the patient's temperature is less than 36ºC, convective hot air should be started until the patient is discharged from the reanimation area or feels comfortable.

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4.7. Aspects derived from anæsthesia

Question to be answered

- What interventions before surgery have shown prevention of problems derived from anæsthesia?
- What interventions during surgery have shown prevention of problems derived from anæsthesia?
- What patients are at risk of presenting with nausea and vomiting in the post-operative phase?
- What factors are linked to a reduction in the risk of presenting with nausea and vomiting in the post-operative phase?
- What antiemetic drugs have shown effectiveness in preventing nausea and vomiting in the post-operative phase?

Anæsthesiology has played a fundamental role in the movement for patient safety, and in establishing standards for safe practice. The first organisation dedicated to patient safety was the Anæsthesia Patient Safety Foundation, which was set up in the USA in 1985. The International Task Force on Anaesthesia Safety was set up in 1989 which, two years later, drew up the *International standards for a safe practice of anaesthesia* (International Task Force on Anaesthesia Safety 1993), which was adopted in 1992 by the World Federation of Societies of Anaesthesiologists and recommended to all its participating societies. In 2008, the World Federation of Societies of Anaesthesiologists' revised and updated those standards (WFSA 2008), and they have been incorporated and evaluated in the WHO initiative Guidelines for Safe Surgery (WHO 2008). Likewise, the *Sociedad Española de Anestesiología, Reanimación y Terapéutica del Dolor* (Spanish Society of Anæsthesiology, Reanimation, and Pain Therapy), also has a "Clinical Practice Guidelinein Anæsthesiology and Reanimation". Below are the main aspects found in these standards.

The standards of the World Federation of Societies of Anaesthesiologists are the main reference for this section. They are classified as highly recommended, recommended, or suggested, and are applicable to each health centre on the basis of its infrastructure. Each section references the documents in which the respective standards are recommended.

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4.7.1. Monitoring during surgery

4.7.1.1. Presence of an anæsthesiologist during anæsthesia

It is highly recommended that an anæsthesiologist be present at all times when the patient is under anæsthesia. The anæsthesiologist must check the anæsthetic apparatus, as well as all the material and drugs for anæsthetic induction and tracheal intubation. In addition to using monitoring technology, continuous clinical observation is required, because the team cannot detect deterioration as quickly as an experienced professional (WFSA 2008, OMS 2008, AAGBI 2007, SEDAR). Moderate quality

If an emergency requires the temporary absence of the person responsible for anæsthesia, it is highly recommended that a judgement be made comparing the emergency with the condition of the anæsthetised patient, and choose the professional who will be responsible for anæsthesia during the absence of the anæsthesiologist (WFSA 2008, OMS 2008, AAGBI 2007).

4.7.1.2. Oxygenation

4.7.1.2.1. Administering oxygen

The administration of supplementary oxygen is highly recommended in all patients who receive general anæsthetia (WFSA 2008, OMS 2008). The anæsthesiologist must check the integrity of the oxygen supply. Moderate quality

It is recommended that inspired oxygen be monitored during anæsthesia with an instrument that is capable of detecting the low concentration of inspired oxygen with an alarm (WFSA 2008, OMS 2008, SEDAR).

It is recommended that an alarm be installed in case of failure of the oxygen supply, as well as a device that gives protection against hypoxic gas mixtures (WFSA 2008, OMS 2008, AAGBI 2007).

Use must be made of secure connexion systems (cylinders and tubing) to prevent errors in connexions to sources of gas (WFSA 2008).

4.7.1.2.2. Patient oxygenation

It is highly recommended that monitoring of patient oxygenation be carried out (WFSA 2008). Moderate quality

It is highly recommended to ensure, whenever possible, that there is adequate lighting and that the pacient is exposed to allow a visual examination (WFSA 2008, SEDAR).

The continuous use of an oxygen monitor, such as the pulse oximeter, is highly recommended (WFSA 2008, OMS 2008, AAGBI 2007, SEDAR).

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4.7.1.3. Airway and ventilation

It is recommended to conduct an assessment of the patient's airway in order to prevent difficulties due to intubation or ventilation. Moderate quality

It is highly recommended to continuously monitor proper intubation and ventilation of the patient, at least and whenever possible, by means of observation and auscultation (WFSA 2008, OMS 2008).

When a ventilation circuit is used, it is highly recommended that the reservoir bag be observed (WFSA 2008).

When mechanical ventilation is applied, the use of a disconnexion alarm during the entire period of application of mechanical ventilation is highly recommended (WFSA 2008, OMS 2008, SEDAR).

It is recommended to continuously monitor the patient using a primordial, pretracheal, or œsophageal stethoscope (WFSA 2008).

It is recommended to confirm that the endotracheal tube is properly fitted, as well as that the concentration and of the graph of expired carbon dioxide are continuously measured (capnography) (WFSA 2008, OMS 2008, SEDAR).

It is suggested to continuously monitor the volumes of gases inspired and/or expired, as well as the concentration of anæsthetic gases (WFSA 2008, OMS 2008).

4.7.1.4. Circulation

4.7.1.4.1. Cardiac frequency and rhythm

It is highly advisable to carry out continuous monitoring of cardiac frequency and rhythm (WFSA 2008, OMS 2008). Moderate quality

It is highly advisable to palpate or observe the pulse and to carry out auscultation of cardiac sounds on a continuous basis (WFSA 2008, OMS 2008).

It is highly recommended to continuously monitorand observe the cardiac frequency using the pulse oximeter (WFSA 2008, OMS 2008).

The use of an electrocardiographic recorder of one or more channels in cascade and V5 precordial derivations for cardiopathic patients is recommended (WFSA 2008, OMS 2008, AAGBI 2007, SEDAR).

It is recommended that a defibrillator be available (WFSA 2008, OMS 2008).

4.7.1.4.2. Tissue perfusion

It is highly recommended to continuously monitor the adequate perfusion of tissue by means of a clinical examination (WFSA 2008). Moderate quality

The use of pulse a pulse oximeter for continuous monitoring is highly recommended (WFSA 2008).

The use of capnography for continuous monitoring is highly recommended (WFSA 2008).

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4.7.1.4.3. Blood pressure

It is highly recommended to determine blood pressure at appropriate intervals (every 5 minutes, or more frequently if indicated by clinical circumstances) (WFSA 2008, OMS 2008, SEDAR). Moderate quality

It is suggested to measure and visualize blood pressure in appropriate cases using non-invasive automatic measuring (WFSA 2008, AAGBI 2007).

4.7.1.5. Temperature

It is highly recommended to ensure that a means of measuring temperature is always available, as well as that it be used at frequent intervals when clinically indicated (WFSA 2008, OMS 2008, AAGBI 2007, SEDAR). Moderate quality

It is recommended to continuously measure the temperature of patients expected to undergoan intentioned or suspected change (WFSA 2008, OMS 2008).

It is recommended to ensure that an electronic system for continuous temperature measurement is available and used if indicated (WFSA 2008, OMS 2008).

4.7.1.6. Neuromuscular function

The use of a quantitative peripheral neurostimulator is recommended when administering drugs that block neuromuscular function (WFSA 2008, OMS 2008, AAGBI 2007). Moderate quality

4.7.1.7. Depth of anæsthesia

It is highly recommended to check the depth of anæsthesia (degree of loss of consciousness) by means of clinical observation (WFSA 2008, OMS 2008). Moderate quality

It is suggested to continuously measure the concentration of anæsthetic gases and volatile agents, both inspired and expired (WFSA 2008).

The application of electronic monitors for measuring brain function (consciousness), although controversial and not recommended as a general rule, should be considered particularly in patients with a high risk of waking up in the intra-operative phase (WFSA 2008).

4.7.1.8. Audible signals and alarms

It is highly recommended to have available audible signals (such as variations in the tone of the pulse oximeter) and audible alarms (with appropriate limiting values) activated during the entire intervention, and that they are sufficiently loud to be heard in the whole operating room (WFSA 2008). Moderate quality

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4.7.2. Preventing nausea and vomiting

4.7.2.1. Identifying patients at risk of presenting with nausea and vomiting in the post-operative phase

Without treatment, post-operative nausea and vomiting (PONV) affects 20-30% of patients, and 70-80% of high-risk patients (Tramèr 2001, Apfel 1999, Apfel 2004). Estimating individual risk of presenting with PONV can indicate which patients may benefit from prophylaxis with antiemetic drugs.

The following PONV risk factors have been described:

- Risk factors associated with the patient: female gender, non-smoker, and a history of PONV or motion sickness (Apfel 1999, Cohen 1994, Koivuranta 1997, Sinclair 1999, Stadler 2003, Roberts 2005, Choi 2005). Low quality
- Risk factors associated with anæsthesia: using a volatile anæsthetic, using nitrous oxides, or using opioids during or after surgery (Apfel 1999, Stadler 2003, Roberts 2005, Choi 2005, aApfel 2002, Khalil 2005, Møiniche 2003, Polati 1997, aTramèr 1999, Sukhani 2002).
- Risk factors associated with surgery: duration of surgery (each increase of 30 minutes in the duration of the intervention increases the risk of PONV by about 60%), type of surgery (laparoscopy, laparotomy, breast surgery, strabismus, plastic surgery, maxillo-facial surgery, gynæcological surgery, abdominal surgery, neurological surgery, ophthalmologic surgery, or urology) (Sinclair 1999, Stadler 2003, Choi 2005).

4.7.2.2. Reducing the risk of presenting with post-operative nausea and vomiting

Reducing the incidence of PONV is very significantly associated with identifying and reducing the risk factors discussed in the previous section.

The following strategies have been identified for reducing the incidence of PONV:

- Avoid general anæsthesia and use regional anæsthesia (Sinclair 1999, Khalil 2005). Low quality
- Use propofol for inducing and maintaining anæsthesia (Apfel 2004, Choi 2005, Tramèr 1997, Gan 1997).
- Avoid nitrous oxide (Apfel 1999, Apfel 2004, Trèmer 1997, Trèmer 1996).
- Avoid volatile anæsthetics (Apfel 2002, Apfel 2002).
- Minimise the use of opioids during or after the intervention (Apfel 1999, Roberts 2005, Apfel 2002, Møiniche 2003, Polati 1997, Sukhani 2002, Apfel 2002, Tramèr 1997).
- Minimise the use of neostigmine (<2.5 mg) (Tramèr 1999, Ho 2005).
- Maintain adequate hydration (Scuderi 2000).

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4.7.2.3. Pharmacological measures to prevent PONV

The recommended first- and second-line antiemetic drugs for the prophylaxis of PONV are serotonin receptor antagonists (ondansetron, dolasetron, granisetron, and tropisetron), steroids (dexamethasone), phenothiazines (prometazine and prochlorperazine), phenylethylamine (ephedrine), butyrophenones (droperidol, haloperidol), antihistamines (dimenhydrinate) and anticholinergic agents (scopolamine). The doses and the timing of administration of antiemetic drugs for preventing PONV are given in the following table.

Dose and time of administration of various anti-emetics for preventing PONV

Drug	Dose	Timing of administration
Dexametasone	4-5 mg ev (Henzi 2000, Wang 2000, Wang 2000)	During induction ([b]Wang 2000)
Dimenhydrinate	1 mg/kg ev ([a]Kranke 2002, Eberhart 1999, Kothari 2000)	
Dolasetron	12.5 mg ev (Graczyk 1997)	At the end of surgery; the timing does not affect its effectiveness (Graczyk 1997)
Droperidol*	0.625-1.25 mg ev (Domino 1999, Fortney 1998)	At the end of surgery ([b]Henzi 2000)
Ephedrine	0.5 mg/kg im (Rothenberg 1991, Hagemann 2000)	At the end of surgery (Rothenberg 1991, Hagemann 2000)
Granisetron	0.35-1.5 mg ev (Sun 1997, Wilson 1996, Mikawa 1977, D'Angelo 2005, Cieslak 1996)	At the end of surgery (Wilson 1996, Mikawa 1977, D'Angelo 2005)
Haloperidol*	0.5-2 mg im/ev (Buttner 2004)	
Prochlorperazine	5-10 mg im/ev (Chen 1998)	At the end of surgery (Chen 1998)
Promethaxzine	6.25-25 mg ev (Khalil 1999, Chia 2004)	During induction (Khalil 1999, Chia 2004)
Ondansetron	4 mg ev ([c]Tramèr 1997)	At the end of surgery (Sun 1997)
Scopolamine	Transdermal patch ([b]Kranke 2002, Bailey 1990)	The night before or four hours before surgery (Bailey 1990)
Tropisetron	2 mg ev (DiBruijn 1992)	At the end of surgery

*Alerts in the US Food and Drug Administration. Abbreviations: ev: endovenous; im: intramuscular.
Adaptation from: Gan TJ, Meyer TA, Apfel CC, Chung F, Davis PJ, Habib AS, *et al.* Society for Ambulatory Anæsthesia guidelines for the management of postoperative nausea and vomiting. Anesth Analg. 2007; 105(6): 1615-28.

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4.7.2.3.1. Serotonin receptor antagonists (ondansetron, dolasetron, granisetron, and tropisetron)

Most studies available on serotonin receptor antagonists focus on ondansetron, which has a greater effect as an antiemetic than as an anti-nausea agent el (Tramèr 1997). A meta-analysis that includes controlled studies using a placebo supports the effectiveness of dolasetronin preventing PONV (Kranke 2002). — High quality

Ganisetron is effective in preventing PONV, although a systematic review shows that some data on ganisetron are not reliable (Graczyk 1997, Wilson 1996, Mikawa 1977, D'Angelo 2005, Chen 2001, Tramèr 1997, Kranke 2002, Kranke 2001). — Moderate quality

Tropisetron was found to be significantly effective reducing the risk of nausea and vomiting, and it is recommended for the prevention of PONV (DiBruijn 1992, Kranke 2002).

Serotonin receptor antagonists have a favourable profile of adverse effects, and are considered to be safe drugs.

4.7.2.3.2. Steroids (dexamethasone)

Dexamethasone is effective in preventing nausea and vomiting (Henzi 2000, Wang 2000). For preventing PONV, the effectiveness of dexamethasone (4 mg ev) appears to be similar to that of ondansetron (4 mg ev) and droperidol (1.25 mg ev) (Apfel 2004). No adverse effects have been observed after administering a single dose of dexamethasone (Henzi 2000). — Moderate quality

4.7.2.3.3. Butyrophenones (droperidol, haloperidol)

The prophylactic dose of droperidol is effective in preventing PONV (Domino 1999, Fortney 1998). The effectiveness of droperidol is equivalent to on-dansetron in preventing PONV (Tramèr 2001, Apfel 2004). It is also effective in reducing the risk of nausea and vomiting induced by opioids when it is administered in combination with controlled analgæsia of the patient (Tramèr 1999, Culebras 2003). Although its use has ben discontinued because of restrictions imposed by the Food and Drug Administration (FDA), it is currently returning to the market with an indication for the prevention of PONV, although the doses used to manage PONV are very low and these levels have not been found to be significantly associated with cardiovascular events (Gan 2002, White 2005, Charbit 2005). — Moderate quality

Haloperidol, which has antiemetic properties at low doses, is currently being investigated as an alternative to droperidol (Buttner 2004, Smith 2005). A meta-analysis with clinical trials, both published and unpublished, suggests that doses far lower than those used to treat psychiatric disturbances bring about an effective reduction of PONV (Smith 2005). Administering haloperidol at those doses carries the risk of extending the QT, which is why it is not recommended as a first-line drug. It can only be considered as an alternative to droperidol if the electrocardiogram is monitored during the six hours following its administration.

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4.7.2.3.4. Antihistamines (dimenhydrinate)

Dimenhydrinate has antiemetic effects. Data from controlled clinical trials with a placebo suggest that its degree of effectiveness as an antiemetic may be similar to that of serotonin receptor antagonists dexamethasone or droperidol (Kranke 2002). — Low quality

4.7.2.3.5. Anticholinergic agents (scopolamine)

A systematic review of transdermal scopolamine showed that it is useful when administered in combination with other antiemetic drugs (Kranke 2002). The adverse effects associated with trandermal patches are moderate (Kranke 2002). — Low quality

4.7.2.3.6. Phenothiazines (promethazine and prochlorperazine)

In two randomised clinical trials, promethaxzine and prochlorperazine showed certain antiemetic effects (Chen 1998, Khalil 1999). Given the scarceness of data, the evidence is not as robust as for other antiemetic drugs. More research is warranted before these drugs can be catalogued as first-line medications. — Low quality

4.7.2.3.7. Phenylethylamine (ephedrine)

Some data suggest that ephedrine may have an antiemetic effect (Rothenberg 1991, Hagemann 2000). — Low quality

4.7.2.3.8. Others

Metoclopramide (at standard clinical doses) ginger root, or cannabiniods (nabione, tetraydracannabinol) did not show effectiveness in preventing PONV (Henzi 1999, Ernst 2000, Morin 2004, Tramèr 2001, Lewis 1994). — Low quality

4.7.2.3.9. New therapies

Preliminary data show promising results for new therapies in preventing PONV, opioid antagonists (naloxone, nalmefene, alvimopan), and neurokinin 1 receptor antagonist (aprepitant). — Very low quality

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4.7.2.3.10. Others

Combination therapy is more effective than monotherapy in preventing PONV (Habib 2001, Eberhart 2000). — Moderate quality

Systematic reviews aimed at specific combinations have shown that the combination of serotonin receptor antagonists and dexamethasone or droperidol is more effective than monotherapy using any of these drugs (Apfel 2004, Henzi 2000, Eberhart 2000, Habib 2004, Eberhart 2000).

Droperidol combined with dexamethasone is more effective than either of these drugs on its own (Apfel 2004).

When the various combinations were compared, no differences were found between "serotonin receptor antagonists plus droperidol", "serotonin receptor antagonists plus dexamethasone" or "droperidol plus dexamethasone" (Apfel 2004, Habib 2004).

Combinations with metaclopramide have not shown a greater reduction in PONV than when compared with monotherapy (Habib 2001, Eberhart 2000, Maddali 2003).

Summary of the evidence

Low quality	Estimating the individual risk of presenting with PONV shows which patients may benefit from prophylaxis using antiemetic drugs. Risk factors that are linked to the patient (female sex, non-smoker, and a history of PONV or motion sickness) (Apfel 1999, Cohen 1994, Koivuranta 1997, Sinclair 1999, Stadler 2003, Roberts 2005, Choi 2005), anæsthesia (using a volatile anæsthetic, using nitrous oxide, or using opioid during or after surgery) (Apfel 1999, Stadler 2003, Roberts 2005, Choi 2005, Apfel 2002, Khalil 2005, Møiniche 2003, Polati 1997, Tramèr 1999, Sukhani 2002), or with the duration and type of surgery (Sinclair 1999, Stadler 2003, Choi 2005) have been identified.
Low quality	Defining risk factors contributes to identifying strategies for reducing the risk of PONV. Some of these strategies include favouring regional anæsthesia over general anæsthesia, using propofol in inducing and maintaining anæsthesia, avoiding nitrous oxide and volatile anæsthetics, minimising the use of opioids and of neostigmine, and carrying out over-hydration (15-25 ml/kg of crystalloids) (Apfel 1999, Roberts 2005, Apfel 2002, Møiniche 2003, Polati 1997, Sukhani 2002, Apfel 2004, Tramèr 1997, Sinclair 1999, Khalil 2005).
High quality	Antiemetic drugs recommended for PONV prophylaxis are serotonin receptor antagonists (Kranke 2002), steroids (Henzi 2000, Wang 2000, Apfel 2004), or butyrophenones (Tramèr 2001, Apfel 2004).
Moderate quality	Phenothiazines, phenylehthylamine, antihistamines, and anticholinergic agents, although in lesser measure, also showed an effect in preventing PONV (Chen 1998, Khalil 1999, Kranke 2002).
Moderate quality	Combination therapies have shown effectiveness greater than that of monotherapy in preventing PONV (Habib 2001, Eberhart 2000).

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Recommendations

Strong	Identify risk factors associated with PONV in each patient who is due to undergo surgery.
Strong	Prophylaxis using antiemetics should be considered in patients with a moderate to high risk of presenting with PONV.
Weak	If patients are allowed to choose on anæsthesia, they must be advised that the risk of PONV decreases with the use of regional rather than general anæsthesia.
Weak	Regional anæsthesia should be considered in patients with high risk of presenting PONV. If general anæsthesia is used, risk factors should be reduced whenever possible.
Weak	The use of opioids should be minimised in interventions. Professionals should evaluate the balance between risks and benefits of administering opioids in relation to the risk of PONV.
Strong	The prevention of PONV through the administration of dexamethasone, ondansetron, or droperidol should be taken into consideration.
Weak	Patients with high risk of presenting with PONV should receive combination therapy for preventing PONV.

4.7.3. Implications of the WHO checklist

In 2007, the WHO, through the World Alliance for Patient Safety, set the Second Global Challenge for patient safety with the slogan "Safe Surgery Saves Lives" (WHO 2008). This programme is aimed at improving surgical safety and reducing complications and mortality associated with surgery around the world based on four strategies: i) offering information to health-care professionals and managers on the importance of the culture of safety in the field of surgery, ii) defining unitary measures to build a minimum register of data that would allow monitoring of surgical care, iii) identifying basic actions to improve surgical safety and implement them worldwide, and iv) evaluating those strategies so that they can be disseminated and implemented them in hospitals around the world.

The main outcome of this initiative is the "Surgical Safety Checklist", which, based on 19 items, puts forward oral verification by surgical staff of a series of safe practices at three critical moments of peri-operative care: i) before administering anæsthetic, ii) before the skin incision, and iii) before the patient leaves the operating theatre (**Appendix 2**).

Till now, only one observational study that pilot-tested the "Surgical Safety Checklist" in operating rooms in eight hospitals in various parts of the world has been published. It showed a significant reduction in surgical complications and mortality (Haynes 2009).

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The study was designed with pre- and post-controls, and it included 3733 adult patients who underwent non-cardiac surgery before the implementation of the "Surgical Safety Checklist", and 3955 patients with similar characteristics after implementation, with a 30-day monitoring period. The main variable was the appearance of any surgical complication, including mortality (based on a classification by the American College of Surgeons). A variable that looked at compliance with basic safety measures by surgical staff was also evaluated. The results were analysed by logistic regression analysis, and initial results were checked in order to rule out the influence of variables such as geography or type of patient.

Low quality

The rate of complications fell by one-third (from 11% before implementation of the checklist in operating rooms to 7% after the checklist was used; P<0.001). Similarly, mortality fell from 1.5 to 0.8% after the tool was used (P=0.003). These results were also observed in infections of the surgical wound, which fell by half (6.2% *vs* 3.4%; P<0.001) or the need for unscheduled surgical re-intervention (2.4 *vs* 1.8; P=0.047). Compliance with safety measures also increased considerably (from 34 to 56%; P<0.001).

The mechanisms to which these results can be attributed, as well as the challenges related to the changes needed in the health system and in the behaviour of surgical staff are still unknown. However, the results of implementing the "Surgical Safety Checklist" are truly important, and some health systems, such as the one in the United Kingdow, have already initiated the immediate implementation of this strategy (Patient Safety Alerts 2009). The Public Health System in Andalusia has also incorporated this list into the framework of the Agreement on Safe Practices signed by the Ministry of Health and Consumption ("BOE (*Boletín Oficial del Estado* – Government Gazette, Spain) 22 December 2008).

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Summary of the evidence

Low quality	Using the "Surgical Safety Checklist", based on oral checks of a series of points in surgical interventions that are started before the administration of anæsthetia, significantly reduces complications and mortality associated with surgery (WHO 2008, Haynes 2009).

Recommendations

Strong	The "Surgical Safety Checklist" must be implemented in all surgical procedures to improve the safety of surgical interventions and to reduce avoidable complications.

5. Diffusion and implementation

The GPC comes in two versions: the full version, and the short version. Both versions are available in HTML format and in PDF format on the web page of GuíaSalud (www.guiasalud.es). The short version is in paper format, and contains the CD-ROM with the full version.

Strategies for diffusing and implementing this GPC include:

- Official presentation of the guide by the health authorities
- Individualised despatch of copies to professionals and potential users
- Diffusing the guide in electronic format on the web pages of the health services, and the companies involved with the project
- Presenting the guide in scientific activities (open days, conferences, meetings).
- Publishing the guide in medical journals.

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Appendices

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Appendix 1. Table classifying the quality of evidence and graduating the strength of the recommendation

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Classifying the quality of the evidence using the GRADE system

Quality of scientific evidence	Design of the study	Reduce quality if	Increase quality if
High	RCT	Limitation to the design: Significant (-1) Very significant (-2)	Association: Scientific evidence of a strong association (RR>2 or <0.5 based on observational studies with no confusing factors) (+1).
Moderate		Inconsistency (-1)	
Low	Observational studies	Direct evidence: Some (-1) uncertainty Great (-2) uncertainty as to whether the evidence is direct	Scientific evidence of very strong association Association (RR>5 o <0.2 based on studies without possibility of bias)(+2)
Very low	Other types of design	Imprecise data (-1) Notification bias: high probability of (-1)	Dose-response curve (+1) All possible confounding factors may have reduced the observed effect

Implications of the degrees of recommendation in the GRADE system

Implications of a strong recommendation:		
Patients	**Clinical**	**Managers/Planners**
The vast majority of persons would agree with the recommended action, and only a small proportion would not agree.	The majority of patients should receive the recommended intervention.	The recommendation can be adopted as health policy in the majority of situations.
Implications of a weak recommendation:		
Patients	**Clinical**	**Managers/Planners**
The majority of persons would agree with the recommended action, but with a significant number in disagreement.	Recognises that different options would be appropriate for different patients, and the physician should help each patient to reach the decision that is most consistent with the patient's values and preferences.	There is a need for significant debate and the participation of interest groups.

Appendix 2. World Health Organisation Surgical Safety Checklist

<table>
<tr><th>ENTRY
Before induciton of anæsthesia</th><th>PAUSE
Before skin incision</th><th>EXIT
Before the patient leaves the operating room</th></tr>
<tr><td>The patient has confirmed
– her / his identity
– site of surgery
– Procedure
– Informed consent</td><td>Confirm that each membner of the team has introduced herself / himslef by name and function

Surgeon, anæsthesiologist, and nurse to confirm verbally:
– the patient's identity
– site of surgery
– procedure</td><td rowspan="6">Nurse confirms verbally with the rest of the team

– Name of procedure carried out
– If applicable, an inventory of gases, needles, and other instruments
– Identifying biological samples (including the patient's name) and their handling
– If there is any problem with the material that needs to be solved

Surgeon, anæsthesiologist, and nurse review and record in the clinical history the most relevant aspects relating to the patient's recovery and care</td></tr>
<tr><td>Mark the site on the body / Not applicable</td><td rowspan="3">Foreseeing critical events:
– Surgeon reviews:
– unforeseen or critical steps
duration of the intervention
– expected loss of blood
– Anæsthesiologist checks if the patient presents any situation that arouses suspcion

– Nurse evaluates:
– Sterility has been checked (with results from the indicators)
– If there are any doubts or problems concerning the instrumentaiton or the equipment</td></tr>
<tr><td>Anæsthesia safety check</td></tr>
<tr><td>Is the pulse oximeter on the patient and functioning</td></tr>
<tr><td rowspan="3">Does the patient have any known allergies?
No
Yes

Difficulties in the airway / risk of aspirtation?
No
Yes, and the necessary equipment and assitance are available

Risk of bloiod loss >500 ml/7 ml/kg in children?
No
Yes, and an adequate access way and the necessary fluids are available</td></tr>
<tr><td>Hass antibiotic prophylaxis been administered in the last 60 minutes?
Yes
Not applicable</td></tr>
<tr><td>Can essential diagnostic images be seen?
Yes
Not applicable</td></tr>
</table>

Adapted from: www.who.int/patientsafety/safesurgery/tools_resources/sssl_checklist_spanish.pdf
www.juntadeandalucia.es/agenciadecalidadsanitaria/observatorioseguridadpaciente/gestor/sites/PortalObservatorio/es/galerias/descargas/cirugia/listado_verificacion_seguridad_quirurgica_090522.pdf

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Appendix 3. Glossary

Alfa-2 agonist: Andrenergic agonist that inhibits the activity of the enzyme andenylyl cyclase, and reduces the activation of the sympathetic nervous system. Used as an antihypertensive.

Anæsthesia: Absence of normal sensations, especially the ability to feel pain, as induced by means of an anæsthetic substance or through hypnosis, or resulting from wounds to nerve tissue. Induced anæsthesia for medical and surgical purposes can be topical, local, regional, or general, and is classified on the basis of the anæsthetic agent used, the method or procedure followed, and the area or organ anæsthetised.

Calcium antagonist: Organic compound that blocks calcium ion current, used in the treatment of hypertension.

Anticoagulant: Drug administered to prevent the formation of blood clots. Some are administered orally, e.g. warfarin, whilst others can be injected, e.g. heparin.

Beta-blocker: Beta-andrenergic blocking agent used in treating disruptions to the cardiac rhythm and in cardioprotection after a myocardial infarction.

Best clinical practice (BPC): Recommendation based on clinical experience, in the absence of solid clinical proof.

Contaminated surgery: Surgical wound that meets the following requirements: i) failure in sterile technique or outpouring of gastrointestinal liquid, ii) signs of acute non-purulent inflammation, iii) open traumatic wound about 12 to 24 hours old.

Clean surgery: Surgical wound without inflammation, with no interruption of sterile technique, and into which the respiratory, digestive, or genito-urinary tracts do not penetrate.

Clean-contaminated surgery: Surgical wound with penetration by the respiratory, digestive, or genito-urinary tract under controlled conditions and with no contamination.

Dirty surgery: surgical wound that meets the following requirements: i) wound in an intervention involving perforated viscera; ii) during the intervention, signs are found of acute inflammation with pus, iii) traumatic wound in which treatment is delayed, with fæcal contamination or devitalised tissue.

Co-morbidity: Co-existence of more than one illness, or presence of an illness in addition to the one that is being treated in a patient.

Autologous blood donation: Donation in which the patient acts as her/his own donor, which is the least risky form of blood donation.

Pulmonary embolism: Blood clot that that comes away from the veins and moves towards the pulmonary arteries. Most deaths through thrombo-embolism are due to pulmonary embolism.

Randomised clinical trial (RCT): Experimental study in which participants are assigned randomly to intervention and control groups, with monitoring to examine differences in results between the groups.

Erythropoietin: Glycoprotein hormone that stimulates the formation of erythrocytes.

Statin: IHMG-CoA reductase inhibitors with hypolipemniant action used to reduce cholesterol.

Cohort study: Observational study based on retrospective or prospective monitoring. The group of persons that is monitored is defined on the basis of the presence or absence of exposure to a presumed risk factor or of the intervention. A cohort study can be compared, in which case two or more groups are chosen on the basis of differences in their exposure to the agent of interest.

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Adverse event: Unforeseen or unexpected accident that causes wounding and/or incapacity and/or an extension of hospital stay and/or death, derived from healthcare and not from the basal illness of the patient.

Avoidable adverse event: Event that would not have occurred if there had been compliance with appropriate standards of daily routine care.

Auricular fibrillation: Cardiac arrhythmia, in which the auricles or upper chambers of the heart beat in an uncoordinated and disorganised fashion, producing a rapid and irregular cardiac rhythm.

Degree of recommendation: Every recommendation must be given a degree of confidence (strong or weak) according to which there is an expectation of obtaining more benefits than drawbacks through its application. It is based on the quality of the evidence of the tests on which the recommendation is based, the balance between risks and benefits, the patient's values and preferences, and costs.

Guide development group: Multidisciplinary group of professionals that selects the clinical questions of the guide, reads the evidence critically, and develops recommendations.

Heparin: Enzyme produced mainly in the liver and lungs and that prevents the development of blood clots. Two types of heparin are used as anticoagulant treatment: low-molecular-weight heparins and unfractionated heparins.

Infection: Colonisation of a host organism by external microorganisms that cause disease.

Immunomodulation: Change in the body's immune system caused by substances that activate or that weaken its function.

Confidence interval (CI): A range of values calculated on the basis of a population sample, that contains the real value of the population with predetermined precision or "confidence" (conventionally 95%). 95% confidence means that if the study and the method used to calculate the interval of time were replicated independently, in 95% of the cases, its estimates will contain the true value for the whole population.

Methodological limitations: Design or presentation featires of a clinical study that are known to be associated with a risk of bias or lack of validity.

Meta-analysis: Statistical technique in the context of a systematic review of the literature that combines the results of a series of studies that deal with the same question, and that show results of interest. The aim is to obtain information that is clearer and more precise from a set of independent data.

Quality of the evidence: The degree of confidence (high, moderate, low, or very low) that the result of a study or of a set of studies represents the "real" value of the intervention(s) evaluated for a research question.

Peri-operative: Period that runs from admission to hospital to undergo surgery until the patient is discharged. Pre-operative refers to the period before surgery, intra-operative refers to the period during surgery, and post-operative refers to the period starting with the patient's departure from the operating room.

Prophylaxis: Measure or procedure established to prevent an illness or complication.

Antibiotic prophylaxis: Preventing infectious complications using antimicrobial therapy (normally: antibiotics).

Vertical mattress stitch: Continuous suture in which each stitch crosses the wound perpendicularly, in the opposite direction to the previous stitch.

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Odds ratio (OR): A measure of the effectiveness of treatment. It expresses the probability of an event in the treatment group, in comparison with or in relation to the probability of an event in the control group.

Cochrane review: A systematic review of scientific literature on the effect of interventions in health or in healthcare, produced by the Cochrane Collaboration.

Systematic review: The research that summarises the tests on a question, clearly formulated, using systematic, explicit methods to identify, choose, and evaluate pertinent studies and to extract, compile, and inform on its conclusions.

Relative risk (RR): A measure of association that shows the effectiveness of a treatment. It is a ratio between the risk in the group exposed to an intervention and the risk in the comparison group.

Surgical clothing: Health products for single or multiple use. Fundamentally, it refers to: surgical gowns and cloths, and suits for clean atmospheres, used in surgery. Standard EN 13795 has standardised the following terms relating to surgical clothing: i) **clean suit**: to reduce to a minimum contamination of the surgical wound, caused by microorganisms from the suit wearer that may be in suspension in the air of the operating room; ii) **single-use product**: for use only in one surgical procedure before being disposed of; iii) **reusable product**: to be reused after disinfection and/or sterilisation; iv) **surgical gown**: long item of clothing with sleeves and tied closed, worn by a member of the surgical team to prevent the transfer of infectious agents, v) **surgical cloth**: a piece of material that covers the patient or the surgical team to prevent the spread of infectious agents, and vi) **critical area**: area of surgical clothing with the greatest probability of exposure and transfer of infectious agents.

Continuous suture: A first stitch is inserted, but the ends remain uncut, so that the thread is inserted continuously along the length of the incision.

Discontinuous suture: Closing the edges of the laceration by inserting simple stitches that are knotted separately.

Allogenic transfusion: Application of blood or blood components from one individual to another.

Venous thrombo-embolism: Formation of a clot in a deep vein (e.g. in the leg or pelvis) that can be asymptomatic, or that may be associated with symptoms (swelling or pain), and that may lead to complications if it moves, resulting in a pulmonary embolism.

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Appendix 4. Abbreviations

ACCP	American College of Chest Physicians
AF	Atrial fibrillation
AHRQ	Agency for Healthcare Research and Quality (USA)
ASA (1)	acetylsalicylic acid
ASA (2)	American Society of Anesthesiologists
BMI	body-mass index
cc	cubic centimetre(s)
CHADS	Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischæmic attack
CI	confidence interval
CPG	Clinical Practice Guideline
DM	mean difference
DMP	weighted mean difference
ENEAS	National Study of the Adverse Effects linked to Hospitalisation (*Estudio Nacional sobre los Efectos Adversos ligados a la Hospitalización*)
ev	endovenous
g / l	grams per litre
GRADE	Grading of Recommendations Assessment, Development and Evaluation
Hb	hæmoglobin
HIV	human immunodeficiency virus
HR	hazard ratio
IHC	immunohistochemistry
im	intramuscular
INR	International Normalised Ratio
iv	intravenous
LDL	low-density lipoproteins
LMWH	low-molecular-weight heparin
mg	milligrams
mg / dl	milligrams per decilitre
mg / k	milligrams per kilo
MI	myocardial infarction
ml.	millilitre
MRSA	methicillin-resistant *Staphylococcus aureus*
NHMRC	National Health and Medical Research Council (Australia)
NICE	National Institute for Health and Clinical Excellence (UK)
NNT	number needed to treat
OAC	oral anticoagulants
ºC	degrees Celsius
OR	odds ratio
PONV	peri-operative nausea and vomiting
RCT	randomised clinical trial
RR	relative risk
S. aureus	*Staphylococcus aureus*
SIGN	Scottish Intercollegiate Guidelines Network
SR	systematic review
SSI	surgical site infection
TIA	transient ischæmic attack
VTE	venous thrombo-embolism
WFSA	World Federation of Societies of Anæsthesiologists
WHO	World Health Organisation

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Appendix 5. Declaration of interest

The declaration of interest of the authors and revisors has been made using a predefined form included in the methodological manual of the SNS.

Authors:

All the signing authors are members of the GPC Working Group for the Safety of Surgical Patients and have declared an absence of conflicts of interest.

Revisors and expert collaborators:

José Luís Aguayo-Albasini, Jesús Aranaz Andrés, María José Castro Ruiz, Sergio Minué Lorenzo, Arturo Martí Carvajal, Joaquín Morís de la Tassa, Anna Oller Castells, Pedro Ruiz López, Sergi Sabaté Tenas, Vicente Santana López, and Antonio José Torres García have declared an absence of conflicts of interest.

Pere Vila Caral declares that he has received funds to attend meetings or conferences and to participate as a speaker of Schering-Plough. He also received support from Prostakan research for his research. Rosa María Muñoz Albarracín declares that she has received funds to attend meetings or conferences from Steris, as well as honoraria for being a speaker of 3M.

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Appendix 6. Main documents and useful resources

As was stated in the Methodology, during the development of the Guide to Clinical Practice, other high-quality GPCs were identified that covered the majority of the topics covered herein. Because of their rigour and clarity, some of those documents have been used to adapt recommendations in some sections. Given below is a list and the link to the full text of the main documents that, by reason of their quality or for being recent publications, may be an importance source of consultation for users of this guide.

Reference: American College of Cardiology/American Heart Association Task Force on Practice Guidelines. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Circulation. 2007;116(17): e418-99.
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