# 1 The Burden of Surgical Site Infections: Pathophysiology and Risk Factors—Preoperative Measures to Prevent Surgical Site Infections

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A semantic approach to "the burden of surgical site infections" could give us an interesting and wide point of view on the topic.

A straight definition of burden is: a load, typically a heavy one, carried by someone or something.

In the context of Healthcare associated infections the use of this word is constantly rising, involving a wide group of "carriers" sharing the load with a different level of implications.

A very explicative figure is a trunk of pyramid with the number of patients affected by HAI at the lower base (high load in terms of morbidity-mortality-quality of life) and all the stakeholders in the upper part (reduced and different kind of load: professional responsibility, legal/insurance implications).

A relevant part, hidden and not even quantifiable, is under the pyramid and represents all the caregivers (part of social costs).

The smallest and actually missing part is the highest one representing the apex: politics, lawmakers, and industries' strategists.

The semantic and etymology of surgical site infections aids us in understanding almost everything in three words: to work with hands (from ancient Greek **χειρ εργον**) creating the opportunity for pathogenic microorganisms to spread into tissues and organs.

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## 1.1 History of Surgical Site Infections in a Nutshell

- Before the mid-nineteenth century fever, wound pus, sepsis, and death were routine sequelae of surgical procedures. Ignaz Semmelweis and Joseph Lister were the pioneers in infection control by introducing the principles of antisepsis and contributing to the clear reduction of post-surgical complications.
- In the 1980s, an infection increased the hospitalization period by approximately 10 days with an additional cost of 2000 dollars; in 1992, each SSI determined 7.3 additional days of hospitalization after the operation, with an additional charge of 3152 dollars.
- In the decade 1986–1996, the data of the National Nosocomial Infections Surveillance (NNIS), showed 15,523 SSI on 593,344 surgical operations (CDC). The SSIs were the most common HAIs (38% of the total): the two-thirds superficial or deep, one-third organ/space. 77% of deaths were attributable to infection most (93%) of which were organ/space.

## 1.2 Results Below Expectations

- In the last 30 years progress in the control of SSI has affected every aspect of assistance (from sterilization to the architecture of operating rooms) and the interventions applied are recognized as effective at the level of literature, yet the SSI remain a source of morbidity and mortality.

  Why

- The reasons are similar to those, more general, of HAI: antimicrobial resistant pathogens, increase in surgical patients, their age and comorbidities.
- Multiple factors have been identified in a patient's surgical path that contribute to the development of the infection.
- The prevention of surgical site infections is complex and requires a strategy that integrates a wide range of interventions before, during and after surgery, relating the different professionals involved in patient management.
- The implementation of these interventions is not standardized. National guidelines are available but there are discrepancies in the interpretation of scientific evidence, recommendations and in the application of good practices.

### 1.2.1 Burden

SSI data (and HAI's) are not included in the list of diseases for which the global burden is regularly evaluated by WHO or other international organizations working on global health.

The incidence of SSI varies worldwide (160,000 to 300,000 in the US and leading HAI reported in low-medium income countries) but numbers are understated,

given the surveillance challenges. Despite the presence of robust data in some countries or regions, we lack accurate SSI rates and numbers about the economic effect (direct and indirect).

Use of SSI rates as a pay-for-performance metric, a target of quality-improvement efforts, a quality indicator and comparison benchmark for health-care facilities, countries and the public, is strictly linked to robust numbers to ensure valid comparisons. It's mandatory to have unique SSI definitions, strength and valid SSI data and to conduct sheer economic studies.

Surgical site infections (SSIs) are the most common and costly of all hospital-acquired infections (HAI), accounting for 20% of HAI. SSIs are associated with increased length of stay and morbidity, a 2- to 11-fold increase in the risk of mortality (77% of this is due to the infection itself); sequelae include prolonged antimicrobial treatment, redo-surgeries, reduced quality of life, post-hospital rehabilitation, lost work, and productivity [1].

The financial burden of SSI is considerable; it ranks as the third most costly of the hospital-acquired infections (doubled since 2005). The annual cost of SSI in the US is estimated at $3.5 to $10 billion.

Increased direct costs from SSIs are driven by prolonged length of stay, intensive care unit stay, reoperation, surgical techniques, emergency department visits, risk of readmission and medical resources erosion (diagnostic test, medical staff, operative, and treatment costs). Indirect costs are related to patients' quality of life, work absence, and earnings loss.

In addition to the economic burden, the development of an SSI and the subsequent prolonged hospitalization will likely have a negative impact on patient physical and mental health; patients who require absence from work constitute an economic cost in terms of lost income and reduced work productivity; infected patients diagnosed after their discharge from hospital may not have the same access to treatment with more distress than for in hospital diagnosed patients.

Furthermore infections detected after discharge may result in an underreporting, as well as the costs associated with community healthcare visits.

Medical costs, given variations across the globe, have been estimated to range from 15,800 to 43,900 $ per SSI.

SSI (in the US) extends hospital length of stay by 9.7 days and increases the cost of hospitalization by more than $20,000 per admission. More than 90,000 readmissions annually are attributed to SSIs, costing an additional $700 million per year. We have to consider that up to 60% of SSIs were estimated to be preventable with the use of evidence-based measures.

In a recent Centers for Disease Control and Prevention (CDC) report on the rates of national and state (US) HAIs based on data from 2018, 3345 acute care hospitals reported 21,265 SSI among 2,808,659 surgical procedures (all National Healthcare Safety Network—NHSN) performed in that year and an overall Standardized Infection Ratio (SIR) of 0.954 (95% CI 0.941–0.967) [2].

Of note, between 2017 and 2018, there was no significant change in overall SSI related to the 10 select procedures tracked in the CDC report (no changes in 336,585 performed abdominal hysterectomy and in 329,729 performed colon surgery).

Applying two different consumer price index adjustments to account for the rate of inflation in hospital resource prices, the CDC estimated that the attributable patient hospital costs for SSI is between $1087 and $29,443.

SSI is considered (using the consumer price index for urban consumers and inpatient hospital services) as the HAI with the largest range of annual costs (US$ 3.2–8.6 billion and US$ 3.5–10 billion, respectively).

The estimated economic costs of SSIs in Europe (in 2004) range between € 1.47–19.1 billion. It predicted also that the average patient stay would increase by approximately 6.5 days and cost three times as much. The analysis suggested that the SSI-attributable economic burden at that time was likely to be underestimated.

In 2017, 12 EU Member States and one EEA country reported SSIs for nine types of surgical procedure to ECDC. During this period, 10,149 SSIs were reported from a total of 648,512 surgical procedures. The percentage of SSIs varied from 0.5% to 10.1%. The incidence density of in-hospital SSIs per 1000 postoperative patient-days varied from 0.1 to 5.7. From 2014 to 2017, a statistically significant increasing trend was observed for both the percentage of SSIs and the incidence density of in-hospital SSIs following laparoscopic cholecystectomy (CHOL) [3].

Overall, 648,512 surgical procedures from 1639 hospitals were reported in 2017. Of these procedures, 622,999 were reported using patient-based surveillance, and 25,513 used the unit-based surveillance. The most frequently reported types of surgical procedure were HPRO operations, followed by KPRO operations and CSEC operations. 10,149 SSIs were reported using patient-based or unit-based surveillance. Of these, 4739 (47%) were superficial, 3088 (30%) deep, and 2274 (22%) organ/space SSIs. In 48 (0.5%) SSIs, the type of SSI was unknown. The proportion of deep or organ/space SSIs was 19% in CSEC operations, 42% in laparoscopic CHOL operations, 46% in open CHOL operations, 50% in open COLO operations, 53% in CABG operations, 54% in LAM operations, 61% in laparoscopic COLO, 71% in KPRO operations, and 77% in HPRO operations. Thirty-four per cent of the SSIs were diagnosed in hospitals, whereas 52% were detected after discharge; for 14% the discharge date was unknown. The proportion of SSIs diagnosed in hospital varied from 12% in KPRO operations to 67% in open COLO operations.

Detailed costs from five European countries (France, Germany, Italy, Spain, and the UK) were recently reviewed and published:

- France—following head and neck cancer surgery, patients who developed an SSI constitute a total per-patient medical cost €17,434 higher than those patients who did not develop an SSI
- Germany—matched case–control study demonstrated that total medical cost per patient was significantly elevated in SSI patients [$49,449 vs $18,218 (€36,261 vs €13,356)] and that intensive care unit (ICU) and ward-care costs accounted for the largest part (27.7% and 24.7%, respectively)
- Italy—in orthopedic and trauma surgery patients, SSI was associated to an average cost of €9560 ranging from 3411 to 22,273 (without specifications of resources and costs)

- Spain—across multiple surgical specialties, the sum of all costs (hospital, temporary and permanent incapacity for work, premature deaths and caregivers costs) per SSI patient is $97,433; healthcare costs only accounted for about 10% of the total financial burden
- UK—in general surgery an SSI constituted an additional financial burden of £10,523 per patient (operating theater and medical staff costs accounted for 11% and 18% of the total) [4].

## 1.3 Pathophysiology

Microbial contamination of the surgical site is a necessary precursor of SSI. The risk of SSI can be conceptualized according to the following relationship Dose of bacterial contamination x virulence / resistance of the host patient = Risk of SSI. Quantitatively, it has been shown that if a surgical site is contaminated with $>10^5$ microorganisms per gram of tissue, the risk of SSI is markedly increased [5]. However, the dose of contaminating microorganisms required to produce infection may be much lower when foreign material is present at the site (i.e., 100 staphylococci per gram of tissue introduced on silk sutures or mesh or prosthesis). Microorganisms may contain or produce toxins and other substances that increase their ability to invade a host, produce damage within the host, or survive on or in host tissue.

Pathogens' source is the endogenous flora of the patient's skin, mucous membranes or hollow viscera [6].

When mucous membranes or skin are incised, the exposed tissues are at risk for contamination with endogenous flora (aerobic gram-positive cocci, anaerobic bacteria, and gram-negative aerobes from fecal flora when incisions are close to the perineum or groin). When a gastrointestinal organ is opened during an operation and is the source of pathogens, gram-negative bacilli (e.g., *E. coli*), gram-positive organisms (e.g., enterococci), and sometimes anaerobes (e.g., *Bacillus fragilis*) are the typical SSI isolates.

Another SSI source is seeding from a distant focus of infection in patients who have prosthesis or other implant placed during the operation. Any device provides a nidus for attachment of the organism.

Exogenous sources include surgical personnel (members of the surgical team), the operating room environment (including air), tools, instruments and materials brought to the sterile field during a procedure. Exogenous flora are primarily aerobes (gram-positive organisms). Anal, vaginal, or nasopharyngeal carriage of group A streptococci by operating room personnel has been implicated as a cause of several SSI outbreaks. Carriage of gram-negative organisms on the hands has been shown to be greater among surgical personnel with artificial nails. Rarely, outbreaks or clusters of surgical site infections caused by unusual pathogens have been traced to contaminated dressings, bandages, irrigants, or disinfection solutions. Fungi (particularly *Candida albicans*) have been isolated from an increasing percentage of SSIs. This trend probably is due to the widespread use of prophylactic and empiric

antibiotics, increased severity of illness, and greater numbers of immunocompromised patients undergoing surgical procedures.

Bacteria contaminate all surgical wounds; a minority of wounds actually demonstrates clinical infection. In most patients, infection does not develop because innate host defenses are efficient against contaminants at the surgical site.

Surgical incision activates 5 critical initiators of the human inflammatory response:

- Coagulation proteins and platelets (hemostatic mechanism)
- Mast cells and complement proteins
- Bradykinin (produced from its ubiquitous protein precursor).

The effect is vasodilation and increased local blood flow with velocity reduction in order to aid the margination of phagocytes. The increasing vascular permeability and local vasodilation facilitates the formation of edema, creating more space between endothelial cells and providing phagocytic access to the injured soft tissue and aqueous conduits for their navigation through the normally condensed extracellular tissues.

After this phase we have both nonspecific chemoattractant signals and specific chemokine signals (from mast cells) that "draw" neutrophil, monocyte and other leukocyte populations into the area of the surgical site.

"Phagocytes' recruitment" into the wound before bacterial contamination actually occurs from the procedure itself (innate host defenses) and gives the patient an advantage against infection as an outcome.

Chemoattractant signaling proteins bind to local vascular endothelial cells and upregulate selectin proteins on their endothelial surface.

Neutrophils move on the endothelial surface within the post-capillary venule. Further interaction between neutrophil and endothelial cell adhesion proteins link the neutrophil to endothelial cell's surface and the chemoattractant gradient leads neutrophil to the site of injury inducing systematic ingestion and digestion of any microbial contaminants.

During the first 24 h monocytes enter the surgical site. If microbial contamination has been minimal and the early arriving neutrophils have been able to adequately control the bacteria, then monocytes produce local chemical signals to regulate the wound-healing process. Myofibrocytes migrate into the fibrin matrix of the wound and collagen deposition displaces its fibrin latticework.

Otherwise, if microbial contamination and proliferation overwhelm the initial neutrophil infiltration, the monocyte becomes a proinflammatory cell with cytokines' release (Tumor necrosis factor—TNF—alpha). The effects are:

- Potent paracrine signal to upregulate neutrophil activity
- TNF-alpha-stimulated neutrophils consume microbes, and lysosomal vacuoles may release reactive oxygen intermediates and acid hydrolases into the extracellular space from its lysosomal vacuoles.

- The extracellular release of reactive oxygen intermediates and the acid hydrolases results in lipid peroxidation of the local environment, with further tissue injury and further activation of the initiator signals.
- The inflammatory response is further intensified.
- Interleukin (IL)-1, IL-6, and other proinflammatory signals are released by the activated monocyte and serve as endocrine signals responsible for fever, stimulation of acute-phase reactants, and other responses.
- The wound is, actually, a host-pathogen battlefield, filled with necrotic tissue, neutrophils, bacteria, and proteinaceous fluid that together constitute pus.

The viable tissues around exhibit the classic signs of inflammation:

- Rubor reflects local vasodilation.
- Calor is the warmth of the vasodilated tissues resulting in increased heat conduction.
- Tumor is due to edema.
- Dolor occurs from stimulation of nerve nociceptors by the numerous products of the inflammatory cascade and tissue injury and distension.
- Functio Laesa is the unavoidable inhibition of normal anatomical function.

Four different determinants lead to either uneventful wound healing or SSI: (1) inoculum of bacteria, (2) virulence of bacteria, (3) adjuvant effects of microenvironment, and (4) innate and acquired host defenses.

Contaminants may enter the wound from the air in the OR, from the instruments or surgeon(s). Skin bacteria are always present. The largest inoculum occurs when the operation involves a body structure heavily colonized by bacteria, such as the bowel ($10^3$–$10^4$ bacteria/mL distal in small bowel, $10^5$–$10^6$ bacteria/mL in right colon, and $10^{10}$–$10^{12}$ bacteria/g of stool in rectosigmoid colon). Bacteria are also present in the stomach of older patients who have hypo or achlorhydria. Significant concentrations of bacteria are encountered in the biliary tract (patients older than 70 years of age, obstructive jaundice, common bile duct stones, acute cholecystitis). Procedures involving the female genital tract will encounter $10^6$–$10^7$ bacteria/mL [7–9]

The more virulent the contaminant, the greater the probability of infection. Coagulase-positive staphylococci require a smaller inoculum than the coagulase-negative species. Uncommon but virulent strains of *Clostridium perfringens* or Group A streptococci require only a small inoculum to cause an especially severe necrotizing infection at the surgical site. *Escherichia coli* has endotoxin in its outer cell membrane that gives it a particular virulence. *Bacteroides fragilis* and other Bacteroides species are ordinarily organisms of minimal virulence as solitary pathogens, but when combined with other oxygen-consuming organisms, they will result in microbial synergism and cause very significant infection following operations of the colon or female genital tract. Due to the intrinsic features of this variable (related to procedure and patient's colonizing bacteria) it's difficult to control it by preventive strategies.

Adjuvant factors (secondary to the surgical procedure) in the microenvironment of the wound may result in clinical infection:

- Hemoglobin by the release of ferric iron during the degradation of red blood cells and stimulation of microbial proliferation
- Necrotic tissue can act as a haven for contaminants avoiding phagocytic action
- Foreign bodies (braided sutures)
- Dead space

Impaired host defenses could be innate or acquired.

In the first case is difficult to elaborate strategy based on the measure of differences between groups of patients (more or less "competent" against infections).

Otherwise, acquired impairment is linked to increased rates of SSI. Shock and hypoxemia are positively associated with SSI, especially in trauma patients. Transfusion appears to be immunosuppressive. Chronic illnesses, hypoalbuminemia (is the most robust predictor of infectious complications after major abdominal surgery) and malnutrition are significant factors. Hypothermia and hyperglycemia are also responsible.

Medications (especially corticosteroids) may also adversely affect the host and increase SSI rates.

The pathophysiology of SSI is complex, even more if we consider all the determinants in a common context focusing on specific causes of an infection (the so called "Aggregate Effect").

### 1.3.1 Risk Factors

Numerous risk factors have been identified for the development of an SSI and we can identify two broad categories affecting the outcome at three different levels:

intrinsic (patient related level, modifiable, or non-modifiable) factors
extrinsic (operative level and institutional level) factors

Patient related factors are:

- Individual characteristics (sex, age, frailty, dependence, socioeconomic status)
- Lifestyle (smoking, alcohol)
- Comorbidities (diabetes, chronic obstructive pulmonary disease, congestive heart failure, acute myocardial infarction, renal insufficiency, hypertension, osteoporosis, Charlson comorbidity score)
- Medications (immunosuppression)
- Prior environment (preoperative length of stay, admission from a long-term facility)
- Risk calculators—scoring system (NNIS, ASA)
- Operative level

- Procedure
  - Incision class
  - Type of surgery
  - Elective vs emergency procedure
  - Case complexity
  - Surgery duration
  - Blood loss / Transfusions
  - Medical device implant
- Institutional level
- Current environment
  - Safety culture
- Hospital
  - Size
- Experience
  - Physician
  - Facility

Potentially modifiable patient risk factors include glycemic control and pre-surgery diabetic evaluation, alcohol and smoking abuse, preoperative albumin <3.5 mg/dL, total bilirubin >1.0 mg/dL, obesity, and immunosuppression. Non-modifiable patient factors include increasing age, recent radiotherapy, and history of skin or soft tissue infection.

Procedure-related factors include emergency and more complex surgery and wound classification.

Facility risk factors include inadequate ventilation, increased operating room (OR) traffic, and appropriate sterilization of equipment. Preoperative risk factors include presence of a preexisting infection; inadequate skin preparation; hair removal; and antibiotic choice, administration, and duration. Intraoperative risk factors include duration of surgery, blood transfusion, maintenance of asepsis, poor-quality surgical hand scrubbing and gloving, hypothermia, and poor glycemic control.

Different surgical sites may contribute to the risk of developing clinical infection. Stratification into groups that have similar risks for infection is crucial to implement preventive strategies among similar patients and to identify infection rates variation from benchmark within an institution. Assessment of gross SSI rates without stratification is likely to be a reflection of patient risk rather than quality of performance. SSIs are a significant healthcare quality issue, resulting in increased morbidity, disability, length of stay, mortality, resource utilization, and costs. Identification of high-risk patients may improve preoperative counseling, inform resource utilization and allow modifications in perioperative management to optimize outcomes.

Many risk factors are beyond practitioner control, but optimizing perioperative conditions can certainly help decrease infection risk.

High-risk surgical patients may be identified on the basis of individual risk factors or combinations of them. In particular, statistical models and risk calculators may be useful in predicting infectious risks, both in general and for SSIs. These models differ in the number of variables; inclusion of preoperative, intraoperative or postoperative variables; ease of calculation and specificity for particular procedures. Furthermore, the models differ in their accuracy in stratifying risk.

Although multiple strategies exist for identifying surgical patients at high risk for SSIs, no one strategy is superior for all patients, and further efforts are necessary to determine if risk stratification in combination with risk modification can reduce SSIs in this patients' population [10].

Early evaluation of perioperative SSI risk factors and patient risk stratification could be of great value in the development of predictive risk models. Predictive risk models could, in turn, assist surgeons and their patients in the clinical decision-making process (e.g., counseling patients on the appropriateness and risks of surgery). In addition, risk models could be used to develop targeted perioperative prevention strategies and diagnostic care process models and improve risk adjustment for risk modeling used in the public reporting of SSI as a quality metric.

However, a study reviewing SSIs in patients undergoing colorectal resections (C-SSIs), identified from an institutional ACS-NSQIP dataset (2006–2014), showed that risk prediction models do not accurately predict C-SSI in their own independent institutional dataset.

Published C-SSI risk scores: the National Nosocomial Infection Surveillance (NNIS), Contamination, Obesity, Laparotomy, and American Society of Anesthesiologists (ASA) class (COLA), Preventie Ziekenhuisinfecties door Surveillance (PREZIES) and NSQIP-based models were compared with receiver operating characteristic (ROC) analysis to evaluate discriminatory quality.

There were 2376 cases included, with an overall C-SSI rate of 9% (213 cases). None of the models produced reliable and high quality C-SSI predictions. For any C-SSI, the NNIS c-index was 0.57 vs 0.61 for COLA, 0.58 for PREZIES, and 0.62 for NSQIP: all well below the minimum "reasonably" predictive c-index of 0.7. Predictions for superficial, deep, and organ space SSI were similarly poor.

Published C-SSI risk prediction models do not accurately predict C-SSI in their independent institutional dataset. Application of externally developed prediction models to any individual practice must be validated or modified to account for institution and case-mix specific factors. This questions the validity of using externally or nationally developed models for "expected" outcomes and interhospital comparisons.

### 1.3.2 Preop Measures

Thirteen recommendations (made by the WHO) were published on Lancet in 2016 covering the preoperative path of surgical patients and taking into account evidence quality, cost and resource use implications, patient values and preferences.

### 1.3.3 Perioperative Discontinuation of Immunosuppressive Agents

It's not indicate to discontinue immunosuppressive medication before surgery to prevent SSI (conditional recommendation, very low quality of evidence). The decision should be made on an individual basis, involving the prescribing physician, the patient, and the surgeon.

### 1.3.4 Enhanced Nutritional Support

It's possible to consider the administration of oral or enteral multiple nutrient-enhanced nutritional formulas to prevent SSI in underweight patients who undergo major surgical operations (conditional recommendation, very low quality of evidence). Multiple nutrient-enhanced formulas can be used to prevent SSIs in adult patients undergoing major surgery. However, it is expensive and requires additional work for clinical staff, including expertise from dietitians and pharmacists. When considering this intervention in the context of a priority assessment approach to reduce the SSI risk, resources and product availability should be carefully assessed, particularly in settings with limited resources.

### 1.3.5 Preoperative Bathing

Good clinical practice requires that patients bathe or shower before surgery. Both a plain or antimicrobial soap can be used for this purpose (conditional recommendation, moderate quality of evidence. Evidence was insufficient to formulate any recommendation on the use of chlorhexidine gluconate-impregnated cloths for the purpose of reducing SSIs.

Decolonization with mupirocin ointment with or without CHG body wash in nasal carriers of *Staphylococcus aureus* undergoing cardiothoracic and orthopedic surgery / other types of surgery

Patients undergoing cardiothoracic and orthopedic surgeries, who are known nasal carriers of *S. aureus*, should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of chlorhexidine gluconate body wash (strong recommendation, moderate quality of evidence). It's to consider the use of the same treatment in patients with known nasal carriage of *S. aureus* undergoing other types of surgery (conditional recommendation, moderate quality of evidence). *S. aureus* is one of the most common health-care-associated pathogen worldwide with increased mortality when it has methicillin-resistance patterns.

*S. aureus* nasal carriage is a well-defined risk factor for subsequent infection in various patient groups. Mupirocin nasal ointment (usually applied twice daily for 5 days) is an effective, safe, and fairly cheap treatment for the eradication of *S. aureus* carriage and is generally used in combination with a whole body wash. A

meta-regression analysis showed that the effect on the *S. aureus* infection prevalence did not differ between different types of surgery ($p = 0.986$). To avoid unnecessary treatment and resistance spread, this intervention should be done only on known *S. aureus* carriers. Therefore, these recommendations apply to facilities where screening for *S. aureus* is feasible, and indeed, studies were done mostly in high-income countries. There is no recommendation on the role of screening for *S. aureus* carriage or the surgical patient population that should undergo screening.

### 1.3.6 MBP with/without the Use of Oral Antibiotics

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) and MBP alone (without administration of oral antibiotics) should not be used (strong recommendation, moderate quality evidence). There is no recommendation on the preferred type of oral antibiotic, including the timing of administration and dosage, but an activity against both facultative Gram-negative and anaerobic bacteria should be guaranteed and non-absorbable antibiotics should be used preferably. The choice should be made according to local availability, updated resistance data within institutions and the volume of surgical activity. This intervention is for preoperative use only and should not be continued postoperatively. The use of oral antibiotics in association with MBP does not replace the need for intravenous surgical antibiotic prophylaxis.

### 1.3.7 Hair Removal

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 (strong recommendation, moderate quality of evidence).

When hair is removed, clipping significantly reduces SSIs compared with shaving (OR 0.51; 0.29–0.91). Because they have similar potential to cause microscopic skin trauma, no hair removal and clipping were combined in an additional meta-analysis, which showed that they are associated with significantly reduced prevalence of SSIs compared with shaving (combined OR 0.51; 0.34–0.78). No recommendation regarding the timing of hair removal could be formulated as only one study assessed this question with no relevant results, but the panel suggested that removal by clipping shortly before surgery is the safest approach, if required.

### 1.3.8 Optimal/Precise Timing for Administration of SAP

Is suggested the administration of SAP before surgical incision, if indicated, depending on the type of operation (strong recommendation, low quality of evidence); it

should be done within the 120 min before the incision, while considering the half-life of the antibiotic (strong recommendation, moderate quality of evidence).

Successful SAP requires delivery of the antimicrobial agent in effective concentrations to the operative site through intravenous administration at the appropriate time.

On the basis of the available evidence, a more precise timing of less than 120 min before incision cannot be defined, and the widely implemented recommendation of within 60 min before incision is not supported by evidence. The half-life of the agent used, the underlying condition(s) of the individual patient (e.g., body-mass index, or renal or liver function), the time needed to complete the procedure, and the protein binding of the antibiotic should be taken into account to achieve adequate serum and tissue concentrations at the surgical site at the time of incision and up to wound closure—in particular to prevent incisional SSI. Administration should be closer to the incision time (<60 min before) for antibiotics with a short half-life (cefazolin, cefoxitin, and penicillins in general). Most available guidelines recommend a single preoperative dose; intraoperative redosing is indicated if the duration of the procedure exceeds two half-lives of the drug, or if there is excessive blood loss during the procedure.

### 1.3.9 Surgical Hand Preparation

Surgical hand preparation should be done either by scrubbing with a suitable antimicrobial soap and water or using a suitable alcohol-based hand rub (ABHR) before donning sterile gloves (strong recommendation, moderate quality of evidence).

Is crucial to maintain the least possible contamination of the surgical field, especially in the case of sterile glove puncture during the procedure. Appropriate surgical hand preparation is recommended in the WHO guidelines on hand hygiene in health care issued in 2009 and in all other existing national and international guidelines for the prevention of SSIs.

When selecting an ABHR, health-care facilities should procure products with proven efficacy according to international standards and position no-touch or elbow-operated dispensers in surgical scrub rooms. In LMICs in which ABHR availability might be low, WHO strongly encourages facilities to undertake the local production of an alcohol-based formulation (feasible and low-cost).

Alternatively, antimicrobial soap, clean running water, and disposable or clean towels for each health-care worker should be available in the scrub room.

### 1.3.10 Surgical Site Preparation

Alcohol-based antiseptic solutions (based on chlorhexidine gluconate) should be used for surgical site skin preparation in patients undergoing surgical procedures (strong recommendation, low to moderate quality of evidence).

The aim is to reduce the microbial load on the patient's skin as much as possible before incision. The most common agents include chlorhexidine gluconate and

povidone-iodine in alcohol-based solutions, but aqueous solutions are also widely used in LMICs, particularly those containing iodophors.

Operating room staff should be trained and informed about the potential harms associated with the solutions used for surgical site preparation. Alcohol-based solutions should not be used on neonates or come into contact with mucosa or eyes and caution should be exercised because of their flammable nature. Chlorhexidine gluconate solutions can cause skin irritation and must not be allowed to come into contact with the brain, meninges, eye or middle ear. Alcohol-based solutions might be difficult to procure and expensive in LMICs, particularly when combined with an antiseptic compound. Local production could be affordable and feasible in these settings, provided that adequate quality control is in place.

### 1.3.11 Antimicrobial Skin Sealants

Antimicrobial sealants should not be used after surgical site skin preparation for the purpose of reducing SSI (conditional recommendation, very low quality of evidence).

Antimicrobial skin sealants are sterile, film-forming cyanoacrylate-based sealants commonly applied as an additional antiseptic measure after using standard skin preparation on the surgical site and before skin incision. They are 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. To avoid unnecessary costs, antimicrobial sealants should not be used after surgical site skin preparation for the purpose of reducing SSIs.

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