GLOBAL GUIDELINES FOR THE PREVENTION OF SURGICAL SITE INFECTION

World Health Organization

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ABBREVIATIONS AND ACRONYMS

ABHR	alcohol-based handrub
AMR	antimicrobial resistance
ASHP	American Society of Health-System Pharmacists
CDC	Centers for Disease Control and Prevention
CHG	chlorhexidine gluconate
CI	confidence interval
ECDC	European Centre for Disease Prevention and Control
ESBL	extended spectrum beta-lactamase
FiO2	fraction of inspired oxygen
GDFT	goal-directed fluid therapy
GDG	Guidelines Development Group
GRADE	Grading of Recommentations Assessment, Development and Evaluation
HAI	health care-associated infection
IDSA	Infectious Diseases Society of America
IPC	infection prevention and control
LMICs	low- and middle-income countries
MBP	mechanical bowel preparation
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-susceptible *Staphylococcus aureus*
MTX	methotrexate
NHSN	National Healthcare Safety Network
NICE	National Institute for Health and Care Excellence
NNIS	National Nosocomial Infections Surveillance System
OR	odds ratio
PAHO	Pan American Health Organization
PHMB	polyhexamethylene biguanide
PICO	Population, Intervention, Comparison, Outcomes
pNPWT	prophylactic negative pressure wound therapy
PVP-I	povidone-iodine
RCT	randomized clinical trial
SAP	surgical antibiotic prophylaxis
SHEA	Society of Healthcare Epidemiology of America
SIGN	Scottish Intercollegiate Guidelines Network
SREG	Systematic Reviews Expert Group
SSI	surgical site infection/s
THA	total hip arthroplasty
TKA	total knee arthroplasty
TNF	tumour necrosis factor
UK	United Kingdom
USA	United States of America
v/v	volume/volume
WHO	World Health Organization
WP	wound protectors

GLOSSARY OF TERMS

Alcohol-based handrub refers to an alcohol-based preparation designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Such preparations may contain one or more types of alcohol, other active ingredients with excipients and humectants.

Antimicrobial skin sealants refer to sterile, film-forming cyanoacrylate-based sealants that are commonly used as additional antimicrobial skin preparation after antisepsis and prior to skin incision. These sealants are intended to remain in place and block the migration of flora from surrounding skin into the surgical site by dissolving for several days postoperatively.

Grading of Recommendations Assessment, Development and Evaluation (GRADE) is an approach used to assess the quality of a body of evidence and to develop and report recommendations.

Health care-associated infection, also referred to as "nosocomial" or "hospital" infection, is an infection occurring in a patient during the process of care in a hospital or other health care facility, which was not present or incubating at the time of admission. Health care-associated infections can also appear after discharge. They represent the most frequent adverse event during care.

Hygienic handrub refers to the treatment of hands with an antiseptic handrub to reduce the transient flora without necessarily affecting the resident skin flora. These preparations are broad spectrum and fast-acting, and persistent activity is not necessary.

Hygienic handwash refers to the treatment of hands with an antiseptic handwash and water to reduce the transient flora without necessarily affecting the resident skin flora. It is broad spectrum, but it is usually less efficacious and acts more slowly than hygienic handrub.

Interactive (advanced) wound dressings refer to modern (post-1980) dressing materials that are designed to promote the wound healing process through the creation and maintenance of a local, warm, moist environment underneath the chosen dressing when left in place for a period indicated through a continuous assessment process. Examples are alginates, semipermeable film membranes, foams, hydrocolloids and fibrous hydrocolloids, non-adherent wound contact materials and combinations of those.

Iodophors refer to a preparation containing iodine complexed with a solubilizing agent, such as a surfactant or povidone (forming povidone-iodine). The result is a water-soluble material that releases free iodine when in solution. Iodophors are prepared by mixing iodine with the solubilizing agent; heat can be used to speed up the reaction.

Low- and middle-income countries: WHO Member States are grouped into four income groups (low, lower-middle, upper-middle, and high) based on the World Bank list of analytical income classification of economies for the 2014 fiscal year, calculated using the *World Bank Atlas* method. For the current (2016) fiscal year, low-income economies are defined as those with a gross national income (GNI) per capita of US$ 1045 or less in 2014; middle-income economies are those with a GNI per capita of more than US$ 1045, but less than US$ 12 736; (lower-middle-income and upper-middle-income economies are separated at a GNI per capita of US$ 4125) high-income economies are those with a GNI per capita of US$ 12 736 or more.

Mechanical bowel preparation refers to the

preoperative administration of substances to induce voiding of the intestinal and colonic contents.

Paediatric population: infants, children, and adolescents, within an age limit usually ranging from birth up to 18 years of age.

Point prevalence (survey) refers to the proportion of individuals with a particular disease or attribute measured on a particular date.
Note: Prevalence differs from incidence in that prevalence includes all cases, both new and preexisting, in the population at the specified time, whereas incidence is limited to new cases only.

Primary closure is defined as closure of the skin level during the original surgery, regardless of the presence of wires, wicks, drains, or other devices or objects extruding through the incision. This category includes surgeries where the skin is closed by some means. Thus, if any portion of the incision is closed at the skin level, by any manner, a designation of primary closure should be assigned to the surgery.

Resident flora refers to microorganisms residing under the superficial cells of the *stratum corneum* and found also on the surface of the skin.

Standard antibiotic prophylaxis refers to the prevention of infectious complications by administering an effective antimicrobial agent prior to exposure to contamination during surgery.

Surgical hand preparation refers to an antiseptic handwash or antiseptic handrub performed preoperatively by the surgical team to eliminate transient flora and reduce resident skin flora. Such antiseptics often have persistent antimicrobial activity.

Surgical handrub(bing) refers to surgical hand preparation with a waterless alcohol-based handrub.

Surgical handscrub(bing)/presurgical scrub refers to surgical hand preparation with antimicrobial soap and water.

Surgical procedure refers to an operation where at least one incision (including a laparoscopic approach) is made through the skin or mucous membrane, or reoperation via an incision that was left open during a prior operative procedure AND takes place in an operating room.

Surgical site infection refers to an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only. Other surgical site infections are more serious and can involve tissues under the skin, organs, or implanted material.
(Source: United States Centers for Disease Control and Prevention. https://www.cdc.gov/HAI/ssi/ssi.html, accessed 11 July 2016.).

Surgical site infection is also defined as an infection that occurs within 30 days after the operation and involves the skin and subcutaneous tissue of the incision (superficial incisional) and/or the deep soft tissue (for example, fascia, muscle) of the incision (deep incisional) and/or any part of the anatomy (for example, organs and spaces) other than the incision that was opened or manipulated during an operation (organ/space).
(Source: European Centre for Disease Prevention and Control. http://ecdc.europa.eu/en/publications/Publications/120215_TED_SSI_protocol.pdf, accessed 16 August 2016).

SSI-attributable mortality refers to deaths that are directly attributable to SSI. The numerators refer to surgical patients whose cause of death was directly attributable to SSI and the denominator usually refers to all surgical patients in a patient population.

Surgical site infection rates per 100 operative procedures are calculated by dividing the number of surgical site infections by the number of specific operative procedures and multiplying the results by 100. Surgical site infection rate calculations can be performed separately for the different types of operative procedures and stratified by the basic risk index.

Surgical instruments are tools or devices that perform such functions as cutting, dissecting, grasping, holding, retracting, or suturing the surgical site. Most surgical instruments are made from stainless steel.

Surgical wound refers to a wound created when an incision is made with a scalpel or other sharp cutting device and then closed in the operating room by suture, staple, adhesive tape, or glue and resulting in close approximation to the skin edges.

Transient flora refers to microorganisms that colonize the superficial layers of the skin and are more amenable to removal by routine handwashing/handrubbing.

Underweight is a term describing a person whose body weight is considered too low to be healthy. The definition usually refers to people with a body mass index of under 18.5 or a weight 15-20% below the norm for their age and height group.

Surgical wounds are divided into four classes.

1. **Clean** refers to an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating (blunt) trauma should be included in this category if they meet the criteria.

2. **Clean-contaminated** refers to operative wounds in which the respiratory, alimentary, genital or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.

3. **Contaminated** refers to open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (for example, open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered ,including necrotic tissue without evidence of purulent drainage (for example, dry gangrene), are included in this category.

4. **Dirty or infected** includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.
(Source: United States Centers for Disease Control and Prevention. https://www.cdc.gov/hicpac/SSI/table7-8-9-10-SSI.html, accessed 11 July 2016.)

DECLARATION OF INTERESTS

In accordance with WHO regulations, all members of the Guidelines Development Group (GDG) were required to complete and submit a WHO Declaration of interests form prior to participating in each meeting. External reviewers and members of the Systematic Reviews Expert Group were also required to submit a Declaration of interest form. The secretariat then reviewed and assessed each declaration. In the case of a potential conflict of interest, the reason was presented to the GDG.

Procedures for the management of declared conflicts of interest were undertaken according to the WHO *guidelines for declaration of interests (WHO experts).* Where a conflict of interest was not considered significant enough to pose any risk to the guideline development process or reduce its credibility, the experts were only required to openly declare the potential conflict at the beginning of the Technical Consultation. However, the declared conflicts were considered irrelevant on all occasions and did not warrant any exclusion from the GDG. Therefore, all members participated fully in the formulation of the recommendations and no further action was taken.

The following interests were declared by GDG members:
Joseph Solomkin, chair of the GDG, is also the chief executive officer of OASIS Global (USA), an organization that provided funds to partially support the salary of a WHO consultant assisting in initiating the guideline development process.

Andreas Widmer declared that he received a research support grant of 200 000 Swiss francs from the Swiss National Science Foundation for a study on antibiotic prophylaxis in 2014.

Peter Nthumba declared that his attendance at a workshop on surgical site infections in 2014 was supported by Ethicon Surgical Care (Johnson & Johnson).

Marja A Boermeester declared that her attendance at a meeting was supported by Johnson & Johnson in 2014 and that she obtained a research grant of € 49 000 from Johnson & Johnson on a subject not related to these guideline recommendations. She also received grants or honoraria for delivering lectures on surgical site infection or serving on scientific advisory boards for Abbott/Mylan, Acelity, Bard, Baxter, GSK, Ipsen and Johnson & Johnson.

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Xavier Guirao declared that he received personal fees of about € 1000 from Merck, Pfizer, Astra-Zeneca, and Novartis; these activities were not related to the guideline recommendations.

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Val Robertson declared that she received a research grant of US$ 3500 from the International Federation of Infection Control in 2015 and that she currently receives a monthly honorarium of US$ 2241 as a technical advisor to the Zimbabwe Infection Prevention and Control Project.

EXECUTIVE SUMMARY

Introduction

Health care-associated infections (HAI) are acquired by patients while receiving care and represent the most frequent adverse event affecting patient safety worldwide.

Recent work by the World Health Organization (WHO) shows that surgical site infection (SSI) is the most surveyed and frequent type of HAI in low- and middle-income countries and affects up to one third of patients who have undergone a surgical procedure. Although SSI incidence is lower in high-income countries, it remains the second most frequent type of HAI in Europe and the United States of America (USA).

Many factors in the patient's journey through surgery have been identified as contributing to the risk of SSI. Therefore, the prevention of these infections is complex and requires the integration of a range of preventive measures before, during and after surgery. However, the implementation of these measures is not standardized worldwide. No international guidelines are currently available and inconsistency in the interpretation of evidence and recommendations among national guidelines is frequently identified.

The aim of these guidelines is to provide a comprehensive range of evidence-based recommendations for interventions to be applied during the pre-, intra- and postoperative periods for the prevention of SSI, while also considering aspects related to resource availability and values and preferences.

Although the guidelines are intended for surgical patients of all ages, some recommendations do not apply to the paediatric population due to lack of evidence or inapplicability and this is clearly stated.

Target audience

The primary target audience for these guidelines is the surgical team, that is, surgeons, nurses, technical support staff, anaesthetists and any professionals directly providing surgical care. Pharmacists and sterilization unit staff will also be concerned by some aspects of these guidelines. The recommendations are also intended to be used by policy-makers, senior managers and infection prevention and control (IPC) professionals as the basis for developing national and local SSI protocols and policies, and supporting staff education and training.

Guideline development methods

The guidelines were developed according to the processes described in the WHO *Handbook for guideline development* issued in 2014. In summary, the process included:
(1) identification of the primary critical outcomes and priority topics and formulation of a series of questions structured in a PICO (Population, Intervention, Comparison, Outcomes) format;
(2) retrieval of the evidence through specific systematic reviews of each topic using a standardized agreed methodology;
(3) assessment and synthesis of the evidence;
(4) formulation of recommendations; and
(5) writing of the guideline content and planning for its dissemination and associated implementation strategy.

The development of the guidelines involved the formation of four main groups to guide the process: the WHO Guideline Steering Group; the Guidelines Development Group (GDG); the Systematic Reviews Expert Group; and the External Review Group.

Using the list of priority topics, questions and critical outcomes identified by the WHO Guideline

Steering Group, the GDG and the guideline methodologist in a scoping meeting convened by WHO in September 2013, the Systematic Reviews Expert Group conducted 27 systematic reviews to provide the supporting evidence for the development of the recommendations; summaries of the systematic reviews are available as web appendices of the guidelines. The scientific evidence was synthesized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. WHO convened four GDG technical consultations between June 2014 and November 2015 to formulate and approve the recommendations based on the evidence profiles. In agreement with the methodologist and the WHO Guidelines Review Committee secretariat, five recommendations were re-discussed through GDG on-line consultations after the meetings and slightly modified, based on either comments by the external peer reviewers or emerging new evidence.

The guidelines consist of a core section including a dedicated chapter for each recommendation, which is divided into subsections according to their application in the pre-, intra- and postoperative periods. This is preceded by a section including other important issues in the approach to SSI prevention that were not the subject of recommendations, but of which users should be fully aware. A summary of main existing national guidelines on SSI prevention is also provided as a web appendix of the guidelines.

Recommendations

The WHO technical consultations led to the adoption of 29 recommendations covering 23 topics for the prevention of SSI in the pre-, intra- and postoperative periods (see Table). For four topics, the GDG considered that the available evidence was not sufficient to develop related recommendations. For each recommendation, the quality of evidence was graded as “very low”, “low”, “moderate” or “high”. The GDG qualified the direction and strength of each recommendation by considering the quality of evidence and other factors, including the balance between benefits and harms, the values and preferences of stakeholders and the resource implications of the intervention. To ensure that each recommendation is correctly understood and applied in practice, the GDG has provided additional remarks where needed. Guideline users should refer to these remarks, as well as to the summary of the evidence provided in each chapter of the recommendations. The summaries of the systematic reviews, including the risk of bias assessments and the GRADE tables, are available in full as on-line appendices of the guidelines. Each chapter also features a research agenda identified by the GDG for each topic.

The recommendations for the prevention of SSI to be applied or considered in the pre-, intra- and postoperative periods are summarized in the Table below, together with the associated PICO questions and their strength and evidence quality. In accordance with WHO guideline development procedures, these recommendations will be reviewed and updated following identification of new evidence at least every five years. WHO welcomes suggestions regarding additional questions for inclusion in future updates of the guidelines.

Table 1. **Summary of core topics, research questions and recommendations for the prevention of surgical site infection**

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Preoperative bathing	1. Is preoperative bathing using an antimicrobial soap more effective in reducing the incidence of SSI in surgical patients compared to bathing with plain soap? 2. Is preoperative bathing with CHG-impregnated cloths more effective in reducing the incidence of SSI in surgical patients compared to bathing with antimicrobial soap?	It is good clinical practice for patients to bathe or shower prior to surgery. The panel suggests that either plain soap or an antimicrobial soap may be used for this purpose. The panel decided not to formulate a recommendation on the use of CHG-impregnated cloths for the purpose of reducing SSI due to the very low quality of evidence.	Conditional	Moderate
Decolonization with mupirocin ointment with or without CHG body wash for the prevention of *Staphylococcus aureus* infection in nasal carriers	Is mupirocin nasal ointment in combination with or without CHG body wash effective in reducing the number of *S. aureus* infections in nasal carriers undergoing surgery?	The panel recommends that patients undergoing cardiothoracic and orthopaedic surgery with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. The panel suggests considering to treat also patients with known nasal carriage of *S. aureus* undergoing other types of surgery with perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash.	Strong Conditional	Moderate Moderate
Screening of ESBL colonization and the impact on antibiotic prophylaxis	1. Should SAP be modified in high (>10%) ESBL prevalence areas? 2. Should SAP be modified in patients who are colonized with or a carrier of ESBL? 3. Should patients be screened for ESBL prior to surgery?	The panel decided not to formulate a recommendation due to the lack of evidence.	NA	NA

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Optimal timing for preoperative SAP	How does the timing of SAP administration impact on the risk of SSI and what is the precise optimal timing?	The panel recommends that SAP should be administered prior to the surgical incision when indicated (depending on the type of operation). The panel recommends the administration of SAP within 120 minutes before incision, while considering the half-life of the antibiotic.	Strong Strong	Low Moderate
Mechanical bowel preparation and the use of oral antibiotics	Is mechanical bowel preparation combined with or without oral antibiotics effective for the prevention of SSI in colorectal surgery?	The panel suggests that preoperative oral antibiotics combined with mechanical bowel preparation should be used to reduce the risk of SSI in adult patients undergoing elective colorectal surgery. The panel recommends that mechanical bowel preparation alone (without administration of oral antibiotics) should **not** be used for the purpose of reducing SSI in adult patients undergoing elective colorectal surgery.	Conditional Strong	Moderate Moderate
Hair removal	1. Does hair removal affect the incidence of SSI? 2. What method and timing of hair removal is associated with the reduction of SSI?	The panel recommends that in patients undergoing any surgical procedure, hair should either **not** be removed or, if absolutely necessary, it should be removed only with a clipper. Shaving is strongly discouraged at all times, whether preoperatively or in the OR.	Strong	Moderate
Surgical site preparation	Should alcohol-based antiseptic solutions or aqueous solutions be used for skin preparation in surgical patients and, more specifically, should CHG or PVP-I solutions be used?	The panel recommends alcohol-based antiseptic solutions based on CHG for surgical site skin preparation in patients undergoing surgical procedures.	Strong	Low to moderate

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Antimicrobial skin sealants	Should antimicrobial sealants (in addition to standard surgical site skin preparation) be used in surgical patients for the prevention of SSI compared to standard surgical site skin preparation only?	The panel suggests that antimicrobial sealants should **not** be used after surgical site skin preparation for the purpose of reducing SSI.	Conditional	Very Low
Surgical hand preparation	1. What is the most effective type of product for surgical hand preparation to prevent SSI? 2. What is the most effective technique and ideal duration for surgical hand preparation?	The panel recommends that surgical hand preparation should be performed by scrubbing with either a suitable antimicrobial soap and water or usng a suitable alcohol-based handrub before donning sterile gloves.	Strong	Moderate
Preoperative and/or intraoperative measures				
Enhanced nutritional support	In surgical patients, should enhanced nutritional support be used for the prevention of SSI?	The panel suggests considering the administration of oral or enteral multiple nutrient-enhanced nutritional formulas for the purpose of preventing SSI in underweight patients who undergo major surgical operations.	Conditional	Very Low
Perioperative discontinuation of immunosuppressive agents	Should immunosuppressive agents be discontinued perioperatively and does this affect the incidence of SSI?	The panel suggests not to discontinue immunosuppressive medication prior to surgery for the purpose of preventing SSI.	Conditional	Very Low
Perioperative oxygenation	How safe and effective is the perioperative use of an increased fraction of inspired oxygen in reducing the risk of SSI?	The panel recommends that adult patients undergoing general anaesthesia with endotracheal intubation for surgical procedures should receive an 80% fraction of inspired oxygen intraoperatively and, if feasible, in the immediate postoperative period for 2-6 hours to reduce the risk of SSI.	Strong	Moderate

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Maintaining normal body temperature (normothermia)	Should systemic body warming vs. no warming be used for the prevention of SSI in surgical patients?	The panel suggests the use of warming devices in the OR and during the surgical procedure for patient body warming with the purpose of reducing SSI.	Conditional	Moderate
Use of protocols for intensive perioperative blood glucose control	1. Do protocols aiming to maintain optimal perioperative blood glucose levels reduce the risk of SSI? 2. What are the optimal perioperative glucose target levels in diabetic and non-diabetic patients?	The panel suggests the use of protocols for intensive perioperative blood glucose control for both diabetic and non-diabetic adult patients undergoing surgical procedures to reduce the risk of SSI. The panel decided not to formulate a recommendation on this topic due to the lack of evidence to answer question 2.	Conditional	Low
Maintenance of adequate circulating volume control/ normovolemia	Does the use of specific fluid management strategies during surgery affect the incidence of SSI?	The panel suggests the use of goal-directed fluid therapy intraoperatively to reduce the risk of SSI.	Conditional	Low
Drapes and gowns	1. Is there a difference in SSI rates depending on the use of disposable non-woven drapes and gowns or reusable woven drapes and gowns? 1.1. Is there a difference in SSI rates depending on the use of disposable non-woven or reusable woven drapes? 1.2. Is there a difference in SSI rates depending on the use of disposable non-woven or reusable woven gowns?	The panel suggests that either sterile, disposable non-woven or sterile, reusable woven drapes and gowns can be used during surgical operations for the purpose of preventing SSI. No specific evidence was retrieved to answer to questions 1.1 and 1.2.	Conditional	Moderate to very low
	2. Does the use of disposable, adhesive, incise drapes reduce the risk of SSI?	The panel suggests **not** to use plastic adhesive incise drapes with or without antimicrobial properties for the purpose of preventing SSI.	Conditional	Low to very low

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Wound protector devices	Does the use of wound protector devices reduce the rate of SSI in open abdominal surgery?	The panel suggests considering the use of wound protector devices in clean-contaminated, contaminated and dirty abdominal surgical procedures for the purpose of reducing the rate of SSI.	Conditional	Very low
Incisional wound irrigation	Does intraoperative wound irrigation reduce the risk of SSI?	The panel considered that there is insufficient evidence to recommend for or against saline irrigation of incisional wounds before closure for the purpose of preventing SSI.	NA	NA
		The panel suggests considering the use of irrigation of the incisional wound with an aqueous PVP-I solution before closure for the purpose of preventing SSI, particularly in clean and clean-contaminated wounds.	Conditional	Low
		The panel suggests that antibiotic incisional wound irrigation should **not** be used for the purpose of preventing SSI.	Conditional	Low
Prophylactic negative pressure wound therapy	Does prophylactic negative pressure wound therapy reduce the rate of SSI compared to the use of conventional dressings?	The panel suggests the use of prophylactic negative pressure wound therapy in adult patients on primarily closed surgical incisions in high-risk wounds for the purpose of the prevention of SSI, while taking resources into account.	Conditional	Low
Use of surgical gloves	1. When is double-gloving recommended? 2. What are the criteria for changing gloves during an operation? 3. What type of gloves should be used?	The panel decided not to formulate a recommendation due to the lack of evidence to assess whether double-gloving or a change of gloves during the operation or the use of specific types of gloves are more effective in reducing the risk of SSI.	NA	NA

Topic	Research questions	Recommendations	Strength	Quality of evidence
Preoperative measures				
Changing of surgical instruments	At the time of wound closure, is there a difference in SSI when instruments are changed for fascial, subcutaneous and skin closure using a new set of sterile instruments?	The panel decided not to formulate a recommendation on this topic due to the lack of evidence.	NA	NA
Antimicrobial -coated sutures	Are antimicrobial-coated sutures effective to prevent SSI? If yes, when and how should they be used?	The panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery.	Conditional	Moderate
Laminar flow ventilation systems in the context of OR ventilation	1. Is the use of laminar air flow in the OR associated with the reduction of overall or deep SSI?	The panel suggests that laminar airflow ventilation systems should **not** be used to reduce the risk of SSI for patients undergoing total arthroplasty surgery.	Conditional	Low to very low
	2. Does the use of fans or cooling devices increase SSIs? 3. Is natural ventilation an acceptable alternative to mechanical ventilation?	The panel decided not to formulate a recommendation on these topics due to the lack of evidence to answer questions 2 and 3.	NA	NA
Postoperative measures				
SAP prolongation	Does continued postoperative SAP reduce the risk of SSI compared with preoperative and (if necessary) intraoperative prophylaxis only?	The panel recommends **against** the prolongation of SAP after completion of the operation for the purpose of preventing SSI.	Strong	Moderate
Advanced dressings	In surgical patients, should advanced dressings vs. standard sterile wound dressings be used for the prevention of SSI?	The panel suggests **not** using any type of advanced dressing over a standard dressing on primarily closed surgical wounds for the purpose of preventing SSI.	Conditional	Low
Antimicrobial prophylaxis in the presence of a drain and optimal timing for wound drain removal	1. In the presence of drains, does prolonged antibiotic prophylaxis prevent SSI?	The panel suggests that preoperative antibiotic prophylaxis should **not** be continued in the presence of a wound drain for the purpose of preventing SSI.	Conditional	Low
	2. When using drains, how long should they be kept in place to minimize SSI as a complication?	The panel suggests removing the wound drain when clinically indicated. No evidence was found to allow making a recommendation on the optimal timing of wound drain removal for the purpose of preventing SSI.	Conditional	Very low

SSI: surgical site infection; PICO: Population, Intervention, Comparison, Outcomes; CHG: chlorhexidine gluconate; SAP: surgical antibiotic prophylaxis; OR: operating room; ESBL: extended-spectrum beta-lactamase; PVP-I: povidone-iodine; NA: not applicable.

1. BACKGROUND

Health care-associated infections (HAIs) are acquired by patients when receiving care and are the most frequent adverse event affecting patient safety worldwide. Common HAIs include urine, chest, blood and wound infections. HAIs are caused mainly by microorganisms resistant to commonly-used antimicrobials, which can be multidrug-resistant.

Although the global burden remains unknown because of the difficulty to gather reliable data, it is estimated that hundreds of millions of patients are affected by HAIs each year, leading to significant mortality and financial losses for health systems. At present, no country is free from the burden of disease caused by HAIs and antimicrobial resistance (AMR).

Of every 100 hospitalized patients at any given time, seven in developed and 15 in developing countries will acquire at least one HAI. The endemic burden of HAI is also significantly (at least 2-3 times) higher in low- and middle-income countries (LMICs) than in high-income nations, particularly in patients admitted to intensive care units, and neonates.

Recent work by the World Health Organization (WHO) *Clean Care is Safer Care* programme (http://www.who.int/gpsc/en) shows that surgical site infection (SSI) is the most surveyed and frequent type of HAI in LMICs and affects up to one third of patients who have undergone a surgical procedure. In LMICs, the pooled incidence of SSI was 11.8 per 100 surgical procedures (range 1.2 to 23.6) *(1, 2)*. Although SSI incidence is much lower in high-income countries, it remains the second most frequent type of HAI in Europe and the United States of America (USA). In some European countries, it even represents the most frequent type of HAI. The European Centre for Disease Prevention and Control (ECDC) reported data on SSI surveillance for 2010-2011. The highest cumulative incidence was for colon surgery with 9.5% episodes per 100 operations, followed by 3.5%for coronary artery bypass graft, 2.9% for caesarean section, 1.4% for cholecystectomy, 1.0% for hip prosthesis, 0.8% for laminectomy and 0.75% for knee prosthesis *(3)*.

Many factors in a patient's journey through surgery have been identified as contributing to the risk of SSI. The prevention of these infections is complex and requires the integration of a range of measures before, during and after surgery. However, the implementation of these measures is not standardized worldwide and no international guidelines are currently available.

No full guidelines have been issued by WHO on this topic, although some aspects related to the prevention of SSI are mentioned in the 2009 WHO *guidelines for safe surgery (4)*. Some national guidelines are available, especially in Europe and North America, but several inconsistencies have been identified in the interpretation of evidence and recommendations and validated systems to rank the evidence have seldom been used. Importantly, none of the currently available guidelines have been based on systematic reviews conducted ad hoc in order to provide evidence-based support for the development of recommendations. In addition, important topics with a global relevance that can lead to potentially harmful consequences for the patient if neglected are mentioned in only a few guidelines, for example, surgical hand antisepsis or the duration of surgical antibiotic prophylaxis (SAP). Of note, the prolongation of antibiotic prophylaxis is one of the major determinants of AMR.

Given the burden of SSI in many countries and the numerous gaps in evidence-based guidance,

there is a need for standardization based on strategies with proven effectiveness and a global approach. International, comprehensive SSI prevention guidelines should include also more innovative or recent approaches. To ensure a universal contribution to patient safety, recommendations should be valid for any country, irrespective of their level of development and resources.

The aim of these guidelines is to provide a comprehensive range of evidence-based recommendations for interventions to be applied during the pre-, intra- and postoperative periods for the prevention of SSI, while taking into consideration resource availability and values and preferences.

1.1 Target audience

The primary target audience for these guidelines is the surgical team, that is, surgeons, nurses, technical support staff, anaesthetists and any professionals directly providing surgical care. Pharmacists and sterilization unit staff will be concerned also by some recommendations or aspects of these guidelines. The guidelines will be an essential tool for health care professionals responsible for developing national and local infection prevention protocols and policies, such as policy-makers and infection prevention and control (IPC) professionals. Of note, it will be crucial to involve senior managers, hospital administrators, individuals in charge of quality improvement and patient safety and those responsible for staff education and training to help advance the adoption and implementation of these guidelines.

1.2 Scope of the guidelines

Population and outcome of interest

The guidelines focus on the prevention of SSI in patients of any age undergoing any surgical procedure. However, there are recommendations that are either not proven for the paediatric population due to lack of evidence or inapplicable. The primary outcomes considered for developing the recommendations were the occurrence of SSI (SSI incidence rates) and SSI-attributable mortality.

Priority questions

The priority research questions guiding the evidence review and synthesis according to each topic addressed by these guidelines are listed in the table of recommendations included in the executive summary. These were further developed as a series of questions structured in a PICO (Population, Intervention, Comparison, Outcomes) format (available in full in web Appendices 2-27) (www.who.int/gpsc/SSI-guidelines/en).

2. METHODS

2.1 WHO guideline development process

The guidelines were developed following the standard recommendations described in the WHO *Handbook for guideline development (5)* and according to a scoping proposal approved by the WHO Guidelines Review Committee.

In summary, the process included: (i) identification of the primary critical outcomes and priority topics and formulation of the related PICO questions; (ii) retrieval of the evidence through specific systematic reviews of each topic using an agreed standardized methodology; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations; and (v) writing of the guidelines' content and planning for the dissemination and implementation strategy.

The initial plan for the guidelines included a section dedicated to best implementation strategies for the developed recommendations, based on a systematic review of the literature and expert advice. However, given the very broad scope and length of the present document and following consultation with the methodologist and the Guidelines Review Committee secretariat, the Guideline Steering Group decided not to include this section. A short chapter is included to address this aspect, but a separate document dedicated to this topic will be provided to accompany the guidelines.

The development of the guidelines involved the formation of four main groups to guide the process and their specific roles are described in the following sections.

WHO Guideline Steering Group

The WHO Guideline Steering Group was chaired by the director of the Department of Service Delivery and Safety (SDS). Participating members were from the SDS IPC team, the SDS emergency and essential surgical care programme, the Department of Pandemic and Epidemic Diseases, and the IPC team at the WHO Regional Office of the Americas.

The Group drafted the initial scoping document for the development of the guidelines. In collaboration with the Guidelines Development Group (GDG), it then identified the primary critical outcomes and priority topics and formulated the related questions in PICO format. The Group identified systematic review teams, the guideline methodologist, the members of the GDG and the external reviewers. It supervised also the evidence retrieval and syntheses, organized the GDG meetings, prepared or reviewed the final guideline document, managed the external reviewers' comments and the guideline publication and dissemination. The members of the WHO Steering Group are presented in the Acknowledgements section and the full list including affiliations is available in the Annex (section 6).

Guidelines Development Group

The WHO Guideline Steering Group identified 20 external experts and stakeholders from the 6 WHO regions to constitute the GDG. Representation was ensured from various professional and stakeholder groups, including surgeons, nurses, IPC and infectious disease specialists, researchers and patient representatives. Geographical representation and gender balance were also considerations when selecting GDG members. Members provided input for the drafting of the scope of the guidelines, the PICO questions and participated in the identification of the methodology for the systematic reviews. In addition, the GDG appraised the evidence that was

used to inform the recommendations, advised on the interpretation of the evidence, formulated the final recommendations based on the draft prepared by the WHO Steering Group and reviewed and approved the final guideline document. The members of the GDG are presented in the Annex (section 6.1).

Systematic Reviews Expert Group

Given the high number of systematic reviews supporting the development of recommendations for the guidelines, a Systematic Reviews Expert Group (SREG) was created. This group included researchers and professionals with a high level of expertise in the selected topics and the conduct of systematic reviews. While some of the reviews were conducted by the WHO IPC team, most SREG experts volunteered to conduct the systematic reviews as an in-kind contribution of their institutions to the development of the guidelines.

The SREG undertook the systematic reviews and meta-analyses and prepared individual summaries, which are available as web appendices to the guidelines. It assessed also the quality of the evidence and prepared the evidence profiles according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.

Some SREG members were also part of the GDG. However, according to the Guideline Review Committee's instructions and to avoid any intellectual conflict, experts leading the systematic reviews were excluded from consensus decision-making for the development of recommendations related to the topic they reviewed, in particular when voting was necessary. As a member of the SREG, the GDG chair was equally excluded from decision-making on recommendations that were based on systematic reviews conducted by himself and his team. Furthermore, in sessions where the chair presented the evidence from systematic reviews conducted by his team, another GDG member was identified to act as the chair. The members of the GDG are presented in the Acknowledgements and the full list including affiliations is available in the Annex (section 6.1).

External Peer Review Group

This group included five technical experts with a high level of knowledge and experience in the fields of surgery and IPC. The group was geographically balanced to ensure views from both high- and LMICs; no member declared a conflict of interest.

The group reviewed the final guideline document to identify any factual errors and commented on technical content and evidence, clarity of the language, contextual issues and implications for implementation. The group ensured that the guideline decision-making processes had incorporated contextual values and preferences of potential users of the recommendations, health care professionals and policy-makers. It was not within the remit of this group to change the recommendations formulated by the GDG. However, very useful comments were provided in some cases, which led to modifications of the recommendation text or the explanations provided within the remarks. The members of the WHO External Peer Review Group are presented in the Acknowledgements and the full list including affiliations is available in the Annex (section 6.4).

2.2 Evidence identification and retrieval

The SREG retrieved evidence on the effectiveness of interventions for the prevention of SSI from randomized controlled trials (RCTs) and non-randomized studies as needed. The Guideline Steering Group provided the SREG with the methodology and a briefing on the desired output of the systematic reviews and the members of these groups agreed together on the format and timelines for reporting. Using the assembled list of priority topics, questions and critical outcomes from the scoping exercise identified by the WHO Guideline Steering Group, the GDG and the guideline methodologist, the SREG conducted 27 systematic reviews between December 2013 and October 2015 to provide the supporting evidence for the development of the recommendations.

To identify relevant studies, systematic searches of various electronic databases were conducted, including Medline (Ovid), the Excerpta Medica Database, the Cumulative Index to Nursing and Allied Health Literature, the Cochrane Central Register of Controlled Trials and WHO regional databases. All studies published after 1 January 1990 were considered. In a few reviews, the GDG and the SREG judged that relevant studies had been published before 1990 and no time limit was used. Studies in at least English, French and Spanish were included; some reviews had no language restrictions. A comprehensive list of search terms was used, including Medical Subject Headings. Criteria for the inclusion

and exclusion of literature (for example, study design, sample size and follow-up duration) for the reviews were based on the evidence needed and available to answer the specific research questions. Studies from LMICs and high-income countries were considered. Search strategies and summaries of evidence for each systematic review are reported in web Appendices 2-27 (www.who.int/gpsc/SSI-guidelines/en).

Two independent reviewers screened the titles and abstracts of retrieved references for potentially relevant studies. The full text of all potentially eligible articles was obtained and then reviewed independently by two authors based on inclusion criteria. Duplicate studies were excluded. Both authors extracted data in a predefined evidence table and critically appraised the retrieved studies.

Quality was assessed using the Cochrane Collaboration tool to assess the risk of bias of RCTs *(6)* and the Newcastle-Ottawa Quality Assessment Scale for cohort studies *(7)*. Any disagreements were resolved through discussion or after consultation with the senior author, when necessary.

Meta-analyses of available comparisons were performed using Review Manager version 5.3 *(8)*, as appropriate. Crude estimates were pooled as odds ratios (OR) with 95% confidence intervals (CI) using a random effects model. The GRADE methodology (GRADE Pro software; http://gradepro.org/) was used to assess the quality of the body of retrieved evidence *(9, 10)*. Based on the rating of the available evidence, the quality of evidence was graded as "high", "moderate", "low" or "very low" (Table 2.2.1).

Table 2.2.1. **GRADE categories for the quality of evidence**

High: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

The results of the systematic reviews and meta-analyses were presented at four GDG meetings held in June 2014 and in February, September and November 2015. The evidence profiles and decision-making tables were reviewed to ensure understanding and agreement on the scoring criteria. According to a standard GRADE decision-making table proposed by the methodologist, recommendations were formulated based on the overall quality of the evidence, the balance between benefits and harms, values and preferences and implications for resource use. These were assessed through discussion among members of the GDG. The strength of recommendations was rated as either "strong" (the panel was confident that the benefits of the intervention outweighed the risks) or "conditional" (the panel considered that the benefits of the intervention probably outweighed the risks). Recommendations were then formulated and the wording was finalized by consensus. If full consensus could not be achieved, the text was put to the vote and the recommendation was agreed upon according to the opinion of the majority of GDG members.

In some conditional recommendations, the GDG decided to use the terminology "the panel suggests considering..." because they considered that it was important to stimulate the user to undertake a thorough decision-making process and to give more flexibility, especially because these recommendations involve important remarks about resource implications and feasibility in LMICs. Areas and topics requiring further research were also identified. After each meeting, the final recommendation tables were circulated and all GDG members provided written approval and comments, if any.

The systematic reviews targeted patients of any age. In general, these guidelines are valid for both adult and paediatric patients unless specified in

the text of the recommendation or in the remarks. In several systematic reviews, no study was retrieved on the paediatric population and thus the GDG discussed whether the recommendations are valid in this population topic by topic. As a result, there are recommendations that are either inapplicable in the paediatric population or not proven due to lack of evidence.

Draft chapters of the guidelines containing the recommendations were prepared by the WHO secretariat and circulated to the GDG members for final approval and/or comments. Relevant suggested changes were incorporated in a second draft. If GDG comments involved substantial changes to the recommendation, all members participated in online or telephone discussions to reach a final agreement on the text. The second draft was then edited and circulated to the External Peer Review Group and the Guideline Steering Group. The draft document was further revised to address their comments. Suggested changes to the wording of the recommendations or modifications to the scope of the document were not considered in most cases. However, in 3 specific recommendations, most reviewers suggested similar changes and these were considered to be important by the Guideline Steering Group. In these cases, further discussions were undertaken with the GDG through teleconferences and consensus was achieved to make slight changes in the text of the recommendations to meet the reviewers' comments under the guidance of the methodologist.

The guideline methodologist ensured that the GRADE framework was appropriately applied throughout the guideline development process. This included a review of the PICO questions and the results of the systematic reviews and meta-analyses, including participation in re-analyses when appropriate, thus ensuring their comprehensiveness and quality. The methodologist also reviewed all evidence profiles and decision-making tables before and after the GDG meetings and provided guidance to the GDG in formulating the wording and strength of the recommendations.

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3. IMPORTANT ISSUES IN THE APPROACH TO SURGICAL SITE INFECTION PREVENTION

3.1 Surgical site infection risk factors: epidemiology and burden worldwide

Background

SSIs are potential complications associated with any type of surgical procedure. Although SSIs are among the most preventable HAIs *(1, 2)*, they still represent a significant burden in terms of patient morbidity and mortality and additional costs to health systems and service payers worldwide *(3-11)*. SSI is both the most frequently studied and the leading HAI reported hospital-wide in LMICs *(3, 4)*. For these reasons, the prevention of SSI has received considerable attention from surgeons and infection control professionals, health care authorities, the media and the public. In particular, there is a perception among the public that SSIs may reflect a poor quality of care *(12)*. The aim of this review is to provide an update of the global data on SSI with a special focus on LMICs, notably to assess infection rates, associated risk factors and the economic burden.

Summary of the available evidence

1. Burden of SSI

a. Evidence from high-income countries

i. USA

In 2010, an estimated 16 million surgical procedures were performed in acute care hospitals in the USA *(13)*. In a recent report on the rates of national and state HAIs based on data from 2014, 3654 hospitals reported 20 916 SSI among 2 417 933 surgical procedures performed in that year *(5)*.

Of note, between 2008 and 2014 there was an overall 17% decrease in SSI in the 10 main surgical procedures. As an example, there was a decrease of 17% in abdominal hysterectomy and 2% in colon surgery *(5)*.

By contrast, a multi-state HAI prevalence survey conducted in 2011 estimated that there were 157 000 SSIs related to any inpatient surgery and SSI was ranked as the second most frequently reported HAI between 2006 and 2008 *(14)*. Another study reported data from the National Healthcare Safety Network (NHSN) between 2006 and 2008 that included 16 147 SSIs following 849 659 surgical procedures across all groups, representing an overall SSI rate of 1.9% *(15)*.

AMR patterns of HAI in the USA have been described *(16)* and compared to a previous report *(17)*. Among the 1029 facilities that reported one or more SSI, *Staphylococcus aureus* was the most commonly reported pathogen overall (30.4%), followed by coagulase-negative staphylococci (11.7%), *Escherichia coli* (9.4%) and *Enterococcus faecalis* (5.9%). Table 3.1.1 summarizes the distribution of the top seven reported pathogens *(16)*.

Table 3.1.1. **Distribution and percentage of pathogenic isolates associated with SSI and resistant to selected antimicrobial agents, NHSN, 2009-2010***

Rank	Pathogen	No. of pathogens/ total SSI pathogens reported (%)	Antimicrobial agent (s)	No. of isolates tested (%)	Resistance (%)
1	*S. aureus*	6415 (30.4)	OX/METH	6304 (98.3)	43.7
2	Coagulase-negative staphylococci	2477 (11.7)	NA	NA	NA
3	*E. coli*	1981 (9.4)	ESC4	1627 (82.1)	10.9
			FQ3	1876 (94.7)	25.3
			Carbapenems	1330 (67.1)	2
			MDR1	1390 (70.2)	1.6
4	*E. faecalis*	1240 (5.9)	VAN	1187 (95.7)	6.2
5	*Pseudomonas aeruginosa*	1156 (5.5)	AMINOS ESC2	664 (57.4) 1097 (94.9)	6 10.2
			FQ2	1111 (96.1)	16.9
			Carbapenems	872 (75.4)	11
			PIP/PIPTAZ	818 (70.8)	6.8
			MDR2	1053 (91.1)	5.3
6	*Enterobacter spp.*	849 (4.0)	ESC4	816 (96.1)	27.7
			Carbapenems	594 (70.0)	2.4
			MDR1	648 (76.3)	1.7
7	*Klebsiella spp.*	844 (4.0)	ESC4	710 (84.1)	13.2
			Carbapenems	582 (69.0)	7.9
			MDR1	621 (73.6)	6.8

* Modified from reference *16*.
NHSN: National Healthcare Safety Network; SSI: surgical site infection; OX/METH: oxacillin/methicillin; ESC4: extended-spectrum (ES) cephalosporins (cefepime, cefotaxime, ceftazidime, ceftriaxone); FQ3: fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin); MDR1: multidrug resistance 1 gene (pathogen must test as "I" [intermediate] or "R" [resistant] to at least one drug in 3 of the 5 following classes: ESC4, FQ3, aminoglycosides, carbapenems§, and piperacillin [PIP] or piperacillin/tazobactam [PIP/TAZ]); NA: not available; VAN: vancomycin; AMINOS: aminoglycosides (amikacin, gentamicin, tobramycin); ESC2: ES cephalosporins (cefepime, ceftazidime); MDR2: multidrug resistance 2 gene (pathogen must test as I or R to at least 1 drug in 3 of the 5 following classes: ESC2, FQ2, AMINOS, carbapenems, and PIP or PIP/TAZ.
§ Carbapenems are imipenem and meropenem.

To investigate the costs of SSI, a study used the 2005 hospital stay data from the US Nationwide Inpatient Sample, which represents 1054 hospitals from 37 states. Extra hospital stay attributable to SSI was 9.7 days with increased costs of US$ 20 842 per admission. From a national perspective, SSI cases were associated with 406 730 extra hospital days and hospital costs exceeding US$ 900 million. An additional 91 613 readmissions for the treatment of SSI accounted for a further 521 933 days of care at a cost of nearly US$ 700 million *(18)*.

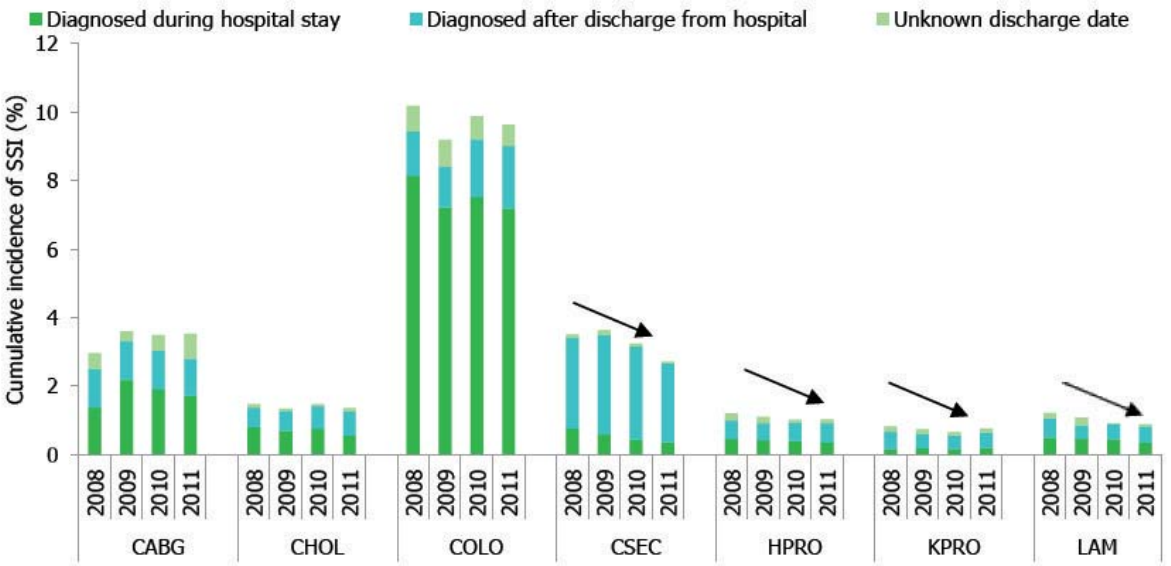
Applying two different consumer price index adjustments to account for the rate of inflation in hospital resource prices, the Centers for Disease Control and Prevention estimated that the aggregate attributable patient hospital costs for SSI infection ranged between US$ 1087 and US$ 29 443 per infection (adjusted for the 2007 US$ level). Using the consumer price index for urban consumers and inpatient hospital services, SSI is considered as the HAI with the largest range of annual costs (US$ 3.2–8.6 billion and US$ 3.5–10 billion, respectively) *(19)*.

ii. European countries

The European point prevalence survey of HAIs and antimicrobial use conducted in 2011-2012 showed that SSIs are the second most frequent HAI in hospitals *(20)*. A recent report from the ECDC on SSI surveillance of SSI provided data for 2010

and 2011 *(6)* from 20 networks in 15 European Union countries and one European Economic Area country using a standardized protocol *(21)*. Hip prosthesis was the most frequently reported surgical procedure and represented 33% of all operations. The cumulative incidence of patients with SSI was the highest in colon surgery with 9.5% (episodes per 100 operations), followed by 3.5% for coronary artery bypass graft, 2.9% for caesarean section, 1.4% for cholecystectomy, 1.0% for hip prosthesis, 0.8% for laminectomy and 0.75% for knee prosthesis *(6)*. The results showed also decreasing trends in SSI incidence in several types of procedure (caesarean section, hip prosthesis and laminectomy) (Figure 3.1.1), thus suggesting that prevention efforts, including surveillance, were successful in participating hospitals *(6, 22)*.

Figure 3.1.1. **Cumulative incidence for SSI by year and type of procedure: European Union/European Economic Area countries, 2008–2011**



Data source: ECDC, HAI-Net SSI patient-based data 2008–2011 (http://ecdc.europa.eu/en/activities/surveillance/Pages/data-access.aspx#sthash.hHYRJ9ok.dpuf, accessed 21 May 2016).

SSI: surgical site infection; CABG: coronary artery bypass graft; CHOL: cholecystectomy; COLO: colon; CSEC: caesarean section; HPRO: hip prosthesis; KPRO: knee prosthesis; LAM: laminectomy.

A study published in 2004 reviewed data from 84 studies and estimated the economic costs of SSIs in Europe to range between € 1.47–19.1 billion. It predicted also that the average patient stay would increase by approximately 6.5 days and cost 3 times as much to treat an infected patient. The analysis suggested that the SSI-attributable economic burden at that time was likely to be underestimated *(10)*.

In **France**, it was estimated that 3% of surgical procedures resulted in infection for a total annual cost of nearly € 58 million. Moreover, patients who experienced SSI had a significantly increased mortality risk (from 4- to 15-fold) and a 3-fold increased length of hospital stay *(23)*.

The prevalence of SSI in **Switzerland** was reported to be 5.4% in a study conducted in 50 acute care hospitals participating in the Swiss Nosocomial Infection Prevalence surveillance programme *(24)*. Another study described a 13-year multicentre SSI surveillance scheme performed from 1998 to 2010. Reported SSI rates were: 18.2% after 7411 colectomies; 6.4% after 6383 appendicectomies; 2.3% after 7411 cholecystectomies; 1.7% after 9933 herniorrhaphies; 1.6% after 6341 hip arthroplasties; and 1.3% after 3667 knee arthroplasties *(25)*.

In **Italy**, the SSI rate reported by the "Sistema Nazionale di Sorveglianza delle Infezioni del Sito Chirurgico" (national SSI surveillance system) from

355 Italian surgical wards between 2009 and 2011 was 2.6% episodes per 100 procedures (1628 cases/60 460 procedures); 60% of SSIs were diagnosed through 30-day post-discharge surveillance. SSI rates were higher in colon (9.0%) and rectal surgery (7.0%), laparotomy (3.1%) and appendectomy (2.1%) *(26)*.

In **England**, the most recent summary of data collected by National Health Service hospitals reported cumulative SSI rates from January 2008 to March 2013. The highest rate was reported among large bowel surgery (8.3%; 95% CI: 7.9–8.7 per 1000 inpatient days), followed by small bowel surgery (4.9%; 95% CI: 4.3–5.7), bile duct, liver and pancreatic surgery (4.9%; 95% CI: 4.1–5.9) and cholecystectomy (4.6%; 95% CI: 3.1–6.6). The lowest rate was reported for knee prosthesis (0.4%; 95% CI: 0.3–0.4) *(8)*.

Data collected from April 2010 to March 2012 estimated that the median additional length of stay attributable to SSI was 10 days (7-13 days), with a total of 4694 bed-days lost over the 2-year period *(27)*.

iii. Australia

A study evaluated the time trends in SSI rates and pathogens in 81 Australian health care facilities participating in the Victorian Healthcare Associated Infection Surveillance System. A total of 183 625 procedures were monitored and 5123 SSIs were reported. *S. aureus was* the most frequently identified pathogen, and a statistically significant increase in infections due to ceftriaxone-resistant *E. coli* was observed (relative risk: 1.37; 95% CI: 1.10–1.70) *(9)*.

iv. Japan

Data from the Japan nosocomial infection surveillance system showed that 470 hospitals voluntarily participated in SSI surveillance in 2013 *(28, 29)*. A retrospective study evaluated also the influence of SSI on the postoperative duration of hospitalization and costs between 2006 and 2008 after abdominal or cardiac surgery. Overall, the mean postoperative hospitalization was 20.7 days longer and the mean health care expenditure was US$ 8791 higher in SSI patients. SSI in abdominal surgery extended the average hospitalization by 17.6 days and increased the average health care expenditure by US$ 6624. Among cardiac surgical patients, SSI extended the postoperative hospitalization by an average of 48.9 days and increased health care expenditure by an average of US$ 28 534 *(30)*. A recent study assessed SSI rates and risk factors after colorectal surgery using the Japan nosocomial infection surveillance system national database. The cumulative incidence of SSI for colon and rectal surgery was 15.0% (6691/44 751 procedures) and 17.8% (3230/18 187 procedures), respectively *(31)*.

v. Republic of Korea

A prospective multicentre surveillance study published in 2000 concluded that SSI constituted 17.2% of all HAIs reported from 15 acute care hospitals *(32, 33)*. The 2009 national SSI surveillance system report described the incidence and risk factors for SSI in 7 types of procedures. The SSI rate per 100 operations was 3.68% (22/1169) after craniotomies, 5.96% (14/235) for ventricular shunt operations, 4.25% (75/1763) for gastric operations, 3.37% (22/653) for colon surgery, 5.83% (27/463) for rectal surgery, 1.93% (23/1190) for hip joint replacement and 2.63% (30/1139) for knee joint replacement *(34)*.

A web-based surveillance of SSIs was performed between 2010 and 2011 to determine the incidence of SSIs after 15 surgical procedures in 43 hospitals. The overall SSI rate represented 2.10% of the total of 18 644 operations and differed after various types of surgery *(35)*. In addition, a systematic review of the literature published between 1995 and 2010 on the epidemiological and economic burden of SSI in the Republic of Korea reported an overall incidence of SSI ranging from 2.0% to 9.7% *(36)*. SSIs were associated with increased hospitalization costs and each episode of SSI was estimated to cost around an additional 2 000 000 Korean Republic won (approximately US$ 1730). Postoperative stays for patients with SSIs were 5 to 20 days longer *(36)*.

In a recent study conducted between 2008 and 2012, the SSI rate following gastrectomy was 3.12% (522/16 918), 2.05% (157/7656) for total hip arthroplasty and 1.90% (152/7648) for total knee arthroplasty. There was a significant trend of decreased crude SSI rates over 5 years *(37)*.

vi. Gulf Council Countries

We were not able to retrieve published national data on SSI rates from any of the Gulf Council Countries (Bahrain, Kingdom of Saudi Arabia, Kuwait, Oman, Qatar and the United Arab Emirates). However, in Saudi Arabia, a 5-year analysis of SSI in orthopaedic surgery in one hospital estimated a rate of 2.55% *(38)*. Another

study from the King Abdulaziz Medical City (Saudi Arabia) compared SSI rates for herniorraphy and cholecystectomy in 2007 to 1999-2000. In 2007, SSI rates per 100 operations in 2007 were 0.88% for herniorrhaphy and 0.48% for cholecystectomy, while in 2007, rates were reduced by 80% for herniorrhaphy (P=0.049) and 74% for cholecystectomy (P=0.270) *(39)*.

vii. Singapore

In a systematic literature review (2000 to 2012) *(40)* of the burden of HAI in South-East Asia, the pooled incidence of SSI was 7.8% (95% CI: 6.3–9.3). A study conducted between January and March 2008 in a tertiary care hospital in Singapore reported an SSI incidence of 8.3% for general, neurologic and orthopaedic surgical procedures *(41)*.

viii. Uruguay

The national incidence data on SSI for 2012-2013 reported that the incidence rate for appendectomy was 3.2%, 2.5% for cardiac surgery, 6.2% for cholecystectomy and 15.4% for colon surgery *(42)*.

ix. Chile

The 2013 national report on HAI surveillance showed a SSI rate of 3.09% for coronary bypass surgery and 1.89% for hip joint replacement. Infection rates in cholecystectomy performed via laparotomy were 4.12% (95% CI: 2.8-6.11) times higher than laparoscopic cholecystectomy (P<0.0001) *(43)*.

Table 3.1.2. **Summary of SSI rates in different countries**

Country (reference)	SSI rate (%) (95% CI [when provided])	Year*	Measurement used	Study design
USA *(5, 15)*	0.9 17% decrease in SSI related to the 10 selected procedures (2014 compared to 2008)	2014	Cumulative incidence (episodes per 100 operations)	NHSN data (incidence design)
European Union *(6)*	9.5 (COLO) 3.5 (CABG) 2.9 (CSEC) 1.4 (CHOL) 1.0 (HPRO) 0.8 (LAM) 0.75 (KPRO)	2010–2011	Cumulative incidence (episodes per 100 operations)	ECDC HAI SSI protocol *(21)*
England *(8)*	Large bowel surgery: 8.3 (7.9–8.7) Small bowel surgery: 4.9 (4.3–5.7) Bile duct, liver and pancreatic surgery: 4.9 (4.1–5.9) CHOL: 4.6 (3.1–6.6) KPRO: 0.4 (0.3–0.4)	2008–2013	Incidence density (episodes per 1000 patient-days)	SSI surveillance - incidence design
Australia *(9)*	2.8	2002–2013	Incidence density (episodes per 1000 patient-days)	Victorian Healthcare Associated Infection Surveillance System
Japan *(29, 31)*	COLO: 15.0 (6691/44 751) Rectal surgery: 17.8 (3230/18 187)	2008–2010	Cumulative incidence (episodes per 100 operations)	National nosocomial infection surveillance system – incidence design

Country (reference)	SSI rate (%) (95% CI [when provided])	Year*	Measurement used	Study design
Republic of Korea *(35, 37)*	Overall: 2.1 Gastrectomy: 3.1 (522/16 918) Total hip arthroplasty: 2.0 (157/7656)	2010–2011 2008–2012	Cumulative incidence (episodes per 100 operations)	National surgical site infection surveillance system – incidence design
Uruguay *(42)*	Appendectomy: 3.2 Cardiac surgery: 2.5 Cholecystectomy: 6.2 COLO: 15.4	2014	Cumulative incidence (episodes per 100 operations)	National nosocomial infection surveillance system
Chile *(43)*	Coronary bypass surgery: 3.1 Hip joint replacement: 1.9	2013		National HAI infection surveillance system
LMICs-WHO	Average: 6.1 (5.0–7.2)	1995–2015	Cumulative incidence (episodes per 100 operations)	Incidence/prospective
South-East Asia *(40)*	7.8 (6.3–9.3)	2000–2012	Pooled incidence review	Systematic literature

* Year of the most recent publication assessing the national SSI rates.
# Unpublished WHO data.

SSI: surgical site infection; CI: confidence interval; NHSN: National Healthcare Safety Network; ECDC: European Centre for Disease Prevention and Control; HAI: health care-associated infection; COLO: colon surgery; CABG: coronary artery bypass graft; CSEC: caesarean section; CHOL: cholecystectomy; HPRO: hip prosthesis; LAM: laminectomy; KPRO: knee prosthesis; UK: United Kingdom; LMIC: low- and middle-income countries.

b. WHO systematic reviews on SSI in LMICs

The WHO report on the global burden of endemic HAI provided SSI data from LMICs. The pooled SSI incidence was 11.8 per 100 surgical patients undergoing surgical procedures (95% CI: 8.6–16.0) and 5.6 per 100 surgical procedures (95% CI: 2.9–10.5). SSI was the most frequent HAI reported hospital-wide in LMICs and the level of risk was significantly higher than in developed countries *(3, 4)*.

Recently, WHO conducted an update of the systematic literature review of from 1995 to 2015 with a special focus on SSI in LMICs (WHO unpublished data). A total of 231 articles in English, French, German, Spanish and Portuguese were included. The pooled SSI rate was 11.2 per 100 surgical patients (95% CI: 9.7–12.8) for incidence/prospective studies. There was no statistical difference in SSI rates when stratified by study quality, patient age groups, geographic regions, country income, SSI definition criteria, type of setting or year of publication. However, there were statistical differences between studies according to the type of surgical population procedures (P=0.0001) and the number of patients per study (P=0.0004).

In incidence studies, the SSI rate was higher for procedures in oncology (17.2%; 95% CI: 15.4–19.1), orthopaedic (15.1%; 95% CI: 10.2–20.6), general surgery (14.1%; 95% CI: 11.6–16.8) and paediatric surgery (12.7%; 95% CI: 6.7–20.3). The SSI rate expressed as the number of SSI infections per 100 surgical operations was reported in 57 (24.7%) studies. The pooled SSI rate using this measure was 6.1% (95% CI: 5.0–7.2) for incidence/prospective studies (Figure 3.1.2).

Some studies *(44-50)* investigated SSI rates after caesarean section surgery and showed a substantial variability in the definition of SSI and in reported rates. High rates of SSI following caesarean section were reported in several LMICs: 16.2% in a study from Nigeria *(44)*, 19% from Kenya *(45)*, 10.9% from Tanzania *(46)* and 9.7% by Viet Nam *(47)*. In 2 studies from Brazil, one reported a rate of 9.6% *(48)* and the other a higher rate of 23.5% *(49)*. In comparison, a much lower average SSI rate of 2.9% is reported in Europe *(6, 21)*.

2. Factors increasing the risk of SSI

Many factors influence surgical wound healing and determine the potential for infection *(51)*. These include patient-related (endogenous) and process/procedural-related (exogenous) variables that affect a patient's risk of developing an SSI. Some variables are obviously not modifiable, such as age and gender. However, other potential factors can be improved to increase the likelihood of a positive surgical outcome, such as nutritional status, tobacco use, correct use of antibiotics and the intraoperative technique.

The usefulness of risk assessment and the definition of risk is debatable as there are very few studies that have an altered patient outcome based on information gained by risk assessment *(52, 53)*. One study analysed a 2-year data report of the NHSN for all surgical procedures and used stepwise logistic regression to develop specific risk models by procedure category. The study concluded that a set of new models using existing data elements collected through the NHSN improved predictive performance, compared to the traditional NHSN risk index stratification *(15)*.

A systematic review of 57 studies from both high-income countries and LMICs identified the following factors associated with an increased risk of SSI in adjusted analysis: a high body mass index; a severe score according to the US National Nosocomial Infections Surveillance (NNIS) risk index; severe wound class; diabetes; and a prolongation of surgery duration *(54)*. A meta-analysis of prospective cohort studies suggested that diabetes mellitus is significantly associated with an increased risk of SSI *(55)*. The national nosocomial surveillance system protocol in Italy identified a longer duration of surgery, an American Society of Anesthesiologists score of at least 3 and a pre-surgery hospital stay of at least 2 days as factors associated with an increased risk of SSI, while videoscopic procedures reduced SSI rates *(26)*. In the Republic of Korea, a systematic review of the epidemiological and economic burden identified diabetes, the absence or >1 hour administration of antibiotic prophylaxis and the type of wound classification (contaminated or dirty) as risk factors significantly associated with SSI by multivariate analyses *(36)*. In addition, the NNIS risk index identified trauma, re-operation and age (60-69 years) as risk factors for SSI after total hip arthroplasty *(37)*.

In a recent unpublished systematic review conducted by WHO, a total of 14 observational studies (no RCTs) *(56-69)* describing the relationship between surgical volume and the risk of SSI were identified. There was a substantial heterogeneity in the definitions of volume, surgical procedures studied and SSI measurement. Thus, separate meta-analyses were performed to evaluate SSI rates between high vs. low and medium vs. low hospital volume, and high vs. low and medium vs. low surgeon volume. A moderate quality of evidence showed that surgical procedures performed in high-/medium-volume hospitals have lower SSI rates compared to low-volume hospitals (OR: 0.69; 95% CI: 0.55-0.87 and OR: 0.80; 95% CI: 0.69-0.94, respectively). In addition, there was a moderate quality of evidence that surgical procedures performed by high- or medium-volume surgeons have lower SSI rates (OR: 0.67; 95% CI: 0.55-0.81 and OR: 0.73; 95% CI: 0.63-0.85, respectively) compared to low-volume hospitals. However, there was controversial evidence when high- and medium-volume hospitals were compared and it remains unclear whether there is a linear relationship between procedure/surgeon volume and the SSI rate.

Conclusions

Despite robust data on the burden of SSI in some countries or regions, accurate estimates of the global burden in terms of SSI rates and the economic aspects still remain a goal for the future. As an example, SSI and overall HAI data are not yet included in the list of diseases for which the global burden is regularly estimated by WHO or other international organizations gathering data on global health. Although SSI rates vary between countries and geographical regions, they represent an important problem, with a significantly higher burden in developing countries. If SSI rates are to serve as a quality indicator and comparison benchmark for health care facilities, countries and the public, they must be determined in a reliable way that produces robust infection rates to ensure valid comparisons. There is a global need to address changes to SSI definitions, strengthen and validate SSI data quality, and to conduct robust SSI economic and burden studies.

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3.2 Surgical site infection surveillance: definitions, methods and impact

The surveillance of HAI is one of the core components of an effective IPC programme *(1, 2)*. However, defining, detecting, reporting and interpreting HAI, including SSI, is challenging and requires expertise, time and resource dedication.

Definitions of surveillance and SSI

Surveillance is defined as "the ongoing, systematic collection, analysis, interpretation and evaluation of health data closely integrated with the timely dissemination of these data to those who need it" *(3)*.

There are many definitions of SSI and a systematic review identified as many as 41 different definitions. However, only five were described as being standardized definitions created by multidisciplinary groups (Table 3.2.1) *(4)*. More than one third of included studies used the US CDC definitions (either 1988 or 1992). While the authors of this review suggest that a single definition allows longitudinal analysis and benchmarking, they conclude by stating that "there is no single, objective gold standard test for surgical wound infection" *(4)*. In addition, many countries use the HAI SSI protocol developed by the ECDC (http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/surgical-site-infections/Pages/SSI.aspx, accessed 20 May 2016).

Table 3.2.1. **Definitions of SSI***

Criterion	CDC 1988	CDC 1992	SISG	NPS	PHLS
Purulent discharge in or exuding from the wound or observed on direct examination	I		✓	✓	✓
Painful spreading erythema indicative of cellulitis			✓	✓	
Purulent drainage	D	SI/D			
Purulent drainage from a drain placed beneath the fascial layer	D				
Purulent drainage from a drain placed through a stab wound into the organ/space		OS			
Organisms isolated from fluid or tissue from the wound	I	SI			
Organisms isolated from fluid or tissue in the organ/space		OS			
Surgeon/physician diagnosis	I/D	SI/DI/OS			
Surgeon deliberately opens wound, unless wound is culture-negative	I/D	SI/DI			
Wound spontaneously dehisces	D	SI/DI			
Pain	D	SI/DI			
Tenderness	D	DI	✓	✓	
Fever › 38°C	D	DI	✓	✓	
Localized swelling (oedema)		SI	✓	✓	
Redness or extending margin or erythema		SI	✓	✓	
Patient still receiving active treatment for a wound with discharged pus				or ✓	
Heat		SI			
Abscess or other evidence of infection found on direct examination	D	DI/OS			

*Reproduced from reference *4*.

CDC: Centers for Disease Control and Prevention; SISG: Surgical Infection Study Group; NPS: National Prevalence Survey; PHLS; Public Health Laboratory Service.

CDC 1988 definitions: I, incisional surgical wound infection; D, deep surgical wound infection. CDC 1992 definitions: SI, superficial incisional; DI, deep incisional; OS, organ/space. The SISG and NPS allow fever (›38°C), tenderness, oedema, an extending margin of erythema or if the patient is still receiving treatment for the wound.

Aims of surveillance

The primary aim of surveillance is the collection of data on SSI rates in order to obtain a measure of the magnitude of the problem. These data must then be analysed to identify and investigate trends, including a careful interpretation of results. Finally, surveillance data should guide the identification of improvement actions and evaluate the effectiveness of these interventions. In this context, the feedback of SSI rates to relevant stakeholders is important.

Should surveillance be conducted?

The positive impact of HAI surveillance was first described in the landmark study on the efficacy of a nosocomial infection control programme conducted in the USA in the 1970s. In this trial, it was shown that an IPC programme with both surveillance and control components could lower SSI rates significantly *(5)*. Importantly, surveillance of SSI is part of the WHO safe surgery guidelines *(6)*. Many countries have introduced mandatory surveillance of HAI, including SSI, such as the UK and certain states in the USA, whereas other countries have voluntary-based surveillance, such as France, Germany and Switzerland. However, there are considerable differences related to the types of surveillance, as well as in the length and type of surveillance *(7, 8)*. Increasingly, national networks and "networks of networks" are being created, such as the CDC NHSN, the ECDC HAI Surveillance Network (HAI-Net) and the International Nosocomial Infection Control Consortium.

By using standardized definitions of HAI and specifically SSI, these networks allow inter-hospital comparisons and benchmarking. An essential component of these surveillance networks is feedback to individual hospitals, as discussed below.

It has been postulated that a "surveillance effect" might occur, similar to the Hawthorne effect in clinical trials, that is, the simple fact of being conscious that one is being observed may independently lead to improved practices or improved adherence to guidelines *(9)*.

Another way in which a successful surveillance programme may decrease SSI rates is that the feedback given to the institution may prompt investigation of why its rates are higher than the benchmark. Certain process indicators (if not already collected) may then identify the reason for "underperformance" and prompt local initiatives to improve performance on these indicators. There is conflicting evidence that conducting surveillance as part of a network has a positive impact on SSI rates (Table 3.2.2). Some studies report a successful reduction of SSI rates after participation in a surveillance network *(10-12)*, while others report no effect *(13)*. However, there is an important methodological issue that could "dilute" the reduction in the time trend of SSI rates, which is the fact of adding smaller hospitals in a network without taking into account their year of participation in the network. This obstacle was overcome in an analysis of German data where hospitals were stratified by year of participation *(9)* and in an analysis of Dutch *(14)* and Swiss *(13)* data where SSI rates were stratified by surveillance time to operation in consecutive one-year periods using the first year of surveillance as a reference. The Dutch and German studies reported decreasing time trends of SSI rates after surveillance, whereas the Swiss study did not.

Conversely, as shown in clinical trials, intensive surveillance may lead to the detection of higher SSI rates than under standard surveillance conditions. As an example, in a recent clinical trial comparing skin antiseptic agents for caesarean section, the SSI rate was 4.0% in one arm and 7.3% in the other *(15)*.These rates seem higher than the most recently available data from the ECDC, which show an SSI rate of 2.9% (inter-country range: 0.4%-6.8%) *(16)*.

Table 3.2.2. **Temporal trends of SSI rates after surveillance in selected networks***

Country (name of network)	Duration of surveillance	Procedures	Change in SSI rate	Reference
England (SSISSF)	5	Orthopaedic	-64 to -69%	*(17)*
France (ISO-RAISIN)	8	Various	-30%	*(11)*
Germany (KISS)	4	Various	-25%	*(10)*
The Netherlands (PREZIES)	5	Various	-57%	*(14)*
Switzerland (regional network)	13	Various	3% to 22%	*(13)*
USA (SENIC)	5	Various	-35%	*(18)*

* Adapted from reference *19*.

SSISS: surgical site infection surveillance service; ISO-RAISIN: Infections du Site Opératoire-Réseau d'alerte, d'investigation et de surveillance des infections nosocomiales; KISS: Krankenhaus Infektions Surveillance System; PREZIES: Preventie Ziekenhusinfecties door surveillance; SENIC: study on the efficacy of nosocomial infection control.

Establishing a surveillance system

According to the US Association for Professionals in Infection Control and Epidemiology *(20)*, there is "no single or "right" method of surveillance design or implementation" *(21)*. However, the following minimal requirements for ensuring quality of surveillance have been identified by the Association *(21)*.

- A written plan that states goals, objects and elements of surveillance process
- Constant rigour of intensity of surveillance
- Consistent elements of surveillance (for example, definitions, calculation methods)
- Adequate human resources (professionals trained in epidemiology)
- Informatic services, computer support
- Evaluation methods.

For a surveillance programme to be successful, there should be a method of data validation to ensure that data are accurate and reliable *(22)*, particularly for benchmarking purposes, as discussed further *(23)*.

Methods for conducting surveillance

In the field of SSI, most surveillance systems target colorectal surgery and total hip and knee arthroplasty. The most common outcome indicator is the cumulative SSI incidence (or SSI rate). Detecting SSI using prevalence methods is less reliable given the high proportion of SSIs that manifest after discharge.

For any given period, denominator data represent the total number of procedures within each category. The number of patients can be used also as the denominator, but it is less precise because more than one infection can occur in the same patient. Numerator data will be the number of SSIs in that same period. Demographic data (age, sex, timing and choice of antimicrobial prophylaxis, American Society of Anesthesiologists score, duration of the operation and wound contamination class) are recorded for all patients, including the site of infection and type of SSI (superficial, deep, organ/space) for those with SSI. Linkage with microbiological data may also be useful.

The gold standard is prospective direct surveillance, although it is time- and labour-intensive and costly *(24)*. The CDC recommendations describe indirect methods of surveillance (sensitivity of 84-89%; specificity 99.8%) as a combination of:

1. Review of microbiology reports and patient medical records.
2. Surgeon and/or patient surveys.
3. Screening for readmission and/or return to the OR.
4. Other information, such as coded diagnoses, coded procedures, operative reports or antimicrobials ordered. *(24)*

The importance of post-discharge surveillance

It is estimated that a significant proportion of SSIs are detected following patient discharge. This proportion varies across settings and according to different definitions, but it has been estimated to be between 13% to 71% *(25)*. The fact that hospital length of stay has been steadily decreasing over the past decades has probably contributed to shifting the burden from inpatient to outpatient infections. Moreover, implant-associated infections may not become apparent until one year after the procedure. For this reason, many surveillance networks recommend the practice of post-discharge surveillance. There is no known gold standard procedure for post-discharge surveillance and a systematic review identified only 7 reports of studies comparing different surveillance methods *(26)*. Due to variations in data collection and classification, as well as missing information regarding diagnostic criteria, no synthesis of post-discharge surveillance data was possible. The authors concluded that more research is required regarding the measurement of SSI after hospital discharge.

There has been recent controversy regarding the CDC decision to shorten post-discharge surveillance to 90 days instead of one year after certain procedures *(27)*. This change was aimed at simplifying post-discharge surveillance and reducing delayed feedback, but it has not been universally adopted as yet *(28)*. A report compared historical prospective SSI surveillance data from a USA network to the retrospective application of the new CDC definitions *(29)*. The authors found that 9.6% of SSIs detected by the former definition went undetected with the new definitions; 28.8% of these undetected SSIs concerned hip and knee prostheses. The proportion of missed SSIs varied by procedure, but they were high for hip (8.8%) and knee prostheses (25.1%). Another report from the Dutch SSI surveillance network analysed the influence of the duration and method of post-discharge surveillance on SSI rates in selected procedures *(30)*. The proportion of missed SSIs was variable, but they were 6% and 14% for hip and knee prostheses, respectively. More importantly, the study showed that the new CDC method of performing post-discharge surveillance was associated with a higher risk of not detecting a SSI when compared with the former method.

How to report surveillance data

Although most surveillance systems report SSI rates, there has been debate in the literature regarding the best choice of outcome indicator. Some authors argue that the incidence density of in-hospital SSI is a more suitable choice of outcome indicator by taking into account different lengths of hospital stay and different post-discharge surveillance methods *(31)*. This indicator requires recording the date of patient discharge.

In order to adjust for variations in case-mix, it is recommended to present risk-adjusted SSI rates in addition to crude rates *(32)*. The most commonly used method of risk adjustment is the NNIS risk index whose aim is to predict the occurrence of an SSI in a given patient *(33)*. This risk index has been updated and includes procedure-specific factors that improve its predictive power, but it is not widely used *(28, 34)*. Of note, collecting data for the NNIS risk index may be difficult in settings with limited resources where very limited information is reported in patient records. As an example, in a recent systematic review conducted by WHO, only 14 of 231 SSI surveillance studies from developing countries reported using the NNIS risk index (WHO unpublished data).

Some surveillance systems report standardized infection ratios, which is the ratio between the observed and the expected infection rates *(35, 36)*. A ratio higher than 1.0 indicates that more SSIs occurred than were expected, whereas a ratio lower than 1.0 indicates the opposite *(36)*. The simplest manner to calculate the expected number of SSIs is by multiplying the number of operations in each procedure category by the SSI rate and dividing by 100. This accounts for the case-mix and is therefore a risk-adjusted summary measure *(36)*.

Other surveillance systems (UK, Switzerland) use a funnel plot to improve the precision of the estimates of SSI rates, which are dependent on the number of operations performed. SSI rates are plotted against the number of procedures for each hospital and 95% CIs are drawn. In this manner, outliers (hospitals with unusually high rates) can be easily identified *(37)*.

Difficulties associated with surveillance

Active surveillance is a resource- and time-consuming activity. Constraints can be both in financial terms and/or in the availability of trained and dedicated staff. Surveillance data need validation and interpretation by supervising IPC professionals and/or epidemiologists. A major and very common constraint to HAI surveillance

in developing countries is the lack of reliable microbiology support. However, this may have a less significant impact on SSI surveillance as a clinical diagnosis can often be made without microbiological confirmation. Thus, the correct collection of clinical data (preferably electronically) is essential for a successful surveillance system. Another difficulty in low-income countries is the high loss of patient follow-up for post-discharge surveillance due to long distances between surgical care services and the patient's place of residence and/or the patient's financial constraints. Based on some interesting publications *(38)*, WHO has developed an adapted approach to SSI post-discharge surveillance by issuing pre-discharge instructions to the patient to allow him/her to recognize signs of infection and maintain follow-up through telephone calls. Finally, in the absence of effective infection control programmes and societies (local and national), it is difficult to introduce a sustainable surveillance system.

Use of surveillance for benchmarking

The use of HAI surveillance data, including SSIs, has been advocated for benchmarking purposes *(23)*. Benchmarking can be used for several purposes, including for the publication of "league tables" as in the UK and USA *(39)*. In addition, it is also used in the USA as the basis for modifying hospital payments to facilities paid by Medicare *(24)*. There are advantages and disadvantages of benchmarking as there are important pitfalls that should be actively avoided. There is a possibility that surveillance systems with more intensive and sensitive surveillance methods that result in higher SSI rates may be unfairly penalised.

Even in the presence of uniform standardized definitions, several studies have shown that inter-rater agreement for SSI is rather low *(40-42)*. One study evaluated inter-rater agreement by submitting 12 case-vignettes of suspected SSI to IPC physicians and surgeons from 10 European countries *(41)*. It was found that there was poor agreement regarding SSI diagnosis and the type of SSI, with variations between and within countries. An analysis of data submitted from 11 countries to the ECDC HELICS (Hospitals in Europe for Infection Control through Surveillance) network showed that there was a substantial variation not only in terms of case-mix (as measured by the NNIS risk index score), but also in the reporting of SSI (highly variable inter-country proportions of superficial SSI ranging from 20-80%) and the length and intensity of postoperative follow-up *(31)*.

An audit of SSI surveillance methods in England showed that differences in data collection methods and data quality were associated with large differences in SSI rates *(43)*. What is striking is that even in the presence of mandatory surveillance with a clearly defined national protocol, a substantial proportion of responders (15%) used alternative definitions *(43)*.

Conclusions

Ideally, surveillance of SSI should be an integral part of IPC programmes of health care organizations and priorities for public health agencies worldwide. However, caution must be exerted when interpreting SSI data, especially when making comparisons, due to a possible heterogeneity of definitions used, surveillance methods, risk stratification and reporting.

Further studies are needed to determine the most sensitive methods of diagnosing SSI, both for in-patients and as part of PDS, and the most efficient methods of collecting data. It is of the utmost importance to develop and test reliable adapted definitions and surveillance methods for settings with limited resources. The role of automated computerized algorithms needs to be also further evaluated. Similarly, the role of SSI surveillance data for benchmarking purposes needs to be clarified, especially when public reporting is involved.

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3.3 Importance of a clean environment in the operating room and decontamination of medical devices and surgical instruments

3.3.1 Environment

For many years, environmental contamination was considered to be less important than many other factors in contributing to HAI. However, recent evidence shows that a contaminated health care environment plays a significant role in the transmission of microorganisms *(1,2)*. It is essential that the operating room (OR) is thoroughly cleaned on a daily basis. Proper mechanical ventilation is also necessary to prevent surgical wound contamination from unfiltered air drawn into the OR and to dilute and remove microorganisms shed in skin scales *(3)*. Specific guidance on the most appropriate ventilation systems in the OR and an evidence-based recommendation on laminar flow are included in chapter 4.23 of these guidelines.

Environmental cleaning and waste management in the OR

Cleaning consists of the removal of dust, soil and contaminants on environmental surfaces and ensures a hygienic and healthy environment both for patients and staff. The environment should be thoroughly cleaned and general principles of good practice should be taken into consideration (Box 3.3.1). Cleaning requirements for various surfaces are detailed in Table 3.3.1.

At the beginning of each day, all flat surfaces should be wiped with a clean, lint-free moist cloth to remove dust and lint. Between cases, hand-touch surfaces (Figure 3.3.1) and surfaces that may have come in contact with patients' blood or body fluids, should be wiped clean first by using a detergent solution and then disinfected according to hospital policy and allowed to dry.

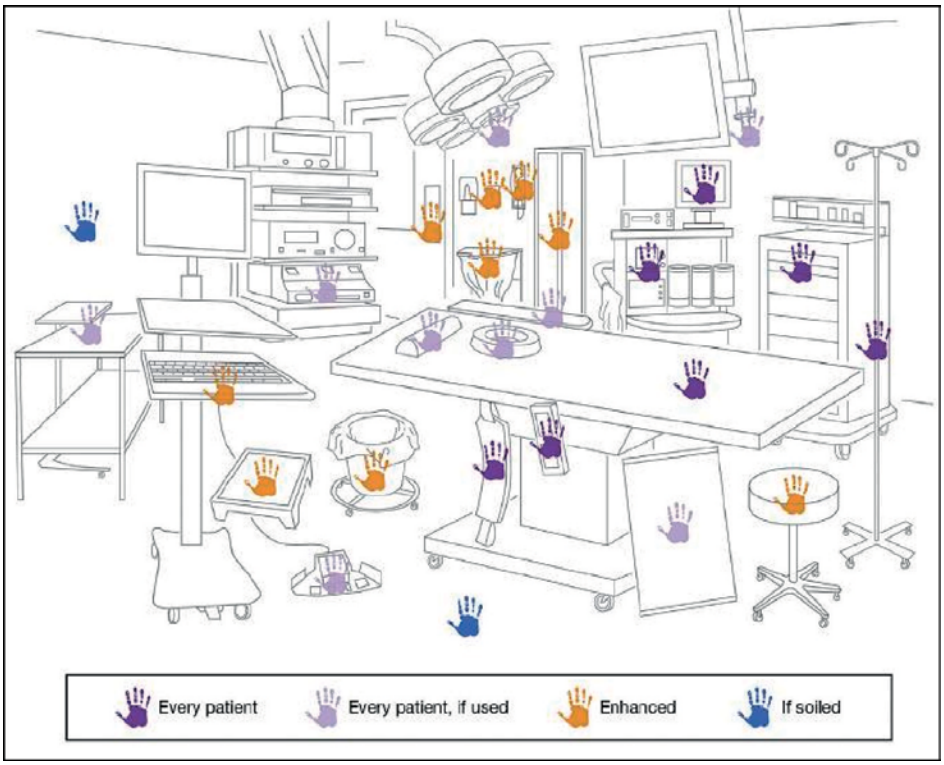
Box 3.3.1. General principles for environmental cleaning

- Cleaning is an essential first step prior to any disinfection process to remove dirt, debris and other materials.
- The use of a neutral detergent solution is essential for effective cleaning. It removes dirt while improving the quality of cleaning by preventing the build-up of biofilms and thus increasing the effectiveness of chemical disinfectants.
- If disinfectants are used, they must be prepared and diluted according to the manufacturer's instructions. Too high and/or too low concentrations reduce the effectiveness of disinfectants. In addition, high concentrations of disinfectant may damage surfaces.
- Cleaning should always start from the least soiled areas (cleanest) first to the most soiled areas (dirtiest) last and from higher levels to lower levels so that debris may fall on the floor and is cleaned last *(4)*.
- Detergent and/or disinfectant solutions must be discarded after each use.
- Avoid cleaning methods that produce mists or aerosols or disperse dust, for example dry sweeping (brooms, etc.), dry mopping, spraying or dusting.
- Routine bacteriological monitoring to assess the effectiveness of environmental cleaning is not required, but may be useful to establish the potential source of an outbreak and/or for educational purposes *(5)*.

Table 3.3.1. **Cleaning requirements for various surface types in ORs**

Surface type	Definition	Cleaning requirement
High hand-touch surface	Any surface with frequent contact with hands.	Requires special attention and more frequent cleaning. *After* thorough cleaning, consider the use of appropriate disinfectants to decontaminate these surfaces.
Minimal touch surface (floors, walls, ceilings, window sills, etc.)	Minimal contact with hands. Not in close contact with the patient or his/her immediate surroundings.	Requires cleaning on a regular basis with *detergent only* or when soiling or spills occur. Also required following patient discharge from the health care setting.
Administrative and office areas	No patient contact.	Require normal domestic cleaning with *detergent only*.
Toilet area	–	Clean toilet areas at least twice daily and as needed.
Medical and other equipment	–	Require cleaning according to written protocols (for example, daily, weekly, after each patient use, etc.). This should include the use of appropriate personal protective equipment, cleaning methods conforming to the type/s of surface and cleaning schedules, etc. Schedules and procedures should be consistent and updated on a regular basis and education and training must be provided to all cleaning staff. Please refer to the manufacturer's instructions for medical equipment to ensure that the item is not damaged by the use of disinfectants.
Surface contaminated with blood and body fluids	Any areas that are visibly contaminated with blood or other potentially infectious materials.	Requires prompt cleaning and disinfection (see below).

Figure 3.3.1. **Example of cleaning frequencies in preoperative and postoperative care areas**



Reproduced with permission from reference *6*.

All spills must be carefully cleaned up and the surface cleaned and disinfected according to hospital policy. Domestic heavy duty gloves should be always worn to undertake this task. Use a single-use plastic apron if contamination of the body is likely. Use of a gown and mask is *not* necessary. If there is a risk of spills with chemicals, the use of a face shield or goggles should be considered, depending on the type of chemical products used for disinfection. All waste from the OR should be collected and removed in closed leak-proof containers; soiled linen should be placed in plastic bags for collection. All reusable medical devices should be sent for reprocessing to the sterile services department or the decontamination unit. The operating table should be cleaned and wiped with a detergent solution, including the mattress and the surface. All surfaces that have come in contact with a patient or a patient's body fluids must be cleaned and disinfected using an appropriate disinfectant solution according to local protocols.

At the end of every day, it is necessary to perform a total cleaning procedure. All areas of the surgical suite, scrub sinks, scrub or utility areas, hallways and equipment should be thoroughly cleaned, regardless of whether they were used or not during the last 24 hours. Soiled linen should be removed in closed leak-proof containers. All contaminated waste containers should be removed and replaced with clean containers. Sharps' containers should be closed and removed when they are three quarters full. All surfaces should be cleaned from top to bottom using a detergent, followed by a disinfectant if necessary, and then allowed to dry. To reduce the microbial contamination of environmental surfaces, such as walls, ceilings and floors, they should be thoroughly cleaned from top to bottom with a detergent and allowed to dry. The routine use of a disinfectant or fumigation of the OR is *not* necessary even after contaminated surgery.

3.3.2 Decontamination of medical devices and surgical instruments

Decontamination is a complex and highly specialized subject. This section provides a brief summary on the decontamination and reprocessing of reusable medical devices and patient care equipment.

In countries with established programmes, decontamination is a speciality in its own right and is an independent, quality-assured and accountable service delivered to health care institutions. The entire process of decontamination is highly regulated and governed by clearly defined guidelines and standards, which are established at both national and international (International Organization for Standardization) levels. This ensures validation of the processes and patient safety *(7-10)*.

In LMICs, decontamination science is in its infancy and few structured decontamination programmes exist, as was evident during the recent Ebola outbreak. In these countries, where the lack of sterile instruments and/or the availability of a properly designed OR and sterile services department have a considerable impact, SSI can be described as surgery-associated infection *(11,12)*. In response to this need, the WHO/Pan American Health Organization (PAHO) have produced a decontamination and reprocessing manual for health care facilities *(13)* to support and guide operational activities to improve standards of care.

In the USA, the term decontamination does not include cleaning and refers to all reprocessing following on thereafter. In the UK and Europe, decontamination relates to the entire process, including cleaning, and this term is used in this chapter (see Table 3.3.2).

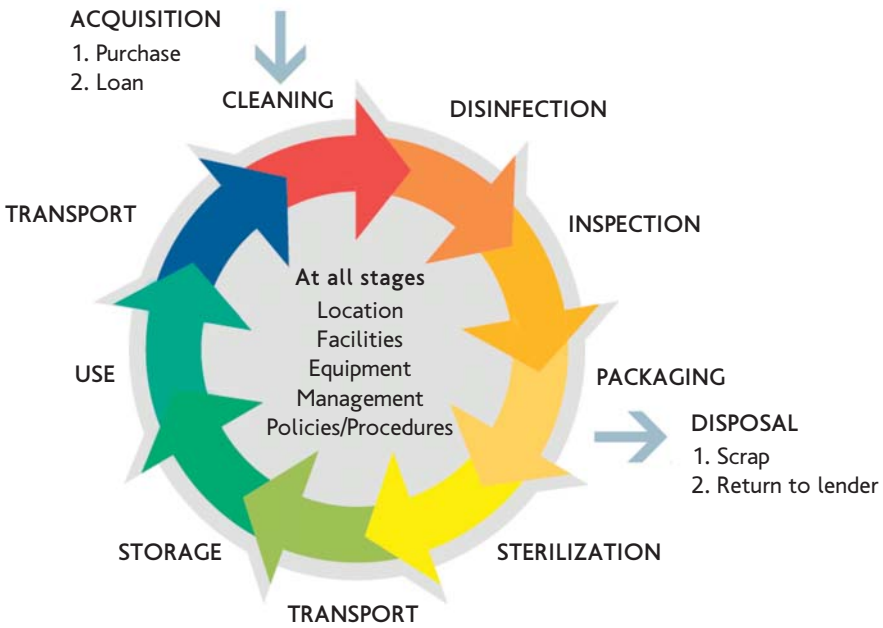
Table 3.3.2. **Glossary of terms**

Decontamination	The use of physical or chemical means to remove, inactivate or destroy pathogenic microorganisms from a surface or item to the point where they are no longer capable of transmitting infectious particles and the surface or item is rendered safe for handling, use or disposal. This term is used to cover cleaning, disinfection and/sterilization. A risk assessment based on the sections below must be conducted to decide the appropriate level of decontamination required.
Cleaning	The removal, usually with detergent and water, of adherent visible soil, blood, protein substances, microorganisms and other debris from the surfaces, crevices, serrations, joints and lumens of instruments, devices and equipment by a manual or mechanical process that prepares the items for safe handling and/or further decontamination. Cleaning is *essential* prior to the use of heat or chemicals.
Disinfection	Either thermal or chemical destruction of pathogenic and other types of microorganisms. Disinfection is less lethal than sterilization because it destroys most recognized pathogenic microorganisms, but not necessarily all microbial forms (for example, bacterial spores). It reduces the number of microorganisms to a level that is not harmful to health or safe to handle.
Sterilization	The complete destruction of all microorganisms including bacterial spores.

Essentials of decontamination

All medical devices that are reprocessed, such as surgical instruments, must undergo rigorous cleaning prior to decontamination and sterilization procedures. Soaking contaminated medical devices prior to cleaning in disinfectants of any kind is not sufficient or recommended *(14)*. Regardless of the type of operative procedure, the decontamination steps in reprocessing surgical instruments and other medical devices are the same. The life cycle of decontamination illustrates *(Figure 3.3.2)* the salient features of decontamination, with each step being as important as the next.

Figure 3.3.2. **The cycle of decontamination of a reusable surgical instrument**



Reproduced with permission from reference *14*.

Risk assessment of contaminated instruments

The risk of transferring microorganisms from instruments and equipment is dependent on the following factors:

- the *presence of microorganisms*, their number, and their virulence;
- the *type of procedure* that is going to be performed (invasive or non-invasive);
- the *body site* where the instrument or equipment will be used.

Risk assessment for the reprocessing of medical devices was best described by Spaulding *(15)* and has since been modified. After thorough cleaning, the decision to disinfect or sterilize is based on whether the device is stable to heat or not. In addition, the body site where the instrument or equipment will be used/have contact with will determine whether cleaning or high level disinfection or sterilization is required. According to the Spaulding classification, medical devices are categorized as critical, semi-critical or non-critical according to the degree of risk of infection transmission (Table 3.3.3).

Table 3.3.3. **Spaulding classification of equipment decontamination *(15)***

Category	Definition	Level of microbicidal action	Method of decontamination	Example of common items/equipment
High (critical)	Medical devices involved with a break in the skin or mucous membrane or entering a sterile body cavity.	Kills all microorganisms.	Sterilization (usually heat if heat-stable or chemical if heat-sensitive).	Surgical instruments, implants, prostheses and devices, urinary catheters, cardiac catheters, needles and syringes, dressing, sutures, delivery sets, dental instruments, rigid bronchoscopes, cystoscopies, etc.
Intermediate (semi-critical)	Medical devices in contact with mucous membranes or non-intact skin.	Kills all microorganisms, except high numbers of bacterial spores.	High-level disinfection by heat or chemicals (under controlled conditions with minimum toxicity for humans).	Respiratory therapy and anaesthetic equipment, flexible endoscopes, vaginal specula, reusable bedpans and urinals/ urine bottles, patient bowls, etc.
Low (non-critical)	Items in contact with intact skin.	Kills vegetative bacteria, fungi and lipid viruses.	Low level disinfection (cleaning).	Blood pressure cuffs, stethoscopes, electrocardiogram leads, etc. Environmental surfaces, including the OR table and other environmental surfaces.

Decontamination facility

The work space

All reprocessing of medical devices must take place in the sterile services department, which should be a separate demarcated department or in a designated decontamination area. Many countries have centralized decontamination areas (central sterile services department) and provide services to the OR, wards and clinical areas. Centralized decontamination processes make the decontamination process cheaper, increase the process safety and enhance its quality. A structured transportation system for clean and used equipment must also be in place. Of note, when the decontamination area space is very limited (usually just one room) and reprocessing is expected to take place in the smallest and least appropriate space with old equipment and overcrowded surfaces, the risk of contamination of clean trays is highly likely. Decontamination of medical devices in clinical areas is not recommended.

Standard operating procedures for decontamination and sterilization

All decontamination units must have written policies and procedures for each stage of the decontamination process and should include:

- formal staff qualification, education/training and competency assessment;
- cleaning;
- high-level disinfection (all processes available);
- preparation and packaging of medical devices;
- sterilizer operating procedures;
- monitoring and documenting of chemical or cycle parameters;
- workplace health and safety protocols specific to the chemical sterilant;
- handling, storage and disposal of the sterilant according to the manufacturer's instructions for use and local regulations;
- use of physical, chemical and/or biological indicators;
- quality systems;
- validation of cleaning, disinfection and sterilization.

Provisions for hand hygiene and personal protective equipment

Equipped hand hygiene stations should be available at the entrance and exit of the sterile services department or decontamination areas. Appropriate personal protective equipment must be provided at each entry point into the sterile services department or decontamination area. Personal protective equipment is designed to be disposable, but it is reused in some low-resource settings. This is acceptable provided that the personal protective equipment, for example, an apron, is cleaned by wiping with a damp cloth and allowed to dry. The apron should then be wiped with 70% alcohol and allowed to dry. A discard bucket for used personal protective equipment must be provided at the exit point, preferably near the wash hand basin.

The workflow

There should be clearly demarcated areas during the reprocessing of medical devices, such as the dirty area where the items are received and cleaned, the inspection-assembly-packaging and the sterilization or high-level disinfection areas, and finally those dedicated to the storage of sterile packs and their transportation. It is recommended that these areas be physically demarcated to avoid cross-contamination from dirty to clean. When this is not possible because of lack of space, obstacles should be placed in order to only permit a unidirectional movement of staff and equipment from dirty to clean without any possibility of overlap.

Transportation of used medical devices

Once devices have been used in the clinical area such as the OR, they should be prepared for transportation to the sterile services department by counting and collecting the devices, rinsing them under cold running water, allowing excess water to drain away, and placing them in a closed container or tray, which will keep them moist until they are removed. These trays (and the accompanying checklist) should be transported in a robust trolley, preferably with closed sides, to the decontamination area. Soaking of medical devices in disinfectant prior to cleaning or during transportation is not recommended as there is a danger of spilling contaminated fluids *(13)* (Box 3.3.2). Used devices should be received, checked and sorted for cleaning in the "dirty" area. Cleaning is normally done either manually or by automated methods.

Box 3.3.2. **Recommendations related to the soaking of instruments in disinfectant prior to cleaning**

Do not soak instruments in desinfectant prior to cleaning

Soaking instruments in 0.5% hypochlorite solution or any other disinfectant before cleaning is not recommended for the following reasons.

- It may damage/corrode the instruments.
- The disinfectant may be inactivated by blood and body fluids, which could become a source of microbial contamination and formation of biofilm.
- Transportation of contaminated items soaked in chemical disinfectant to the decontamination area may pose a risk to health care workers and result in inappropriate handling and accidental damage.
- Soaking may contribute to the development of antimicrobial resistance to disinfectants.

Manual cleaning

Cleaning by hand will require well-trained operators to wear appropriate personal protective equipment (waterproof aprons, domestic heavy duty gloves, face cover to protect mucous membranes and head cover [optional]), dilute the detergent accurately according to the manufacturer's guidelines, open up all the hinges on the devices and clean these by holding the item below the surface of the water (water temperature no more than 50^{o} C) while using a soft nylon brush to remove debris. Visual inspection of the hinges, teeth and serrated edges should be carried out to ensure cleanliness. There is no controlled validation of manual cleaning apart from protein detection, which is expensive. Water or air pressure guns are used to blow through and clear lumen devices.

Automated cleaning

Reprocessing medical devices through a washer disinfector is safer and usually more efficient. Devices are cleaned using water jets, then washed with detergent and warm water, followed by a thermal disinfection cycle (some machines have a drying cycle). The load is substantial, although some washer disinfectors are capable of reprocessing up to 60 trays per hour. Most importantly, each cycle is validated with physical and biological parameters *(13)*.

Inspection, assembly and packaging

Using a magnifying glass and good lighting, clean devices are carefully checked to confirm cleanliness and being fit for purpose and then reassembled. If the medical device is found not to be clean, it is returned for re-cleaning; damaged devices are replaced and the completed tray is wrapped ready for sterilization. Packaging is usually done by double wrapping for surgical trays or sterilization pouches for single items. Packaging material should be robust, permeable to steam, but maintain a fluid barrier, and should protect the sterility of the package prior to use.

Methods of decontamination

Steam sterilization

Most surgical devices are heat-resistant and therefore steam is the preferred sterilizing agent globally. It is inexpensive, efficient, easily maintained and widely available, compared with chemical sterilizers. There are several types of autoclaves/sterilizers. All of them work on the same principle of converting water to steam and holding the steam just below boiling point (saturated) so that there is maximum (latent) heat held in a semi-gaseous state. The steam makes contact with the load in the chamber and releases the heat, thus resulting in sterilization. The time that the steam is in contact with the devices is crucial and is known as the "holding time".

Types of autoclaves

- The *pre-vacuum* steam sterilizer is the most widely-used sterilizer and is suitable for the sterilization of wrapped clean instruments, gowns, drapes, towelling and other dry materials required for surgery. Air removal is part of the cycle and thus it is suitable for medical devices with lumens and porous loads.
- *Downward (gravity) displacement* sterilizers are designed for sterilizing bio-hazardous waste, solutions and instruments. They are now obsolete and have many drawbacks as sterility cannot be assured and they are less reliable than pre-vacuum sterilizers. They are not the best option for wrapped packs or porous materials. Air removal is by gravity displacement and they

are also not suitable for medical devices with lumens.

- *Non-vacuum steam sterilizers*: self-contained (benchtop) sterilizers are sometimes used, but they are only suitable for relatively few or simple items. Table top sterilizers may be used in outpatient departments, dental surgeries and some family planning clinics, but they should not be considered for use in ORs and they are also not suitable for medical devices with lumens.

Sterilization by chemical (low temperature) automatic methods

Chemical gas (low temperature) sterilization is used to sterilize heat- and moisture-sensitive devices. It should be noted that these methods are expensive to install and to run. The mechanics are complex and well-trained staff should be employed if this method is used. Manual chemical sterilization is not recommended because the process cannot be controlled and may lead to occupational health issues.

Use of chemicals, such as chlorine, ortho-phthalaldehyde or glutaraldehyde, is not recommended for sterilization. Although they have sporicidal activity, it is difficult to control the process and there is a risk of contamination during the rinse to removal residual chemicals before patient use. In addition, items cannot be packed and stored, but must be used immediately after rinsing.

Sterilization with gaseous chemical methods should be carried out in chambers with automated cycles that provide safety for the user and guarantee the process. Medical device compatibility will vary with each low temperature sterilization method. Low temperature (gas) sterilization can be achieved using a number of different chemicals for example, ethylene oxide, hydrogen peroxide gas/plasma, ozone, low temperature and steam formaldehyde.

Immediate use sterilization system or "flash" sterilization

An Immediate use sterilization sysstem or "flash" sterilization is a common term that describes the fast sterilization of non-porous and/or non-cannulated surgical instruments in an unwrapped condition in downward displacement steam instrument sterilizers located close to the point where the instruments will be used immediately.

In the past, "flash"sterilization was the main means of providing sterile instruments for surgery. Special high-speed sterilizers are usually located in the OR in order to process unwrapped instruments and instruments for urgent use. For example, the only available hand piece is dropped on the floor in the middle of the procedure and this single instrument needs to be sterilized in a rush. These sterilizers operate at 134° C for 3-10 minutes. "Flash" sterilization delivers the instruments wet and very hot into the OR environment. Of note, "flash" sterilization should never replace the lack of material or instruments for a programmed surgical procedure.

If an immediate use sterilization system must be used, it should be used only after all of the following conditions have been met:

- Work practices should ensure proper cleaning, inspection and arrangement of instruments before sterilization.
- The physical layout of the area ensures direct delivery of sterilized items to the point of use.
- Procedures are developed, followed and audited to ensure aseptic handling and staff safety during transfer of the sterilized items from the sterilizer to the point of use.

Validation

In sterile services, it is the process and not the procedure, which is usually tested and validated to ensure high quality assurance and the reliability of the process. There are both simple and complex methods to check that the surgical package has been through the correct decontamination process. Validation of the sterilization process has to take place at every step and can be quite confusing for the sterile services department staff. For details, please refer to the WHO/PAHO decontamination and reprocessing manual for health care facilities *(13)*.

Loan instruments

It is common practice for expensive medical devices used for operations, such as instruments for orthopaedics, neurology or implants and transplants, to be rented ("loaned") from supply companies and brought to the OR. Often the companies deliver the sets directly to the OR and recuperate them directly, thus bypassing the sterile services department. These medical devices are used between several hospitals and the greatest concern is that often there is no control of correct reprocessing of these devices. In LMICs, many

companies supplying loan instruments do not have facilities to reprocess medical devices and they are often moved from one health care facility to another without adequate reprocessing. In these circumstances, there is often very little documentation about where or how the medical devices have been used. In a very comprehensive document published by the UK Institute of Decontamination Sciences, which outlines the relationship between the OR, the supply company and the sterile services department, it is clear that the ultimate responsibility for patient safety and quality of sterilization lies with the sterile services department in the health care facility and not the supply company *(14)*. Therefore, it is vital that all medical devices destined for the OR must transit via the sterile services department of that health care facility and are validated as safe to use.

Storage of sterile packs

After sterilization, the packs are removed and allowed to cool. If there is an adequate supply of surgical trays and equipment, appropriate storage in the sterile services department has to be provided before the packs are dispatched to the OR. The proper storage of sterile instruments and equipment is essential to ensure that the product maintains its level of sterilization or disinfection. The storage area for sterile packs has specific requirements.

- Store in a clean, dry environment (that is, far from moisture sources) that is protected from any damage. It is recommended that the storage containers should not be made of absorbent material, such as wood.
- The area must be bright, light and airy with good air circulation. The temperature must be moderate without wide fluctuations during the day.
- The storage area should have an adequate level of lighting and the walls should be smooth and easy to clean.
- Access to the area should be restricted.
- The packs should be placed on open racks rather than closed shelves in a single layer to prevent moisture from accumulating between the packs.
- The labels must be visible and clear.
- The pack inspection register should be clearly visible. The racks must be at least 10 cm off the ground and from the ceiling.
- Before use, packages should be inspected in order to verify that they meet the requirements of a sterile product.

User sterility check

It is the duty of the sterile services manager or the person in charge of the sterile services department to ensure that a medical device does not leave the unit unless it is completely safe to use on a human. When there is a lack of equipment in the OR, it is frequent that medical devices are taken for use in the knowledge that the reprocessing cycle has not been completed. However, it is also the responsibility of each health care worker not to allow the use of an unsafe device on a patient. Therefore, all staff should be trained in the checks to be made before a medical device may be used.

Use of sterile instruments in the operating room

1. Role of the nurse who lays out the sterile surgical instruments on the operating trolley in the operating room

The nurse who prepares the operating trolley should check that:

- the preparation area is quiet, clean and undisturbed;
- the packs are not wet (no moisture);
- the packaging of the pack is intact, not torn or opened;
- there are no water marks from condensation indicating non-sterility;
- the chemical indicator strip is present and has a uniform change of colour;
- the internal indicator shows sterilization;
- the devices are clean;
- the surfaces of the devices are intact;
- the devices are fit for use.

2. Role of the scrub nurse

The scrub nurse should check to ensure that:

- the devices are ready and fit for use;
- the devices are not dirty or broken;
- there are an adequate number of devices for the procedure (to avoid opening several packs or resorting to an immediate use sterilization system);
- the pack indicators are placed in the patient notes;
- the surgeon is aware of any shortage of equipment or devices.

3. Role of the surgeon and surgical team

The surgeon should ensure that before making an incision:

- the operating field is sterile and clearly defined;
- the devices are visibly clean;
- the devices are fit for purpose;
- all the necessary equipment is available;
- there is no unnecessary delay on the operating table because of a lack of instruments;
- the pack indicators are in the patient notes and are satisfactory.

On completion of the surgical procedure, OR staff should:

- check that all instruments are present before returning to the sterile services department;
- rinse the instruments as per the standard operating protocol;
- ensure that items are securely contained in a leak-proof container before transportation to the sterile services department;
- inform the sterile services department of any issues with the surgical instruments, for example, a broken device.

Decontamination of endoscopes

An increasing number of diagnostic and therapeutic procedures are now being carried out using rigid or flexible endoscopes *(16)*. Effective decontamination will protect the patient from infection, ensure the quality of diagnostic procedures and samples and prolong the life of the equipment *(17)* (Table 3.3.4). The source of infection may be due to:

- the previous patient or inadequate decontamination of the endoscope before reuse;
- endogenous skin, bowel or mucosal flora;
- contaminated lubricants, dyes, irrigation fluid or rinse water;
- inadequate decontamination of the reprocessing equipment.

Staff should be aware of the complexities of the endoscopes they are processing to ensure that the construction of the endoscope is fully understood. Failures in decontamination, particularly for flexible endoscopes, have been reported due to failure to access all channels of the endoscope. Irrespective of the method of disinfection or sterilization, cleaning is an essential stage in the decontamination procedure and the manufacturers' instructions should be followed at all times. An endorsement of compatibility of the endoscope with the decontamination process is essential.

Rigid endoscopes are relatively easy to clean, disinfect and sterilize as they do not have the sophistication of functionality, construction and channel configuration and compatibility issues that exist with flexible endoscopes. Where possible, all reprocessing of autoclavable endoscopes and their accessories should take place in a sterile services department or dedicated decontamination unit as the process controls and validation are already in place. It should never take place in the clinical area *(17)*.

Flexible endoscopes are heat-sensitive and require chemical disinfection (or low temperature disinfection) *(18)*. Decontamination of flexible endoscopes should take place in a dedicated well-ventilated room (up to 12 air changes per hour) away from the procedure room. There should be adequate ventilation to remove potentially harmful disinfectant vapour. The room should be equipped with a sink with sufficient capacity to accommodate the largest endoscopes and a dedicated wash hand basin equipped with soap and disposable paper towels.

There should be a workflow direction within the room from dirty to clean to avoid the possibility of recontamination of decontaminated endoscopes from those just used on a patient. Systems should be in place to indicate which endoscopes are ready for patient use and recorded either manually or by an automated endoscope reprocessor. Modern units will have a 2-room system with pass-through washer disinfectors to separate the clean and dirty areas. Storage of endoscopes should be organized to avoid any recontamination of processed endoscopes. There should be sufficient storage for the consumables used during the decontamination procedure, for example, personal protective equipment, chemicals, cleaning brushes and sufficient capacity for waste disposal.

Table 3.3.4. **Types of endoscopic procedures**

Types of endoscopes	Rigid endoscope example	Flexible endoscope example	Level of decontamination
Invasive: passed into normally sterile body cavities or introduced into the body through a break in the skin or mucous membrane	Arthroscope Laparoscope Cystoscope	Nephroscope Angioscope Choledochoscope	Sterilization by steam or a low temperature method, for example, gas plasma.
Non-invasive: in contact with intact mucous membrane, but does not enter sterile cavities	Bronchoscope	Gastroscope Colonoscope Bronchoscope	High-level disinfection, for example, immersion in glutaraldehyde, peracetic acid, chlorine dioxide.

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4. EVIDENCE-BASED RECOMMENDATIONS ON MEASURES FOR THE PREVENTION OF SURGICAL SITE INFECTION

PREOPERATIVE MEASURES

4.1 Preoperative bathing

Recommendations

It is good clinical practice for patients to bathe or shower prior to surgery.

The panel suggests that either a plain or antimicrobial soap may be used for this purpose.
(Conditional recommendation, moderate quality of evidence)

The panel decided not to formulate a recommendation on the use of chlorhexidine gluconate (CHG)-impregnated cloths for the purpose of reducing SSI due to the limited and very low quality evidence.

Rationale for the recommendation

- The GDG considers it good clinical practice to bathe or shower before surgery to ensure that the skin is as clean as possible and to reduce the bacterial load, especially at the site of incision. Moderate quality evidence shows that preoperative bathing with antimicrobial soap containing CHG has neither benefit nor harm compared to plain soap in reducing the SSI rate. As no study was available using antimicrobial agents other than CHG, the GDG unanimously agreed that either plain or antimicrobial soap may be used.
- Evaluation of the evidence from 3 observational studies showed that preoperative bathing with 2% CHG-impregnated cloths may have some benefit in reducing the SSI rate when compared to bathing with CHG soap or no preoperative bathing. However, in 2 of these studies, the comparison group was inadequate as it included patients who did not comply with instructions to use the cloths preoperatively. This limited and very low quality evidence was considered as insufficient to make any recommendation regarding the use of CHG cloths. All GDG members agreed not to formulate a recommendation on this topic, apart from one member who would have preferred to have a recommendation discouraging the use of CHG-impregnated cloths due to concerns about the waste of resources if these products are purchased, especially in developing countries.

Remarks

- Although no study including paediatric patients was retrieved, the GDG believes that the good practice statement on the importance of patient bathing applies also to paediatric patients. However, if performed with antimicrobial soap, the manufacturer's instructions should be followed regarding the suitability for this age category.
- The GDG identified possible harm associated with the use of CHG-containing solutions, although it was stressed that this is a rare occurrence. Two studies *(1, 2)* found that CHG solutions may cause skin irritation, delayed reactions, such as contact dermatitis and photosensitivity, and hypersensitivity reactions in very rare cases, such as anaphylactic shock. Some of these potential adverse events may be induced also by ingredients of regular soap, such as fragrances. A concern of the GDG was the possible development of reduced susceptibility to CHG, particularly when using CHG-impregnated cloths *(3)*.
- The GDG also expressed concern about the cost of CHG-impregnated cloths, in particular in settings with limited resources where other interventions may have a higher priority.

Background

Preoperative whole-body bathing or showering is considered good clinical practice to make the skin as clean as possible prior to surgery in order to reduce the bacterial load, especially at the site of incision. This is generally done with an antimicrobial soap (usually CHG 4% combined with a detergent or in a triclosan preparation) in settings where this is available and affordable *(4, 5)*.

Preoperative showering with antiseptic agents is a well-accepted procedure for reducing skin microflora *(6-8)*, but it is less clear whether this procedure leads to a lower incidence of SSI *(7, 8)*. Although rare, patient hypersensitivity and allergic reactions to CHG can occur *(1)*.

When considering the available evidence, the most relevant question is whether preoperative bathing or showering with an antimicrobial soap is more effective than plain soap to reduce SSI. The GDG also considered it relevant to investigate whether using CHG-impregnated cloths rather than bathing with CHG soap is more effective.

Several organizations have issued recommendations regarding preoperative bathing (Table 4.1.1). Most recommend bathing with soap the day of the operation or the day before. Only the US Institute of Healthcare Improvement bundle for hip and knee arthroplasty recommends CHG soap for preoperative bathing. Others state that the use of an antimicrobial soap instead of plain soap is an unresolved issue.

Table 4.1.1. **Recommendations on preoperative bathing according to available guidelines**

Guidelines (year issued)	Recommendations on preoperative bathing and related time of administration
SHEA/IDSA practice recommendation (2014) *(9)*	Unresolved issue.
NICE (2008 and 2013 update) *(10, 11)*	Bathing is recommended to reduce the microbial load, but not necessarily SSI. Soap should be used. The use of antiseptic soap to prevent SSI is inconclusive.
Health Protection Scotland bundle (2013) *(12)*	Ensure that the patient has showered (or bathed/washed if unable to shower) using plain soap on day of or day before surgery.
The Royal College of Physicians of Ireland (2012) *(13)*	Bathing with soap is recommended on the day of or before the procedure.
US Institute of Healthcare Improvement bundle for hip and knee arthroplasty (2012) *(14)*	Preoperative bathing with CHG soap is recommended for at least 3 days before surgery.
UK High impact intervention bundle (2011) *(15)*	Patient showering (or bathing/washing if unable to shower) is recommended preoperatively using soap.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; UK: United Kingdom.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the effectiveness of preoperative bathing or showering with antimicrobial soap (including CHG-impregnated cloths) compared to plain soap and to determine if the former should be recommended for surgical patients to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 2) was to evaluate whether preoperative bathing using an antimicrobial soap is more effective in reducing the risk of SSI than bathing with plain soap. The review evaluated also whether preoperative bathing with CHG-impregnated cloths is more effective than using an antimicrobial soap. The target population included patients of all ages undergoing a surgical procedure. The primary outcome was occurrence of SSI and SSI-attributable mortality.

A total of 9 studies (7 RCTs and 2 observational studies) including a total of 17 087 adult patients *(2, 16-23)* investigated preoperative bathing or showering with an antimicrobial soap compared to plain soap.

There is a moderate quality of evidence that bathing with CHG soap does not significantly reduce SSI rates compared to bathing with plain soap (OR: 0.92; 95% CI: 0.80–1.04).

Three observational studies *(24-26)* examined the effectiveness of bathing with CHG-impregnated cloths on SSI rates. One prospective cohort study *(24)* compared bathing with CHG 2% cloths vs. CHG 4% antiseptic soap. Two other prospective studies *(25, 26)* compared bathing twice preoperatively with CHG 2%-impregnated cloths to no preoperative bathing among orthopaedic surgery patients. In the latter studies, the comparison group was inadequate as it comprised patients who did not comply with instructions to use the cloths preoperatively (and therefore most likely did not bathe). No RCTs meeting the specified inclusion criteria were identified.

There is only very low quality evidence that preoperative bathing with CHG-impregnated cloths may reduce SSI rates when compared to either bathing with CHG soap or no bathing. The body of retrieved evidence focused on adult patients and no studies were available in the paediatric population. No studies reported SSI-attributable mortality rates.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG acknowledged that most people with access to water would bathe prior to surgery. It was highlighted that patients wish to be informed of best clinical practice and they will tend to carry out the procedures that they were told to do by the professional health care worker. Some GDG members highlighted that patients may value CHG-impregnated cloths if access to clean water is limited. However, others emphasized that the evidence on the use of CHG-impregnated cloths is very low quality and their use could contribute to CHG resistance.

Resource use

The GDG pointed out that the availability of and access to clean water can be a problem in rural areas in LMICs and preoperative bathing may be neglected. In addition, antimicrobial soap will place an additional financial burden on the health care facility and/or patients in many of these countries. Similarly, CHG-impregnated cloths will pose an additional important financial burden and availability might be very limited in LMICs. Plain soap is more widely available and cheaper than antimicrobial soap.

A cost-effectiveness study *(16)* found that preoperative whole-body washing with a CHG solution is not a cost-effective intervention for reducing SSI. However, it is important to note that this study predominantly consisted of clean surgical procedures for which the risk of SSI is low. Findings from 2 additional studies suggested that the use of CHG-impregnated cloths could lead to reducing health care costs, mainly by decreasing the incidence of SSI *(27, 28)*.

Research gaps

GDG members highlighted that the available evidence compared only CHG as the antiseptic agent to bathing with plain soap. Further research is needed to compare different antiseptic agents to each other and to plain soap for preoperative bathing. Well-designed RCTs and cost-effectiveness analyses are also needed to examine the timing and duration of bathing and its importance in the context of different types of surgery and wound classes, especially in LMICs. In addition, microbiological studies of contamination levels could be of interest. Finally, well-designed RCTs are needed to produce better quality results on

the effectiveness of CHG-impregnated cloths to reduce SSI and their cost implications, in particular in low-resource settings. The long-term impact of the use of CHG on the possible induction of CHG resistance should also be studied, particularly CHG-impregnated cloths. Further research is also needed to clarify the effect of soap or antiseptics on the skin microbiome.

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4.2 Decolonization with mupirocin ointment with or without chlorhexidine gluconate body wash for the prevention of *Staphylococcus aureus* infection in nasal carriers undergoing surgery

Recommendations

1. **The panel recommends that patients undergoing cardiothoracic and orthopaedic surgery with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash.**
   (Strong recommendation, moderate quality of evidence)

2. **The panel suggests considering to treat also patients with known nasal carriage of *S. aureus* undergoing other types of surgery with perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash.**
   (Conditional recommendation, moderate quality of evidence)

Rationale for the recommendation

- Moderate quality evidence shows that the use of mupirocin 2% ointment with or without a combination of CHG body wash in surgical patients with *S. aureus* nasal carriage has significant benefit when compared to placebo/no treatment in reducing the *S. aureus* SSI rate, as well as the overall *S. aureus* HAI rate.
- The GDG carefully considered this evidence and the additional subgroup analysis conducted by the systematic review team. The GDG concluded that the evidence is most solid for the cardiothoracic and orthopaedic patient population and that recommending the intervention with the same strength for all surgical patients would pose cost and feasibility constraints, including diagnostic implications to identify carriers among all surgical patients.
- As a result, the GDG agreed to recommend that cardiothoracic and orthopaedic surgical patients with known nasal carriage of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. The strength of this recommendation was considered to be strong. Although the risk and consequences of postoperative *S. aureus* infection are more relevant in cardiothoracic and orthopaedic surgery, the GDG noted that the data from the meta-analysis and meta-regression show that patients with known *S. aureus* nasal carriage undergoing other types of surgery might also benefit from perioperative intranasal applications of mupirocin 2% ointment with or without a combination of CHG body wash. The strength of this recommendation was considered to be conditional and the GDG proposed to use the terminology "The panel suggests considering..." to highlight the need for careful local evaluation about whether and how to apply this recommendation, in particular regarding feasibility of carriers' identification in a broader surgical patient population and cost effectiveness.
- In patients undergoing other types of surgery to be targeted with this intervention, it is advisable to take other factors into account, such as the local rates of *S. aureus* and methicillin-resistant *S. aureus* (MRSA) and patient-related factors. Among the latter, the most important are past *S. aureus* infection, known carrier status of community-acquired MRSA, and patients colonized by *S. aureus* in sites other than the nose.
- The GDG emphasized that the recommendation to use mupirocin with or without a combination of CHG body wash is derived from the available evidence as CHG 4% soap was used for full body wash in combination with mupirocin nasal ointment in 2 of the included 6 studies. Moreover, in one study CHG 2% soap body wash was used as standard preoperative clinical practice.
- The GDG highlighted that the studies identified as the evidence base for these recommendations did not assess screening for *S. aureus* as part of the intervention. Consequently, no recommendation can be formulated on the role of screening in this context or the surgical patient population that should undergo screening for *S. aureus* carriage. The GDG noted also that standard operating procedures should be agreed upon according to national recommendations and the decision based

on the local epidemiology, the patient's risk factors for *S. aureus* acquisition, the microbiological capacity and financial resources available at the health care facility. The GDG emphasized that this recommendation applies to facilities where screening for *S. aureus* is feasible. The GDG strongly believes also that decolonization with mupirocin ointment with or without a combination of CHG body wash should be performed on known *S. aureus* carriers only in order to avoid unnecessary treatment and the spread of resistance.

Remarks

- Included studies were performed in adult patients undergoing cardiac, orthopaedic, general, gynaecological, neurological, Mohs micrographic, vascular and gastrointestinal surgery. Based on this evidence, this recommendation is not applicable to paediatric patients.
- The available evidence focused on the nasal carriage of *S. aureus*. Other body sites of frequent and/or known colonization could be considered for decolonization. However, due to the lack of substantial evidence, no recommendation can be made in this direction.
- Studies were performed mostly in high-income countries.
- Mupirocin nasal ointment at a concentration of 2% was used in all included studies. In 2 of the included 6 studies *(1, 2)* CHG 4% soap was used for full body wash in combination with the mupirocin nasal ointment. In one study *(3)* CHG 2% soap body wash was used as standard preoperative clinical practice.
- The application of mupirocin varied from 2 times a day for 5 days *(2, 4, 5)* to 7 days *(3)* before surgery or from the day of hospital admission until the day of surgery *(6)*. Daily administration was continued after surgery for a total of 5 days only in one trial *(1)*. In all studies, at least one administration took place in the immediate preoperative period. Given the variability of treatment protocols, the GDG was unable to give specific instructions about the frequency and duration of mupirocin administration.
- The GDG identified AMR as an important possible harm associated with the use of mupirocin *(7)*. It was emphasized that an approach to treat all patients, regardless of their carriage status, instead of carriers only increases the likelihood of resistance to mupirocin *(8, 9)*. Consequently, monitoring of AMR is recommended in facilities where mupirocin is used *(10-12)*. The available evidence *(3, 5, 6)* and additional studies *(13, 14)* showed no trend towards an increasing prevalence of mupirocin resistance following its short-term use in surgical patients. However, there is evidence that the increased short-term use of mupirocin leads to an increase of resistance to mupirocin and other antibiotics *(15)*. Moreover, in settings known to have a high prevalence of mupirocin resistance, the recommendation to use perioperative intranasal mupirocin ointment may not apply.
- Potential allergic reactions to mupirocin should be accounted for.
- One recent study *(16)* showed a reduction in mortality at one year in patients receiving mupirocin compared to patients receiving placebo. The present review of the evidence based on 3 studies *(1, 3, 5)* did not find an effect on short-term mortality (up to 8 weeks follow-up).
- The GDG identified a possible harm associated with the use of CHG-containing solutions, although it was stressed that this is a rare occurrence. Two studies *(17, 18)* found that CHG solutions may cause skin irritation, delayed reactions (such as contact dermatitis and photosensitivity) and hypersensitivity reactions in very rare cases, such as anaphylactic shock. Some of these potential adverse events may be induced also by ingredients of regular soap, such as fragrances. A concern of the GDG was the possible development of reduced susceptibility to CHG *(19)*.

Background

S. aureus is the leading health care-associated pathogen in hospitals worldwide. These infections are associated with substantial morbidity and mortality and this trend is increasing due to the widespread dissemination of MRSA *(20)*.

Staphylococcal infections occur regularly in hospitalized patients and can have severe consequences, including postoperative wound infections, nosocomial pneumonia and catheter-related bacteraemia *(21-25)*. A recent study of over 7 million hospital admissions in the USA estimated that the annual national impact was 2.7 million additional days in hospital, US$ 9.5 billion excess costs and at least 12 000 in-patient deaths *(26)*. Given the high burden of these infections for the patient and the health system, effective prevention strategies are essential.

Traditionally, the control of *S. aureus* has been focused on preventing cross-transmission between patients *(27)*. However, it has been shown repeatedly that a large proportion (approximately 80% after surgery) of HAI due to *S. aureus* originate from the patients' own flora *(23, 28, 29)*. Nasal carriage of *S. aureus* is now considered a well-defined risk factor for subsequent infection in various patient groups *(22, 30)*.

Mupirocin nasal ointment (usually applied to the nose 2 times daily for 5 days) is an effective, safe and relatively cheap treatment for the eradication of carriage. Mupirocin can be used for the eradication of both methicillin-sensitive *S. aureus* (MSSA) and MRSA, although mupirocin resistance has been reported *(31)*. Several interventional studies have attempted to reduce infection rates by eradicating nasal carriage *(22)*. Recently, rapid molecular diagnostics with the capacity to detect *S. aureus* nasal carriage within hours rather than days have become available *(32, 33)*, thus enabling the prompt pre-emptive treatment of carriers when appropriate.

The SSI prevention guideline published by SHEA/IDSA) *(34)* recommends screening for *S. aureus* and decolonizing surgical patients for high-risk procedures. Some SSI prevention bundles, such as the one issued by the US-based Institute for Healthcare Improvement *(35)* recommend to screen for *S. aureus* and decolonize prior to surgery, if positive (Table 4.2.1). However, these recommendations are not based upon systematic reviews of the literature and meta-analysis or a rigorous evaluation of the quality of the available evidence.

Table 4.2.1. **Recommendations on screening and decolonization of *S. aureus* according to available guidelines and bundles**

Guidelines (year issued)	Recommendations on screening and decolonizations of S. aureus
SHEA/IDSA (2014) *(34)*	Screen for *S. aureus* (**MSSA and MRSA**) and decolonize surgical patients for high-risk procedures, including some orthopaedic and cardiothoracic procedures.
NICE (2008) *(36)*	Do not use nasal decontamination with topical antimicrobial agents aimed at eliminating *S. aureus* routinely to reduce the risk of SSI.
Institute for Healthcare Improvement: hip and knee arthroplasty (2012) *(35)*	Screen for *S. aureus*. If positive, decolonize 3 days before surgery with nasal mupirocin and CHG soap for 5 days in total for both **MSSA and MRSA**.
Health Protection Scotland bundle (2013) *(37)*	Screen for **MRSA** based on clinical risk assessment.
UK High impact intervention bundle (2011) *(38)*	Screen for **MRSA**: follow local guideline. Screen and decolonize prior to surgery, if found positive.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; SSI: surgical site infection; MSSA: methicillin-susceptible *S. aureus*; MRSA: methicillin-resistant *S. aureus*; CHG: chlorhexidine gluconate.

Following the in-depth analysis of the sources and strength of evidence in available guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on the effectiveness of decolonization with mupirocin nasal ointment for the reduction of the *S. aureus* infection rate, including SSI, in patients undergoing surgery with known *S. aureus* nasal carriage.

Summary of the evidence

The purpose of the evidence review (web Appendix 3) was to determine whether decolonization with intranasal mupirocin ointment with or without a combination with CHG soap body wash reduces *S. aureus* overall infection rates, including SSI. The target population included patients of all ages with known *S. aureus* nasal carriage undergoing a surgical procedure. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.

Six RCTs *(1-6)* including 2385 patients comparing mupirocin nasal ointment combined with or without CHG soap body wash to placebo or no treatment were identified. Five trials described surgical patients (cardiac, orthopaedic, general, gynaecological, neurological or Mohs micrographic surgery) and one *(1)* included both surgical (cardiac, vascular, orthopaedic, gastrointestinal or general surgery) and non-surgical patients (internal medicine). According to the selected studies, the following comparisons were evaluated:

1. mupirocin vs. placebo/no treatment with the following outcomes:
    a. all HAI caused by *S. aureus*;
    b. health care-associated SSI caused by *S. aureus*.

Overall, a moderate quality of evidence shows that the use of mupirocin 2% ointment combined with or without CHG soap body wash has a significant benefit for the reduction of the SSI rate caused by *S. aureus* in surgical patients with nasal carriage when compared to placebo/no treatment (OR: 0.46; 95% CI: 0.31–0.69), including the overall health care-associated *S. aureus* infection rate (OR: 0.48; 95% CI: 0.32–0.71). It should be noted that most studies included patients undergoing cardiothoracic and orthopaedic surgery, but 2 trials included also other types of procedures. Indeed, in meta-regression analysis, there was no evidence to suggest that the effect on the *S. aureus* infection rate differed between different types of surgery (*P*=0.986).

The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that patients with nasal *S. aureus* colonization would prefer to be treated with mupirocin ointment nasally with or without a combination of CHG body wash in order to reduce the risk of SSI. Conversely, patients could be concerned about the emergence of AMR, as well as the possible development of reduced susceptibility to antiseptics, such as CHG.

Resource use

The use of mupirocin, including screening for *S. aureus* ("screen-and-treat" strategy), was shown to be cost-effective in 2 studies *(1, 39)*. On average, hospital costs were € 1911 lower per patient treated with mupirocin and CHG soap (n=210) than the costs of care in the placebo arm (n=205; € 8602 vs. € 10 513; *P*=0.01). A subgroup analysis showed that cardiothoracic patients with *S. aureus* nasal carriage treated with mupirocin and CHG cost € 2841 less (n=280; € 9628 vs. €12 469; *P*=0.006) and orthopaedic patients € 955 less than non-treated patients (n=135; € 6097 vs. € 7052; *P*=0.05). Furthermore, based on a nasal *S. aureus* carriage rate of 20%, the authors estimated a saving of approximately € 400 000 per 1000 surgical patients *(39)*.

The GDG highlighted that the access to and availability of nasal mupirocin ointment could be limited for LMICs and pose a financial burden, including also to patients. In addition, antimicrobial soap will pose an additional financial burden to the health care facility and/or patients in many LMICs. The same applies to the technical laboratory capacity and financial burden for the screening process.

Research gaps

Most GDG members emphasized that no further studies are needed on mupirocin. However, given the variability in the timing and duration of mupirocin administration and bathing with CHG across the trials included in this review, additional

well-designed RCTs are needed to clarify this issue in surgical patients. GDG members highlighted that other agents for the decolonization of nasal *S. aureus* carriers scheduled for surgery should be investigated in well-designed double-blind RCTs. It was underlined that the development and implementation of an inexpensive screening process for *S. aureus* is highly desirable for LMICs. In addition, there is a need for effectiveness and cost-effectiveness studies in these settings.

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4.3 Screening for extended-spectrum beta-lactamase colonization and the impact on surgical antibiotic prophylaxis

Recommendation

The panel decided not to formulate a recommendation due to the lack of evidence.

Rationale for the recommendation

The literature search did not identify any relevant studies comparing the tailored modification of SAP for the prevention of SSI in areas with a high prevalence of extended spectrum beta-lactamase (ESBL)-producing Enterobacteriacae (including patients with rectal colonization of ESBL) to no modification of standard antibiotic prophylaxis. Furthermore, no studies comparing routine screening for ESBL (irrespective of ESBL prevalence prior to surgery) with no screening that could inform a recommendation for this question were identified.

Remarks

- The prevalence of ESBL-producing Enterobacteriacae was considered to be high when demonstrating a prevalence of >10% on the total number of all samples submitted to the laboratory for investigation, including both infection and/or colonization.
- The GDG believes that routine screening for ESBL prior to surgery might increase the widespread use of broad-spectrum antibiotics (particularly carbapenems) pre-surgery in ESBL-colonized patients. This practice may be harmful as it is likely to further increase the emergence of resistance in gram-negative bacteria, especially carbapenem-resistant Enterobacteriacae. The WHO global surveillance report on AMR has already highlighted concerns about the emergence of antibiotic-resistant bacteria due to the inappropriate use of antimicrobial agents. Importantly, the options for the treatment of infections are now extremely limited due to the lack of development of a new class of antimicrobial agents over the past decades *(1)*.

Background

In recent years, the prevalence of patients colonized with ESBL-producing bacteria has increased globally both in health care facilities and in the community. Similar to most gram-negative bacteria, ESBL resides in the gastrointestinal tract and decolonization is very difficult to achieve. The most frequent infections caused by ESBL concern the urinary tract and, to a lesser extent, bloodstream infections. Current SSI prevention guidelines do not address the screening, decolonization and modification of SAP in patients who are colonized with these organisms prior to surgery or the effect of these procedures for the prevention of SSI. The GDG decided to conduct a systematic review to assess the effectiveness of these measures.

Summary of the evidence

The purpose of the evidence review (web Appendix 4) was to evaluate whether the tailored modification of SAP in areas with a high prevalence of ESBL-producing Enterobacteriaceae (>10%), including patients known to be colonized with ESBL, is more effective in reducing the risk of SSI than no modification of prophylaxis. A further objective was to investigate whether routine screening for ESBL in both low and high ESBL prevalence areas has an impact on reducing the risk of SSI compared to no screening. The target population included patients of all ages undergoing a surgical operation. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

The literature search did not identify any studies comparing the tailored modification of SAP for the prevention of SSI in areas with a high prevalence of ESBL-producing Enterobacteriaceae (including patients with rectal colonization of ESBL) to no modification of standard prophylaxis. Similarly, no studies were identified comparing routine patient screening for ESBL with no screening as a preventive measure prior to surgery.

Additional factors considered

Resource use

In the absence of evidence, the implementation of routine screening for ESBL to detect faecal colonization prior to surgery would have major cost implications, especially in LMICs. For example, this would include clinical staff who have to take a swab and competent microbiology laboratory services to detect ESBL, perform antibiotic susceptibility tests and then communicate the results to the surgical team in a timely manner. This may be difficult as most laboratories are under-resourced and may lack good quality control programmes, particularly in LMICs. In addition, when the screening swab is positive for ESBL, it is very tempting for a clinical team to use carbapenems on colonized patients. This generates additional costs as they have to be given by the intravenous route, which is costly and time-consuming, notably in settings with low resources where there are already a shortage of nursing and medical power.

Research gaps

The GDG members highlighted that although there is an increase in the emergence of ESBL-producing Enterobacteriacae worldwide, no controlled trials or good quality observational studies have been published to answer the questions of this review, even in countries where ESBL-producing Enterobacteriaceae are endemic. Well-designed, RCTs and good quality observational studies are urgently needed to give guidance to the surgical team and prevent the inappropriate use of broad-spectrum antibiotics and the emergence of multidrug-resistant organisms on a global basis. As a priority, these studies should investigate whether the tailored modification of SAP in areas with a high prevalence of ESBL-producing Enterobacteriacae, including patients known to be colonized with ESBL, is more effective in reducing the risk of SSI than no modification of the standard prophylaxis.

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4.4 Optimal timing for preoperative surgical antibiotic prophylaxis

Recommendations

The panel recommends the administration of SAP prior to the surgical incision when indicated (depending on the type of operation).
(Strong recommendation, low quality of evidence)

The panel recommends the administration of SAP within 120 minutes before incision, while considering the half-life of the antibiotic.
(Strong recommendation, moderate quality of evidence)

Rationale for the recommendations

1. Overall low quality evidence shows that the administration of SAP after the incision causes harm with a significant increase of the SSI risk compared with administration of SAP prior to incision. Adequate tissue concentrations of the antibiotic should be present at the time of incision and throughout the procedure for SAP to be effective. This necessitates administration prior to incision. Further evidence shows that a low tissue concentration of antibiotics at the time of wound closure is associated with higher SSI rates *(1, 2)*. As a result, the GDG unanimously agreed to recommend the administration of SAP prior to incision and decided that the strength of this recommendation should be strong, although the overall quality of evidence is low. It is unlikely that higher quality evidence will be available in the future and indeed it would be unethical to perform a study where SAP is only administered post-incision because of the risk to cause significant harm.

2. A moderate quality of evidence comparing different time intervals prior to incision shows significant harm when SAP is administered before 120 minutes compared to within 120 minutes pre-incision. Given the significant increase of SSI with SAP administration more than 120 minutes before incision, the GDG decided to recommend SAP administration within 120 minutes pre-incision. A further analysis of data from studies assessing the effect of SAP administration on SSI at different time intervals within the 120-minute pre-incision period was performed, that is, 120-60 minutes vs. 60-0 minutes and 60-30 minutes vs. 30-0 minutes. No significant difference was found. Therefore, based on the available evidence, it is not possible to establish more precisely the optimal timing within the 120-minute interval.

   Several GDG members expressed concern that serum and tissue concentrations of antibiotics with a short half-life may be less effective than administration closer to the time of incision if given early in this time interval. For this reason, the GDG recommends to take into account the half-life of the administered antibiotics in order to establish the exact time of administration within 120 minutes pre-incision (for example, administration closer to the incision time [<60 minutes] for antibiotics with a short half-life, such as cefazolin, cefoxitin and penicillins in general).The same attention should be paid to the single antibiotic half-life when considering re-dosing during prolonged surgery. Concerns about antibiotic protein binding may arise when choosing highly-bound antimicrobials, such as ceftriaxone, teicoplanin or ertapenem. Under particular pathophysiological conditions (for example, patients with a low level of serum proteins, such as the critically ill or very elderly individuals), such drug disposition may indeed be affected. In addition, malnourishment, obesity, cachexia or renal disease with protein loss may result in suboptimal antibiotic exposure through increased antibiotic clearance in the presence of normal or augmented renal function, including overexposure and potential toxic effects in the presence of severely impaired renal function.

Remarks

- It is not within the scope of these guidelines to provide recommendations on what type of operations require SAP and the antibiotics, doses and intraoperative redosing rules that should be used. Separate specific guidelines will be made available by WHO on this topic. Examples of procedures that do not require SAP are clean orthopaedic operations not involving implantation of foreign materials or low-risk elective laparoscopic procedures.

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. However, the GDG considers this recommendation valid also for paediatric patients.
- In the included studies, the information was generally unclear regarding the duration of the procedure, re-dosing protocol, exact timing of the administration, infusion time and whether the half-life of the administered antibiotics was taken into account.
- Studies on caesarean section were not included in this review as they compared pre-incisional administration of SAP vs. administration after cord clamping. A recent systematic review on caesarean section indicated that SAP should be administered prior to incision in order to reduce maternal infectious morbidities *(3)*. This aligns with the recommendations in other surgical procedures where SAP is indicated.
- The guidelines of the American Society of Health-System Pharmacists (ASHSP) *(4)* recommend that intraoperative re-dosing is needed if the duration of the procedure exceeds 2 half-lives of the drug or if there is excessive blood loss during the procedure. While the benefit of this approach seems reasonable from a drug pharmacokinetic aspect, the reviewed studies have not addressed in SAP protocols the duration of surgical procedures or re-dosing in relation to SSI. No recommendation could be concluded on the benefit or harm of this approach.
- Some guidelines distinguish that some antibiotics require administration over 1-2 hours, such as fluoroquinolones and vancomycin. Therefore, the administration of these agents should begin within 120 minutes before the surgical incision. The literature search has not identified studies with SSI as an outcome that differentiate between the timing of administration of antibiotics requiring a longer period and those with a shorter administration timing. Clinicians should consider the half-life and protein binding as the most important pharmacokinetic parameters of any single SAP agent in order to ensure adequate serum and tissue concentration at the time of incision and during the entire surgical procedure.

Background

SAP refers to the prevention of infectious complications by administering an effective antimicrobial agent prior to exposure to contamination during surgery *(4)*. Successful SAP requires delivery of the antimicrobial agent in effective concentrations to the operative site before contamination occurs *(5)*. Microbial contamination of the wound during the procedure can be of exogenous or endogenous origin. The benefit of the routine use of SAP prior to non-clean and implant surgery to prevent SSI has long been recognized. Further evidence of its benefit for other clean procedures where the consequences of an infection would be devastating (for example, cardiac and neurosurgery) is also an important research topic. Of note, the effect of SAP does not concern the prevention of SSI caused by postoperative contamination. Within these guidelines, the recommendations have been developed with a focus on the optimal timing of SAP administration and the indication and type of SAP depending on the type of surgery is outside the scope of the document. Some experimental and clinical studies have demonstrated an effect of SAP timing on SSI *(6, 7)*, but the optimal timing is still under debate.

The administration of SAP prior to surgery has been specified in many clinical practice guidelines issued by professional societies or national authorities (Table 4.4.1). Several of these guidelines, such as those published by the ASHP *(4)*, SHEA/ IDSA) *(8)*, the Royal College of Physicians of Ireland *(9)* or Health Protection Scotland *(10)*, recommend administration within 60 minutes prior to incision (120 minutes for vancomycin and fluoroquinolones due to prolonged infusion times) *(3)*. However, these recommendations are not based on systematic reviews of the literature and meta-analysis or a rigorous evaluation of the quality of the available evidence.

Table 4.4.1. **Recommendations on SAP according to available guidelines**

Guidelines (date issued)	Recommendations on SAP and the related time of administration
SHEA/IDSA (2014) *(8)*	Administer only when indicated, within 1 hour before incision with superior efficiency between 0 and 30 minutes prior to incision compared with administration between 30 and 60 minutes.
NICE (2013) *(11).*	Single dose of antibiotic intravenously on starting anaesthesia**.** Prophylaxis should be given earlier for operations in which a tourniquet is used, that is**,** *after* rather than before tourniquet inflation.
ASHSP (2013) *(4)*	Administration of the first dose of the antimicrobial beginning within 60 minutes before surgical incision is recommended. Administration of vancomycin and fluoroquinolones should begin within 120 minutes before surgical incision because of the prolonged infusion times required for these drugs.
The Royal College of Physicians of Ireland (2012) *(9)*	At induction (within 60 minutes prior to incision surgery). If a *tourniquet* is to be applied, a 15-minute period is required between the end of antibiotic administration and tourniquet application. Single dose, except if blood loss (›1.5 L in adults or 25 mL/kg in children) and prolonged surgical procedures (4 hours).
USA Institute of Health Improvement: surgical site infection (2012) *(12)*	Within 60 minutes prior to incision. Discontinue within 24 hours (48 hours for cardiac patients).
Health Protection Scotland bundle (2013) *(10)*	Within 60 minutes prior to incision. Follow SIGN104 guideline.
UK High impact intervention care bundle (2011) *(13)*	Appropriate antibiotics administered within 60 minutes prior to incision and only repeated if there is excessive blood loss, a prolonged surgical procedure or during prosthetic surgery.

SAP: Surgical antibiotic prophylaxis; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; ASHSP: American Society of Health-Care Pharmacists.

Following the in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on the correct timing of SAP administration.

Summary of the evidence

The purpose of the evidence review (web Appendix 5) was to compare the effect of different timings of SAP administration on the risk of SSI and to identify the optimal timing to effectively prevent SSI.
The target population were patients of all ages undergoing surgical interventions where SAP was indicated. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.
A total of 13 observational studies *(7, 14-25)* including a total of 53 975 adult patients were identified; 2 were from multiple centres. No RCTs were identified. The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality. Despite substantial heterogeneity in reporting time intervals between the selected studies, separate meta-analyses were performed to evaluate the following comparisons of SAP timing administration: pre- vs. post-incision within 120 minutes vs. more than 120 minutes prior to incision; more than 60 minutes vs. within 60 minutes prior to incision; and 30-60 minutes vs. 0-30 minutes.

Moderate quality evidence shows that SAP administration before 120 minutes pre-incision is associated with a significantly higher risk of SSI when compared to administration within 120 minutes (OR: 5.26; 95% CI: 3.29–8.39). Furthermore, there is low quality evidence that administration of SAP after incision is associated with a significantly higher risk of SSI compared to administration prior to incision (OR: 1.89; 95% CI: 1.05–3.4). In addition, low quality evidence shows that administration within 60 minutes prior to incision has neither benefit nor harm for the reduction of SSI rates compared to administration between 60 to 120 minutes prior to incision. Similarly, SAP administration within 30 to 0 minutes prior to incision has neither benefit nor harm for the reduction of SSI rates when compared to administration within 60 to 30 minutes prior to incision.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG concluded that all patients, health care providers and policy-makers will favour the intervention for both recommendations. Due to logistic and practical considerations, anaesthesiologists tend to administer SAP in the operating room. This is often close to the start of incision, but it still lies within the 120-minute interval recommended by the GDG.

Resource use

There are no extra costs related to an optimized timing interval for SAP. However, the GDG believes that it is important to define responsibility for timely SAP administration and organizational resources may be required. In-service training including best practices for SAP administration should be provided. Feasibility and equity are not identified as significant issues for both recommendations.

Research gaps

The GDG highlighted the limited evidence available on optimal SAP timing to prevent SSI and the need for further studies on this topic. In particular and as a high priority, RCTs comparing the effect of different time intervals within the 120 minutes prior to incision are needed, that is, 120-60 minutes vs. 60-0 minutes and 60-30 minutes vs. 30-0 minutes. These should clearly state the duration of the procedure, the re-dosing protocol according to the drug chosen, as well as the infusion time and best exact timing of administration, while taking into account the half-lives of the antibiotics. Research is warranted also to identify the best timing according to specific types of surgical procedures. Furthermore, well-designed RCTs are necessary to investigate the relation between the pharmacokinetic and pharmacodynamic parameters of the antimicrobial agents used for SAP, including tissue levels at the incision site and SSI rates. The GDG noted that there are no high quality data examining the effect of dose adjustments or intraoperative re-dosing on SSI rates. Thus, it would be important to conduct RCTs comparing optimal doses of antibiotics and re-dosing protocols.

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4.5 Mechanical bowel preparation and the use of oral antibiotics

Recommendations

1. **The panel suggests that preoperative oral antibiotics combined with mechanical bowel preparation (MBP) should be used to reduce the risk of SSI in adult patients undergoing elective colorectal surgery.**
   (*Conditional recommendation, moderate quality evidence)*

2. **The panel recommends that MBP alone (without administration of oral antibiotics) should not be used for the purpose of reducing SSI in adult patients undergoing elective colorectal surgery.**
   (Strong recommendation, moderate quality evidence)

Rationale for the recommendations

1. Overall moderate quality evidence shows that preoperative oral antibiotics combined with MBP reduce the SSI rate compared to MBP alone. Of note, none of the included studies investigated the effect of oral antibiotics alone, that is, without combining their administration with MBP. All studies also applied standard intravenous antibiotic prophylaxis. Furthermore, the available evidence shows that there is no difference between the intervention and control groups in the occurrence of anastomotic leakage. This result is important because concerns can be raised about the possible higher frequency of leakage if MBP is not performed. Considering the moderate quality of the evidence and the demonstrated effect, the GDG decided to suggest that preoperative oral antibiotics in combination with MBP should be used to reduce the risk of SSI in addition to routine standard intravenous antibiotic prophylaxis, when appropriate.

2. A moderate quality of evidence shows that preoperative MBP alone has no benefit in reducing the SSI rate when compared to performing no MBP. Moreover, the meta-analysis indicates that no MBP has a non-significant beneficial effect in reducing the risk of SSI. In addition, the available evidence shows that there is no difference in the occurrence of anastomotic leakage with or without MBP. Therefore, the GDG unanimously agreed to recommend that MBP alone, without administration of oral antibiotics, should not be used for the purpose of reducing SSI in elective colorectal surgery.

Remarks

- MBP refers to the preoperative administration of substances to induce voiding of the intestinal and colonic contents. Polyethylene glycol and/or sodium phosphate were the agents of choice for MBP in most studies. However, the protocols differed between the trials in terms of dosage, timing of the application and fasting. It was emphasized that suboptimal cleaning of the colon may be more problematic than no bowel preparation at all.
- All studies included adult patients undergoing colorectal surgical procedures; therefore, the effectiveness of these interventions is not proven for paediatric patients.
- Apart from the MBP regimen, the oral antibiotics and the drug of choice for intravenous antibiotic prophylaxis varied across the studies. In 8 trials, oral aminoglycosides were combined with anaerobic coverage (metronidazole *(1-5)* or erythromycin *(6-8)*) and 3 studies *(9-11)* applied a gram-negative coverage only.
- The GDG acknowledges that is difficult to provide a universal statement on the choice of drugs for oral antibiotics to be used for MBP. The combination of the drugs used should guarantee an activity against both facultative gram-negative and anaerobic bacteria. The choice of antimicrobials should be made ideally according to local drug availability, updated resistance data within institutions and the volume of surgical activity.
- The GDG identified possible harms of the intervention of MBP with varying levels of severity. These include patient discomfort, electrolyte abnormalities and potentially severe dehydration at the time of anaesthesia and incision.

- The GDG pointed out that there is an alert issued by the US Food and Drug Administration highlighting that acute phosphate nephropathy (a type of acute renal failure) is a rare but serious adverse event associated with oral sodium phosphate bowel cleansing *(12)*.
- Concerns were also raised with regard to the potential adverse effects of the oral antibiotics used (for example, high risk of idiosyncratic reaction with erythromycin). A further concern was AMR as a potential unintended consequence of this intervention. The effectiveness of oral antibiotics may decrease due to their widespread use, thus triggering the emergence of resistant strains. The GDG noted that there was a widespread belief that non-absorbable antibiotics should be preferably used. In the corresponding comparisons, a combination of non-absorbable and absorbable antibiotics was administered in 8 of 11 RCTs *(1-8)*. Two studies *(9, 10)* applied non-absorbable and one study *(11)* absorbable antibiotics only.
- The GDG emphasized that the intervention of oral antibiotics with MBP is for preoperative use only and should not be continued postoperatively. This intervention should not be referred to as "selective digestive decontamination" (SDD) in order to avoid any confusion with SDD used for the prevention of ventilator-associated pneumonia in the intensive care setting.

Background

The optimal preparation of the bowel of patients undergoing colorectal surgery has been a subject of debate for many years. The main focus has been on whether or not mechanical cleansing of the bowel should be part of the standard preoperative regimen. MBP involves the preoperative administration of substances to induce voiding of the intestinal and colonic contents. The most commonly used cathartics for MPB are polyethylene glycol and sodium phosphate. It was assumed that cleaning the colon of its contents was necessary for a safe operation and could lower the risk of SSI by decreasing the intraluminal faecal mass and theoretically decreasing the bacterial load in the intestinal lumen. Furthermore, it was believed that it could prevent the possible mechanical disruption of a constructed anastomosis by the passage of hard faeces. Finally, MBP was perceived to improve handling of the bowel intraoperatively.

Another aspect of preoperative bowel preparation that has evolved over the last decades concerns the administration of oral antibiotics. Since the 1930s, orally administered antibiotics have been used with the aim to decrease the intraluminal bacterial load. However, these drugs had typically poor absorption, achieved high intraluminal concentrations and had activity against (anaerobic and aerobic) species within the colon. The addition of oral antibiotics that selectively target potentially pathogenic microorganisms in the digestive tract, predominantly gram-negative bacteria, *S. aureus* and yeasts, is known also as "selective digestive decontamination". This term originates from intensive care medicine and usually refers to a regime of tobramycin, amphotericin and polymyxin combined with a course of an intravenous antibiotic, often cefotaxime. Originating from the belief that oral antibiotics would work only when the bowel had been cleansed of its content, a regime of oral antibiotics was frequently combined with MBP.

A few organizations have issued recommendations regarding preoperative MBP and the administration of oral antimicrobials (Table 4.5.1). For example, SHEA/IDSA recommend to use MBP for colorectal procedures, but only combined with oral antibiotics. However, these recommendations are not based on systematic reviews of the literature and meta-analysis or a rigorous evaluation of the quality of the available evidence.

Table 4.5.1. **Recommendations on MBP and the administration of oral antimicrobials according to available guidelines**

Guidelines (year issued)	Recommendations on MBP and the administration of oral antimicrobials
SHEA/IDSA practice recommendation (2014) *(13)*	Use a combination of parenteral antimicrobial agents and oral antimicrobials to reduce the risk of SSI following colorectal procedures. (i) The additional SSI reduction achieved with MBP has not been studied, but the data supporting the use of oral antimicrobials have all been generated in combination with MBP. (ii) MBP preparation without oral antimicrobials does not decrease the risk of SSI.
NICE (2008) *(14)*	Do not use MBP routinely to reduce the risk of SSI.

MBP: mechanical bowel preparation; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; SSI: surgical site infection; NICE: National Institute for Health and Care Excellence.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess the available evidence on the effectiveness of preoperative oral antibiotics and MBP for the prevention of SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 6) was to evaluate whether preoperative MBP is more effective in reducing the risk of SSI than no MBP at all. The review evaluated also whether combining the preoperative administration of oral antibiotics with MBP in addition to the standard preoperative intravenous antibiotic prophylaxis is more effective than MBP alone. The population targeted were patients of any age undergoing elective colorectal surgery. The primary outcome was the occurrence of SSI and SSI-attributable mortality. Data on anastomotic leakage were analysed separately as a secondary outcome. The body of retrieved evidence focused on adult patients and no study was available in the paediatric population.

A total of 24 RCTs *(1-11, 15-27)* were identified. They compared either MBP with no MBP or the combined intervention of MBP and oral antibiotics with MBP and no oral antibiotics.

A total of 11 RCTs *(1-11)* including a total of 2416 patients and comparing preoperative MBP combined with the administration of oral antibiotics vs. MBP and no oral antibiotics were identified. Moderate quality evidence shows that preoperative MBP combined with oral antibiotics reduces the SSI rate when compared to MBP only (OR: 0.56; 95% CI: 0.37–0.83). Using this intervention, there is neither benefit nor harm in the occurrence of anastomotic leakage (OR: 0.64; 95% CI: 0.33–1.22).

A total of 13 RCTs *(15-27)* including a total of 4869 patients and comparing MBP with no MBP were identified. Moderate quality evidence shows that preoperative MBP has neither benefit nor harm for the reduction of SSI rates when compared to no MBP at all (OR: 1.31; 95% CI: 1.00–1.72). The available evidence shows also that there is no difference in the occurrence of anastomotic leakage with or without MBP (OR: 1.03; 95% CI: 0.73–1.44).

Among the studies comparing MBP combined with oral antibiotics vs. MBP alone, only 2 *(8, 11)* reported specifically on SSI-attributable mortality. Both studies reported a lower mortality rate when oral antibiotics were administered, although they failed to report any test for statistical significance. Of the 13 trials comparing MBP with no MBP, 3 reported specifically on SSI-attributable mortality *(18, 23, 27)*, but they did not find any statistical difference in the mortality rate.

None of the identified RCTs specifically evaluated the role of oral antibiotics without a MBP regimen, but some observational studies *(28-30)* using registry databases suggested that oral antibiotics may be effective in reducing the risk of SSI, irrespective of being combined with MBP. In addition, a prospective, randomized study *(31)*

strongly supports the use of oral antibiotics as part of a bundled intervention, but in combination with MBP. In this study, the combination of the preoperative administration of oral antibiotics and MBP was omitted in one group and compared with a standard regimen of oral antibiotics and MBP, while both arms received intravenous antibiotics prior to the surgical incision.

Additional factors considered when formulating the recommendation

Values and preferences

One study *(9)* found a higher incidence of diarrhoea when oral antibiotics were administered. Another study *(1)* assessed patient tolerance with 3 different oral antibiotic regimes. Patients reported more gastrointestinal symptoms (that is nausea and vomiting) at the time of preoperative preparation when given 3 doses of oral antibiotics compared to no oral antibiotics or one dose only. Among the studies comparing MBP with no MBP, 4 reported on patient discomfort. Berrera and colleagues *(15)* reported that half of all patients (50%) receiving MBP reported fair or poor tolerance. The main causes were nausea (56%), vomiting (23%) and cramping abdominal pain (15%). In another study *(16)* including 89 patients with MBP, 17-28% complained of similar disorders which led to a stop of preoperative MBP in 11% of cases. In one study *(17)*, MBP was associated with discomfort in 22% of patients, including difficulty in drinking the preparation, nausea, vomiting and abdominal pain. Zmora and colleagues *(27)* found that diarrhoea in the early postoperative period was more common in the MBP than the non-MBP group and reached statistical significance. The GDG acknowledged that some patients, for example, the elderly or disabled, might prefer not to undergo MBP, regardless of the outcome.

Resource use

It was acknowledged that MBP, including the administration of oral antibiotics, involves an additional workload as this intervention requires organizational resources to ensure its appropriate administration (for example, clear written instructions to patients and staff education). Furthermore, the initial cost is higher compared to not undertaking this intervention, but none of the included studies reported on costs and cost-effectiveness. However, the GDG concluded that the benefits of administering oral antibiotics outweigh these aspects. The antibiotics commonly used for the intervention (erythromycin, metronidazole and an aminoglycoside) are generally inexpensive and readily available, including in LMICs.

Research gaps

The GDG highlighted that there is enough evidence available on MBP alone. However, further research is needed on the effects of using oral antibiotics without MBP for the prevention of SSI. In particular, well-designed RCTs are needed to compare oral antibiotics and adequate intravenous prophylactic antibiotics vs. adequate intravenous prophylactic antibiotics only. The GDG noted also that there is limited evidence on the role of these interventions for patients undergoing laparoscopic procedures. However, some observational studies of mixed populations who underwent open and laparoscopic procedures suggested benefits for MBP across all groups. A RCT was recently published on this topic and showed a significant reduction of SSI in laparoscopic patients receiving oral antibiotics in addition to MBP and standard intravenous antibiotic prophylaxis *(32)*. However, this study could not be included in the systematic review due to the time limits determined for study inclusion.

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4.6 Hair removal

Recommendation

The panel recommends that in patients undergoing any surgical procedure, hair should either not be removed or, if absolutely necessary, it should be removed only with a clipper. Shaving is strongly discouraged at all times, whether preoperatively or in the operating room (OR).
(Strong recommendation, moderate quality of evidence)

Rationale for the recommendation

- For the formulation of the recommendation, the GDG considered the meta-analysis comparing clipping and no hair removal vs. shaving to be the most relevant. Moderate quality evidence shows a clear benefit of either no hair removal or clipping when compared to shaving with a significant decrease of the SSI risk.
- As a result, the GDG unanimously agreed to recommend that hair should either not be removed or, if absolutely necessary, it should be removed only with a clipper and the strength of this recommendation should be strong.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. However, the GDG considers this recommendation valid also for paediatric patients.
- When analysed separately, there was no significant difference between clipping and shaving compared to no hair removal, but clipping was found to be significantly beneficial when compared to shaving. The GDG decided that no hair removal and clipping should be compared to shaving in the same group as they are both similar in nature.
- It was noted that only one study *(1)* compared different times of hair removal (night before vs. day of surgery for both shaving and clipping). This study showed no clear evidence favouring any of the times for either method. Therefore, the GDG agreed that no recommendation regarding the timing of hair removal could be given. However, it was acknowledged that if hair is removed, removal shortly before surgery could be the most practical and safest approach.
- No studies were identified evaluating the effect of settings where hair removal is performed (OR vs. ward or home) with the outcome of SSI. Thus, the GDG agreed that no recommendation could be developed regarding the location of hair removal with clippers when this is necessary.
- The GDG did not identify any possible harm associated with no hair removal or using clippers.

Background

Removal of hair from the intended site of surgical incision has traditionally been part of the routine preoperative preparation of patients undergoing surgery. Hair removal may be necessary to facilitate adequate exposure and preoperative skin marking. Furthermore, suturing and the application of wound dressings can be complicated by the presence of hair. Apart from these practical issues, hair has been associated with a lack of cleanliness and the potential to cause SSI. There is also the belief that hair removal inversely increases the risk of SSI by causing microscopic trauma of the skin. To minimize the potential of skin trauma, the use of clippers instead of razors has been proposed for preoperative hair removal. In contrast to razors that involve a sharp blade drawn directly over the skin, clippers cut the hair close to the skin without actually touching it. A third method for hair removal is the application of depilatory creams containing chemicals. Drawbacks of the use of these creams are the necessity to leave them in place for approximately 15-20 minutes for the hair to be dissolved and the potential for allergic reactions. A Cochrane review published in 2009 and updated in 2011 found no statistically significant difference in SSI rates between hair removal and no hair removal interventions.

However, a significant harm was observed when hair removal with razors was compared with clipping *(2)*.

Among available guidelines, 4 explicitly recommend to avoid routine hair removal as a part of preoperative measures to prevent SSI *(3-6)*.

All other guidelines recommend not using razors. If electric clippers are used, a single-use head should be used (Table 4.6.1). Only a few guidelines provide an evaluation of the quality of the evidence.

Table 4.6.1. **Recommendations on hair removal according to available guidelines**

Guidelines (date issued)	Recommendations on hair removal
SHEA/IDSA (2014) *(6)*	Hair should not be removed at the operative site unless the presence of hair will interfere with the operation. Do not use razors. If hair removal is necessary, remove hair outside the operating room using clippers or a depilatory agent.
NICE (2013) *(7)*	Evidence for preoperative hair removal in reducing SSI rates is insufficient. Razors should not be used for hair removal because they increase the risk of SSI. If hair has to be removed, use electric clippers with a single-use head on the day of surgery as clipping may be associated with a reduced rate of SSI.
The Royal College of Physicians of Ireland (2012) *(4)*	Avoid hair removal. If hair must be removed, then use single-patient use clippers and not razors.
USA Institute for Healthcare Improvement: surgical site infection (2012) *(5)*	Avoid hair removal. If removal is necessary, remove outside the operating room using a single-patient use clipper.
Health Protection Scotland bundle (2013) *(3)*	Avoid hair removal. If removal is necessary, use a single-patient use clipper.
UK High impact intervention bundle (2011) *(8)*	If hair removal is required, use clippers with a disposable head and timed as close as possible to the operating procedure.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; SSI: surgical site infection; NICE: National Institute for Health and Care Excellence; UK: United Kingdom.

Following the in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on the need and correct method for hair removal.

Summary of the evidence

The purpose of the evidence review (web Appendix 7) was to investigate whether the method and timing of hair removal (using clippers, depilatory cream or shaving with razors) or no hair removal affect the incidence of SSI. The target population was patients of all ages undergoing a surgical procedure. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.

A total of 15 RCTs or quasi-randomized trials *(1, 9-22)* comparing the effect of preoperative hair removal vs. no hair removal or different methods of hair removal (shaving, clipping and depilatory

cream) were identified. Meta-analyses were performed to evaluate the following comparisons: shaving, clipping and depilatory cream individually vs. no hair removal, shaving vs. clipping and shaving vs. depilatory cream. As no hair removal and clipping are similar in terms of reduced potential to cause microscopic skin trauma, an additional analysis was performed combining no hair removal and clipping *vs.* shaving.

A low to very low quality of evidence shows that shaving, clipping or the use of depilatory cream has neither benefit nor harm related to the reduction of the SSI rate when compared to no hair removal (OR: 1.78; 95% CI: 0.96-3.29; OR: 1.00;95% CI: 0.06-16.34; and OR: 1.02; 95% CI: 0.42-2.49, respectively).

However, when hair is removed, there is a low quality of evidence showing that clipping has a significant benefit in reducing the SSI rate compared to shaving (OR: 0.51; 95% CI: 0.29-0.91). A very low quality of evidence shows that the use of depilatory cream has neither benefit nor harm when compared to shaving for the prevention of SSI (OR: 2.78; 95% CI: 0.86-9.03). When clipping and no hair removal were combined in the meta-analysis, a moderate quality of evidence showed that both are associated with a significantly lower risk of SSI when compared to shaving (OR: 0.51; 95% CI: 0.34-0.78).

A moderate quality of evidence shows that hair removal the day before surgery does not affect the SSI rate compared to hair removal on the day of surgery (OR: 1.22; 95% CI: 0.44-3.42).

The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

Studies evaluating surgeon or patient preferences for hair removal show variable results. Ilankovan and colleagues investigated patient and surgeon preferences before maxillofacial surgery and showed that patients prefer no hair removal over shaving, while the surgeons' assessment of the difficulty of wound closure did not differ between the two methods *(18)*.

The GDG acknowledged that the preferences of both patients and surgeons may differ according to the body area. Some members expressed the following opinions.

- Surgeons may be hesitant to use clippers in the male genitalia area.
- Women may prefer shaving for surgery in the genital area or even come to the hospital already shaved because of cultural norms.
- Surgeons may prefer to remove hair because of concerns that long hair would interfere with surgery and stick to the drapes.

While acknowledging this variability of approaches and cultural issues, the GDG emphasized that these preferences could be changed with an awareness-raising campaign to highlight the benefits of the recommendation and the harms of shaving practices, together with strong implementation strategies. Furthermore, the GDG was confident that the typical values of the target population regarding the SSI outcome would most probably favour the intervention.

Resource use

The GDG observed that avoiding hair removal has no cost and puts no burden on staff. Clippers are expensive and it might be difficult to procure them in LMICs. It is generally advisable to use single-use clippers/clipper heads, which may again be difficult to procure in LMICs. Of note, when reused, clipper heads can be very difficult to clean and decontaminate. When required for reuse, the GDG suggests that local infection prevention procedures are followed for clipper/clipper head decontamination, taking into account the following basic instructions for the general process: carefully disassemble the blades; clean with soap and water using a cloth and wearing appropriate personal protective equipment; dry with a fresh cloth and wipe with alcohol, again using a fresh cloth. Following the procedure, dispose of cloths and personal protective equipment, cleanse hands and store the clipper in a clean, covered dry storage space to avoid contamination.

Research gaps

Although the evidence to support the recommendation appears to be sufficient, the GDG provided the following directions for additional research on this topic. Studies are needed to evaluate the optimal timing and the most appropriate setting (ward vs. home) for the hair removal procedure when it is considered necessary by the surgeon. It would be important also to conduct surveys on the acceptability of patients

and surgeons regarding hair removal (or not) prior to surgery, particularly for body areas where preferences may vary, for example, genitalia for females and the maxillofacial area for males. The best and most acceptable methods of hair removal in settings with limited resources need to be investigated, including low-cost solutions. In particular, studies with a focus on the use of clippers in LMICs are needed to stimulate research on the design and production of an affordable clipper for these settings, including a cost-effectiveness analysis. For all settings, research is required to develop and test evidence-based procedures on how to decontaminate clippers.

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4.7 Surgical site preparation

Recommendation

The panel recommends alcohol-based antiseptic solutions based on CHG for surgical site skin preparation in patients undergoing surgical procedures.
(Strong recommendation, low to moderate quality of evidence)

Rationale for the recommendation

- Moderate quality evidence shows that the use of alcohol-based antiseptic solutions for surgical site skin preparation are more effective compared to aqueous solutions in reducing SSI. A meta-analysis of available studies (low quality of evidence) showed that alcohol-based CHG is beneficial in reducing SSI rates compared to alcohol-based povidone-iodine (PVP-I). As a result, the GDG agreed to recommend the use of an alcohol-based antiseptic solution preferably based on CHG for surgical site preparation on intact skin. The strength of this recommendation was considered to be strong.
- The GDG discussed whether to formulate the recommendation for adult patients only or to make a recommendation for all patients. The body of evidence focused on adult patients. The paediatric population was not represented as most commercially-available products have no indications for use in these patients due to the lack of studies in this population. By contrast, the GDG emphasized that it is unlikely that high quality evidence will be available in the future on paediatric patients, mainly due to ethical reasons.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, the effectiveness of this intervention is not proven for paediatric patients.
- Although the systematic review time limits for inclusion were set to a publication date between 1990 and 15 August 2014, a relevant trial published on 4 February 2016 was exceptionally included after discussion with the WHO Guidelines Review Committee and the GDG. The GDG was confident that no additional relevant trial had been published since the systematic review set date and therefore the search was not fully updated.
- According to the available studies, a sub-analysis of the comparison of alcohol-based antiseptic solutions vs. aqueous solutions was performed. A significant benefit in reducing the risk of SSI was observed with CHG in an alcohol-based solution compared to PVP-I in an aqueous solution. No significant difference was found between alcohol-based vs. aqueous PVP-I solutions. Most of the included studies used isopropyl alcohol at a concentration of 70-74%. Concentrations of the iodophor compound ranged from 0.7-10% and from 0.5-4% for CHG. Due to this heterogeneity and the lack of data to confirm any one direction, the GDG did not feel comfortable to include a statement about the concentration of the antiseptic compound in the recommendation.
- Washing the patient's skin with detergents or antiseptics is dealt with in chapter 4.1 and should be performed separately outside of the OR, whereas surgical site skin preparation is done prior to surgery within the OR.
- The GDG identified possible harms associated with the use of alcohol-based solutions and it was highlighted that they should not be used on neonates or be in contact with mucosa or eyes. CHG solutions must not be allowed to come into contact with the brain, meninges, eye or middle ear. As alcohol is highly flammable, alcohol-based antiseptic preparations may ignite if used in the presence of diathermy and they must be allowed to dry by evaporation. Therefore, it is advisable to ensure that the drapes are not saturated with alcohol or that the alcohol-based solution has not formed a pool underneath the patient before operating. While possible allergies should be accounted for (for example, to PVP-I), it should be noted that CHG has a potential risk of causing skin irritation. OR staff should be trained and informed about the potential harms associated with the solutions used for surgical site preparation.

Background

Surgical site preparation refers to the preoperative treatment of the intact skin of the patient within the OR. Preparation includes not only the immediate site of the intended surgical incision, but also a broader area of the patient's skin. The aim of this procedure is to reduce the microbial load on the patient's skin as much as possible before incision of the skin barrier. The most widely used agents include CHG and PVP-I in alcohol-based solutions, which are effective against a wide range of bacteria, fungi and viruses. However, aqueous solutions, particularly those containing iodophors, are also widely used, notably in developing countries.

Application techniques for preoperative surgical site preparation are also a topic of interest.

However, 3 trials investigating the effect of the application technique with comparable antiseptic compounds showed no difference in surgical site infection (SSI) rates *(1-3)*. Despite current knowledge of the antimicrobial activity of many antiseptic agents and application techniques, it remains unclear what is the best approach to surgical site preparation *(4, 5)*.

Several guidelines, such as those published by SHEA/IDSA) *(6)*, NICE *(7)* or the Royal College of Physicians of Ireland *(8)*, recommend the use of an alcohol-based solution for surgical site preparation (Table 4.7.1). However, these recommendations are not based upon systematic reviews of the literature and meta-analysis or a rigorous evaluation of the quality of the available evidence.

Table 4.7.1. **Recommendations on surgical site skin preparation according to available guidelines**

Guidelines (date issued)	Recommendations on surgical site skin preparation
SHEA/IDSA (2014) *(6)*	Wash and clean skin around the incision site. Use a dual agent skin preparation containing alcohol, unless contraindications exist.
NICE (2013) *(7)*	PVP-I or CHG, although alcohol-based solutions may be more effective than aqueous solutions. The most effective antiseptic for skin preparation before surgical incision remains uncertain.
The Royal College of Physicians of Ireland (2012) *(8)*	CHG 2% in isopropyl 70% alcohol solution; PVP-I with alcohol for patients who are allergic to CHG.
USA Institute for Healthcare Improvement: hip and knee arthroplasty (2012) *(9)*	Combining either an iodophor or CHG with alcohol is better than PVP-I alone.
Health Protection Scotland bundle (October 2013) *(10)*	CHG 2% in isopropyl 70% alcohol solution; PVP-I with alcohol for patients who are allergic to CHG.
UK High impact intervention bundle (2011) *(11)*	CHG 2% in isopropyl 70% alcohol solution; PVP-I with alcohol for patients who are allergic to CHG.

PVP-I: povidone-iodine; CHG: chlorhexidine gluconate; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence.

Following the in-depth analysis of the sources and strength of evidence in available guidelines, the GDG decided to conduct a systematic review to assess the available evidence on the efficacy of solutions and antiseptic agents used for surgical site skin preparation.

Summary of the evidence

The purpose of the evidence review (web Appendix 8) was to compare the effect of different solutions (alcohol-based vs. aqueous preparations) and antiseptic agents (CHG vs. PVP-I) used for surgical site skin preparation in order to prevent SSI. The target population included patients of all ages undergoing a surgical procedure. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.

A total of 17 RCTs *(2, 12-27)* comparing antiseptic agents (PVP-I and CHG) in aqueous or alcohol-based solutions were identified. According to the selected studies, the following comparisons were evaluated:

1. Alcohol-based antiseptic solutions vs. aqueous solutions
    a) CHG in an alcohol-based solution vs. PVP-I in an aqueous solution
    b) PVP-I in an alcohol-based solution vs. PVP-I in an aqueous solution

2. CHG vs. PVP-I - both in alcohol-based solutions

Moderate quality evidence shows that alcohol-based antiseptic solutions are overall more effective compared to aqueous solutions in reducing the risk of SSI (OR: 0.60; 95% CI: 0.45–0.78). More specifically, a low quality of evidence shows a significant reduction of the SSI risk with the use of alcohol-based CHG compared to PVP-I in alcohol-based solutions (OR: 0.58; 95% CI: 0.42–0.80). Moderate quality evidence shows also a significant benefit in using CHG alcohol-based solutions compared to aqueous PVP-I for the reduction of SSI rates (OR 0.65; 95% CI: 0.47–0.90). However, very low quality evidence suggests that there is no significant difference between PVP-I alcohol-based solutions and PVP-I aqueous solutions (OR 0.61; 95% CI: 0.19–1.92).

The literature search did not identify any studies that used aqueous CHG for surgical site skin preparation. The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Furthermore, most commercially available products have no indications for use in paediatric patients due to the lack of studies in this population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patients' values and preferences with regards to this intervention. The GDG concluded that most patients wish to receive this intervention in order to reduce the risk of SSI.

However, the use of alcohol might be refused by patients and/or health care workers because of religious reasons. This issue was addressed as part of the WHO *Clean Care is Safer Care* programme of work and a chapter on this topic is included in the WHO *guidelines on hand hygiene in health care (28)*, which recommends the preferred use of alcohol-based handrub (ABHR) for hand cleansing. The engagement of cultural and religious leaders (for example, in the hand hygiene campaign in health care facilities) proved useful to overcome such barriers and positive solutions were found. Indeed, an encouraging example is the statement issued by the Muslim Scholars' Board of the Muslim World League during the Islamic High Council's meeting held in Mecca, Saudi Arabia, in January 2002: "It is allowed to use medicines that contain alcohol in any percentage that may be necessary for manufacturing if it cannot be substituted. Alcohol may be used as an external wound cleanser, to kill germs, and in external creams and ointments." There may be a necessity to resume the discussion with religious leaders and individual patients with regards to the recommendation to use alcohol-based solutions for surgical site skin preparation.

Resource use

The GDG highlighted that the availability of alcohol-based solutions is limited in LMICs, particularly when combined with an antiseptic compound. These commercial products may represent a financial burden to health care facilities and patients if they are required to provide care supplies. The GDG discussed the implementation of this recommendation in LMICs and argued that local production may be a more affordable and feasible option in these settings, provided that adequate quality control is put in place. As an example, in

the context of the Surgical Unit-based Safety Programme, instructions for the local production of an alcohol- and CHG-based preparation were produced and implemented by WHO in 5 African hospitals (http://www.who.int/gpsc/susp/en/). A cost-effectiveness study *(29)* found that although CHG is more expensive, its effectiveness to reduce SSI makes it up to 36% more cost-effective than PVP-I.

Research gaps

GDG members highlighted that the use of alcohol-based solutions in surgical site skin preparation per se is no longer a research topic. There is a need for well-designed RCTs comparing specific preparations containing CHG, PVP-I and other antiseptics in alcohol-based and other solutions, taking into consideration their effectiveness, toxicity and costs. The GDG remarked that studies should focus on SSI as the critical endpoint and defined according to the CDC criteria. Furthermore, there is a need to compare commercial products with locally-produced solutions in health facilities in LMICs in effectiveness and cost-effectiveness studies. As there are no studies investigating the use of these solutions in paediatric patients, studies in this population would be particularly welcome. Currently, a few alcohol-based or aqueous solutions with antiseptic compounds contain colouring agents. Adding these agents to preparations can be helpful to indicate where surgical site preparation products have been applied on the patient's skin, but further studies would be needed if new colouring agents are proposed in order to ascertain effectiveness and tolerability.

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4.8 Antimicrobial skin sealants

Recommendation

The panel suggests that antimicrobial sealants should not be used after surgical site skin preparation for the purpose of reducing SSI.
(Conditional recommendation, very low quality of evidence)

Rationale for the recommendation

- Overall very low quality evidence from eight RCTs and one quasi-randomized trial shows that the preoperative application of antimicrobial skin sealants, in addition to standard surgical site skin preparation, produces neither benefit nor harm in reducing the SSI rate. The GDG unanimously agreed that there is no advantage in using antimicrobial sealants and suggested not using them. Given the quality of the evidence, the GDG decided that the strength of this recommendation should be conditional.

Remarks

- The body of retrieved evidence mainly focused on adult patients, but one study also included children. This recommendation is valid for both patient populations.
- The GDG observed that most studies investigating cyanoacrylate-based antimicrobial sealants were funded by manufacturers of commercial sealants.
- All included studies investigated the use of antimicrobial sealants on the skin of the surgical site before incision.
- Although the type and concentration of the antiseptics used for skin preparation varied among the included studies, the GDG underlined that the intervention and control groups in each of the studies received the same skin preparation technique, while antimicrobial sealants were added in the intervention group.
- The GDG identified skin irritation and allergic reactions as possible harms associated with the use of antimicrobial sealants.

Background

The endogenous bacteria on a patient's skin is believed to be the main source of pathogens that contribute to SSI *(1)*. Surgical site skin preparation commonly includes scrubbing or applying alcohol-based preparations containing antiseptic agents prior to incision, such as CHG or iodine solutions. Additional technologies are being researched and developed to reduce the rate of contamination at the surgical site and subsequent SSI.

Antimicrobial skin sealants are sterile, film-forming cyanoacrylate-based sealants commonly applied as an additional antiseptic measure after standard skin preparation of the surgical site and prior to skin incision. The sealant is intended to remain in place and block the migration of flora from the surrounding skin into the surgical site by dissolving over several days postoperatively. As an antimicrobial substance, sealants have been shown to reduce bacterial counts on the skin of the operative site *(2)*. However, most studies reported only changes in bacterial colonization and did not investigate SSI rates. Therefore, the use of antimicrobial sealants for the purpose of preventing SSIs is still under debate.

Currently available SSI prevention guidelines do not address the use of antimicrobial skin sealants and their effect to prevent SSI. The GDG decided to conduct a systematic review to assess the effectiveness of their use.

Summary of the evidence

The purpose of the evidence review (web Appendix 9) was to evaluate whether the use of antimicrobial skin sealants in addition to standard surgical site skin preparation is more effective in reducing the risk of SSI than standard surgical site skin preparation only. The target population were patients of all ages undergoing a surgical procedure. The primary outcome

was the occurrence of SSI and SSI-attributable mortality.

A total of nine studies including a total of 1974 patients and comprising 8 RCTs *(3-10)* and one prospective quasi-randomized trial *(11)* were identified. The studies compared the effect of the addition of antimicrobial skin sealants to standard skin preparation in the intervention group vs. standard skin preparation only in the control group.

Very low quality evidence shows no benefit or harm for the reduction of SSI rates when using the addition of antimicrobial sealants compared to standard surgical site skin preparation only (OR: 0.69; 95% CI: 0.38–1.25).

The body of retrieved evidence mainly focused on adult patients, but one study also included children. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was retrieved on patient values and preferences with regards to this intervention. However, the GDG observed that some studies *(8, 12)* reported that patients may suffer skin irritation due to the antimicrobial sealants as they remain on the skin for some time. Therefore, patients may prefer not to experience skin irritation, particularly when there is no evidence of benefit in using antimicrobial sealants to prevent SSI.

Resource use

The GDG pointed out that the availability of antimicrobial sealants may be limited in LMICs and their cost was a potential major resource concern. Lipp and colleagues observed that no studies included in a meta-analysis reported the cost of cyanoacrylate sealants as a preoperative preparation of the surgical site and no benefit was shown in preventing SSI *(13)*.

In addition to economic concerns, the availability of these commercial products may be an added barrier in LMICs. Furthermore, training in the proper technique and resources for their use would need to be available for surgical staff.

Research gaps

GDG members highlighted that many of the available RCTs have a high risk of bias and potential conflicts of interest. Several studies were excluded because they reported only bacterial colonization and not SSI as the primary outcome. Further studies are needed to identify evidence associated with important outcomes, including SSI rates (rather than microbial data), length of stay, cost-effectiveness and adverse effects on skin.

Most of the included studies investigated the use of cyanoacrylate-based sealants in contaminated procedures and the use of these agents may be more or less effective in other procedures. Importantly, the protocol for standard surgical site skin preparation with antiseptics varied across studies, thus making it difficult to discern the actual effect of the sealant alone. The GDG considers that more well-designed RCTs with adequate power are needed. These should focus on SSI as the primary outcome, rather than a reduction in the microbial load. Conducting trials with a more diverse surgical patient population will also further support evidence-based guidance on the use of antimicrobial sealants. For example, more evidence is needed in paediatric surgical patients.

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4.9 Surgical hand preparation

Recommendation

The panel recommends that surgical hand preparation be performed either by scrubbing with a suitable antimicrobial soap and water or using a suitable ABHR before donning sterile gloves.
(Strong recommendation, moderate quality of evidence)

Rationale for the recommendation

- The GDG noted that surgical hand preparation is vitally important to maintain the lowest possible contamination of the surgical field, especially in the event of sterile glove puncture during the procedure. Appropriate surgical hand preparation is recommended in the WHO *guidelines on hand hygiene in health care (1)* issued in 2009 and in all other existing national and international guidelines on the prevention of SSI.
- Moderate quality evidence shows the equivalence of handrubbing with an ABHR and handscrubbing with antimicrobial soap and water for surgical hand preparation for the prevention of SSI.

Remarks

- The available evidence on SSI as an outcome is limited to three RCTs. The trials compared handrubbing (with alcohol-based preparations) vs. handscrubbing (with PVP-I, CHG or plain soap) for surgical hand preparation and showed no significant difference between the two methods.
- Evidence from additional studies using the bacterial load on participants' hands as the outcome demonstrated that some ABHR formulations are more effective to reduce colony-forming units than scrubbing with water and antimicrobial or plain soap. The relevance of this outcome to the risk of SSI remains uncertain and the GDG considered this as indirect evidence and concluded that the recommendation could not be developed based on this surrogate outcome. Only evidence from RCTs with an SSI outcome was taken into account for the recommendation development.
- The WHO hand hygiene guidelines recommend preferably using "a product ensuring sustained activity". It was assumed that the sustained activity ensured by certain products (for example, CHG) was desirable, but there was no evidence that these products were more effective in directly reducing the risk of SSI. In the absence of such evidence, the GDG decided not to make any recommendations on specific products with or without a sustained effect and it emphasized the need to define what is considered a "suitable" product.
- The hands of the surgical team should be clean upon entering the OR by washing with a non-medicated soap. Once in the operating area, repeating handrubbing or scrubbing without an additional prior handwash is recommended before switching to the next procedure.
- It should be kept in mind that the activity of ABHRs may be impaired if hands are not completely dried before applying the product or by the handwashing itself. Hence, surgical handscrub and surgical handrub with alcohol-based products should not be combined sequentially *(1)*.
- When choosing ABHR, health care facilities should regularly procure products with proven efficacy (that is, complying with European norms or those of the American Society for Testing and Materials or equivalent international standards) to implement this recommendation and position no-touch or elbow-operated dispensers in surgical scrub rooms. Alternatively, antimicrobial soap, clean running water and disposable or clean towels for each health care worker should be available in the scrub room.
- In LMICs where ABHR availability is limited, WHO strongly encourages facilities to undertake the local production of an alcohol-based formulation according to WHO guidance, which has been demonstrated to be a feasible and low-cost solution *(1, 2)*.
- Skin irritation, dryness, dermatitis and some rare allergic reactions are adverse events that can occur following frequent scrubbing for surgical hand preparation. Although these are less frequent with

ABHRs and more frequent with iodophors, even well-tolerated ABHRs containing emollients may cause a transient stinging sensation at any site of broken skin (cuts, abrasions). Allergic contact dermatitis or contact urticaria syndrome caused by hypersensitivity to alcohol or to various additives present in some ABHRs are rare occurrences. ABHR preparations with strong fragrances may be poorly tolerated by a few health care workers with respiratory allergies. Studies of surgeon preferences indicate a primary preference for ABHRs with a higher tolerability and acceptability, due mostly to the shorter application time required and fewer skin reactions.

- Care must be taken to avoid contact with the eyes when using preparations with CHG 1% or greater as it may cause conjunctivitis or serious corneal damage. Ototoxicity precludes its use in surgery involving the inner or middle ear. Direct contact with brain tissue and the meninges should be avoided. The frequency of skin irritation is concentration-dependent, with products containing 4% most likely to cause dermatitis when used frequently for antiseptic handwashing. True allergic reactions to CHG are very uncommon *(1)*.
- Alcohols are flammable and health care workers handling alcohol-based preparations should respect safety standards.

Background

The purpose of routine hand hygiene in patient care is to remove dirt, organic material and reduce microbial contamination from transient flora. In contrast to hygienic hand hygiene through handwash or handrub, surgical hand preparation must eliminate the transient flora and reduce the resident flora. In addition, it should inhibit the growth of bacteria under the gloved hand *(1)*. Despite the limited scientific evidence on the effect of surgical hand preparation (usually called "handscrubbing") in reducing SSIs, the aim of this preventive measure is to reduce the release of skin bacteria from the hands of the surgical team to the open wound for the duration of the procedure, particularly in the case of an unnoticed puncture of the surgical glove. A rapid multiplication of skin bacteria occurs under surgical gloves if hands are washed with a non-antimicrobial soap, whereas it occurs more slowly following preoperative scrubbing with a medicated soap. The skin flora, mainly coagulase-negative staphylococci, *Propionibacterium* spp. and *Corynebacteria* spp., are rarely responsible for SSI, but in the presence of a foreign body or necrotic tissue, even inocula as low as 100 colony-forming units can trigger such infections *(3)*.

The spectrum of antimicrobial activity for surgical hand preparation should be as broad as possible against bacteria and fungi. Viruses are rarely involved in SSI and are not part of test procedures for licensing in any country. Similarly, activity against spore-producing bacteria is not part of international testing procedures. According to the European Committee for Standardization *(4, 5)* and the American Society for Testing and Materials *(6)*, antiseptic preparations intended for use as surgical hand preparations are evaluated for their ability to reduce the number of bacteria released from hands for immediate and persistent activity, thus targeting both transient and resident flora. Therefore, to be considered efficacious, antiseptic preparations should comply with either the European norm 12791 *(7)* or the American Society for Testing and Materials E-1115 standards *(8)*.

The WHO *guidelines on hand hygiene in health care (1)* (Table 4.9.1) recommend to keeping nails short and to remove all jewellery, artificial nails or nail polish before surgical hand preparation. If hands are visibly soiled, the guidelines recommend to wash hands and remove debris from underneath fingernails using a nail cleaner (not brushes), preferably under running water (sinks should be designed to reduce the risk of splashes). Surgical hand antisepsis should be performed using either (but not combined) a suitable antimicrobial soap or ABHR, preferably with a product ensuring sustained activity, before donning sterile gloves. Hands and forearms should be scrubbed with antimicrobial soap for the length of time recommended by the manufacturer, usually 2–5 minutes. The guidelines stipulate that if the quality of water is not assured in the OR, surgical hand antisepsis using ABHR is recommended. A sufficient amount of ABHR should be applied to *dry* hands and forearms for the length of time recommended by the manufacturer, typically 1.5 minutes, and hands and forearms allowed to dry before donning sterile gloves. Several organizations have issued recommendations regarding surgical hand preparation and these are summarized in Table 4.9.1.

Table 4.9.1. **Summary of recommendations on surgical hand preparation according to available guidelines**

Guidelines (date issued)	Recommendations on surgical hand preparation
WHO *Guidelines on hand hygiene in health care* (2009) *(1)*	• Surgical hand antisepsis should be performed using either a suitable antimicrobial soap or suitable ABHR, preferably with a product ensuring sustained activity, before donning sterile gloves. • If the quality of water is not assured in the OR, surgical hand antisepsis using an ABHR is recommended before donning sterile gloves when performing surgical procedures. • When performing surgical hand antisepsis using an antimicrobial soap, scrub hands and forearms for the length of time recommended by the manufacturer, typically 2–5 minutes. Long scrub times (for example, 10 minutes) are not necessary. • When using an alcohol-based surgical handrub product with sustained activity, follow the manufacturer's instructions for application times. Apply the product to dry hands only. Do not combine surgical handscrub and surgical handrub with alcohol-based products sequentially. • When using an ABHR, use a sufficient amount of the product to keep hands and forearms wet with the handrub throughout the surgical hand preparation procedure. • After application of the ABHR as recommended, allow hands and forearms to dry thoroughly before donning sterile gloves.
SHEA/IDSA (2014) *(9)*	• Use an appropriate antiseptic agent to perform preoperative surgical scrub, scrubbing the hands and forearms for 2–5 minutes for most products.
NICE (2008 and 2013) *(10,11)*	• The operating team should wash their hands prior to the first operation on the list using an aqueous antiseptic surgical solution and ensure that hands and nails are visibly clean, with a single-use brush or pick for the nails. • Before subsequent operations, hands should be washed using either using an ABHR or an antiseptic surgical solution. • If hands are soiled, they should be washed again with an antiseptic surgical solution. • The revised version of this guideline published in 2013 repeats the same surgical hand preparation recommendation with the addition of ensuring the removal of any hand jewellery, artificial nails and nail polish before starting surgical hand decontamination.

OR: operating room; ABHR: alcohol-based handrub; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence.

A Cochrane systematic review was published in 2008 *(12)* and very recently updated in 2016 *(13)*. The update included 14 RCTs; four trials reported rates of SSIs as the primary outcome, while the other studies measured the numbers of colony-forming units on participants' hands. The main finding was that that there is no firm evidence that one type of hand antisepsis (either ABHRs or aqueous scrubs) is better than another in reducing SSIs, but the quality of the evidence was considered low to very low. However, moderate or very low quality evidence showed that ABHRs with additional antiseptic ingredients may be more effective to reduce colony-forming units compared with aqueous scrubs *(12, 13)*.

Following an in-depth analysis of the sources and strength of the evidence in current guidelines, which are not based on systematic reviews and GRADE methodology, the GDG decided to address the issue of what type of products and scrubbing technique should be used for surgical hand preparation.

Summary of the evidence

The purpose of the evidence review (web Appendix 10) was to compare the effect of different techniques (that is, handrubbing vs. handscrubbing), products (that is, different ABHR formulations and plain or medicated soap) and application times for the same product. The primary outcome was the occurrence of SSI and SSI-attributable mortality. The target population included patients of all ages undergoing a surgical procedure.

Only six studies comprising 3 RCTs *(14-16)* and three observational studies *(17-19)* were identified with SSI as the primary outcome. All studies compared handrubbing to handscrubbing for surgical hand preparation. Handrubbing was performed by using either Sterilium® (Bode Chemie GmbH, Hamburg-Stellingen, Germany; 75% aqueous alcohol solution containing propanol-1, propanol-2 and mecetronium), the WHO-recommended formulation II (75% (volume/volume [v/v]) isopropyl alcohol, 1.45% (v/v) glycerol, 0.125% (v/v) hydrogen peroxide), Avagard® (3M, Maplewood, MN, USA; 61% ethanol plus CHG 1% solution) or Purell® (Gojo Industries Inc., Akron, OH, USA; 62% ethyl alcohol as an active ingredient; water, aminomethyl propanol, isopropyl myristate, propylene glycol, glycerine, tocopheryl acetate, carbomer and fragrance as an inactive ingredient). Handscrubbing products contained either CHG or PVP-I and/or plain soap. Five studies compared ABHR to handscrubbing with an antimicrobial soap containing either PVP-I 4% or CHG 4% and showed no significant difference in SSI. The same result was found in a cluster randomized cross-over trial comparing ABHR to handscrubbing with plain soap *(15)*. It was not possible to perform any meta-analysis of these data as the products used for handrubbing and/or handscrubbing were different.

The systematic review also identified 58 studies conducted either in laboratory or hospital settings, which evaluated participants' hand microbial colonization following surgical hand preparation with different products and techniques. There was a high variability in the study setting, microbiological methods used, type of product and time of sampling. The GDG decided not to take this indirect evidence into consideration to formulate the recommendation. Evidence from RCTs with only a SSI outcome was taken into account for the development of the recommendation, which is rated as moderate due to inconsistency. The overall evidence shows no difference between handrubbing and handscrubbing in reducing SSI.

The systematic review did not identify any studies comparing different durations of the technique for the same product with an SSI outcome. Only studies assessing the bacterial load on hands were found. After evaluation of this indirect evidence, the GDG decided not to develop any recommendation on the duration of surgical hand preparation and to continue to recommend following the manufacturer's instructions for each product.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. Given that surgical hand preparation has been considered to be best clinical practice since almost 200 years and is recommended in all surgical guidelines, the GDG is confident that the typical values and preferences of the target population regarding the outcome would favour the intervention.

Studies of surgeon preferences indicate a primary preference for ABHR. In general, studies show that ABHRs are more acceptable by surgeons compared to handscrubbing, due mainly to the reduced time required for surgical hand preparation and fewer skin reactions. The included studies provided some data on acceptability and tolerability of the products. According to a user survey in a study conducted in Kenya *(15)*, OR staff showed a preference for ABHR as it was faster to use, independent of the water supply and quality and did not require drying hands with towels. No skin reactions were reported with either ABHR or plain soap and water. Parienti and colleagues *(14)* assessed 77 staff for skin tolerance and found that skin dryness and irritation was significantly better in the handrubbing periods of the study. Although Al-Naami and colleagues *(16)* failed to show a significant difference, a survey of OR staff in a Canadian surgical hand preparation intervention

study *(18)* showed that 97% of responders approved of the switch to handrubbing and four persons even noted an improvement in their skin condition. All studies reported fewer (one or none) episodes of substantial dermatitis with ABHR compared to handscrubbing. In one study, some surgeons noted the occasional reversible bleaching of the forearm hair after the repeated use of handrub *(15)*.

Resource use

Observational studies with SSI outcome show a significant cost benefit of handrubbing. A Canadian study *(18)* showed that the standard handscrub-related costs of direct supplies were evaluated to be around Can$ 6000 per year for 2000 surgical procedures, not including the cost of cleaning and sterilizing surgical towels. The actual expenses incurred after a full year of handrub use were Can$ 2531 for an annual saving of approximately Can$ 3500. A dramatic decrease in surgical towel use (an average of 300 fewer towels per week) added to the savings. Two other studies *(17, 19)* from the USA and Cote d'Ivoire showed lower costs with Avagard® and Sterilium® when compared to the use of antiseptic-impregnated hand brushes and a PVP-I product, respectively. One RCT *(15)* also supported these findings and showed that the approximate total weekly cost of locally-produced ABHR according to the modified WHO formula was just slightly higher than plain soap and water (€ 4.60 compared with € 3.30; cost ratio: 1:1.4).

Despite this evidence on the cost-effectiveness of ABHRs, they may still have a high cost and limited availability in LMICs, even if local production is promoted. The barriers to local production may include the difficulty to identify staff with adequate skills, the need for staff training, constraints related to ingredient and dispenser procurement and the lack of adequate quality control. However, the GDG strongly emphasized that local production still remains a promising option in these circumstances. A WHO survey *(20)* of 39 facilities from 29 countries demonstrated that the WHO ABHR formulations can be easily produced locally at low cost and are very well tolerated and accepted by health care workers. Although the contamination of alcohol-based solutions has seldom been reported, the GDG emphasized the concern that top-up dispensers, which are more readily available, impose a risk for microbial contamination, especially in LMICs. According to the survey, the reuse of dispensers at several sites helped to overcome difficulties caused by local shortages and the relatively high costs of new dispensers. However, such reuse may lead to handrub contamination, particularly when empty dispensers are reprocessed by simple washing before being refilled, and the "empty, clean, dry, then refill" strategy to avoid this risk may require extra resources.

The feasibility and costs related to the standard quality control of locally-produced products is another consideration. In the WHO survey *(20)*, 11/24 assessed sites could not perform quality controls locally due to lack of equipment and costs. However, most sites were able to perform basic quality control with locally-purchased alcoholmeters. The use of soap and water will require disposable towels, which adds to the cost. Towel reuse is not recommended in the health care setting and towels should be changed between health care workers, thus resulting in resource implications.

Research gaps

The GDG noted that there are major research gaps and heterogeneity in the literature regarding comparisons of product efficacy, technique and duration of the scrubbing methods with SSI as the primary outcome. In particular, it would be useful to conduct RCTs in clinical settings to compare the effectiveness of various antiseptic products with sustained activity to reduce SSI vs. ABHR or antimicrobial soap with no sustained effect. Well-designed studies on the cost-effectiveness and tolerability/acceptability of locally-produced formulations in LMICs would be also helpful. Furthermore, research is needed to assess the interaction between products used for surgical hand preparation and the different types of surgical gloves, in relation to SSI outcome.

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Surgical Handrubbing Technique

- Handwash with soap and water on arrival to OR, after having donned theatre clothing (cap/hat/bonnet and mask).
- Use an alcohol-based handrub (ABHR) product for surgical hand preparation, by carefully following the technique illustrated in Images 1 to 17, before every surgical procedure.
- If any residual talc or biological fluids are present when gloves are removed following the operation, handwash with soap and water.

Put approximately 5ml (3 doses) of ABHR in the palm of your left hand, using the elbow of your other arm to operate the dispenser.

Dip the fingertips of your right hand in the handrub to decontaminate under the nails (5 seconds).

Images 3-7: Smear the handrub on the right forearm up to the elbow. Ensure that the whole skin area is covered by using circular movements around the forearm until the handrub has fully evaporated (10-15 seconds).

Images 8-10: Now repeat steps 1-7 for the left hand and forearm.

Put approximately 5ml (3 doses) of ABHR in the palm of your left hand as illustrated, to rub both hands at the same time up to the wrists, following all steps in images 12-17 (20-30 seconds).

Cover the whole surface of the hands up to the wrist with ABHR, rubbing palm against palm with a rotating movement.

Rub the back of the left hand, including the wrist, moving the right palm back and forth, and vice-versa.

Rub palm against palm back and forth with fingers interlinked.

Rub the back of the fingers by holding them in the palm of the other hand with a sideways back and forth movement.

Rub the thumb of the left hand by rotating it in the clasped palm of the right hand and vice versa.

When the hands are dry, sterile surgical clothing and gloves can be donned.

Repeat this sequence (average 60 sec) the number of times that adds up to the total duration recommended by the ABHR manufacturer's instructions. This could be two or even three times.

World Health Organization

PREOPERATIVE AND/OR INTRAOPERATIVE MEASURES

4.10 Enhanced nutritional support

Recommendation

The panel suggests considering the administration of oral or enteral multiple nutrient-enhanced nutritional formulas for the purpose of preventing SSI in underweight patients who undergo major surgical operations.
(Conditional recommendation, very low quality of evidence)

Rationale for the recommendation

- Multiple nutrient-enhanced nutritional formulas contain any combination of arginine, glutamine, omega-3 fatty acids and nucleotides.
- After careful appraisal of the included studies, the research team and the GDG decided to perform meta-analysis comparisons including only studies in which the oral and enteral routes were used and excluding those where the parenteral route was used. The main reason was that the parenteral route is very different and the experts considered it inappropriate to administer enhanced nutritional formulas only for the purpose of preventing SSI when considering the infectious risk related to intravenous access.
- Overall very low quality evidence from eight RCTs and two observational studies shows that multiple nutrient-enhanced formulas demonstrate a benefit in reducing the risk of SSI compared to standard nutritional support. The population studied were adult patients undergoing major surgical procedures (mainly cancer and cardiac patients).
- Overall low quality evidence from five RCTs and one observational study (very low quality) shows that a single nutrient-enhanced formula (containing either arginine or glycine or omega-3 fatty acids) produces neither benefit nor harm when compared to standard nutritional support in reducing the risk of SSI.
- As a result of these evaluations and comparisons, the GDG agreed to suggest that underweight patients who are undergoing major surgical operations (particularly oncology and cardiovascular procedures) may benefit from the administration of oral or enteral multiple nutrient-enhanced nutritional formulas for the purpose of preventing SSI. Given the very low quality of the evidence, the strength of this recommendation was considered to be conditional and the GDG proposed to use the terminology "The panel suggests considering..." to highlight the need for careful local and patient-by-patient evaluation about whether and how to apply this recommendation, in particular depending on the availability of nutritional formulas and costs.
  Note: "underweight" is a term describing a person whose body weight is considered too low to be healthy. The definition usually refers to people with a body mass index of under 18.5 or a weight 15-20% below the norm for their age and height group.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, the effectiveness of the intervention is not proven for paediatric patients and is valid for adult patients only.
- There is little evidence as to whether the timing of administration of multiple nutrient-enhanced nutritional formulas modifies the effect on the prevention of SSI. Therefore, the GDG was unable to identify an optimal timing and duration of the administration of these formulas.
- The GDG emphasized that most patients included in the studies were receiving enteral feeding through a tube for other reasons than the prevention of SSI. When inserting a feeding tube solely to administer multiple nutrient-enhanced nutritional formulas for the purpose of SSI prevention, it is important to be aware of the possible discomfort and harm ranging from mucosal irritation and the development of sinusitis to perforation. The GDG does not encourage the insertion of a feeding tube for the sole purpose of preventing SSI. In particular, it considers that improving nutritional status should not in any way lead to a delay in surgery.

- The GDG identified contaminated preparations as a potential harm, especially due to contaminated water and/or a break in the aseptic technique during preparation. This risk is increased when the feeding takes place at the patient's home. It is good practice to follow clinical and IPC guidelines and aseptic precautions when preparing nutritional formulas.

Background

Malnutrition, including protein-energy and micronutrient deficiencies, continues to be a major public health problem, particularly in developing countries. It affects also the rapidly growing elderly population in high-income countries *(1, 2)*. Nutritional status can have a profound impact on the immune system *(3)* as documented by some studies *(2-4)*. These alterations in host immunity may make patients more susceptible to postoperative infections and malnutrition was reported as a threat to surgical outcome, such as delayed recovery, higher rates of morbidity and mortality, prolonged hospital stay, increased health care costs and a higher early readmission rate *(2-7)*.

Some studies showed that early nutritional support can improve the outcome following major surgery and decrease the incidence of infectious complications in selected malnourished or severely injured patients. The hypothesis is that the immune system may be modulated by the use of specific types of nutritional support *(2, 3, 6, 8)*.

Surgery also induces an altered metabolism of protein, marked by a negative nitrogen balance and changes in amino acid patterns in blood. In addition, inflammation is integral to the recovery after stress, such as a surgical procedure. Therefore, nutritional support is being used more and more as a means to increase protein and caloric intake during the perioperative period, particularly by using formulas high in specific amino acids, antioxidants and anti-inflammatory nutrients *(9, 10)*.

Given the role of nutrition in the host response to surgery, many researchers believe that nutritional interventions would reduce SSI and the related morbidity. However, an epidemiological association between incisional SSI and malnutrition has been difficult to demonstrate consistently for all surgical subspecialties. There is very little consensus on the optimal timing and dosage of multiple nutrient-enhanced nutrition, especially for the prevention of SSI.

At present, there are no formal recommendations for nutrition supplementation for SSI prevention. Recent recommendations from SHEA/IDSA state that the preoperative administration of parenteral nutrition should not delay surgery *(11)*. Following an in-depth analysis of the resources and limited recommendations from other guidelines, the GDG members decided to conduct a systematic review on the effectiveness of nutrition supplementation for SSI prevention.

Summary of the evidence

The purpose of the evidence review (web Appendix 11) was to evaluate the effect of enhanced nutritional support compared to standard nutrition for the prevention of SSI. The population targeted were patients of all ages undergoing surgical procedures. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.

A total of 23 studies comprising 19 RCTs *(12-30)* and four observational studies *(31-34)* were identified with SSI as a reported outcome. Studies included adult patients undergoing cardiac surgical procedures (one study) or undergoing elective surgical procedures for head and neck, gastrointestinal, colorectal or gynaecological cancer. No study was available in the paediatric population. There was a substantial variation in the route of administration, nutritional formulas used and the definition of SSI. After careful appraisal of the included studies, the research team and the GDG decided to perform meta-analysis comparisons including only studies in which the oral and enteral routes were used and excluded those using the parenteral route.

Despite the above-mentioned heterogeneity, two meta-analyses were performed to evaluate the following comparisons: a multiple nutrient-enhanced nutritional formula vs. standard nutrition and a single nutrient-enhanced nutritional formula vs. standard nutrition, administered through either oral or enteral routes.

A total of 10 studies were identified. They comprised

eight RCTs *(15, 19-21, 23, 26, 28, 29)* and two observational studies *(31, 33)* including a total of 1434 patients and comparing the use of multiple nutrient-enhanced nutritional formulas (containing any combination of arginine, glutamine, omega-3 fatty acids and nucleotides) to standard nutrition. One study *(19)* involved data from multiple centres. Very low quality evidence shows that a multiple nutrient-enhanced nutritional formula has a significant benefit when compared to a standard nutritional formula in reducing the risk of SSI. The combined OR was 0.53 (95% CI: 0.30–0.91) for the RCTs and 0.07 (95% CI; 0.01–0.53) for the observational studies.

Furthermore, six studies including 397 patients and comprising of five RCTs *(14, 16-18, 29)* and one observational study *(32)* compared the use of nutritional supplements enhanced with a single nutrient (either arginine, glycine or branched chain amino acids) to standard nutrition. These studies included adult patients undergoing elective surgical procedures with head and neck cancer, hepatocellular carcinoma and cardiac disease. Low quality evidence shows that a single nutrient-enhanced formula has neither benefit nor harm for the reduction of SSI when compared to standard nutrition (RCTs: OR: 0.61; 95% CI: 0.13–2.79; observational study: OR: 0.29; 95% CI: 0.06–1.39).

The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. It was acknowledged that although patients may value measures to prevent SSI, they do not wish to be exposed to discomfort or possible harm due to a feeding tube inserted solely for that purpose. The GDG is confident that patients would very likely accept the administration of multiple nutrient-enhanced nutritional formulas if they are already receiving enteral feeding. Moreover, if oral feeding is possible, this would be an alternative likely welcomed by most patients. Some of the formulas were dairy-based, which may represent a problem for individuals who avoid dairy products for dietary, ethical or cultural reasons.

Resource use

No cost-effectiveness studies were identified. However, the use of enhanced nutrition support is expensive and requires additional work for clinical staff. In facilities where these formulas are used, there is a special need for dieticians and pharmacists, including the training of staff on their appropriate use and preparation. It is essential that all oral feeds be prepared in a clean dedicated area using an aseptic technique. Furthermore, the availability of enhanced nutrition formulas may be limited, particularly in LMICs, including the availability of ingredients for the preparation of the formulas (for example, clean drinking water). IPC measures for the preparation of the formulas need to be implemented. Given the very low quality of evidence for a benefit, the GDG was uncertain whether the benefits outweigh the costs of multiple nutrient-enhanced nutritional formulas.

Research gaps

The GDG highlighted that the few trials studying the efficacy of enhanced nutritional support for the prevention of SSI are small and generally of low quality. In addition, they are often conducted in populations that are at a high risk of malnutrition (for example, gastrointestinal cancer), which limits their generalizability. Many studies were funded by manufacturers of proprietary formulas and this could increase the potential for bias.
Future well-designed RCTs should be independent of manufacturers and performed in larger populations of individuals undergoing a variety of general surgical procedures. The impact of nutritional support should be investigated further in LMICs. Studies should investigate the benefit of other nutritional elements (for example, iron, zinc) and vitamins. Finally, the optimal timing and duration of the administration of nutritional support in relation to the time of surgery should be further assessed by well-designed RCTs.

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4.11 Perioperative discontinuation of immunosuppressive agents

Recommendation

The panel suggests not discontinuing immunosuppressive medication prior to surgery for the purpose of preventing SSI.
(Conditional recommendation, very low quality of evidence)

Rationale for the recommendation

- Very low quality evidence shows that the perioperative discontinuation of methotrexate (MTX) might be harmful or have no effect on the risk of SSI compared to its continuation. Furthermore, very low quality evidence from two observational studies showed that the perioperative discontinuation of tumour necrosis factor (TNF) inhibitors (anti-TNF) might have a benefit for the reduction of the SSI rate when compared to the continuation of anti-TNF. Taking into consideration (1) the very limited evidence (for anti-TNF) or lack of evidence and even potential harm (for MTX) to support a discontinuation of treatment, and (2) the risk associated with the discontinuation of treatment on the patient's underlying disease/s, the GDG unanimously agreed to suggest that immunosuppressive medication should not be discontinued for the purpose of preventing SSI.

Remarks

- The GDG emphasized that the decision to discontinue immunosuppressive medication may be made on an individual basis, involving the prescribing physician, the patient and the surgeon.
- No relevant evidence was found on the perioperative discontinuation of long-term corticosteroid therapy.
- The population investigated in the studies on MTX included patients with rheumatoid arthritis *(1-5)* and Crohn's disease *(6)*. Studies on anti-TNF investigated a population with rheumatoid arthritis *(7)* and other inflammatory rheumatic diseases *(8)*.
- The time point and time interval of discontinuation of the immunosuppressive agent were very heterogeneous across studies or not specified.
- The GDG identified the occurrence of a flare-up of the underlying disease as a potential harm associated with discontinuation of immunosuppressive therapy. The risk of major adverse events associated with discontinuation is high in patients taking immunosuppressive therapy after organ transplantation or for rheumatoid arthritis, whereas it might be lower in those taking immunosuppressive agents for inflammatory bowel disease *(4, 5, 9-14)*.

Background

Immunosuppressive agents are drugs that inhibit or prevent activation of the immune system. They are commonly prescribed to prevent rejection of transplanted organs or for the treatment of inflammatory diseases, such as rheumatoid arthritis or inflammatory bowel disease. Some observational studies indicate that the immunosuppressive effect of the drugs could lead to impaired wound healing and increased risk of infection in patients treated with these agents *(8)*. Conversely, the discontinuation of immunosuppressive treatment could induce flares of disease activity and long-term interruptions of therapy might induce the formation of anti-drug antibodies and subsequently decrease the effect of the immunosuppressives *(15)*.

To date, only one SSI prevention guideline has issued a recommendation regarding the administration of immunosuppressive agents in the perioperative period. This guideline was published by SHEA/IDSA and recommends avoiding the use of immunosuppressive agents in the perioperative period if possible *(16)*. However, this recommendation is not based on systematic reviews of the literature and meta-analyses or a rigorous evaluation of the quality of the available evidence. Of note, several other SSI prevention guidelines do not address this topic.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess the influence of immunosuppressive agents on the

incidence of SSI and whether a discontinuation of immunosuppressive medication in the perioperative period is effective to prevent SSI in surgical patients.

Summary of the evidence

The purpose of the evidence review (web Appendix 12) was to evaluate whether a discontinuation of immunosuppressive medication in the perioperative period is more effective in reducing the risk of SSI than continuation of the medication. The target population was patients of all ages taking immunosuppressive agents and undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

A total of eight studies comparing the perioperative discontinuation of immunosuppressive medication vs. continuation were identified and included a total of 2461 patients. They comprised one RCT *(5)*, one quasi-RCT *(3)* and six observational studies *(1, 2, 4, 6-8)*. Six studies comprising one RCT *(5)*, one quasi-RCT *(3)* and four observational *(1, 2, 4, 6)* investigated MTX and two observational studies *(7, 8)* investigated anti-TNF. The time point and time interval of discontinuation of the immunosuppressive agent were as follows: seven days before surgery *(5)*; one week prior to surgery and the week of surgery *(2)*; two weeks before surgery until two weeks after surgery *(3)*; within four weeks prior to surgery *(6)*; four weeks before surgery *(1)*; and one, four or eight weeks before and reintroduced one week after surgery *(8)*. The remaining two studies gave a rather unspecific description of the time point and time interval of discontinuation, that is, more than four times the half-life of the agent *(7)* or more than one week during the perioperative period *(4)*.

According to the selected studies the following comparisons were evaluated:

Discontinuation vs. continuation of:

a. MTX
b. anti-TNF.

Very low quality evidence shows that the perioperative discontinuation of MTX might be harmful or have no effect on the risk of SSI when compared to continuation of MTX. The combined OR was 7.75 (95% CI: 1.66–36.24) for the controlled trials and 0.37 (95% CI: 0.07–1.89) for the observational studies. Furthermore, there is very low quality evidence from two observational studies *(7, 8)* that the perioperative discontinuation of anti-TNF might have a benefit in reducing the SSI rate compared to the continuation of anti-TNF (OR: 0.59; 95% CI: 0.37–0.95).

The body of retrieved evidence focused mainly on adult patients, although a few studies also included a paediatric population *(6, 8)*. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients value the prevention of SSI, but they also do not want to be exposed to the risk of flare-ups or progression of their underlying disease due to the discontinuation of immunosuppressive therapy. Furthermore, most patients would like to be fully informed about the consequences of these decisions and to be involved in the decision making process.

Resource use

No cost-effectiveness data are available on the continuation or discontinuation of immunosuppressive therapy. The GDG pointed out that when making any decision on discontinuation, the physician treating the underlying disease or another senior physician will have to be involved, which may generate additional costs.

Research gaps

GDG members highlighted that well-designed RCTs are urgently needed to clarify this issue. Trials should examine also the optimal time between discontinuation of immunosuppressive agent(s) and time of surgery. In addition, the importance of the optimal dose of the various immunosuppressive therapy agents with regards to the SSI rate should be investigated. Studies should take into account new immunosuppressive agents. The GDG pointed out that surveillance and registry data are very likely to contribute also to the evidence in this field of research.

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4.12 Perioperative oxygenation

Recommendation

The panel recommends that adult patients undergoing general anaesthesia with endotracheal intubation for surgical procedures should receive an 80% fraction of inspired oxygen (FiO_2) intraoperatively and, if feasible, in the immediate postoperative period for 2-6 hours to reduce the risk of SSI.
(*Strong recommendation, moderate quality of evidence*)

Rationale for the recommendation

- A moderate quality of evidence shows that providing high FiO_2 (80%) is beneficial in patients undergoing procedures under general anaesthesia with endotracheal intubation and results in a significant decrease of the risk of SSI compared to 30-35% FiO_2. As a result, the GDG unanimously agreed to recommend that patients undergoing surgical procedures under general anaesthesia should receive 80% FiO_2 intraoperatively and in the immediate postoperative period for 2-6 hours, if feasible, and that the strength of this recommendation should be strong.
- FiO_2 was chosen as the unit of measurement because it was used in the studies retrieved, which led to the recommendation. The key point recognized by initial investigations is that O_2 saturation is reflective of oxygen bound to haemoglobin. Various studies have demonstrated that as a consequence of passive diffusion of oxygen from blood exposed to FiO_2 = 80%, tissue concentrations far exceed those attributable to haemoglobin release.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, the effectiveness of this intervention is not proven for paediatric patients.
- After careful appraisal of the included studies, the research team and the GDG decided to perform meta-analysis comparisons including only patients under general anaesthesia with endotracheal intubation and mechanical ventilation. Studies using neuraxial anaesthesia with a facemask or nasal cannula were excluded. Indeed, according to a meta-regression analysis introducing general anaesthesia with endotracheal intubation as a significant covariate, the type of anaesthesia proved to independently modify the effect of hyperoxygenation. In neuraxial anaesthesia with a nasal cannula or facemask, the control of ventilation (and thereby control of the actual administration of high FiO_2 to the lungs) is limited and was therefore considered different from an intervention with mechanical ventilation.
- The benefit of hyperoxygenation tended to be greater in open colorectal surgery than in other types of surgery, but no significant association was found between the type of surgery and the effect of hyperoxygenation.
- The GDG emphasized that the benefits of this intervention can be observed only when it can be implemented both by intubation during the operation and by using a high flux mask in the immediate postoperative period.
- Other potential sources of heterogeneity were discussed, including the age of the population (older patients may benefit more) and duration of surgery. It is known that colorectal surgery has a higher risk for SSI compared to other surgical procedures and hyperoxygenation may be beneficial in this group of patients due to the predominance of anaerobic flora in the colonic flora.
- None of the clinical trials that reported adverse events when investigating the administration of 80% FiO_2 showed a significant difference in pulmonary complications or other adverse events *(1-4)*. However, the GDG discussed the possible harms of hyperoxemia, in particular in patients with obstructive lung disease (for example, chronic obstructive pulmonary disease), such as absorption atelectasis with exposure to high oxygen tension and the possibility of depressing ventilation drive, particularly in the postoperative period. It was also pointed out that adverse events may not have been addressed adequately in the included trials. In addition, there was a considerable variation in the exclusion criteria for underlying lung disease, especially chronic obstructive pulmonary disease.

- The GDG discussed the results of one study indicating that long-term survival may be better with normal oxygenation *(5)*. However, the trial was underpowered for survival and the shorter survival was predominantly observed in a subgroup of patients with malignant disease, which is biologically implausible. The long-term follow-up of the Enigma trial showed no difference in survival *(2)*. Therefore, the GDG concluded that there was no convincing evidence of increased mortality attributable to high FiO2 during the perioperative period.
- The GDG highlighted that the benefits of hyperoxygenation would be maximized when normothermia and normovolemia are maintained. (See chapters 4.13 and 4.15 for the recommendations on normothermia and normovolemia.)
- The GDG acknowledged also that the studies were performed in high-income countries only.

Background

There is evidence that an optimized blood flow to the surgical incision reduced SSI rates through the avoidance of hypothermia, hypoxia and decreased perfusion *(6)*. Since 2000, several trials have been published on the use of high FiO_2 concentrations during the perioperative period and the potential association with lower rates of SSI (see *Summary of the evidence*). These studies include RCTs, meta-analyses and the long-term survival follow-up of original cohorts.

The intervention consists of providing patients with 80% oxygen compared to the usual administration of 30% oxygen. Patients are routinely given 100% oxygen for 30 seconds to 2 minutes prior to intubation and then maintained on either "normoxia", defined as oxygen at 30% or 35% FiO_2, or "hyperoxia", defined as oxygen at 80% FiO_2.

The arguments for providing oxygen levels beyond the standard 30% standard are largely based on two notions *(7)*. The first is that the surgical incision may not be adequately perfused and therefore might receive substantially higher oxygen if there is a higher partial pressure of oxygen in the blood *(8)*. The other notion is that the host defence systems might be further improved by higher oxygen partial pressures, particularly by enhancing neutrophil oxidative killing *(9)*.

The argument regarding enhanced killing devolves down to the affinity of the nicotinamide adenine dinucleotide phosphate oxidase for oxygen. The Km (Michaelis constant) of the enzyme for oxygen is 5-20 μM Hg O2 *(10, 11)*. It has been shown that the oxygen tension at infected sites is greatly reduced compared with that of most uninfected tissues, with PO2 approximating 25 mM of oxygen, equivalent to 3% oxygen *(12)*.

Perioperative oxygenation has been specified in clinical practice guidelines issued by professional societies or national authorities (Table 4.12.1). SSI prevention bundles from both England's High impact intervention approach and Health Protection Scotland, as well as guidelines from the Royal College of Physicians of Ireland and the UK-based NICE, recommend maintaining a haemoglobin oxygen saturation of at least 95% *(13-16)*. The SSI prevention guidelines of SHEA/IDSA recommend optimizing tissue oxygenation by administering supplemental oxygen during and immediately following surgical procedures involving mechanical ventilation *(17)*.

Table 4.12.1. **Recommendations on oxygenation preparation according to available guidelines**

Guidelines (date issued)	Recommendations on oxygenation preparation
SHEA/IDSA (2014) *(17)*	Optimize tissue oxygenation by administering supplemental oxygen during and immediately following surgical procedures involving mechanical ventilation.
NICE (2008) *(15)*	Sufficient oxygen to maintain a haemoglobin saturation of more than 95%.
The Royal College of Physicians of Ireland (2012) *(18)*	Haemoglobin saturation is maintained above 95% (or greater if there is underlying respiratory insufficiency).
Health Protection Scotland bundle (2013) *(13)*	Haemoglobin saturation is maintained above 95% (or greater if there is underlying respiratory insufficiency).
UK High impact intervention bundle (2011) *(16)*	Haemoglobin saturation is maintained above 95% (or greater if there is underlying respiratory insufficiency) both during the intra- and postoperative stages (recovery room).

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; England.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on optimal perioperative oxygenation.

A recent systematic review assessed the same PICO question as these guidelines *(19)*. However, the conclusions by Wetterslev and colleagues differ substantially from those presented here. Although the same data were used in the analysis performed for this review, the authors did not conduct a subgroup analysis based on the type of anaesthesia (that is, general with endotracheal intubation vs. neuraxial with facemask or nasal cannula) as was done here, following to the strong suggestion by the GDG. In the review by Wetterslev and colleagues, general anaesthesia was not identified as a significant covariate and, consequently, it was not taken into account in the final analysis, thus resulting in a different outcome. The GDG strongly believes that the approach chosen here is superior and the difference in outcome is of critical importance for the presented recommendation.

Summary of the evidence

The purpose of the evidence review (web Appendix 13) was to compare the effect of increased (80%) FiO_2 with standard (30-35%) FiO_2 on the risk of SSI. The target population included patients of all ages undergoing a surgical procedure. The primary outcomes were the occurrence of SSI and SSI-attributable mortality.

We identified 15 RCTs *(1, 2, 20-32)* including a total of 7237 adult patients, which investigated the perioperative use of increased FiO_2 and reported SSI as an outcome. All studies compared the administration of 80% FiO_2 to 30-35% FiO_2 (14 studies 30%; one study *(24)* 35%). The type of anaesthesia and respiratory control varied between neuraxial anaesthesia with a facemask or nasal cannula *(29-32)* and general anaesthesia with endotracheal intubation and mechanical ventilation *(1, 2, 20-28)*. Operative procedures differed also between colorectal surgery *(20, 22, 23, 26)*, acute and elective abdominal surgery *(1, 2, 24)*, gynaecological procedures and breast surgery *(28)*, tibial fixation *(27)* and caesarean section *(29-32)*. The body of retrieved evidence

focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

After careful appraisal of the included studies, the research team and the GDG decided to perform meta-analysis comparisons including only studies in which patients were under general anaesthesia with endotracheal intubation and mechanical ventilation *(1, 2, 20-28)*. Those using neuraxial anesthesia with a facemask or nasal cannula *(29-32)* were excluded for the recommendation. In a meta-regression analysis introducing general anaesthesia with endotracheal intubation as a significant covariate, the type of anaesthesia proved to independently modify the effect of hyperoxygenation. In neuraxial anaesthesia with a facemask or nasal cannula, the control of ventilation (and thereby control of the actual administration of the high FiO_2 to the lungs) is limited and was considered different from the intervention with mechanical ventilation. No significant association was found between the type of surgery and the effect of hyperoxygenation.

A meta-analysis of 11 RCTs was conducted to compare increased (80%) perioperative FiO_2 with standard (30-35%) FiO_2 in patients undergoing procedures under general anaesthesia with endotracheal intubation *(1, 2, 20-28)*. An overall moderate quality of evidence shows that increased perioperative FiO_2 is beneficial in reducing SSI compared to standard perioperative FiO_2 in this patient population (OR: 0.72; 95% CI: 0.55–0.94). The quality of the evidence for this comparison was moderate due to inconsistency.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG concluded that all patients, health care providers and policy-makers will favour the intervention. The GDG acknowledged that oxygen administration with a mask might be quite uncomfortable for patients in the postoperative period when they are extubated and waking up from anaesthesia.

Resource use

In LMICs, oxygen availability (procurement and distribution) and the related costs are a problem and a burden on available resources; thus, the local production of oxygen in hospitals should be encouraged. However, it was pointed out that even when it is implemented, the equipment for both the concentration and production of oxygen (that is, oxygen generation tanks/pumps) may not be cost effective or readily available. Lack of quality control (for example, contamination of the tanks with bacteria and fungi can occur, especially during condensation), incorrectly labelled tanks, maintenance of production and infrastructure challenges (for example, electricity) are other considerations in resource-limited settings. It was noted also that a high flux mask would be needed to maintain high-flow oxygen in the postoperative period in extubated patients, which would be an additional cost. Furthermore, as it may be uncomfortable for patients to wear a mask for 2-6 hours after surgery, it could be an additional burden on staff. In settings where medical oxygen is scarce, policy-makers may not consider this recommendation as a priority.

Research gaps

The GDG members highlighted the limited evidence available in some areas and additional research is required on the effect of hyperoxygenation in reducing SSI rates. In particular, studies should be conducted in the paediatric population outside the neonatal period. Further research is needed in settings with limited resources, while ensuring that basic IPC measures are in place and including different surgical procedures. Research is also needed to investigate the benefit of post-extubation hyperoxemia, including different durations, concentrations and oxygen administration routes. As the underlying mechanism of the effect of hyperoxygenation on the incidence of SSI is not entirely understood, translational research investigating these mechanisms is needed. These studies should also take into consideration the importance of normovolemia and normothermia. All studies should be RCTs with the SSI outcome defined according to CDC criteria and sub-specified as superficial, deep and organ space occupying.

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4.13 Maintaining normal body temperature (normothermia)

Recommendation

The panel suggests the use of warming devices in the operating room and during the surgical procedure for patient body warming with the purpose of reducing SSI.
(Conditional recommendation, moderate quality of evidence)

Rationale for the recommendation

- Overall moderate quality evidence from two RCTs shows that the maintenance of normothermia has a significant benefit in reducing the risk of SSI when compared to non-warming standard care. The GDG unanimously agreed that warming devices should be used to avoid patient hypothermia in the operating room and during the surgical procedure in order to reduce the risk of SSI and, more importantly, other complications associated with surgery (see below). Considering the quality of the evidence (moderate, but relying only on 2 small RCTs), the GDG did not reach full consensus about the strength of this recommendation and most members (11 vs. 4) voted for a conditional recommendation. The GDG appraised that the available evidence supporting this recommendation is limited. It was noted also that no observational studies investigating body warming with a SSI outcome were identified.
- However, the GDG emphasized that there are additional relevant benefits of warming strategies, such as a decrease in myocardial events, blood loss and transfusion requirements.
- The GDG agreed that the evidence was insufficient to identify a target temperature to be reached and maintained or an optimal device for warming the patient (for example, fluid warmers or simple blankets). The generally accepted target is core temperature ›36°C, considering that "hypothermia" (or low body temperature) is defined as a core temperature below 36°C and is common during and after major surgical procedures lasting more than two hours. However, it was not possible to reach an agreement regarding the optimal pre- and postoperative time for warming.

Remarks

- Included studies were conducted in high-income countries and in adult patient populations. However, the GDG considers this recommendation valid also for paediatric patients.
- The systematic review team and the GDG decided to exclude the study by Wong and colleagues *(1)* because the PICO question asks for a comparison of warming vs. non-warming, whereas the study by Wong applies warming procedures in both groups. Nevertheless, the GDG acknowledged that the study showed a tendency towards reduced SSI in the intervention group, which employed more intensive warming.
- The GDG identified a potential harm of skin burns, depending on the warming device (possible with conductive warming mattresses).
- It was mentioned also that the increased temperature within the work environment may be a concern for surgical staff. Of note, raising the room temperature is not an option to warm the patient as it causes thermal discomfort for the surgical staff, with an increased risk of dripping sweat onto the surgical site.

Background

Hypothermia (or low body temperature) is defined as a core temperature below 36°C and is common during and after major surgical procedures lasting more than two hours. The human body has a central compartment comprising the major organs where temperature is tightly regulated and a peripheral compartment where temperature varies widely *(2)*. Heat loss is compensated by reducing blood flow through the skin and by increasing heat production, mainly by inducing muscular activity (shivering) and increasing the basal metabolic rate. Typically, the periphery compartment may be 2-4°C cooler than the core compartment *(2)*.

Exposure to a cold operating room environment and anaesthetic-induced impairment of thermoregulatory control are the most common

events leading to hypothermia *(3, 4)*. Skin surface exposure during the perioperative period can increase heat loss. Furthermore, cool intravenous and irrigation fluids directly cool patients. Sedatives and anaesthetic agents inhibit the normal response to cold, resulting in improved blood flow to the periphery and increased heat loss *(3, 4)*. During the early period of anaesthesia, these effects are observed as a rapid decrease in core temperature caused by redistribution of heat from the central to the peripheral compartment. This early decrease is followed by a more gradual decline, reflecting ongoing heat loss. With epidural or spinal analgesia, the peripheral blockade of vasoconstriction below the level of the nerve block results in vasodilatation and greater ongoing heat loss.

For the above reasons, inadvertent non-therapeutic hypothermia is considered to be an adverse effect of general and regional anaesthesia *(5)*. Published research has correlated unplanned perioperative hypothermia with impaired wound healing, adverse cardiac events, altered drug metabolism and coagulopathies *(5-7)*.

It is unclear how the maintenance of normothermia in the core body compartment might reduce the incidence of SSI. All available studies measure core and not peripheral temperature. However, it is highly likely that the reported lower core temperatures result in reduced cutaneous temperature at the operative site. Nonetheless, incisional warming has not been shown to decrease SSI rates *(8)*. A recent Cochrane review of the effect of warmed intravenous fluids found no statistically significant differences in core body temperature or shivering between individuals given warmed and room temperature irrigation fluids *(9)*, but SSI was not the primary outcome. Another Cochrane review of interventions used for treating inadvertent postoperative hypothermia concluded that active warming reduces the time to achieve normothermia. Several warming devices have been studied, including forced-air warming, circulating hot water devices, radiant blankets, radiant warmers and electric blankets. Again, SSI was not among the primary outcomes of the review *(10)*. Temperature monitoring can be performed non-invasively either orally or by infrared ear temperature measurement, which is inaccurate. Intraoperatively, acceptable semi-invasive temperature monitoring sites are the nasopharynx, oesophagus and urinary bladder *(11)*.

Some of the current health care bundles and guidelines recommend that body temperature be maintained above 35.5-36°C during the perioperative period, although there is no consensus among these recommendations for the lower limit or optimal timing for normothermia (Table 4.13.1).

Table 4.13.1. **Recommendations on body temperature control (normothermia) according to available guidelines**

Guidelines (date issued)	Recommendations on body temperature control (normothermia)
SHEA/IDSA (2014) *(12)*	Maintain normothermia (temperature of 35.5°C or more) during the perioperative period in surgical patients who have an anaesthesia duration of at least 60 minutes.
Royal College of Physicians of Ireland (2012) *(13)*	Body temperature maintained above 36° C in the perioperative period (excludes cardiac patients).
Health Protection Scotland bundle (2013) *(14)*	Body temperature maintained above 36° C in the perioperative period (excludes cardiac patients).
UK High impact intervention bundle (2011) *(15)*	Body temperature maintained above 36° C in the perioperative period.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; England

Following an in-depth analysis of the sources and strength of evidence in available guidelines, the GDG decided to conduct a systematic review to assess the effectiveness of body warming on the prevention of SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 14) was to assess whether perioperative body warming vs. no warming is more effective in reducing the risk of SSI. The target population was patients of all ages undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Two RCTs *(16, 17)* including a total of 478 patients were identified (one was a multicentre study). Both studies compared the effect of body warming in the intervention group vs. no warming in the control group. Both studies addressed pre- and intraoperative warming; no studies were identified that assessed the effect of postoperative warming on SSI. The population studied were adult patients undergoing elective colorectal, hernia repair, vascular and breast surgical procedures. No study was available in the paediatric population. No observational study with SSI as the primary outcome was identified. The literature search did not identify any studies that reported on SSI-attributable mortality.

Moderate quality evidence shows that body warming has a significant benefit when compared to no warming in reducing the risk of SSI (OR: 0.33; 95% CI: 0.17–0.62).

Additional factors considered when formulating the recommendation

Values and preferences

No study was retrieved on patient values and preferences with regards to this intervention. The GDG emphasized that pain, nausea and shivering are among the most frequently reported adverse events following cooling down of the body temperature in the OR. Therefore, the GDG acknowledged that patients may prefer being kept warm during the surgical procedure and would also favour the intervention in order to reduce the risk of SSI. By contrast, the GDG is confident that patients wish to be protected from skin burns due to temperature and contact pressure (for example, conductive warming mattress).

Resource use

The GDG highlighted that the use of warming devices, such as forced-air warming devices or radiant blankets, increases the space and energy needed to store and run the equipment. The equipment and maintenance costs represent also a substantial financial burden, especially for LMICs. Availability and procurement are additional issues in LMICs. It was pointed out that the use of warming devices may decrease the risk of adverse outcomes and overall hospital costs *(18-20)*.

The GDG observed that given the lack of evidence to identify the optimal warming devices, it is arguable that simple blankets might function as efficiently as electrically-run devices in warming the patient, particularly in low-resource settings,

Research gaps

The GDG highlighted that well-designed RCTs are needed to identify the target temperature, the optimal devices (fluid warmers, mattresses, simple blankets, etc.) and the proper timing and duration of warming (pre-/intra-/postoperative). Trials should focus on SSI as the primary outcome and ideally address the cost-effectiveness of the intervention. It was emphasized also that there is no evidence from LMICs or in the paediatric population, which represent important research areas.

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4.14 Use of protocols for intensive perioperative blood glucose control

Recommendation

The panel suggests the use of protocols for intensive perioperative blood glucose control for both diabetic and non-diabetic adult patients undergoing surgical procedures to reduce the risk of SSI.
(Conditional recommendation, low quality of evidence)

Rationale for the recommendation

- Overall low quality evidence shows that a protocol with more strict blood glucose target levels has a significant benefit in reducing SSI rates when compared to a conventional protocol. There was evidence that the effect was smaller in studies that used intensive blood glucose controls intraoperatively only compared to studies that used an intensive protocol postoperatively or both intra- and postoperatively. Among the intensive protocols, the effect was similar in studies with a target blood glucose level of ≤110 mg/dL (6.1 mmol/L) and an upper limit target level of 110-150 mg/dL (6.1-8.3 mmol/L). Similar to meta-regression analysis, there was no evidence that the effect of intensive blood glucose control differed between studies of diabetic and non-diabetic patients. Thus, the GDG unanimously agreed that the recommendation to use protocols for intensive perioperative blood glucose control should apply to both diabetics and non-diabetics. However, the GDG decided that the available evidence did not allow the definition of an optimal target level of blood glucose. The strength of this recommendation was considered to be conditional.

Remarks

- The GDG observed that most studies were done in intensive care settings, with no studies in paediatric populations. Therefore, the effectiveness of this intervention is not proven for paediatric patients.
- In general, blood glucose target levels in the intensive protocol group were ≤150 mg/dL (8.3 mmol/L), whereas blood glucose target levels in the conventional protocol group were all ‹220 mg/dL (12.2 mmol/L).
- Intravenous insulin administration was performed in the intensive protocol group in all studies and in the conventional protocol group in most studies. Three trials *(1-3)* used subcutaneous administration in the conventional group. Some studies used continuous insulin administration, whereas others used intermittent. One study *(4)* administered a fixed high dose of intravenous insulin with dextrose 20% infused separately to maintain a blood glucose level between 70 and 110 mg/dL (“insulin clamp”).
- Duration and timing of glucose control differed between studies. The definitions of postoperative glucose control varied from 18 hours and “until enteral nutrition” to a maximum of 14 days.
- Five trials *(1-3, 5, 6)* studied diabetic patients, 8 studies *(4, 7-13)* included both diabetic and non-diabetic individuals, and 2 studies *(14, 15)* concerned only non-diabetic patients. The most frequent surgical procedures were cardiac surgery. Some studies focused on patients undergoing other major surgical procedures, including abdominal surgery.
- The GDG emphasized that hypoglycaemia is a possible harm associated with protocols with strict blood glucose target levels. Hypoglycaemia has a serious risk of life-threatening complications, such as cardiac events. Different definitions for hypoglycaemic events were used in the studies and varied from blood glucose levels ≤40 mg/dL (2.2 mmol/L) to ≤80 mg/dL (4.4 mmol/L).
- Data from the available evidence showed no difference in the risk of death and stroke with the use of an intensive protocol compared to a conventional protocol.

Background

Blood glucose levels rise during and after surgery due to surgical stress. Surgery causes a stress response that results in a release of catabolic hormones and the inhibition of insulin. Moreover, surgical stress influences pancreatic beta-cell function, which results in lower plasma insulin levels. Taken together, this relative

hypoinsulinaemia, insulin resistance and excessive catabolism from the action of counter-regulatory hormones make surgical patients at high risk for hyperglycaemia, even non-diabetic individuals *(16)*.

Several observational studies *(17-20)* showed that hyperglycaemia is associated with an increased risk of SSI and therefore an increased risk of morbidity, mortality and higher health care costs in both diabetic and non-diabetic patients and in different types of surgery. Conflicting results have been reported regarding the different treatment options to control hyperglycaemia in diabetic and non-diabetic patients, the optimal target levels of blood glucose and the ideal timing for glucose control (intra- and/or postoperative). Moreover, some studies targeting relatively low perioperative glucose levels have highlighted the risk of adverse effects associated with intensive protocols as they may cause hypoglycaemia *(21-24)*.

Several organizations have issued recommendations regarding perioperative blood glucose control (Table 4.14.1). While most recommendations focus on the diabetic patient only, those issued by SHEA/IDSA *(25)* and the American College of Physicians *(26)* apply to all surgical patients. They recommend either target levels between 140-200 mg/dL (7.8-11.1 mmol/L) or upper limits of 180 mg/dL (10mmol/L) or 198 mg/dL (11mmol/L). Due to the risk of hypoglycaemia, targeting lower levels should be avoided *(26, 27)*.

Table 4.14.1. **Recommendations on perioperative blood glucose control according to available guidelines**

Guidelines (year issued)	Recommendations on perioperative blood glucose control
SHEA/IDSA practice recommendation (2014) *(25)*	Control blood glucose during the immediate postoperative period for cardiac and non-cardiac surgery patients. a) Maintain postoperative blood glucose at 180 mg/dL or lower. b) Intensive postoperative glucose control (targeting levels less than 110 mg/dL) has not been shown to reduce the risk of SSI and may actually lead to higher rates of adverse outcomes, including stroke and death.
NICE (2008) *(28)*	Do not give insulin routinely to patients who do not have diabetes to optimize blood glucose postoperatively as a means of reducing the risk of SSI.
Health Protection Scotland bundle (2013) *(29)*	Ensure that the diabetic patient's glucose level is kept at <11 mmol/L throughout the operation.
The Royal College of Physicians of Ireland (2012) *(30)*	Ensure that if the patient is diabetic that the glucose level is kept at <11 mmol/L throughout the operation.
UK High impact intervention bundle (2011) *(31)*	A glucose level of <11 mmol/L has to be maintained in diabetic patients.
The Society of Thoracic Surgeons practice guideline series (2009) *(27)*	All patients with diabetes undergoing cardiac surgical procedures should receive an insulin infusion in the operating room and for at least 24 hours postoperatively to maintain serum glucose levels ≤180 mg/dL.
American College of Physicians: clinical practice guideline (2011) *(26)*	Do not use intensive insulin therapy (4.4 to 6.1 mmol/L [80 to 110 mg/dL]) to normalize blood glucose in SICU/MICU patients with or without diabetes mellitus. A target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) is recommended if insulin therapy is used in SICU/MICU patients.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; SICU: surgical intensive care unit; MICU: medical intensive care unit.

Following an in-depth analysis of the sources and strength of the evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the impact of perioperative blood glucose levels on the risk of SSI and to determine the optimal perioperative target levels in diabetic and non-diabetic surgical patients to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 15) was to evaluate whether the use of protocols for intensive perioperative blood glucose control is more effective in reducing the risk of SSI than conventional protocols with less stringent blood glucose target levels. The population studied were patients of all ages, both diabetic and non-diabetic, and undergoing several types of surgical procedures. The primary outcome was the occurrence of SSI and SSI-attributable mortality. A total of 15 RCTs *(1-15)* including a total of 2836 patients and comparing intensive perioperative blood glucose protocols vs. conventional protocols with less stringent blood glucose target levels were identified. Eight studies were performed in adult patients undergoing cardiac surgery *(1, 2, 4, 6, 9-11, 15)*, 6 in patients undergoing abdominal or major non-cardiac surgery *(3, 5, 7, 12-14)*, and one other study in patients undergoing emergency cerebral aneurysm clipping *(8)*. No study was available in a paediatric population. In 2 studies *(4, 7)*, glucose control was performed intraoperatively only. Eight studies *(1, 2, 6, 8, 9, 11, 13, 15)* investigated intra- and postoperative glucose control and 5 studies *(3, 5, 10, 12, 14)* focused on postoperative glucose control.

None of the studies had SSI as their primary outcome. Most studies had a combined outcome of postoperative complications. The definition of SSI was also different in most studies.

There was substantial heterogeneity among the selected studies in the population, notably regarding the timing when intensive blood glucose protocols were applied in the perioperative period and intensive blood glucose target levels. For this reason, separate meta-analyses were performed to evaluate intensive protocols vs. conventional protocols in different settings (that is, in diabetic, non-diabetic and a mixed population) with intraoperative, intra- and postoperative glucose control, and in trials with intensive blood glucose upper limit target levels of ≤110 mg/dL (6.1 mmol/L) and 110-150 mg/dL (6.1-8.3 mmol/L) (web Appendix 15).

Overall, there is low quality evidence that a protocol with more strict blood glucose target levels has a significant benefit in reducing SSI rates when compared to a conventional protocol (OR: 0.43; 95% CI; 0.29–0.64). In addition, there was no evidence in meta-regression analyses that the effect of intensive blood glucose control differed between studies of diabetic and non-diabetic patients (*P*=0.590). There was evidence that the effect was smaller in studies that used intensive blood glucose control intraoperatively only (OR: 0.88; 95% CI: 0.45-1.74) compared to studies that used controls postoperatively or both intra- and postoperatively (OR: 0.47; 95% CI: 0.25-0.55; *P*=0.049 for the difference between ORs). Among the intensive protocols, the effect was similar in studies with upper limit target blood glucose levels of ≤110 mg/dL (6.1 mmol/L) and 110-150 mg/dL (6.1-8.3 mmol/L) (*P*=0.328).

Data from the available evidence showed no difference in the risk of postoperative death and stroke with the use of an intensive protocol compared to a conventional protocol (OR: 0.74; 95% CI: 0.45-1.23 and OR: 1.37; 95% CI: 0.26-7.20, respectively). The study by Ghandi and colleagues was the only one that reported more strokes and deaths in the intensive group *(11)*. This study had comparable 24-hour achieved blood glucose levels in the intensive care unit in both groups, although they were significantly lower in the intensive group intraoperatively and at baseline. Other studies showed equal or even less strokes and/or deaths in the intensive group, but these findings were not significant. In meta-regression analyses, there is no evidence for a difference in risk between studies with an upper limit target blood glucose level of ≤110 mg/dL (6.1 mmol/L) and an upper limit level of 110-150 mg/dL (6.1-8.3 mmol/L) (*P*=0.484 for mortality and *P*=0.511 for stroke).

Meta-analysis of hypoglycaemic events in the 8 RCTs with a blood glucose upper limit target level of ≤110 mg/dL (6.1 mmol/L) showed an increased risk of hypoglycaemic events with the use of an intensive protocol over a conventional protocol (OR: 4.18; 95% CI: 1.79–9.79). However, 2 of the 8 studies included in this analysis had no hypoglycaemic events *(4, 13)* and only 3 studies *(3, 7, 14)* found significantly more hypoglycaemic events with the use of the intensive protocol. A meta-analysis of 4 studies *(1, 2, 6, 10)* showed an increased risk of hypoglycaemic events with the use of a strict protocol with a blood glucose upper

limit target level of 110-150 mg/dL (6.1-8.3 mmol/L) compared to a conventional protocol (OR: 9.87; 95% CI: 1.41–69.20). Two studies included in this analysis had no hypoglycaemic events *(1, 2)*. Among the studies that could not be included in the meta-analysis due to missing data, 2 reported significantly more hypoglycaemic events in the intensive group *(8, 12)*, while no difference in risk was observed in another study *(9)*. Overall, there is an increased risk for hypoglycaemic events with the use of either intensive protocol for blood glucose control (OR: 5.55; 95% CI: 2.58–11.96). In meta-regression analyses, there is no evidence for a difference in the risk of hypoglycaemia between studies with a target blood glucose level of ≤110 mg/dL (6.1 mmol/L) and an upper limit target level of 110-150 mg/dL (6.1-8.3 mmol/L) (P=0.413).

The GDG underlined that there are many observational studies showing a reduction in SSI with intensive blood glucose control in non-diabetic populations. However, after discussion, the GDG agreed not to include the data from the observational studies.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients wish to receive this intervention in order to reduce the risk of SSI. Patients are concerned about hypoglycaemic events, as well as being monitored for the blood glucose target level on a regular (sometimes a few times daily) basis, which might be associated with frequent needle pricks.

Resource use

The GDG members emphasized that apart from in intensive care settings, patients are more likely to receive a conventional protocol because of concerns regarding resources and the ability to monitor blood glucose adequately. The GDG highlighted that the purchase and storage (refrigerator) of insulin is a financial burden in LMICs and the availability of insulin is a concern. The equipment for the application of frequent glucose control is also expensive and may be limited in availability in such settings. In addition, the medical staff has to be carefully trained to correctly monitor the blood glucose level and treat hypoglycaemic events. There are no data available to determine the cost-effectiveness of different protocols.

Research gaps

GDG members highlighted that the available evidence mostly consists of intensive care and cardiac surgery populations. There is a need for studies in the paediatric setting, as well as in non-ICU surgical patients and those undergoing different types of surgical procedures. Adequately-powered RCTs should be performed to compare different blood glucose target levels in order to better define the optimal level for the purpose of SSI prevention, but with only a very limited risk of hypoglycaemia. For a given target level, there should be studies investigating the optimal route of insulin administration, as well as studies on the duration of continued postoperative glucose control. In particular, the GDG noted that research on cost-effectiveness and studies from LMICs are needed.

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4.15 Maintenance of adequate circulating volume control/normovolemia

Recommendation

The panel suggests the use of goal-directed fluid therapy (GDFT) intraoperatively to reduce the risk of SSI.
(Conditional recommendation, low quality of evidence)

Rationale for the recommendation

- Overall low quality evidence shows that intraoperative GDFT has significant benefit in reducing the SSI rate compared to standard fluid management. This effect is shown also for GDFT in the postoperative period.
- Considering that both fluid overload and hypovolemia are likely to affect other clinical outcomes, the GDG agreed to emphasize that specific fluid management strategies, such as GDFT or restrictive fluid management, may be used during surgery for purposes other than the reduction of SSI, for example, to support cardiovascular and renal functions.
- Considering the low quality evidence, as well as the above-mentioned factors, the GDG agreed to suggest the use of GDFT intraoperatively and decided that the strength of this recommendation should be conditional.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, this effectiveness of this intervention is not proven for paediatric patients.
- GDFT refers to a haemodynamic treatment based on the titration of fluid and inotropic drugs according to cardiac output or similar parameters.
- Restrictive fluid management refers to the administration of a regimen with a reduced volume of fluids in the bolus and/or over time compared to local standard fluid maintenance.
- Standard fluid maintenance in the control group refers to the administration of fluid regimens at the discretion of the treating medical team or according to the local standard.
- Most trials among the included studies compared the efficacy of specific fluid management strategies with standard fluid regimens in the intraoperative period. Fourteen RCTs investigated GDFT *(1-14)* and 5 RCTs focused on restrictive fluid management *(15-19)*. As the PICO question focused on fluid management during surgery, these comparisons were used to formulate the recommendation.
- Further trials compared specific fluid management strategies vs. standard fluid management in the preoperative *(20)* and/or postoperative period *(21-24)*.
- It was discussed that the actual physiological effect of administered fluids may also differ, depending on several other factors, such as surgical stress, normothermia and tissue oxygenation.
- The GDG argued that both fluid overload and hypovolemia are likely to increase mortality and morbidity *(25)*.
- Although the optimal strategy for GDFT cannot be identified from the published data due to the heterogeneity of the protocols used in the included studies, the panel suggests administering haemodynamic therapy based on a goal-directed approach during the entire surgical procedure. Optimization is preferably based on dynamic pre-load parameters (that is, pulse pressure variation, systolic pressure variation) derived from arterial catheter measurements (when an arterial line is indicated) or minimal invasive alternatives.
- The GDG felt that using an algorithm is helpful, while taking into account that local resources and expertise may vary and limit possibilities for the optimal strategy. Indeed, the variety of effective algorithms on a multitude of outcomes indicates that having an algorithm for a specific goal is the most important factor, more than any particular algorithm associated with the effect of GDFT.

Background

Wound healing and resistance to infection is dependent on tissue oxygen tension. In addition, sufficient tissue oxygenation is essential for collagen synthesis and wound repair *(17)* and is improved by adequate arterial oxygenation. Ideally, perioperative fluid therapy prevents tissue hypoxia by maximizing the cardiac output and thus improving arterial oxygenation. However, the optimal perioperative fluid strategy remains a subject of debate. A large variability exists between regimens in daily practice and both fluid overload (hypervolemia) and hypovolemia have been associated with increased mortality and morbidity. Fluid overload leads to a decrease in muscular oxygen tension. Due to surgical trauma, a systemic inflammatory response arises, which leads to a fluid shift to the extravascular space. Following a large fluid shift, generalized oedema may occur, which decreases tissue oxygenation and impedes tissue healing. By contrast, hypovolemia leads to arterial and tissue hypoxia due to a decrease in cardiac output.

The optimal fluid (colloid or crystalloid) or strategy of fluid management (GDFT, liberal or restricted) remains a subject of controversy. GDFT uses cardiac output or similar parameters to guide intravenous fluid and inotropic administration, but the disadvantage of this strategy is the difficulty to adequately assess normovolemia. Liberal and restrictive fluid strategies use standard fluid regimens not based on cardiac output. Nevertheless, an adequate assessment of normovolemia in these strategies remains complicated. In addition, the physiological effects of any given volume of fluid may differ, depending on the magnitude of the surgical stress response and not solely on the volume of fluids administered. At present, there is no universal definition of normovolemia or a standardized method for its assessment. Some studies assess normovolemia by urinary output or serum markers, whereas others use more invasive techniques, such as cardiac output or cardiac index.

Few organizations have issued recommendations regarding the maintenance of normovolemia (Table 4.15.1). The UK-based NICE recommends maintaining adequate perfusion during surgery *(26)*. Based on an evidence update in 2013, it is stated that haemodynamic GDFT appears to reduce SSI rates *(27)*. The SHEA/IDSA guidelines do not formulate a specific recommendation on the maintenance of normovolemia for SSI prevention. However, in a statement on oxygen therapy, it is indirectly recommended to maintain an appropriate volume replacement *(28)*.

Table 4.15.1. **Recommendations for the maintenance of normovolemia according to available guidelines**

Guidelines (year issued)	Recommendations for the maintenance of normovolemia
SHEA/IDSA practice recommendation (2014) *(28)*	No specific recommendation on the maintenance of normovolemia for SSI prevention. Indirect recommendation: "Supplemental oxygen is most effective when combined with additional strategies to improve tissue oxygenation, including maintenance of normothermia and **appropriate volume replacement**".
NICE (2008) *(26)*	Maintain adequate perfusion during surgery.
NICE (2013 update) *(27)*	Haemodynamic goal-directed therapy (titration of fluid and inotropic drugs to reach normal or supraoptimal physiological endpoints, such as cardiac output and oxygen delivery) appears to reduce SSI rates.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; SSI: surgical site infection; NICE: National Institute for Health and Care Excellence;

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the effectiveness of specific fluid management strategies compared with standard fluid regimens and to determine if certain fluid management strategies during surgery might be beneficial to prevent SSI in surgical patients.

Summary of the evidence

The purpose of the evidence review (web Appendix 16) was to evaluate whether specific fluid management strategies for the maintenance of normovolemia are more effective in reducing the risk of SSI than standard fluid regimens administered during surgery. The target population included patients of all ages undergoing a surgical operation. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Twenty-four RCTs *(1-24)* including a total of 4031 patients and comparing specific strategies of fluid management with standard fluid management were identified. Types of surgical procedures included were colorectal, abdominal, general, urology, gynaecological, cardiothoracic, vascular, orthopaedic and other surgery.

Due to heterogeneity among the selected studies in the type of specific fluid management strategy used throughout the perioperative period, separate meta-analyses were performed for GDFT or restrictive fluid regimens vs. standard fluid regimens in the pre-, intra- and postoperative periods.

Overall, there is low quality evidence that intraoperative GDFT has a significant benefit in reducing the SSI rate compared to standard fluid management (OR: 0.56; 95% CI: 0.35–0.88). By contrast, very low quality evidence indicated that intraoperative restrictive fluid management has neither benefit nor harm compared to standard intraoperative fluid management in reducing the SSI rate (OR: 0.73; 95% CI: 0.41–1.28).

One study *(20)* compared GDFT vs. standard fluid management preoperatively and demonstrated no benefit in reducing the risk of SSI (OR: 0.47; 95% CI: 0.13–1.72), whereas a meta-analysis of 2 RCTs *(22, 23)* comparing GDFT vs. standard fluid management in the postoperative period showed a decrease of the risk of SSI in the GDFT group (OR: 0.24; 95% CI: 0.11–0.52). One study *(24)* comparing restrictive vs. standard fluid management postoperatively showed no difference in risk (OR: 6.20; 95% CI: 0.68–56.56). Similarly, one RCT *(21)* compared GDFT vs. standard fluid management pre- and postoperatively combined and demonstrated no benefit (OR: 0.75; 95% CI: 0.16–3.52).

The retrieved evidence focused on adult patients only. No study was available in a paediatric population. Five RCTs reported that either fluid overload or hypovolemia seem to be associated with increased mortality and morbidity *(15, 18, 19, 23, 24)*.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG pointed out that patients are seldom informed about fluid management.

Resource use

The GDG underlined that there are no studies on the costs or cost-effectiveness of different fluid management strategies during surgery. However, the GDG noted that GDFT might require more resources, including the fact that the medical staff needs to be specifically trained. It was noted that in low-resource settings, anaesthesia is often provided by non-specialized professionals and there may also be a limitation in the type of intravenous fluids available.

Research gaps

The GDG highlighted that a widely-accepted definition for normovolemia is needed. Future studies including large well-designed RCTs with clear definitions should aim at identifying the most accurate and least invasive method of measuring normovolemia and assess its influence with regard to tissue oxygenation and normothermia. In particular, studies should be conducted in LMICs. More research is required to investigate the effectiveness of different fluid management strategies in paediatric populations.

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4.16 Drapes and gowns

Recommendations

1. **The panel suggests that either sterile, disposable, non-woven or sterile, reusable woven drapes and surgical gowns can be used during surgical operations for the purpose of preventing SSI.**
   (Conditional recommendation, moderate to very low quality of evidence)

2. **The panel suggests not to use plastic adhesive incise drapes with or without antimicrobial properties for the purpose of preventing SSI.**
   (Conditional recommendation, low to very low quality of evidence)

Rationale for the recommendations

- It is good clinical practice to use sterile drapes and gowns for surgery. To determine what type of surgical drapes and gowns are the most effective for the purpose of preventing SSI, the GDG decided to focus on disposable non-woven and reusable woven drapes, including plastic adhesive incise drapes with or without antimicrobial properties. Non-woven and woven drapes and gowns with antimicrobial properties were not considered a priority and no relevant evidence was found.
- Available evidence from one RCT, one quasi-RCT and 2 observational studies (moderate quality for RCTs and very low for observational) shows that the use of sterile disposable non-woven drapes and sterile surgical gowns has neither benefit nor harm when compared to sterile reusable woven drapes and surgical gowns in reducing the SSI rate. Considering the quality of the evidence, the GDG unanimously agreed to suggest that either sterile disposable non-woven or sterile reusable woven drapes and surgical gowns can be used. The strength of this recommendation was considered to be conditional.
- The GDG pointed out that there is no evidence for the potential effect of the timing or usefulness of changing surgical drapes or gowns in the course of a surgical operation for the purpose of preventing SSI.
- Evidence available from one RCT, one quasi-RCT and 2 observational studies (overall very low quality for both RCTs and observational) shows that the use of adhesive iodophor-impregnated incise drapes has neither benefit nor harm when compared to no adhesive incise drapes in reducing the SSI rate.
- Available evidence from 2 RCTs (overall low quality) shows that the use of plastic, adhesive, non-impregnated incise drapes has neither benefit nor harm when compared to no adhesive incise drapes in reducing the SSI rate.
- Considering the lack of evidence that plastic adhesive incise drapes (with or without antimicrobial properties) prevent SSI, the GDG unanimously agreed that they should not be used. Given the quality of the evidence (moderate to very low), the strength of this recommendation was considered to be conditional.

Remarks

- The GDG highlighted that if the material of the disposable and reusable surgical drapes and gowns is permeable to liquids, it can expose health care workers to body fluids and also represents a risk for patients. Ideally, the material should be impermeable to prevent the migration of microorganisms. The GDG remarked that both reusable and disposable drapes and gowns commercially available are in permeable or impermeable forms.
- The GDG identified possible harms associated with the use of disposable drapes in that the adhesive bands of single-use drapes may provoke skin rash or eczema and devices may be dislodged when removing adhesive drapes after the surgical procedure *(1)*.
- Regarding plastic, adhesive incise drapes, the GDG identified allergic reactions as a possible harm associated with the use of iodophor-impregnated incise drapes *(2)*. The GDG noted also that a further possible harm could be that pieces of the adhesive film might remain in the wound.

Background

Sterile surgical drapes are used during surgery to prevent contact with unprepared surfaces and maintain the sterility of environmental surfaces, equipment and the patient's surroundings. Similarly, sterile surgical gowns are worn over the scrub suit of the operating team during surgical procedures to maintain a sterile surgical field and reduce the risk of the transmission of pathogens to both patients and staff *(3)*.

Surgical gowns and drapes are fabricated from either multiple- or single-use materials. In addition, there is a considerable variation in design and performance characteristics within each of these two broad categories, which reflects the necessary trade-offs in economy, comfort and degree of protection required for particular surgical procedures *(4)*.

During surgical procedures, the risk of pathogen transmission increases if the barrier materials become wet. Consequently, the multiple- or single-use materials of the drapes and gowns used in a surgical procedure should prevent the penetration of liquids. Reusable materials are typically composed of different tightly woven textiles and/or knitted cotton or other fabrics possibly blended with polyester and/or chemically treated. These products have to be durable and provide protection after many cycles of processing and treatment. Disposable surgical drapes and gowns are typically composed of non-woven material of synthetic and/or natural origin, possibly combined with chemical treatment *(3)*.

Adhesive plastic incise drapes, either plain or impregnated with an antimicrobial agent (mostly an iodophor), are used on the patient's skin after completion of the surgical site preparation. The film adheres to the skin and the surgeon cuts through the skin and the drape itself *(5)*. Such a drape is theoretically believed to represent a mechanical and/or microbial barrier to prevent the migration of microorganisms from the skin to the operative site *(6)*. However, some reports have shown an increased recolonization of the skin following antiseptic preparation underneath adhesive drapes compared to the use of no drapes *(7)*.

A Cochrane review *(8)* and its updates *(5, 9)* of the effect of adhesive incise drapes to prevent SSI found that there is no evidence that plastic adhesive drapes reduce SSI. No recommendation is available on the use of sterile disposable or reusable drapes and surgical gowns for the purpose of SSI prevention.

This topic is addressed in a few of the recent available guidelines, but with conflicting recommendations. The recent SHEA/IDSA guidelines issued in 2014 recommend that plastic adhesive drapes with or without antimicrobial properties should not be used routinely as a strategy to prevent SSI *(10)*. However, the UK-based NICE issued a guideline in 2008 recommending that an iodophor-impregnated drape should be used if a plastic adhesive drape is required *(11)*.

Following an in-depth analysis of the available resources and given the limited recommendations from other guidelines, the GDG decided to conduct a systematic review to assess the effect of the use of sterile disposable or reusable drapes and surgical gowns, including plastic adhesive incise drapes, for the purpose of SSI prevention.

Summary of the evidence

The purpose of the evidence review (web Appendix 17) was to evaluate 3 important questions: (1) whether sterile disposable non-woven drapes and gowns or sterile reusable woven drapes and gowns should be used to prevent SSI; (2) whether changing drapes during operations affect the risk of SSI; and (3) whether sterile, disposable, adhesive incise drapes should be used to reduce the risk of SSI. The target population included patients of all ages undergoing a surgical procedure, with the presence of postoperative drainage. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

A total of 11 studies *(1, 12-21)* related to these topics with SSI as the primary outcome were identified and included 4 RCTs *(12, 17, 20, 21)*.

Regarding the first question, five studies including a total of 6079 patients and comprising one RCT *(12)*, one quasi-RCT *(13)* and three observational *(1, 14, 15)* were identified. Studies included clean and clean-contaminated (for example, general, cardiothoracic, orthopaedic, neurosurgery and plastic surgery) procedures. Four studies *(1, 12, 13, 15)* compared the use of sterile, disposable non-woven drapes and gowns vs. sterile, reusable woven drapes and gowns. One study *(14)* compared the use of sterile, disposable fenestrated drapes designed originally for cardiac catheterization with traditional draping that involved the use of multiple

reusable cloth drapes. There was a substantial variation among studies in the definition of SSI and the type and material of the single-use and reusable drapes and gowns.

After careful appraisal of the retrieved studies, a meta-analysis including the studies evaluating sterile, disposable non-woven vs. sterile, reusable woven drapes and gowns was performed. A moderate (RCTs) and very low (observational studies) quality of evidence showed that the use of sterile disposable non-woven drapes and gowns has neither benefit nor harm compared to sterile reusable woven items (OR: 0.85; 95% CI: 0.66–1.09 for RCTs; OR: 1.56; 95% CI: 0.89–2.72 for observational studies).

Regarding the second question, no studies assessing whether changing drapes during operations affects the risk of SSI were identified.

Regarding the third question, 6 studies (3 RCTs *(17, 20, 21)*, one quasi-RCT *(16)* and 2 observational *(18, 19)*) including a total of 1717 adult patients with SSI as an outcome were identified. Studies included clean and clean-contaminated (for example, cardiac, hip fracture fixation, open appendectomy, hernia repair and liver resection for hepatocellular carcinoma) surgical procedures. There was a substantial variation in the definition of SSI among studies.

Two separate meta-analysis comparisons were performed to evaluate sterile, disposable, antimicrobial-impregnated adhesive incise drapes vs. sterile non-adhesive incise drapes, and sterile, non-antimicrobial-impregnated adhesive incise drapes vs. sterile non-adhesive incise drapes. There is a very low quality of evidence suggesting that the use of sterile, disposable, antimicrobial-impregnated adhesive incise drapes has neither benefit nor harm compared to sterile non-adhesive incise drapes in reducing the risk of SSI (OR: 2.62; 95% CI: 0.68–10.04 for RCTs; OR: 0.49; 95% CI: 0.16–1.49 for observational studies). There is a low quality of evidence from 2 RCTs that the use of sterile, disposable non-antimicrobial-impregnated adhesive incise drapes has neither benefit nor harm compared to sterile non-adhesive incise drapes in reducing the risk of SSI (OR: 1.10; 95% CI: 0.68–1.78).

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to the interventions addressed in the recommendations. The GDG is confident that most patients would not want to be involved in the decision of whether to use disposable or reusable drapes and surgical gowns as long as the risk of SSI is minimized. It was acknowledged also that although patients may value measures to prevent SSI, they do not wish to be exposed to discomfort or possible harm due to skin irritation or allergic reactions to drapes (for example, associated with some adhesive disposable drapes or adhesive incise drapes).

Resource use

The GDG acknowledged that many different aspects need to be taken into account when evaluating the resource implications for the use of sterile disposable vs. sterile reusable drapes and surgical gowns. These include (but are not limited to) direct purchase costs and costs related to laundry and sterilization, labour required for reprocessing and waste disposal *(22)*. Two studies *(23, 24)* showed lower costs associated with the use of disposable drapes and gowns, whereas a cost-benefit analysis *(22)* found costs for sterile disposable drapes and gowns to be relatively higher compared with reusable ones. Other authors reported that costs were similar for disposable and reusable items *(25, 26)*. The heterogeneous findings of the available data on resource implications suggest that disposable and reusable surgical drapes and gowns are probably similar in costs.

In LMICs, the availability of disposable drapes and gowns and adhesive incise drapes may be limited and costs may represent a high financial burden, whereas labour costs for reprocessing reusable items may be less of an issue. The disposal of single-use drapes and gowns and the ecological impact should be considered as their use generates additional clinical waste. Taking into account the lack of evidence of any benefit for the prevention of SSI, the additional cost for plastic adhesive incise drapes is not justified, irrespective of the setting.

Research gaps

The GDG highlighted that the available evidence regarding the interventions addressed in the recommendations is limited and comes mainly

from high-income countries. More well-designed RCTs investigating the use of sterile disposable compared to sterile reusable drapes and surgical gowns in terms of SSI prevention are needed, particularly in LMICs. A cost-effectiveness analysis is highly recommended, especially in low-resource settings. Further research should focus also on different types of materials (including permeable and impermeable materials) and address environmental concerns (water, energy, laundry, waste, etc.). Another research priority is to investigate whether drapes should be changed during the operation and if this measure has an effect on SSI rates. The GDG highlighted that the use of adhesive incise drapes is not considered a high priority topic in the field of SSI prevention research. Nevertheless, well-designed RCTs should be encouraged to further investigate the potential benefits of these products, which are aggressively promoted by the manufacturing companies.

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4.17 Wound protector devices

Recommendation

The panel suggests considering the use of wound protector (WP) devices in clean-contaminated, contaminated and dirty abdominal surgical procedures for the purpose of reducing the rate of SSI. *(Conditional recommendation, very low quality of evidence)*

Rationale for the recommendation

- Overall very low quality evidence shows that a single- or double-ring WP device has benefit in reducing the rate of SSI compared with regular wound protection. Meta-regression analysis showed no strong evidence for a difference in the effect between single- and double-ring WPs. There was also no evidence that the effect differed between clean-contaminated or contaminated or dirty surgery and other surgery.
- The GDG agreed to suggest the use of either WP device in abdominal surgery with laparotomy for the purpose of reducing SSI. Given the very low quality evidence, the strength of the recommendation was considered to be conditional and the GDG proposed to use the terminology "The panel suggests considering..." to highlight the need for careful local evaluation about whether and how to apply this recommendation, in particular regarding the availability of these devices and associated costs.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, the effectiveness of this intervention is not proven for paediatric patients.
- Two differently designed types of commercially-available WP devices have been used as an intervention in the included studies, that is, single- *(1-6)* and double-ring WPs *(7-11)*.
- With regard to the degree of wound contamination in abdominal surgery, 5 studies included clean-contaminated *(3-7)*, 5 studies included contaminated *(2-6)* and 6 studies investigated dirty procedures *(2-6, 9)*.
- The GDG identified possible harms associated with the use of WP devices, particularly in patients with abdominal adhesions. In these cases, the insertion of a WP device may be difficult and lead to the need to enlarge the incision, to injuries to the small bowel and to the prolongation of the procedure. A further concern is the limited space to access the surgical field after insertion of the WP.
- Although poorly assessed by the studies included, no serious adverse effects have been reported.
- The GDG emphasized that the operating surgeon needs to be familiar with handling a WP device during placement, in the operative phase and upon removal to avoid wound contamination at these critical time points, particularly when WP is used in patients with a high intra-abdominal bacterial load, such as diffuse peritonitis.
- The GDG highlighted that these are single-use devices that must not be reused.

Background

Although surgeons have progressively paid more attention to the control of operative wound contamination during surgical procedures, incisional SSI is still a frequent postoperative adverse event jeopardizing patient safety and increasing health care costs.

Conventional surgical drapes are commonly used by surgeons to limit the aseptic surgical area and to cover the freshly-made wound edges. Nevertheless, this non-fixed mechanical barrier may become dislodged or potentially contaminated.

To better reinforce the aspects related to wound edge isolation, surgical WP devices have been fabricated and marketed, unlike new developed drugs that need different controlled studies before approval by regulatory bodies. These new surgical devices comprise a non-adhesive plastic sheath

attached to a single or double rubber ring that firmly secures the sheath to the wound edges. The device is intended to facilitate the retraction of the incision during surgery without the need for additional mechanical retractors and cloths. Theoretically, commercially-available WPs are intended to reduce wound edge contamination to a minimum during abdominal surgical procedures, including contamination from outside (clean surgery) and inside the peritoneal cavity (clean-contaminated, contaminated and dirty surgery). Although these surgical devices are already on the market, their real usefulness and cost-effectiveness warrants additional evidence-based analysis.

Few organizations have issued recommendations regarding the use of WP devices (Table 4.17.1). The UK-based NICE states that wound edge protection devices may reduce SSI rates after open abdominal surgery, but no recommendation is given due to the lack of further high quality evidence *(12)*. However, SHEA/IDSA guidelines recommend the use of impervious plastic WPs for gastrointestinal and biliary tract surgery *(13)*.

Table 4.17.1. **Recommendations on the use of WP devices according to available guidelines**

Guidelines (year issued)	Recommendations on the use of WP devices
SHEA/IDSA practice recommendation (2014) *(13)*	Use impervious plastic WPs for gastrointestinal and biliary tract surgery.
NICE (2013 update) *(12)*	Wound edge protection devices may reduce the SSI rate after open abdominal surgery, but the current lack of high quality studies implies that more research is needed.

WP: wound protector; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence.

Following the in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess the effectiveness of WP devices compared with standard wound edge protection and to determine if they might be beneficial to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 18) was to evaluate whether the use of a WP device is more effective in reducing the risk of SSI than conventional wound protection, which is mainly through placing wet towels between the wound edge in combination with steel retractors. The target population included patients of all ages undergoing either elective or urgent abdominal surgery through conventional open access. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Eleven trials comparing the use of a WP device with conventional wound protection in abdominal surgical procedures with laparotomy were identified. These included a total of 2949 patients and comprised 10 RCTs *(1, 3-11)* and one prospective controlled trial *(2)*. There is very low quality evidence for the benefit of either a single- or double-ring WP device in reducing the SSI rate when compared with standard wound protection (OR: 0.42; 95% CI: 0.28–0.62).

This beneficial effect was observed both for single- (OR: 0.51; 95% CI; 0.34–0.76) and double-ring WPs (OR: 0.25; 95% CI: 0.13–0.50). Similarly, meta-regression analysis showed no strong evidence for a difference in the effect between single- and double-ring WPs (P=0.107). There was also no evidence that the effect differed between clean-contaminated (P=0.244), contaminated (P=0.305) or dirty (P=0.675) surgery and other surgery. The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients wish to receive this intervention in order to reduce the risk of SSI. Patients will prefer also to be treated by surgeons who are familiar with the use of WP devices in order to reduce the risk of complications.

Resource use

In LMICs, the availability of WP devices may be limited and represent a high financial burden. The GDG pointed out that this intervention may not be prioritized in resource-limited settings compared to other interventions to reduce SSI. It was highlighted that there is a need for staff training, irrespective of the setting. Few studies addressed the cost-effectiveness of the intervention. Two small studies found the use of WP to be cost-effective *(6, 9)*, while one larger trial did not *(14)*.

Research gaps

The GDG highlighted that the available evidence consists mainly of low quality small studies. There is a need for properly designed multicentre RCTs. The SSI outcome should be defined according to the CDC criteria and sub-specified as superficial, deep and organ/space occupying infections. Specific and relevant surgical procedures should be reported regarding the level of wound contamination and the rate of incisional SSI (for example, colorectal surgery and laparotomy for peritonitis). Investigators should consider comparing single- with double-ring WP devices. Trials should report adverse events related to the intervention. Finally, cost-effectiveness studies are also needed.

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4.18 Incisional wound irrigation

Recommendations

The panel considers that there is insufficient evidence to recommend for or against saline irrigation of incisional wounds before closure for the purpose of preventing SSI.

The panel suggests considering the use of irrigation of the incisional wound with an aqueous PVP-I solution before closure for the purpose of preventing SSI, particularly in clean and clean-contaminated wounds.

The panel suggests that antibiotic incisional wound irrigation before closure should not be used for the purpose of preventing SSI.
(Conditional recommendations/low quality of evidence)

Rationale for the recommendation

- RCTs comparing wound irrigation vs. no wound irrigation or wound irrigation using different solutions with SSI as an outcome were evaluated. Evidence was available on intraperitoneal, incisional wound and mediastinal irrigation in patients undergoing various surgical procedures.
- Considering the substantial heterogeneity in the available evidence, the GDG decided to focus only on incisional wound irrigation. In particular, the GDG agreed not to consider intraperitoneal irrigation for the formulation of recommendations as the identified studies described contaminated and dirty intra-abdominal procedures (for example, peritonitis). Therefore, wound irrigation was likely to represent a therapeutic intervention, rather than a prophylactic measure.
- Very low quality evidence shows that incisional wound irrigation with saline solution has neither benefit nor harm compared to no irrigation.
- Low quality evidence shows that the irrigation of the incisional wound with an aqueous PVP-I solution is beneficial with a significant decrease of the risk of SSI when compared to irrigation with a saline solution.
- Very low quality evidence shows that the irrigation of the incisional wound with antibiotic solutions has neither benefit nor harm compared to irrigation with a saline solution or no irrigation.
- The GDG agreed that there is insufficient evidence to issue a recommendation for or against the saline solution irrigation of incisional wounds for the purpose of preventing SSI. The GDG also decided to suggest considering the use of irrigation of the incisional wound with an aqueous PVP-I solution. The term "considering" was proposed to highlight that a decision-making process is needed, especially focusing on clean and clean-contaminated wounds. Finally, the GDG agreed to suggest that antibiotic incisional wound irrigation should not be used for the purpose of preventing SSI. The strength of these recommendations should be conditional due to the low quality of the evidence.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, the effectiveness of irrigation of the incisional wound with an aqueous PVP-I solution is not proven for paediatric patients.
- The available evidence from 7 RCTs *(1-7)* (10 estimates) showed that irrigation of the incisional wound with an aqueous PVP-I solution was beneficial in reducing the risk of SSI when compared to irrigation with a saline solution. Stratification of the evidence by contamination showed that the effect was attributable to incisional wound irrigation in clean and clean-contaminated procedures rated as wound classes I and II according to the CDC system *(8)*.
- The evidence on irrigation of incisional wounds with aqueous PVP-I is available from studies investigating PVP-I 10% in open abdominal surgery (CDC wound classes I-IV; 3 RCTs), PVP-I 1% in appendectomies (CDC wound classes II-IV; one RCT) and PVP-I 0.35% in orthopaedic spine surgery (CDC wound class I; 3 RCTs). There was no evidence for a dose-response effect with regard to the concentration of the PVP-I solution used.

- Two RCTs showed that the pulse pressure irrigation of incisional wounds with a normal saline solution was beneficial in reducing the risk of SSI in CDC wound classes I and II-III compared to normal irrigation with a saline solution. One RCT showed that irrigation with a normal saline solution applied with pressure to the incisional wound was beneficial compared to no irrigation. Nevertheless, the GDG considered that there is insufficient evidence to issue a recommendation for or against the saline solution irrigation of incisional wounds as one RCT investigating regular irrigation with a saline solution showed neither benefit nor harm when compared to no irrigation. When saline solution irrigation is used, the use of pulse pressure irrigation may be considered.
- The available evidence from 5 RCTs shows that the antibiotic irrigation of the incisional wound has neither benefit nor harm in reducing SSI when compared to no or saline solution irrigation.
- Of the included studies, 3 RCTs *(5, 9, 10)* described sterility of the irrigation fluid. The other studies did not report whether the irrigation fluid was sterile or not.
- The GDG discussed allergic reactions and metabolic adverse events as potential harms of iodine uptake. However, clinical signs of iodine toxicity were not reported in the included studies *(5)*. In the case of known or presumed allergy to iodine, other products (for example, chlorhexidine) should be used if incisional wound irrigation is performed. PVP-I must not be allowed to come into contact with exposed meninges and neural tissues, such as the brain or spinal cord *(11)*. Based on in vitro studies *(12, 13)*, the GDG also raised concerns about the potential toxic effects of PVP-I on fibroblasts, the mesothelium and the healing of tissue. No study assessed undesirable outcomes for pulse pressure irrigation.
- The GDG highlighted the risk of emergence of AMR associated with the use of antibiotics for wound irrigation. Considering that the evidence shows that this procedure has no benefit with regard to SSI prevention, the GDG strongly emphasized that this practice is associated with an unnecessary risk of contributing to AMR. Furthermore, the GDG underlined that there is no standardized procedure to prepare an antibiotic solution for wound irrigation and no certainty of target attainment by using this method.

Background

Intraoperative wound irrigation is the flow of a solution across the surface of an open wound to achieve wound hydration and it is widely practised to help prevent SSI *(14-16)*. It is intended to act as a physical cleaner by removing cellular debris, surface bacteria and body fluids, to have a diluting effect on possible contamination, and to function as a local antibacterial agent when an antiseptic or antibiotic agent is used. Up to 97% of surgeons state that they use intraoperative irrigation *(14)*.

However, practices vary depending on the patient population, the surface of application and solutions used. Similar variations in methodology and results can be observed in studies investigating the effect of wound irrigation *(17)*. Some experimental studies have also raised concerns about the cytotoxicity of some bactericidal additives, but the clinical relevance of these findings is unclear. Moreover, most of the literature investigating wound irrigation dates from an era when infection prevention measures were incomparable to practice today.

Two clinical practice guidelines issued by professional societies and a national authority have included contradictory recommendations regarding intraoperative wound irrigation (Table 4.18.1). The SHEA/IDSA guideline recommends performing intraoperative antiseptic wound lavage (grade II level of evidence) *(18)*. The UK-based NICE guideline states that there is only limited evidence suggesting a benefit for intraoperative wound irrigation with PVP-I. However, although wound irrigation with PVP-I may reduce SSI, PVP-I is not licensed for open wounds by the US Food and Drug Administration *(19)*. Therefore, the NICE guideline recommends that wound irrigation should not be used to reduce the risk of SSI *(20)* .

Table 4.18.1. **Recommendations on wound irrigation according to available guidelines**

Guidelines (date issued)	Recommendations on wound irrigation to reduce the risk of SSI
SHEA/IDSA (2014) *(18)*	Perform antiseptic wound lavage (for example, with diluted PVP-I).
NICE (2008) *(20)*	Do not use wound irrigation to reduce the risk of SSI.

SSI: surgical site infection; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence.

Following the in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on wound irrigation.

Summary of the evidence

The purpose of the evidence review (web Appendix 19) was to investigate whether intraoperative wound irrigation (with or without active agents or pressured application) affects the incidence of SSI. The population studied were adult patients undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality. Only studies investigating wound irrigation (flow of solution across the surface of an open wound, with or without active additives) were included. Studies investigating the topical application of antibiotics or antiseptics (powder, gels, sponges, etc.) other than intraoperative wound irrigation were not included. To ensure that only evidence relevant to the current standard of infection prevention measures was included in our analyses, studies where SAP was not administered appropriately (that is, preoperatively and intravenous) were excluded. In addition, studies where wound irrigation represented a therapeutic intervention for a pre-existent infection rather than a prophylactic measure were also excluded.

A total of 21 RCTs comparing (active) wound irrigation vs. no (active) wound irrigation in patients undergoing various surgical procedures were identified with SSI as the outcome (web Appendix 19). There was substantial heterogeneity in the available evidence. The main differences were related to the irrigated surface, the composition of the irrigation fluid and the surgical procedure with the associated wound contamination level. After careful appraisal of the included studies, the research team and the GDG decided to restrict the recommendation to incisional wound irrigation as too little (and heterogeneous) evidence was available to address other applications of irrigation (that is, intraperitoneal or mediastinal irrigation). In particular, the GDG agreed not to consider intraperitoneal irrigation for the formulation of recommendations as the identified studies described contaminated and dirty intra-abdominal procedures (for example, peritonitis). Therefore, wound irrigation was likely to represent a therapeutic intervention, rather than a prophylactic measure.

Meta-analyses were performed to evaluate the following comparisons in incisional wound irrigation: saline solution vs. no irrigation; syringe pressure irrigation with saline solution vs. no irrigation; pulse pressure irrigation with saline solution vs. normal saline solution; aqueous PVP-I vs. saline solution; and antibiotic vs. saline solution or no irrigation.

One study *(21)* compared irrigation of the incisional wound with normal saline solution to no irrigation in women undergoing a caesarean section (CDC wound class II). The study demonstrated no significant difference between wound irrigation and no irrigation on the incidence of incisional wound infection (OR: 1.09; 95% CI: 0.44-2.69; *P*=0.85). The quality of evidence was very low due to risk of bias and imprecision. When different methods of irrigation were compared, a low quality of evidence from 2 studies *(22, 23)* demonstrated a significant benefit for pulse pressure irrigation in preventing SSI compared to normal irrigation with a saline solution (OR: 0.30; 95% CI: 0.08-0.86; *P*=0.0003). A moderate quality of evidence from another study *(24)* demonstrated a significant benefit for irrigation with a normal saline solution applied with force compared to no irrigation (OR: 0.35; 95% CI: 0.19-0.65; *P*=0.0009).

Seven RCTs *(1-7)* compared irrigation of the incisional wound with aqueous PVP-I solutions in

different concentrations to irrigation with a saline solution. Meta-analysis of these studies demonstrated a significant benefit for incisional wound irrigation with an aqueous PVP-I solution (OR: 0.31; 95% CI: 0.13-0.73; *P*=0.007). However, the quality of evidence was low due to risk of bias and imprecision. Stratification for wound contamination and PVP-I solution showed that the effect was attributable to incisional wound irrigation in clean and clean-contaminated procedures with PVP-I 10% and PVP-I 0.35%.

Five studies *(25-29)* compared irrigation of the incisional wound with an antibiotic solution to irrigation with a normal saline solution or no irrigation in CDC wound classes I-IV. A meta-analysis of the 5 RCTs demonstrated no significant difference between antibiotic irrigation of the incisional wound and no irrigation or only with a saline solution (OR: 1.16; 95% CI: 0.64-2.12; P=0.63). The quality of evidence was very low due to risk of bias and imprecision.

Factors considered when formulating the recommendation

Values and preferences

Patient values and preferences were not assessed by the studies, but the GDG argued that the recommendation was in line with the values and preferences of most patients.

Resource use

The GDG pointed out that there is a lack of data on costs or the cost-effectiveness of interventions using wound irrigation. Although the GDG recognized that saline and PVP-I solutions are usually readily available in most settings, the availability of sterile products may be limited in LMICs. In many settings, the availability and costs of pulse pressure devices, including their purchase, waste disposal, procurement, energy and machine maintenance, represent a high financial burden, especially in LMICs. Moreover, the use of pressure devices introduces the need for staff protection, such as gowns and face shields.

Research gaps

The GDG highlighted that the available evidence comes from old studies mainly conducted in the 1980s. This represents a serious limitation as IPC measures have changed significantly since that period. New well-designed RCTs using standard of care protocols for SAP are needed to evaluate and compare the most commonly-used irrigation practices with a special emphasis on the agent used and a focus on the prevention of SSI in different surgical procedures. In particular, it is unclear as to what is the best alternative agent to PVP-I in the case of an adverse event with this solution. These studies should be conducted in both high-income and LMICs. In addition, trials should address also the cost-effectiveness of the intervention and the harm associated with irrigation and the agents used for irrigation.

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4.19 Prophylactic negative pressure wound therapy

Recommendation

The panel suggests the use of prophylactic negative pressure wound therapy (pNPWT) in adult patients on primarily closed surgical incisions in high-risk wounds, for the purpose of the prevention of SSI, while taking resources into account.
(Conditional recommendation, low quality of evidence)

Rationale for the recommendation

- Overall low quality evidence shows that pNPWT has a benefit in reducing the risk of SSI in patients with a primarily closed surgical incision following high-risk wounds (for example, in case of poor tissue perfusion due to surrounding soft tissue/skin damage, decreased blood flow, bleeding/hematoma, dead space, intraoperative contamination) when compared to conventional postoperative wound dressings.
- The GDG emphasized that the devices used for pNPWT are expensive and may not be available in low-resource settings. Thus, the prioritization of this intervention should be carefully considered according to resources available and other priority measures for the prevention of SSI.
- It was also noted that there were no trials comparing different levels of negative pressure or different durations of applying negative pressure to the wound. In addition, studies did not report subgroup analyses by type of surgery or the degree of wound contamination. In stratified meta-analyses, there was little evidence that the effects differed by type of surgery, wound class or the level and duration of applying negative pressure. The GDG concluded that the effect appears to be independent of these factors and that no recommendations can be made on the optimal level of pressure or duration of application.
- As a result of the low quality evidence and the other above-mentioned factors, the majority of GDG members agreed to suggest the use of pNPWT on primarily closed surgical incisions in high-risk procedures, but taking resources into account. One GDG member disagreed with the recommendation because he considered the evidence insufficient to support it. The GDG decided that the strength of this recommendation should be conditional.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. Therefore, this recommendation is not proven for paediatric patients. The GDG pointed out that all RCTs were performed in clean surgery (4 in orthopaedic and trauma surgery), apart from one study that also included abdominal procedures. By contrast, the included observational studies were performed in clean, clean-contaminated, contaminated and dirty procedures. As pNPWT devices are commonly used in abdominal surgery, the GDG considered that observational studies should be included.
- Negative pressure devices were set between 75 mm Hg and 125 mm Hg with the postoperative duration ranging from 24 hours up to 7 days. The control group used sterile dry gauze, tape, occlusive or absorbent dressings.
- The overall quality of evidence was low for the RCTs due to risk of bias and imprecision and low for the observational studies.
- The GDG discussed potential mechanisms for the observed benefit of pNPWT, including less wound dehiscence, better removal of fluids and protection against microorganisms entering the wound from the surrounding environment.
- The GDG identified the appearance of blisters *(1)* or maceration as possible harms associated with the use of use of negative pressure devices. No other relevant adverse event was identified through the available evidence.

Background

Negative Pressure Wound Therapy consists of a closed sealed system connected to a vacuum pump, which maintains negative pressure on the wound surface. pNPWT is used on primarily closed surgical incisions to prevent SSI. Although negative pressure wound therapy has been used since the late 1990s for several purposes, such as open bone fractures *(2)*, diabetic ulcers *(3)* and management of open abdomen wounds *(4)*, its use for the prevention of SSI is relatively new. After the first report of its use in orthopaedic surgery in 2006 *(5)*, several studies have followed.

Current SSI prevention guidelines do not offer a recommendation on the use of pNPWT. Only the UK-based NICE addresses this topic in a recent evidence update of its guidelines, but without formulating a recommendation. These guidelines state that "NPWT appears to reduce SSI rates after the invasive treatment of lower limb trauma, but may be less effective in other patient groups, such as those with multiple comorbidities. Further research is needed." *(6)*.

Following discussion about the interest in this topic and the lack of recommendations in other guidelines, the GDG decided to conduct a systematic review to assess the effectiveness of the use of pNPWT to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 20), was to evaluate whether the use of pNPWT is more effective in reducing the risk of SSI than the use of conventional wound dressings without negative pressure therapy. The target population included patients of all ages undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Nineteen articles describing 20 studies that compared the use of pNPWT with conventional wound dressings were identified. These included a total of 6122 patients and comprised six RCTs *(1, 5, 7-9)* and 14 observational studies *(10-23)* (RCTs, 562; observational studies, 5560). One article *(5)* described two separate studies and another article assessed and analysed separately two different patient populations (breast and colorectal) *(20)*.

Due to heterogeneity among the selected studies regarding the type of surgical procedure or wound contamination class, as well as the level and duration of applying negative pressure, additional separate meta-analyses were performed. These concerned the type of surgical procedure, wounds classified as clean and clean-contaminated, the duration of pNPWT for ‹5 days vs. ›5 days and a pressure level of ‹100 mmHg vs. ›100 mmHg (web Appendix 20).

Overall, there is low quality evidence from RCTs and observational studies that pNPWT has a significant benefit in reducing the risk of SSI in patients with a primarily closed surgical incision when compared to conventional postoperative wound dressings (RCTs: OR: 0.56; 95% CI: 0.32–0.96; observational studies: OR: 0.30; 95% CI: 0.22–0.42). When stratified by the type of surgery (web Appendix 20), the most relevant meta-analyses results showed no statistically significant benefit in the reduction of the risk of SSI in orthopaedic and/or trauma surgery. By contrast, a significant benefit was observed in reducing SSI rates with the use of pNPWT compared to conventional wound dressings in abdominal (9 observational studies; OR: 0.31; 95% CI: 0.19–0.49) and cardiac surgery (2 observational studies; OR: 0.29; 95% CI: 0.12–0.69).

In the stratification by wound contamination class (web Appendix 20), the most relevant meta-analyses results showed a significant benefit in reducing SSI rates with the use of pNPWT compared to conventional wound dressings in clean surgery (8 observational studies; OR: 0.27; 95% CI: 0.17–0.42) and in clean-contaminated surgery (8 observational studies; OR: 0.29; 95% CI: 0.17–0.50).

When considering different durations of pNPWT (for either ‹ or ≥ 5 days) and a pressure level (of either ‹ or ≥ 100 mmHg), the significant benefit observed with the use of pNPWT remained unchanged (web Appendix 20).

The body of retrieved evidence focused on adult patients only. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients would

wish to receive this intervention in order to reduce the risk of SSI. However, there are concerns about comfort and convenience as some devices can be noisy and may disturb sleep. The GDG pointed out that the use of pNPWT may prolong hospital stay, but this could be prevented by the use of portable suction systems.

Resource use

The availability and costs of these devices and the potential extension of hospital stay are major concerns, mainly in LMICs, but also in high-resource settings. The GDG remarked that patients are generally more likely to receive a conventional dressing instead of pNPWT due to lack of material and evidence of cost-effectiveness. However, studies in gynaecological patients showed that the intervention may be cost-effective *(24-26)*. The GDG acknowledged that it may be possible to construct a non-portable, locally-made device at low cost for LMICs. It was highlighted also that there is a need to train staff in handling these devices, regardless of the setting.

Research gaps

The GDG highlighted that additional well-designed RCTs investigating the use of pNPWT for SSI prevention are needed, especially in LMICs. Future research is likely to have an important impact on our confidence in the estimate of effect. The main research priority is to identify the groups of patients in whom this intervention is cost-effective, including those undergoing contaminated and dirty procedures. Further research is also needed to identify the optimal level of negative pressure and duration of application.

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4.20 Use of surgical gloves

Recommendation

The panel decided not to formulate a recommendation due to the lack of evidence to assess whether double-gloving or changing of gloves during the operation or using specific types of gloves is more effective in reducing the risk of SSI.

Remarks

- Gloving refers to the use of sterile gloves by the surgical team during the operation.
- During the operation, glove decontamination with alcohol or other products for the purpose of reuse should never be performed.
- Sterile surgical gloves (as well as medical examination gloves) are single-use items and should not be reused.
- The literature search failed to identify relevant studies on the following topics of interest that ultimately could inform a recommendation for these questions with regard to the prevention of SSI: a comparison of double-gloving vs. using a single pair of gloves; the intraoperative changing of gloves vs. retaining gloves; and latex gloves vs. other types of gloves.
- The GDG emphasized that most surgeons prefer to double-glove because it is plausible that bacterial contamination of the surgical field may occur in the event of glove perforation. Moreover, most surgeons prefer to wear double gloves for their own protection against injury from sharps and/or bloodborne infections. In the case of double-gloving, a routine change of the outer gloves during long surgeries is often recommended by health care practitioners. However, no evidence was found to support these practices.

Background

The invasive nature of surgery introduces a high risk for the transfer of pathogens that may cause bloodborne infections in patients and/or the surgical team, as well as SSI. This risk may be reduced by implementing protective barriers, such as wearing surgical gloves.

A Cochrane review *(1)* published in 2009 investigated whether additional glove protection reduces the number of SSIs or bloodborne infections in patients or the surgical team and the number of perforations to the innermost pair of surgical gloves. There was no direct evidence that additional glove protection worn by the surgical team reduces SSI in patients. However, the review had insufficient power for this outcome as only two trials were found with the primary outcome of SSI, both of which reported no infections. No trials were found with transmitted bloodborne infections as an outcome in surgical patients or the surgical team in relation to the gloving method. Thirty-one RCTs were identified with the outcome of glove perforation, leading to the result that the use of a second pair of surgical gloves, triple gloving, knitted outer gloves and glove liners significantly reduces perforations to the innermost gloves.

Few organizations have issued recommendations regarding the use of gloves (Table 4.20.1). The latest WHO *guidelines for safe surgery* published in 2009 *(2)* recommend that the operating team should cover their hair and wear sterile gowns and sterile gloves during the operation, but without any indication on single or double-gloving. The SHEA/IDSA guidelines *(3)* recommend that all members of the operative team should double-glove and change gloves when perforation is observed. However, the modalities and frequency of changing gloves have not been included in any guidelines or recommendations *(2-4)*.

Table 4.20.1. **Recommendations on gloving according to available guidelines**

Guidelines (year issued)	Recommendations on the use of gloves
WHO guidelines for safe surgery (2009) *(2)*	The operating team should cover their hair and wear sterile gowns and sterile gloves during the operation.
SHEA/IDSA practice recommendation (2014) *(3)*	All members of the operative team should double-glove and change gloves when perforation is observed.

WHO: World Health Organization; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess the effectiveness of double-gloving and the changing of gloves at a specific time during the operation to reduce SSI. The question of whether a specific type of gloving is beneficial in reducing the risk of SSI was also addressed.

Summary of the evidence

The purpose of the evidence review (web Appendix 21) was to evaluate whether double-gloving or the changing of gloves during the operation is more effective in reducing the risk of SSI than single-glove use or no change of gloves. In a third approach, it was evaluated whether specific types of gloving (that is, glove liners, coloured perforation indicator systems, cloth/steel outer gloves, triple gloves) are more effective in reducing the risk of SSI than the use of latex gloves. The target population included patients of all ages undergoing a surgical operation. The primary outcome was the occurrence of SSI and SSI-attributable mortality. Bacterial contamination of the gloves was considered as a surrogate outcome.

Ten studies comprising 8 RCTs *(5-12)* and 2 observational studies *(13, 14)* were identified. Among these, one observational study compared the efficacy of double-gloving with the use of a single pair of gloves with an SSI outcome *(13)* and another (observational) with a cerebrospinal fluid shunt infection outcome *(14)*. Six studies compared the changing of gloves during the operation with the retaining of gloves (3 RCTs with an SSI outcome *(6, 7, 10)*, 2 RCTs *(5, 11)* focusing on bacterial contamination and one RCT *(12)* reporting on both). Two RCTs with an SSI outcome compared specific types of gloving with the use of latex gloves *(8, 9)*. Types of surgery included were neurosurgery, hernia repair, caesarean section, orthopaedic and vascular surgery.

Due to heterogeneity among the selected studies regarding comparison, design and outcome, quantitative meta-analyses were not performed.

Whereas one observational study *(14)* showed that the cerebrospinal fluid shunt infection rate was significantly higher in the single-glove group compared to the double-glove group, another observational study *(13)* found no difference in the risk of SSI between double- vs. single-gloving in patients undergoing hernia repair. Three RCTs *(6, 7, 10)* showed no difference in risk for post-caesarean SSI or endometritis when comparing changing of gloves or removal of the external second pair of gloves after delivery of the placenta or fetus to retaining the gloves during the entire procedure. One RCT *(12)* reported a reduction of superficial SSI when changing of gloves was performed vs. no change of gloves before the first contact with the vascular prosthesis in synthetic vascular graft surgery. Three RCTs *(5, 11, 12)* and one additional non-comparative observational study *(15)* showed that changing of the external second pair of gloves in the course of the operation significantly decreases the incidence of bacterial contamination of the gloves. Two RCTs *(8, 9)* showed no difference in SSI when comparing different types of gloves (double-gloving) in orthopaedic surgery.

The methodological quality of most of the selected studies was poor as most trials did not provide sufficient details of their process of randomization, allocation, sample size calculation and blinding. SSI

definitions varied across the studies. There were few studies with SSI as the primary outcome. Included studies with bacterial contamination as a surrogate outcome showed a great heterogeneity in the setting, design and outcome measures. There is no direct evidence demonstrating the link between bacterial contamination and SSI rates.

The body of retrieved evidence focused on adult patients and no study was available in a paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered

Resource use

The availability of surgical gloves could be limited in LMICs, particularly specific types, such as glove liners, coloured perforation indicator systems, cloth steel outer gloves. In limited resource settings, an acceptable quality of gloves needs to be ascertained as patients are often asked to purchase surgical gloves themselves, which could be of substandard quality.

Research gaps

GDG members highlighted that well-designed RCTs investigating the effectiveness of double-gloving compared to the use of a single pair of gloves would be welcome, especially in LMICs. In addition, RCTs evaluating whether a change of gloves during the operation is more effective in reducing the risk of SSI than no change of gloves are needed, including an assessment of the criteria for changing gloves during the surgical procedure. It would be interesting also to compare different types of gloving to address the question of the optimal type of gloves to be used. All studies should focus on SSI as the primary outcome and be defined according to the CDC criteria and sub-specified as superficial, deep and organ space-occupying.

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4.21 Changing of surgical instruments

Recommendation

The panel decided not to formulate a recommendation on this topic due to the lack of evidence.

Remarks

- Surgical instruments are tools or devices that perform functions such as cutting, dissecting, grasping, holding, retracting or suturing. Most surgical instruments are made from stainless steel.
- The literature search failed to identify relevant studies comparing wound closure using new, sterile surgical instruments with wound closure with previously-used instruments in contaminated surgery for the purpose of preventing SSI.
- The GDG believes that changing instruments for wound closure in contaminated surgery is common practice. A change of instruments prior to wound closure after contaminated surgical procedures seems logical, particularly after colorectal surgery or in patients operated on for diffuse peritonitis. Nevertheless, there is no evidence to support this practice.

Background

SSI is caused by microorganisms either from the patient's own skin flora or from the environment surrounding the patient. In both cases, there is a potential for microorganisms to adhere to surgical instruments and consequently contaminate the incisional wound, particularly during contaminated surgical procedures. Therefore, it is common practice to exchange surgical instruments used in contaminated surgical procedures for a new sterile set of surgical instruments before wound closure.

Current SSI prevention guidelines do not address the exchange of surgical instruments prior to wound closure and its effect to prevent SSI. The GDG decided to conduct a systematic review to assess the effectiveness of this practice.

Summary of the evidence

The purpose of the evidence review (web Appendix 22) was to evaluate whether wound closure employing new, clean surgical instruments is more effective in reducing the risk of SSI than wound closure with previously-used surgical instruments. The target population included patients of all ages undergoing contaminated surgical operations. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

The literature search did not identify any studies comparing wound closure using new, sterile surgical instruments and wound closure with previously-used surgical instruments in contaminated surgery.

Two studies, one RCT *(1)* and one observational study *(2)*, investigated the change of instruments in colorectal surgery in combination with other interventions performed before wound closure, including the change of drapes, gowns and gloves, wound lavage and rescrubbing (not homogeneous in terms of interventions). Both studies showed no benefit for the prevention of SSI.

Research gaps

The GDG highlighted that well-designed RCTs investigating the change of instruments prior to wound closure would be welcome. SSI outcome should be defined according to CDC criteria and studies should be conducted in LMICs and high-income countries and include different surgical procedures. However, several GDG members pointed out that such trials are unlikely to be done. In the future, it is more likely that further studies of combined interventions will be conducted.

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4.22 Antimicrobial-coated sutures

Recommendation

The panel suggests the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery.
(Conditional recommendation, moderate quality of evidence)

Rationale for the recommendation

Overall low to moderate quality evidence shows that antimicrobial-coated sutures have significant benefits in reducing SSI rates in patients undergoing surgical procedures when compared to non-coated sutures. The effect seems to be independent of the type of suture, procedure or wound contamination classification. In meta-regression analysis, there was no evidence that the effect of antimicrobial-coated sutures differed between braided and monofilament sutures, clean, cardiac or abdominal surgery, and other surgeries. However, the GDG highlighted that the available trials examined triclosan-coated, absorbable sutures only. There were no studies identified that investigated other antimicrobial agents. Considering the low to moderate quality of the evidence and the low quality of comparisons in the subgroups of the RCTs included in the meta-regression analyses, the GDG agreed that the strength of the recommendation should be conditional.

Remarks

- The body of retrieved evidence mostly focused on adult patients and only one study was available in a paediatric population. This recommendation can be applied to paediatric patients, but the manufacturer's instructions should be checked to evaluate any contraindication for paediatric patients.
- The GDG discussed the available evidence and agreed to consider only studies comparing the same type of suture in order to prevent confounding by type of suture (monofilament or braided).
- The overall quality of evidence was moderate for the RCTs due to risk of bias and low for the observational studies. The GDG discussed whether or not to consider indirectness for the overall comparison of antimicrobial-coated vs. non-coated sutures. The agreement was that indirectness does not apply because the PICO question is very broad.
- Included studies were performed in high- and middle-income countries.
- Types of surgical procedures included were colorectal, abdominal, breast, head and neck, lower limb, spinal, cardiac, vascular and other surgery.
- The types of sutures investigated in the included studies were triclosan-coated polydioxanone suture vs. polydioxanone suture featuring a monofilament suture construction (3 RCTs *(1-3)*); triclosan-coated polyglactin 910 suture vs. polyglactin 910 suture featuring a braided (multifilament) suture construction (7 RCTs *(4-10)* and 4 observational studies *(11-14)*); and polyglactin 910 and poliglecaprone 25 (both triclosan-coated) sutures vs. polyglactin 910 and poliglecaprone 25 sutures featuring a braided (polyglactin 910) and a monofilament (poliglecaprone 25) suture construction (3 RCTs *(15-17)* and one observational study *(18)*).
- No adverse events have been associated in the included studies with the use of antimicrobial-coated sutures. However, the GDG pointed out that there is limited evidence that triclosan may have negative effects on wound healing *(19)* or lead to contact allergy *(20)*. Although the development of resistance is mentioned as a concern, the daily absorption of triclosan from consumer products (for example, commercially-available hand soap) is higher than a single triclosan suture *(21-23)*.

Background

Surgical suture material is used to adequately adapt the wound edges and thus it is in direct contact with the wound itself. To prevent microbial colonization of the suture material in operative incisions, sutures with antibacterial activity have been developed. Triclosan (5-chloro-2-[2.4-dichlorophenoxy] phenol) is a broad-spectrum bactericidal agent that has been used for more than 40 years in various products, such as toothpaste and soaps. Higher concentrations of triclosan work as a bactericide by attacking different structures in the bacterial cytoplasm and cell membrane *(24)*. At lower concentrations, triclosan acts as a bacteriostatic agent binding to enoyl-acyl reductase, a product of the Fab I gene and thus inhibiting fatty acid synthesis *(25, 26)*.

Several trials have shown that the use of triclosan-coated sutures leads to a reduction of the number of bacteria in vitro and also of wound infections in animal and clinical studies *(27-29)*. Of note, this effect is not confined to any particular tissue or organ system *(23)*. Apart from triclosan, several novel antimicrobial coatings are now becoming available *(30, 31)*, but there are still no reported clinical studies comparing the efficacy of novel antibacterial sutures with non-coated ones. Triclosan-coated polyglactin 910, triclosan-coated polydioxanone, and triclosan-coated poliglecaprone 25 are commercially-available sutures with antimicrobial properties. Commonly-used non-coated sutures are polyglactin 910, polydioxanone, poliglecaprone 25, polyglycolic acid and polyglyconate sutures.

Few organizations have issued recommendations regarding the use of antimicrobial-coated sutures (Table 4.22.1). The UK-based NICE suggests that antimicrobial-coated sutures may reduce the SSI risk compared to non-coated sutures, although this effect may be specific to particular types of surgery, such as abdominal procedures *(32)*. The SHEA/IDSA guidelines indicate that antiseptic-impregnated sutures should not be used routinely as a strategy to prevent SSI *(33)*.

Table 4.22.1. **Recommendations on the use of antimicrobial-coated sutures according to available guidelines**

Guidelines (year issued)	Recommendations on the use of antimicrobial-coated sutures
SHEA/IDSA practice recommendation (2014) *(33)*	Do not routinely use antiseptic-impregnated sutures as a strategy to prevent SSI.
NICE (2013 update) *(32)*	Antimicrobial-coated sutures may reduce the SSI risk compared to uncoated sutures, although this effect may be specific to particular types of surgery, such as abdominal procedures.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; SSI: surgical site infection.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess if the use of antimicrobial-coated sutures might be beneficial for surgical patients to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 23) was to evaluate whether the use of antimicrobial-coated sutures is more effective in reducing the risk of SSI than the use of non-coated sutures. The target population included patients of all ages undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Eighteen studies (13 RCTs *(1-10, 15-17)* and five cohort studies *(11-14, 18)*) including a total of 7458 patients (RCTs, 5346; observational studies, 2112) and comparing the use of antimicrobial- with non-coated sutures were identified.

Seven studies compared the efficacy of antimicrobial-coated sutures with non-coated sutures in mixed wounds (5 RCTs *(2-5, 8)* and 2 observational studies *(12, 14)*). A further 7 studies (5 RCTs *(6, 10, 15-17)*

and 2 observational studies *(11, 18)*) made the same comparison in clean wounds, mainly cardiac and breast cancer surgery, and 4 studies (3 RCTs *(1, 7, 9)* and one observational study *(13)*) concerned clean-contaminated wounds in abdominal surgery.

Due to heterogeneity among the selected studies regarding the type of suture used, type of surgical procedure or wound contamination class, additional separate meta-analyses were performed for triclosan-coated polydioxanone suture vs. polydioxanone suture, triclosan-coated polyglactin 910 suture vs. polyglactin 910 suture, and polyglactin 910 and poliglecaprone 25 (both triclosan-coated) sutures vs. polyglactin 910 and poliglecaprone 25 sutures, as well as in clean, clean-contaminated and mixed types of wounds (web Appendix 23).

Overall, there is moderate to low quality evidence that antimicrobial-coated sutures have significant benefit in reducing SSI rates in patients undergoing surgical procedures when compared to non-coated sutures (moderate quality for RCTs: OR: 0.72; 95% CI: 0.59–0.88; low quality for observational studies: OR: 0.58; 95% CI: 0.40–0.83).
In meta-regression analysis, there was no evidence that the effect of antimicrobial-coated sutures differed between braided and monofilament sutures (P=0.380), or between clean (P=0.69), cardiac (P=0.900) or abdominal (P=0.832) and other types of surgery. According to these analyses, the effect seems to be independent of the type of suture, procedure or wound contamination classification.

Regarding the comparisons of specific types of sutures (web Appendix 23), only the meta-analyses of the studies comparing triclosan-coated polyglactin 910 suture vs. polyglactin 910 suture featuring a braided suture construction showed that the use of antimicrobial-coated sutures has significant benefit compared to non-coated sutures in reducing SSI rates (OR: 0.62; 95% CI: 0.44–0.88 for RCTs; OR: 0.58; 95% CI: 0.37–0.92 for observational studies).

Some limitations of the included studies should be noted. The quality of the included RCTs was moderate to low. Indeed, some studies had an unclear or high risk of blinding of participants, care-providers and outcome assessors, and/or a high risk of incomplete outcome data. Furthermore, some studies had industrial sponsorship or conflicts of interest with a commercial company.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that most patients wish to receive this intervention in order to reduce the risk of SSI, but patients must be informed about the small and unconfirmed risk of allergy to triclosan. The GDG emphasized that patients would like to be part of the process by being involved and informed.

Resource use

The GDG emphasized that sutures are expensive in general. Moreover, the availability of antimicrobial-coated sutures is limited in LMICs. In settings where patients have to pay for the material themselves, an increase in costs would represent an additional personal financial burden. At the time of formulating this recommendation, the GDG noted that manufacturers sold the antimicrobial-coated and non-coated sutures for approximately the same price. However, the GDG is not aware of the future pricing policy of manufacturers. The use of antimicrobial-coated sutures could increase the cost per patient, but it might reduce the mean length of hospital stay and reduce potential costs to the health care system due to the avoidance of the risk of SSI *(5, 8, 34)*.

The body of retrieved evidence mostly focused on adult patients and only one study *(4)* was available in a paediatric population. The literature search did not identify any studies that reported on SSI attributable-mortality.

Research gaps

The GDG highlighted the limited evidence available in some areas and the need for further research on the effects of antimicrobial-coated sutures in reducing SSI rates. In particular, studies should be conducted in LMICs and include different surgical procedures. Comparisons between antimicrobial-coated and non-coated sutures should be performed with the same type of suture material, including non-absorbable sutures. In particular, comparisons with an alternative antimicrobial agent to triclosan would be welcome. More research is required to investigate the effectiveness of antimicrobial-coated sutures in the paediatric population and in various types of settings. All studies should be designed as a RCT with the SSI outcome defined according to CDC criteria and sub-specified as superficial, deep and organ space

occupying. Adverse events related to the intervention should be clearly reported, including the need to assess the risk of allergy. Importantly, possible emerging AMR to the antimicrobial agent should be monitored. Moreover, cost-effectiveness studies are also needed. Of note, research investigating the effectiveness of antimicrobial-coated sutures should be independently funded with a limited influence of industry sponsorship.

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4.23 Laminar airflow ventilation systems in the context of operating room ventilation

Recommendation

The panel suggests that laminar airflow ventilation systems should not be used to reduce the risk of SSI for patients undergoing total arthroplasty surgery.
(Conditional recommendation, low to very low quality of evidence)

Rationale for the recommendation

Very low quality evidence shows that in both total hip (THA) and knee (TKA) arthroplasty, laminar airflow ventilation has no benefit when compared to conventional ventilation in reducing the SSI rate. In THA, conventional ventilation had a non-significant beneficial effect in reducing the risk of SSI. Therefore, the GDG unanimously agreed that laminar airflow ventilation systems should not be used as a preventive measure to reduce the risk of SSI for total arthroplasty surgery. The strength of this recommendation was considered to be conditional, considering the very low quality of the supporting evidence. For other types of procedures, the available evidence consisted of single observational studies only and the GDG considered this body of evidence to be insufficient to lead to any specific recommendation. Moreover, laminar airflow ventilation has been of interest mainly as a preventive measure in orthopaedic arthroplasty surgery.

Remarks

- Conventional ventilation systems pass air with a mixed or turbulent flow into the OR. These systems aim to homogenize the fresh air and the air, aerosols and particles within the room. This leads to an accelerated dilution of the air volume and an irregular movement of the particles. Conventional turbulent ventilation systems are used for any type of surgery. Systems with laminar airflow are frequently used in an environment where a contamination with particles is a highly adverse event, for example, in orthopaedic implant surgery. The goal of laminar airflow is to pass the fresh air unidirectionally with a steady velocity and approximately parallel streamlines to create a zone where the air, aerosols and particles within the room are being driven out.
- No possible harms associated with the recommendation were identified. However, the cooling effect of the fresh air from a laminar airflow system on the surgical wound and the patient may lead to lower intraoperative tissue temperatures in the surgical wound or systemic hypothermia if the temperature is not monitored intraoperatively *(1)*.
- The GDG underlined that most data are from national surveillance databases or registries. Although these studies have a large sample size, they are not designed specifically for this comparison. Indeed, comparisons were between hospitals with laminar flow and those with conventional ventilation, rather than comparisons within the same hospital. This may lead to major confounding by factors such as differences in hospital/surgeon volume, characteristics of admitted patients and/or the extent of implementation of other SSI prevention measures.
- The systematic review investigated also the use of fans or cooling devices and natural ventilation in the operating room compared to conventional ventilation with regards to the risk of SSI. However, the literature search did not identify studies that evaluated these interventions. One observational study *(2)* that evaluated natural ventilation in the operating room compared to conventional ventilation following THA and TKA found no difference in the SSI risk.
- Given the very limited evidence on natural ventilation and fans/cooling systems, the GDG decided not to develop a recommendation on these topics. Nevertheless, it is advisable to ensure a proper ventilation rate of the operating room and an adequate maintenance of the components of the installed ventilation system *(3)*.

Background

The ventilation system in the operating room is designed to provide certain functions, primarily to create thermal comfort for the patient and staff and to maintain constant air quality by eliminating aerosols and particles within the room. It serves also to maintain certain air pressure requirements between communicating rooms. Special ventilation systems supplying filtered air at positive pressure are required in the operating room. Ideally, around 20 air changes per hour are necessary to dilute microorganisms generated in the operating room and to exclude ingress from surrounding areas *(3)*.

There are various systems used to ventilate an operating room. Natural ventilation is the most basic way and refers to airflow by natural forces. WHO provides the following definition *(4)*: "use of natural forces to introduce and distribute outdoor air into or out of a building. These natural forces can be wind pressures or pressure generated by the density difference between indoor and outdoor air". Exploiting natural ventilation may be a suitable solution for settings with limited resources and it is considered as an option for IPC by WHO. However, there is no evidence available for its use in operating rooms *(4)*.

A well-designed ventilation system that takes advantage of natural air movements is still complex to achieve and is limited to a benign local climate *(4)*. If natural ventilation alone is not sufficient to fulfil the desired functions mentioned above, fans and cooling or warming devices are commonly installed, mostly to maintain the air temperature and humidity at a comfortable level. Limitations of these devices might be an inadequate rate of air changes per hour and control of the direction of airflow in the operating room and the spread of particles and dust, thus resulting in an insufficient elimination of aerosols and particles.

In most LMICs, operating rooms do not have a full mechanical ventilation system and the air conditioning used is a recirculating cooling device. If such a system is used, it should be wall-mounted rather than floor standing, and should be maintained regularly, including filters checked, cleaned or changed. The use of fans in the operating room is not recommended and should be used only as a last resort if the lack of air circulation affects the surgeon's performance. Any fans in the operating room or preparation room should be cleaned on a regular basis.

In well-resourced environments, conventional ventilation systems that pass air with a mixed or turbulent flow into the operating room are the most widely installed. These systems aim to homogenize the fresh air and the air, aerosols and particles within the room. This leads to an accelerated dilution of the air volume and an irregular movement of the particles. Conventional turbulent ventilation systems are used for all types of surgery. Systems with laminar airflow are frequently used in an environment where contamination with particles is a highly adverse event, for example, orthopaedic implant surgery. The goal of passing the fresh air unidirectionally with a steady velocity and approximately parallel streamlines is to create a zone where the air, aerosols and particles within the room are being driven out. Limitations to this principle are all forces disrupting the parallel airflow.

In many countries, the use of high efficiency particulate air filters (at least 99.97% efficient in removing particles ≥0.3 µm in diameter) in the operating room ventilation system is mandatory by law. Of note, the utmost importance must be paid to the maintenance of any kind of ventilation system and its components. The operating room ventilation system should be regularly checked and filters changed (the need for this is assessed by monitoring the pressure differential across the filters) according to local standard operating procedures, which should be based on the manufacturer's instructions and international guidelines.

A systematic review *(5)* published in 2012 on the influence of laminar airflow on prosthetic joint infections found laminar airflow ventilation to be a risk factor for the development of a severe SSI.

Some guidelines have issued recommendations regarding the ventilation systems in the operating room (Table 4.23.1), but several other SSI prevention guidelines do not address this topic. These range from a technical advice for proper air handling in the operating room *(6)* to leaving this question as an unresolved issue *(3)*. However, these recommendations are not based on systematic reviews of the literature and meta-analysis or a rigorous evaluation of the quality of the available evidence.

Table 4.23.1. **Recommendations on ventilation systems in the operating room according to available guidelines**

Guidelines (year issued)	Recommendations on ventilation systems in the operating room
SHEA/IDSA practice recommendation (2014) *(5)*	Follow the American Institute of Architects' recommendations for proper air handling in the operating room.
CDC/HICPAC Guidelines for environmental infection control in health-care facilities (2003) *(3)*	No recommendation for orthopaedic implant operations in rooms supplied with laminar airflow.

SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; CDC: Centers for Disease Control and Prevention; HICPAC: Healthcare Infection Control Practices Advisory Committee.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG decided to conduct a systematic review to assess the effectiveness of ventilation systems in the operating room for the prevention of SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 24) was to evaluate whether a laminar airflow ventilation system is more effective in reducing the risk of SSI than a conventional ventilation system. The review investigated also whether fans or cooling devices and natural ventilation are acceptable alternatives to conventional ventilation for the prevention of SSI. The target population was patients of all ages undergoing a surgical procedure. The primary outcome was the occurrence of SSI and SSI-attributable mortality. Definitions in included studies that related to severe SSI, periprosthetic infection and deep infections requiring revision were considered as deep SSI.

Twelve observational studies *(9-20)* comparing laminar airflow with conventional ventilation were identified. No RCTs were identified. Most data were obtained from national surveillance systems and registries. Of note, although these sources had a large sample size, the databases were not specifically designed for this comparison. Most studies focused on THA (33 0146 procedures) and TKA (134 368 procedures). Only single studies were available for other types of surgery (appendectomy *(8)*, cholecystectomy *(8)*, colon surgery *(8)*, herniorrhaphy *(8)*, gastric *(10)* and vascular surgery *(7)*). The population studied were mostly adult patients. According to the selected studies, the following comparisons were evaluated.

1. Laminar airflow ventilation vs. conventional ventilation
    a. in THA
    b. in TKA.

Very low quality evidence shows that laminar airflow ventilation has no benefit when compared to conventional ventilation in reducing the SSI rate in THA (OR: 1.29; 95% CI: 0.98–1.71) or TKA (OR: 1.08; 95% CI: 0.77–1.52).

In single observational studies, laminar flow was found to be associated with an increased overall risk of SSI in patients undergoing appendectomy; no significant association was shown in colon surgery, cholecystectomy and herniorraphy.
In gastric and open vascular surgery, the absence of laminar flow was found to increase the risk of SSI.

The search did not identify data that evaluated the use of fans or cooling devices in the operating room and their impact on the risk of SSI compared to a normal/conventional ventilation system.
One observational study *(2)* that evaluated natural ventilation in the operating room compared with conventional ventilation and its impact on the risk of SSI following THA and TKA found no difference in the risk of SSI.

The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

No study was found on patient values and preferences with regards to this intervention. The GDG is confident that the typical values and preferences of the target population regarding the outcome would not favour the intervention and therefore would agree with the recommendation. The GDG believes also that patients would not have an opinion about a hospital ventilation system, as long as other aspects are being taken into account to prevent infections.

Resource use

Cost-effectiveness analyses found laminar airflow to be more expensive compared to a conventional ventilation system. An Italian study *(18)* evaluated an increase of 24% in building costs and an increase of 36% in annual operating costs. A model calculation study from Australia *(19)* evaluated additional costs of AUD$ 4.59 million per 30 000 THAs performed. Additional costs of € 3.24 procedure (1000 procedures per year for 15 years) were calculated by a German study group *(20)*. The GDG highlighted that the implementation of laminar airflow is difficult in low-income settings due to the lack of resources, technical expertise and infrastructure.

Research gaps

The GDG highlighted the very low quality evidence available on the topic and the need for further research on the effects of laminar flow in reducing the SSI rate, particularly well-designed clinical trials in the field of endoprosthetic surgery. The GDG acknowledged that RCTs may not be reasonable as they would require a massive investment with a high sample size to have enough power to see a difference. In addition, cluster trials could be problematic as it would be almost impossible to control for confounding factors, such as different surgeons operating in the same operating room. Nationwide databases may provide the best affordable information, but adherence to international definitions and more information about confounders need to be obtained from country surveillance systems and registries. The lack of evidence on the impact of fans/cooling devices and natural ventilation on the SSI rate compared to conventional ventilation emphasizes the need for further research in this field in order to evaluate whether these systems might be an alternative in resource-limited countries when properly designed and maintained.

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POSTOPERATIVE MEASURES

4.24 Surgical antibiotic prophylaxis prolongation

Recommendation

The panel recommends against the prolongation of SAP administration after completion of the operation for the purpose of preventing SSI.
(Strong recommendation/moderate quality of evidence)

Rationale for the recommendation

- Moderate quality evidence from a high number of RCTs (44 studies included in the overall meta-analysis) shows that prolonged SAP postoperatively has no benefit in reducing SSI after surgery when compared to a single dose. However, there was some evidence (low to very low quality) that a prolonged postoperative administration of antibiotics may be beneficial to reduce the risk of SSI in cardiac, vascular and orthognathic surgery when compared to single-dose prophylaxis. Considering this limited and low to very low quality evidence in support of SAP prolongation in the above-mentioned procedures, as well as the possible harm associated with the prolonged duration of antibiotic administration, the GDG agreed to recommend against the prolongation of antibiotic administration after completion of the operation for the purpose of preventing SSI.
- Considering the possible adverse events, the risk of generating AMR linked to SAP prolongation and the high number of available studies of moderate quality showing no benefit, the strength of the recommendation was decided to be strong.

Remarks

- In the included studies, "single dose" usually refers to a preoperative dose with or without intraoperative re-dosing, depending on the duration of the operation and the half-life of the drug. The included studies always compared the same antibiotic agent in the same dose per administration.
- The guidelines of the American Society of Health-System Pharmacists *(1)* recommend that intraoperative re-dosing is needed if the duration of the procedure exceeds 2 half-lives of the drug or if there is excessive blood loss during the procedure. While the benefit of this approach seems reasonable from a drug pharmacokinetic aspect, the reviewed studies have not addressed the duration of surgical procedures or re-dosing in relation to SSI in standard antibiotic prophylaxis protocols. No recommendation could be concluded on the benefit or harm of this approach.
- For cardiac (2 RCTs *(2, 3)*) and orthognathic surgery (3 RCTs *(4-6)*), there was some evidence that prolonging antibiotic administration after completion of the operation may be beneficial in reducing the risk of SSI when compared to single-dose prophylaxis. By contrast, other RCTs *(7-13)* showed no benefit of prolonging antibiotic prophylaxis beyond 24 hours compared to prophylaxis for up to 24 hours in these types of surgery.
- In vascular surgery, there was some evidence from one RCT *(14)* that prolonging antibiotic prophylaxis until intravenous lines and tubes are removed may be beneficial in reducing the risk of SSI when compared to single-dose prophylaxis.
- The GDG highlighted the risk of promoting AMR if antibiotics are prolonged in the postoperative period, both in the individual patient and at the health care facility level. In addition, this practice might negatively affect the patient microbiome and lead to short- and long-term gastrointestinal complications. A relevant harm possibly linked to prolonged SAP is the intestinal spread of *C. difficile* with a higher risk of a clinical manifestation of infection.

Background

The preventive effect of the routine use of SAP prior to non-clean and implant surgery has long been recognized. However, the benefit of continuing SAP after completion of the procedure is unclear. While current guidelines recommend a maximum postoperative SAP duration of 24 hours, increasing evidence shows that there may be non-inferiority of a single preoperative dose (and possible additional intraoperative doses according to the duration of the operation). Despite this, surgeons still have a tendency to routinely continue SAP up to several days after surgery *(15, 16)*.

The use and duration of postoperative prophylaxis have been specified in clinical practice guidelines issued by professional societies or national authorities (Table 4.26.1). Several guidelines, such as those published by SHEA/IDSA *(17)* and the American Society of Health-System Pharmacists *(1)*, recommend discontinuing SAP within 24 hours after surgery. The 2012 SSI prevention bundle from the US Institute of Healthcare Improvement *(18)* recommends discontinuing SAP within 24 hours in general and within 48 hours in cardiac surgery. Other guidelines published by the UK-based NICE *(19)*, the Scottish Intercollegiate Guidelines Network (SIGN) *(20)*, the Royal College of Physicians of Ireland *(21)* and the UK Department of Health *(22)*, recommend a single dose of preoperative SAP and no postoperative continuation with or without exceptions for specific surgical procedures.

Table 4.24.1. **Recommendations on SAP according to available guidelines**

Guidelines (date issued)	Recommendations on SAP duration
SHEA/IDSA (2014) *(17)*	Stop agent within 24 hours after the procedure for all procedures.
American Society of Health-System Pharmacists *(1)*	Discontinue antibiotic prophylaxis within 24 hours after surgery.
NICE (2008) *(19)*	Consider giving a single dose of antibiotic prophylaxis intravenously on starting anaesthesia.
The Royal College of Physicians of Ireland (2012) *(21)*	With the exception of a small number of surgical indications (see below), the duration of surgical prophylaxis should be a single dose. Duration of prophylaxis involving more than a single dose, but not for more than 24 hours: open reduction and internal fixation of compound mandibular fractures, orthognathic surgery, complex septorhinoplasty (including grafts), head and neck surgery. Duration for more than 24 hours, but not for more than 48 hours: open heart surgery.
USA Institute for Healthcare Improvement: surgical site infection (2012) *(18)*	Discontinue antibiotic prophylaxis within 24 hours and 48 hours for cardiac patients.
SIGN: Antibiotic prophylaxis in surgery (2014) *(20)*	A single dose of antibiotic with a long enough half-life to achieve activity throughout the operation is recommended. Up to 24 hours of antibiotic prophylaxis should be considered for arthroplasty.
UK High impact intervention bundle (2011) *(22)*	Appropriate antibiotics were administered within 60 minutes prior to incision and only repeated if there was excessive blood loss, a prolonged operation or during prosthetic surgery.

SAP: surgical antibiotic prophylaxis; SHEA: Society for Healthcare Epidemiology of America; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; SIGN: Scottish Intercollegiate Guidelines Network.

Following an in-depth analysis of the sources and strength of evidence in current guidelines, the GDG members decided to conduct a systematic review to assess the available evidence on the effectiveness of prolonged antibiotic prophylaxis to prevent SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 25) was to investigate whether prolonged SAP in the postoperative period is more effective in reducing the risk of SSI than perioperative prophylaxis (single dose before incision and possible intraoperative additional dose/s according to the duration of the operation). The target population included patients of all ages undergoing a surgical procedure for which SAP is indicated. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Sixty-nine RCTs *(2-9, 11-14, 23-79)* including a total of 21 243 patients and investigating the optimal duration of antibiotic prophylaxis in a variety of surgical procedures were identified: appendectomy *(23-27)*; colorectal surgery *(28-30, 60-64, 75)*; upper gastrointestinal tract surgery *(31-34)*; cholecystectomy *(35, 65)*; hepatobiliary surgery *(76, 80)*; mixed general surgery *(37-42, 79)*; caesarean section *(43-45)*; gynaecological surgery *(46, 47, 74)*; orthopaedic and trauma surgery *(48, 49)*; spine surgery *(50, 66)*; cardiac surgery *(2, 3, 7, 8, 77)*; thoracic surgery *(51)*; vascular surgery *(14)*; transplantation surgery *(52)*; head and neck surgery *(53, 67-69, 78, 81)*; ear, nose and throat surgery *(55, 70)*; maxillofacial surgery *(56-59, 71)*; orthognathic surgery *(4-6, 9, 11-13, 72)*; and others *(73)*. Both intervention and control groups received the same preoperative regimen in all included studies and they only differed in the postoperative continuation of antibiotic prophylaxis. There were variations in the antibiotic regimens and in the duration of SAP prolongation. The first dose of the antibiotic prophylaxis was always administered preoperatively.

Considering the heterogeneity among the selected studies regarding the duration of SAP prolongation postoperatively and the type of surgical procedure, several separate meta-analyses were performed according to the following comparisons (web Appendix 25).

1. Any prolonged regimen vs. no postoperative dose (44 RCTs).
2. A prolonged regimen less than 24 hours postoperatively vs. a single postoperative dose (one RCT).
3. A prolonged regimen more than 24 hours postoperatively vs. a prolonged regimen less than 24 hours postoperatively (23 RCTs).
4. A prolonged regimen more than 48 hours postoperatively vs. a prolonged regimen less than 48 hours postoperatively (3 RCTs).
5. Type of procedure with a prolonged antibiotic regimen:
   a. cardiac surgery
   b. vascular surgery
   c. orthognathic surgery.

Overall, there is a moderate quality of evidence that prolonged postoperative antibiotic prophylaxis has no benefit in reducing the SSI rate when compared to a single dose of antibiotic prophylaxis (OR: 0.89; 95% CI: 0.77–1.03).

In cardiac *(2, 3)* and orthognathic surgery *(4-6)*, there is some low quality evidence that SAP continuation after completion of the operation may be beneficial in reducing SSI when compared to a single dose of prophylaxis (OR: 0.43; 95% CI: 0.25–0.76 and OR: 0.30; 95% CI: 0.10–0.88, respectively). Conversely, other RCTs *(7-13)* showed no benefit in SSI prevention by prolonging SAP beyond 24 hours compared to SAP for up to 24 hours in both cardiac *(7, 8)* (OR: 0.74; 95% CI: 0.32–1.73; very low quality of evidence) and orthognathic surgery *(9-13)* (OR: 0.34; 95% CI: 0.08–1.44; very low quality of evidence). In vascular surgery, there was some evidence from one RCT *(14)* that prolonging antibiotic prophylaxis until intravenous lines and tubes are removed may be beneficial in reducing the risk of SSI when compared to a single dose (OR: 0.50; 95% CI: 0.25–0.98).

The retrieved evidence focused mostly on adult patients. Only 2 studies *(27, 61)* addressed specifically the paediatric population. Fifteen studies *(4, 6, 11-13, 25, 26, 37, 39, 41, 42, 57, 70, 82, 83)* included some paediatric patients, but with a majority of adult patients. Among the 69 included studies, 14 *(4, 6, 9, 11, 13, 26, 38, 43-45, 56, 57, 70, 77)* were conducted in LMICs. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

Patient values and preferences were not assessed by the studies. The GDG argued that the recommendation was likely to be similar to the values and preferences of most patients. The GDG pointed out that some patients feel reassured by receiving prolonged antibiotic prophylaxis, while others would prefer to receive the lowest number of drugs possible and, in particular, to discontinue antibiotics as soon as possible.

Resource use

Studies addressing cost-effectiveness reported a cost reduction associated with shorter antibiotic prophylaxis regimens. This varied from US$ 36.90 to US$ 1664 and was attributable to the lower number of antibiotic doses administered and a reduced treatment of side-effects and duration of hospitalization *(24, 47, 52, 55, 74, 84)*.
The GDG emphasized that the recommendation may generate cost savings due to reduced expenses in drugs and materials, staff time and reduced costs due to the prevention of adverse events associated with prolonged antibiotic prophylaxis. The GDG highlighted that there is a need to raise awareness and provide education on the rational use of antibiotics and antibiotic stewardship among both health care workers (surgeons in particular, with reference to this recommendation) and patients.

Research gaps

The GDG highlighted that there is a need for further well-designed RCTs in cardiac and vascular surgery, as well as in in the paediatric population. Importantly, it would be crucial that studies include the selection of the most appropriate antibiotic according to the surgical procedure. Future trials should investigate the effect of prolonged antibiotic prophylaxis on the microbiome.

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4.25 Advanced dressings

Recommendation

The panel suggests not using any type of advanced dressing over a standard dressing on primarily closed surgical wounds for the purpose of preventing SSI.
(Conditional recommendation/low quality of evidence)

Rationale for the recommendation

- Advanced dressings used in the included studies were of the following types: hydrocolloid; hydroactive; silver-containing (metallic or ionic); and polyhexamethylene biguanide (PHMB) dressings. Standard dressings were dry absorbent dressings.
- Low quality evidence from 10 RCTs shows that advanced dressings applied on primarily closed incisional wounds do not significantly reduce SSI rates compared to standard wound dressings. The GDG unanimously agreed that advanced dressings should not be used as a preventive measure to reduce the risk of SSI. Given the low quality of the evidence, the GDG decided that the strength of this recommendation should be conditional.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. However, the GDG considered this recommendation valid also for paediatric patients.
- The GDG identified possible harms associated with the use of silver-containing dressings. Allergic reactions or skin irritations may develop in some patients *(1)*.
- Regarding ionic silver dressings, the GDG was concerned about the possible exposure of patients and health care workers to nanoparticles. It was also pointed out that microbial resistance to silver and PHMB may develop.
- The GDG also highlighted that the availability of advanced dressings may be limited in LMICs and their purchase might represent a financial burden.
- The GDG emphasized that dressings used on primarily closed surgical wounds should be sterile and should be applied with an aseptic technique.
- The studies included did not investigate negative pressure dressings. pNPWT is dealt with in chapter 4.19 of these guidelines.

Background

The term "surgical wound" used in this document refers to a wound created when an incision is made with a scalpel or other sharp cutting device and then closed in the operating room by suture, staple, adhesive tape, or glue and resulting in close approximation to the skin edges. It is common practice to cover such wounds with a dressing. The dressing acts as a physical barrier to protect the wound from contamination from the external environment until the wound becomes impermeable to microorganisms. The dressing can also serve to absorb exudate from the wound and keep it dry.

A wide variety of wound dressings are available (web Appendix 26). Advanced dressings are mainly hydrocolloid or hydrogels or fibrous hydrocolloid or polyurethane matrix hydrocolloid dressings and vapour-permeable films.

A Cochrane review *(2)* and its update *(3)* of the effect of dressings for the prevention of SSI found no evidence to suggest that one dressing type was better than any others.

The UK-based NICE issued a clinical guideline for SSI prevention and treatment in 2008 which recommended covering surgical incisions with an appropriate interactive dressing at the end of the procedure *(4)*. The 2013 evidence update of these guidelines suggests that no particular type of dressing emerges as the most effective in reducing the risk of SSI, although silver nylon dressings may be more effective than gauze.

The update recommends further research to confirm the effectiveness of modern types of dressing *(5)*. Postoperative care bundles recommend that surgical dressings be kept undisturbed for a minimum of 48 hours after surgery unless leakage occurs. However, there are currently no specific recommendations or guidelines regarding the type of surgical dressing *(6-8)*.

Following an in-depth analysis of the sources and strength of evidence in current guidelines and reviews, the GDG members decided to conduct a systematic review to assess the effectiveness of advanced dressings compared to standard surgical wound dressings for the prevention of SSI.

Summary of the evidence

The purpose of the evidence review (web Appendix 26) was to evaluate whether the use of advanced dressings is more effective in reducing the risk of SSI than standard wound dressings. The target population included patients of all ages undergoing a surgical procedures. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Ten RCTs *(1, 9-17)*, including a total of 2628 patients, evaluated advanced dressings compared to standard dressings. Patients were adults undergoing sternotomy and elective orthopaedic, cardiac, vascular, plastic, abdominal and colorectal cancer surgical procedures. There were variations in the interventions as some studies used hydrocolloid, hydroactive and silver- or PHMB-impregnated dressings. In addition, there were variations in the definition of SSI and the duration of postoperative follow-up.

Despite the heterogeneity of the types of advanced dressings used in the selected studies, separate meta-analyses were performed to evaluate (1) an overall comparison of advanced vs. standard dressings, and (2) hydrocolloid or silver-impregnated or hydroactive or PHMB dressings vs. standard dressings.

Overall, there is low quality evidence that advanced dressings do not significantly reduce SSI rates compared to standard dressings (OR: 0.80; 95% CI: 0.52–1.23). In particular, compared to standard dressings, very low quality evidence showed neither benefit nor harm for hydrocolloid dressings (OR: 1.08; 95% CI: 0.51–2.28), silver-impregnated dressings (OR: 0.67; 95% CI: 0.34–1.30) and hydroactive dressings (OR: 1.63; 95% CI: 0.57–4.66). There is also low evidence for PHMB-containing dressings (OR: 0.20; 95% CI: 0.02–1.76).

The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. In addition, no studies reported SSI-attributable mortality rates.

Additional factors considered when formulating the recommendation

Values and preferences

There are many factors that may contribute to the preferences of surgeons and/or patients with regard to the use of particular dressings. Although no difference in SSI prevention was shown in the meta-analysis of 10 RCTs, other outcomes were reported in some studies. Two RCTs included in these analyses assessed patient comfort and reported that hydrocolloid dressings were more comfortable than standard dressings *(16, 17)*. Another study reported better cosmetic results in patients whose incisions were dressed with hydrocolloid dressings compared to incisions covered with standard dressings, despite no SSI events in either group *(13)*. It was acknowledged that patients may prefer a low frequency of dressing change.

Resource use

The cost and availability of advanced dressings may be a limitation, particularly in LMICs. The added cost of using hydrogel, hydrocolloid or silver-containing dressings has been investigated by several studies included in this review. Two studies reported fewer dressing changes for hydrogel dressings compared to standard dressings *(10, 16)*. Although the hydrogel dressings were associated with a cost 2 to 5 times higher than standard dressings, they may be beneficial for patients unable to change dressings or requiring a return to hospital for subsequent dressing changes *(16)*. One study attributed increased nursing time with standard dressings, which is a consideration for hospitals with a small nursing staff. Another study reported higher costs for hydrocolloid compared to standard dressings *(17)*. In addition to cost, it may be difficult for some LMICs to acquire and properly use moist or metallic dressings. However, one study reported that hydrocolloid dressings were less complicated to apply *(15)*.

Research gaps

It was emphasized that there are very few large, high-quality trials investigating different types of dressings with SSI prevention as a primary outcome.

Future clinical studies should focus on generating a large sample size and include blind outcome assessment. Well-designed studies conducted in LMICs are needed, as well as in the paediatric population. The GDG highlighted a special interest in investigating the use of silver-containing dressings in orthopaedic and cardiac surgery with regard to SSI prevention. Assessment of adverse events should be considered in the trials, including the possible effects of silver nanoparticles. In addition, it would be interesting to explore the comparison of opaque dressings with transparent ones in terms of postoperative visual examination and the duration of keeping the primary dressing in place, ultimately with regard to SSI prevention.

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4.26 Antimicrobial prophylaxis in the presence of a drain and optimal timing for wound drain removal

Recommendations

1. **The panel suggests that perioperative antibiotic prophylaxis should not be continued to the presence of a wound drain for the purpose of preventing SSI.**
   (Conditional recommendation, low quality of evidence)

2. **The panel suggests removing the wound drain when clinically indicated. No evidence was found to recommend an optimal timing of wound drain removal for the purpose of preventing SSI.**
   (Conditional recommendation, very low quality of evidence)

Rationale for the recommendation

- Overall low quality evidence (from 7 RCTs) indicates that prolonged antibiotic prophylaxis in the presence of a wound drain has neither benefit nor harm in reducing SSI when compared to perioperative prophylaxis alone (single dose before incision and possible intraoperative additional dose/s according to the duration of the operation). Considering the lack of evidence that prolonged antibiotic prophylaxis prevents SSI and the possible associated harms (see below), the GDG unanimously agreed that antibiotic prophylaxis should not be continued in the presence of a wound drain. Given the low quality of the evidence, the strength of this recommendation was considered to be conditional.
- Very low quality evidence (from 11 RCTs) shows that the early removal of wound drains has neither benefit nor harm in reducing the SSI rate when compared to late removal of drains (at postoperative day 6 or later). In particular, no benefit was shown when comparing early removal (from postoperative days 1 to 5) with removal on or after postoperative day 6. Results were also similar when comparing early removal with removal determined according to the volume of drainage. Considering the very low quality evidence and the finding that the body of evidence does not identify an optimal time point for wound drain removal with regard to the prevention of SSI, the GDG decided to suggest that the wound drain should be removed when clinically indicated. Given the very low quality of evidence, the strength of this recommendation was considered to be conditional.

Remarks

- The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. However, the GDG considers this recommendation valid also for paediatric patients.
- The GDG emphasized that the body of evidence does not identify an optimal time point of wound drain removal with regard to the reduction of SSI. Definitions for the early removal of drains varied across the studies from 12 hours to 5 days postoperatively. In addition, the definitions for the late removal of drains varied from removal when the drainage volume became minimal (that is, ‹30 or ‹50 mL/day) or at specific time points, such as postoperative days 2 to 10.
- The GDG pointed out that the evidence on the optimal time for drain removal consists of studies that were done with closed wound drains. Therefore, the related recommendation refers to the use of closed wound drainage systems.
- The available evidence on the optimal time for drain removal was limited to studies conducted in breast and orthopaedic surgery.
- It was noted that the great majority of available studies on the topics of these recommendations were conducted in high- and middle-income countries; only one study is available from a low-income country.
- The GDG identified possible harms associated with the prolonged duration of antibiotic administration, such as the selection and emergence of resistant bacteria, the risk of fungal superinfections and *Clostridium difficile* infection and side effects of antibiotics. Furthermore, early removal of the wound drain may be associated with possible postoperative complications, such as an increase of the occurrence of seroma and haematoma requiring treatment *(1)*.
- The GDG highlighted that wound drains are single-use devices and must not be reused.

Background

The use of drainage tubes in surgical wounds has a long history *(2)*. Prophylactic placement postoperatively has been widely practiced since the mid-1800s with the dictum of Lawson Tait, the 19th century British surgeon, "When in doubt, drain", well known to all surgical trainees. However, some studies have called into question the benefits of routine drainage *(3, 4)*. It is even argued that drains might adversely affect surgical outcomes, for example, affecting anastomotic healing by causing infection in the anastomotic area and the abdominal wound *(5, 6)*. Thirty-four systematic reviews investigating the effect of drains compared to no wound drainage in terms of the related infection risk in surgical patients have been published so far. A meta-review summarizing these reviews (web Appendix 27) demonstrated that most meta-analyses showed a tendency towards a beneficial effect of not using a wound drain with regard to a reduced risk of wound infection, but no significant differences were achieved.

The aim of drainage tubes is to remove any fluid or blood that may collect in the wounds and cavities created by the surgical procedure and thus may cause complications. When used, the optimal time for drain removal after surgery is still unknown. Drains are usually left in place until the amount of fluid draining out of them in a 24-hour period has reduced to a certain volume (typically less than 30 mL to 100 mL). However, some surgeons will remove the drains at a particular time point after surgery, which may vary from hours to more than a week. In most cases, antibiotic prophylaxis is continued postoperatively when a drain is used, but this practice is not evidence based.

With the presence of drainage tubes, the need for perioperative antibiotic prophylaxis and the optimal regimen requires further assessment and investigation given the dramatic increase in AMR worldwide. In recognition of the fact that AMR is now considered a major health problem, the implementation of global and national programmes to optimize the use of antibiotic agents in humans has been strongly urged by WHO *(7)*.

There are currently no formal recommendations for antimicrobial prophylaxis in the presence of a drain or regarding wound drain removal for the prevention of SSI. Following an in-depth analysis of the resources and lack of recommendations from other guidelines, the GDG decided to conduct a systematic literature review on these topics.

Summary of the evidence

The purpose of the evidence review (web Appendix 27) was to evaluate whether prolonged antibiotic prophylaxis in the presence of a wound drain is more effective in reducing the risk of SSI than perioperative prophylaxis alone (single dose before incision and possible intraoperative additional dose/s according to the duration of the operation). The review evaluated also whether the early removal of wound drains is more effective than late removal to prevent SSI. The target population included patients of all ages undergoing a surgical operation with the presence of postoperative drainage. The primary outcome was the occurrence of SSI and SSI-attributable mortality.

Seven RCTs *(8-14)* were identified. They included a total of 1670 patients and investigated whether antibiotics should be administered preoperatively as a single dose and possibly re-dosed according to the duration of the operation, or if their administration should be extended to the postoperative period.

Three studies reported a prolonged antibiotic administration until the wound drain was removed *(8, 9, 11)*. In the remaining 4 trials, patients received a 3-day *(10, 14)* or 5-day intravenous course *(13)*. Patients enrolled in the studies underwent general surgery *(8-10, 14)*, kidney transplantation *(11)* and pilonidal sinus surgery *(13)*. One trial *(12)* determined whether prolonged antibiotic prophylaxis reduced the risk of infectious complications for patients undergoing elective thoracic surgery with tube thoracostomy. The antibiotic was continued for 48 hours after the procedure or until all thoracostomy tubes were removed, whichever came first.

There is low quality evidence that prolonged antibiotic prophylaxis in the presence of a wound drain has neither benefit nor harm in reducing SSI when compared to perioperative prophylaxis alone (OR: 0.79; 95% CI: 0.53–1.20).

Eleven RCTs *(1, 15-24)* including a total of 1051 patients and comparing early vs. late removal of drainage were identified. Nine studies investigated the duration of drains in patients undergoing mastectomy *(1, 15-22)* and 2 studies after hip or knee arthroplasty *(23, 24)*. Study definitions

for early drain removal varied from removal at 12 hours, 24 hours and 48 hours to 3, 4 or 5 days postoperatively. Late removal was either defined as removal when the drainage volume became minimal (that is, <30 mL/day or <50 mL/day) or as specific time points, such as postoperative days 2, 6, 8 and 10. One trial *(24)* compared 3 different time points of drain removal (12 hours, 24 hours and 48 hours).

Despite this heterogeneity, two subgroup analyses were performed based on two main classifications for the indication of late wound drain removal, that is, specific time points with drain removal at postoperative day 6 or later (3 studies *(17, 19, 22)*) and drainage volume (6 studies *(1, 15, 16, 18, 20, 21)*). Early removal was considered to be from postoperative days 1 to 5. Therefore, 2 studies that compared drain removal at postoperative day 1 vs. postoperative day 2 *(23)* and 12 hours/24 hours vs. postoperative day 2 *(24)* were not included in the subgroup comparisons.

There is very low quality evidence that the early removal of wound drains has neither benefit nor harm in reducing the SSI rate when compared to late removal (OR: 0.86; 95% CI: 0.49–1.50). When this comparison was sub-classified by late removal at specific time points (postoperative day 6 or later) and drainage volume, the results remained unchanged (OR: 0.63; 95% CI: 0.07–5.70 and OR: 0.93; 95% CI: 0.51–1.70, respectively).

The body of retrieved evidence focused on adult patients and no study was available in the paediatric population. The literature search did not identify any studies that reported on SSI-attributable mortality.

Additional factors considered when formulating the recommendation

Values and preferences

The GDG is confident that most patients do not wish to receive prolonged antibiotic prophylaxis to reduce SSI in the absence of good evidence for a benefit, including the possibility of potential harms, such as the development of AMR, antimicrobial-related adverse events and *C. difficile* infection.

The GDG acknowledged that wound drains are uncomfortable and inconvenient for patients. One survey showed that patients prefer early wound drain removal *(15)*. Even patients who developed seromas requiring aspiration indicated their preference for early removal with a return to hospital for further aspiration if necessary. In one trial on mastectomy, Barton and colleagues *(1)* reported that early drain removal increased the occurrence of seromas requiring treatment and this trial was even halted because of the significantly higher rate of adverse events in the early removal group.

Resource use

The GDG noted that the availability of antibiotics might be limited, particularly in LMICs. The additional costs of prolonged antibiotic prophylaxis in the presence of a wound drain, including the acquisition of wound drains, may represent not only a financial burden to the health system/ medical centre in low-resource settings, but also to the patients themselves. The GDG emphasized that there is a need to raise awareness and education on the rational use of antibiotics and antibiotic stewardship among both health care workers (surgeons in particular, with reference to this recommendation) and patients. Early removal of drains may shorten hospital length of stay and therefore lead to cost savings *(22)*.

Research gaps

GDG members highlighted that the available evidence on the time point of wound drain removal is limited to the fields of breast and orthopaedic surgery only. The GDG observed that the number of studies evaluating specific time points is very limited and there is therefore a need for RCTs to focus on specific time points for drain removal, rather than on drainage volume. All future studies should use SSI as the outcome, defined according to CDC criteria, and report any adverse events related to the time of drain removal. There is a need also for well-designed RCTs, especially in orthopaedic joint replacement and cardiac surgery. All included studies were in adult patients and more research is required to investigate the benefit of early drain removal in paediatric populations and among neonates. The great majority of the available evidence comes from high- and middle-income countries and more studies in low-income countries are required.

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5. DISSEMINATION AND IMPLEMENTATION OF THE GUIDELINES

The overall aim of this guideline is to improve the quality of care and outcome of patients undergoing surgical procedures through the prevention of SSI.

Uptake of the guidelines by all players included in the target audience is essential. In particular, adoption of the recommendations within national and local IPC and safe surgery guidelines and policies is a key element. Their translation into practice in surgical services and operating rooms is the ultimate and most important goal to achieve a reduction of harm due to SSI through the continuum of the patient's surgical journey. The dissemination and implementation of these guidelines are crucial steps that should be undertaken by the international community, as well as by national and local health services.

Guidelines implementation

The IPC team of the WHO Service Delivery and Safety Department works with experts and a separate document to accompany the guidelines will be dedicated to strategies for their implementation. This work is based on a systematic literature review aimed at identifying successful strategies and protocols for the implementation of SSI prevention measures, included those recommended by these guidelines.

The team is also considering the results of some key projects that WHO and other partners have led in the field of safe surgery and SSI prevention over the last years. The results and impact of the dissemination and adoption of the WHO safe surgery checklist will be evaluated and included in the implementation strategy document. Furthermore, over the last 3 years, the WHO IPC team and the Johns Hopkins Armstrong Institute for Patient Safety and Quality (Baltimore, MD) led the implementation of the Surgical Unit-based Safety Programme in hospitals in the WHO African Region and the USA. This was a quasi-experimental before/after study implementing a range of SSI prevention measures, together with infection surveillance, combined with an improvement of the patient safety culture. The quantitative results have shown a significant reduction of SSI and improvement of the patient safety climate, while qualitative evaluations have provided insightful lessons learned on barriers and facilitating factors for implementation. As demonstrated by the Surgical Unit-based Safety Programme and other projects, IPC guidelines are most successfully implemented when embedded in an enabling environment supportive of a patient safety culture. Following expert consultation, the results of all these pieces of work will be included in the implementation strategy document. In addition, a package of more than 20 implementation tools was produced for the Surgical Unit-based Safety Programme. This tool package is in the process of being revised and updated by WHO and it will be issued as the formal implementation package accompanying these guidelines. The package will include SSI prevention, as well as patient safety culture building tools.

Guidelines dissemination and evaluation

The recommendations in these guidelines will be disseminated through a broad network of international technical partners and stakeholders in the field of IPC, surgery and patient safety, including professional societies and patient organizations. More specifically, the WHO Global Infection Prevention and Control network and the Global Initiative for Emergency and Essential Surgical Care forum will be targeted. Other WHO teams working on IPC projects, WHO country and regional offices, ministries of health, WHO collaborating centres, other United Nations agencies and nongovernmental organizations will be targeted through specific communications and

support and collaboration will be provided for dissemination and implementation as appropriate. Dissemination will be done also through all facilities participating in the WHO *Save Lives: Clean Your Hands* and *Safe Surgery Saves Lives* global campaigns. Plans are being developed to conduct pilot implementation in some countries, particularly in the African Region and the Region of the Americas. All these activities will be supported by specific communication messages and, importantly, by the implementation strategy document and tool package planned to be issued shortly after publication of the guidelines.

Dissemination through the scientific literature is considered crucial for the successful uptake and adoption of the recommendations and WHO and members of the Systematic Reviews Expert Group have already submitted some papers for publication in peer-reviewed journals.

The WHO IPC team will continue to work with all stakeholders and implementers to identify and assess the priorities, barriers and facilitators to guideline implementation. The team will support also the efforts of stakeholders to develop guideline adaptation and implementation strategies tailored to the local context. The recommendations contained in the present guideline should be adapted into locally appropriate documents that are able to meet the specific needs of each country and its health service. Modifications to the recommendations, where necessary, should be limited to conditional recommendations and justifications for any changes should be made in an explicit and transparent manner.

To assess and follow-up the implementation of these guidelines, an evaluation framework will be developed by the WHO IPC team and colleagues from regional offices. This work will also be based on already available tools from Surgical Unit-based Safety Programme and other IPC projects.

6. ANNEXES

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