Italian Consensus Document

RECOMMENDATIONS FOR THE PERIOPERATIVE PREVENTION OF SURGICAL SITE INFECTIONS

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RECOMMENDATIONS FOR THE PERIOPERATIVE PREVENTION OF SURGICAL SITE INFECTIONS

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Publication executed with the unconditioned contribution of Becton Dickinson Italia SpA.

Edition reserved for Doctors

Out of commerce

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Foreword: the aim of this document

This document (the result of the work of many Italian experts) is not meant to be yet another set of guidelines in the field of prevention of post-surgery infections, but it does acknowledge that the situation in Italy requires the systematic application of evidence-based recommendations, which have already been set out by excellent international guidelines. The most updated versions of those guidelines are here analysed, combined and adjusted according to applicability and function criteria specifically designed for Italy. The eminently practical purpose of this document is shown by the availability of some educational tools that help implement and apply the recommendations contained here. These include a checklist and a poster that is a simplification in pictures of the bundle's contents, which are all available for free and can be downloaded from http://documentodiconsensoSSI.edizioniedra.it.

Introduction

Surgical site infections (SSIs) are infections occurring within 30 days after the operation or up to one year after the operation if an implant is in place (definition of the European Centre for Disease Prevention and Control [ECDC]) (1). SSIs can be classified as incisional or organ/space. The former can be defined as superficial incisional (if only skin or subcutaneous tissue is involved) and deep incisional (if the infection involves deep soft tissue, such as the fascia and/or muscles). Organ/space SSIs involve any part of the anatomy other than the incision that has been opened or manipulated during an operation (2).

Extent of the problem

According to a recent survey by the World Health Organisation (WHO), SSIs are the most frequent kind of hospital acquired infections (HAIs) in low- and middle-income countries. They affect approximately one third of patients who undergo surgery. Although the incidence is lower in high-income countries, SSIs are the second most common type of HAIs in Europe and the USA (3). In the USA, SSIs affect 2-5% of surgical patients, which, considering the approximately 16 million surgical operations performed each year, correspond to 320,000-800,000 cases per year (4). Over 2.5 million cases of HAIs are reported each year in Europe and SSIs represent about 20% of them. They are outnumbered only by infections in the lower respiratory tract (23.5%) and represent one of the main causes of post-operative morbidity and mortality (5).

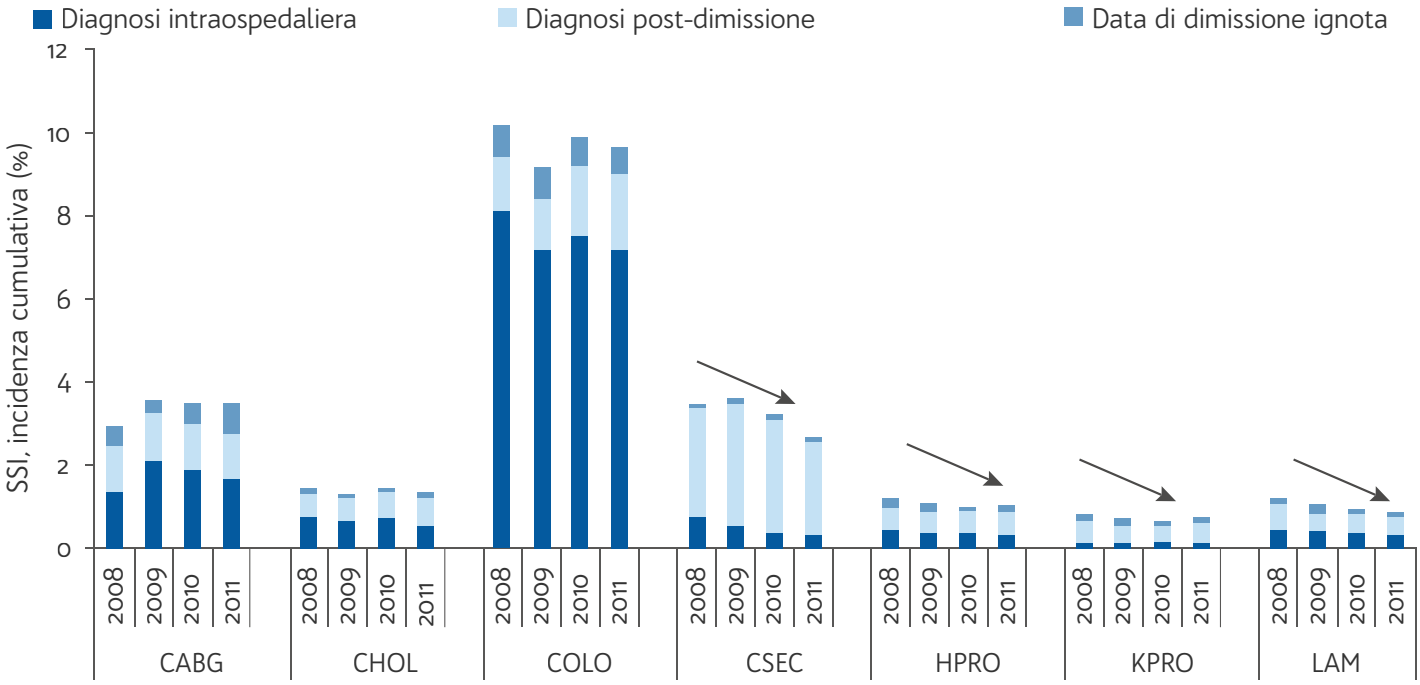
A significant percentage of SSIs (between 13% and 71%) are diagnosed after hospital discharge. Signs of implant-associated infections may occur up to a year after surgery. An increase in the above infections in the last ten years is also related to earlier discharges from hospital after surgery. This means that incidence data based only on hospital evidence risks underestimating the true incidence of SSIs (3).

SSIs are complications potentially associated with any kind of surgery, but the incidence varies depending on the kind of operation. A recent ECDC surveillance study, which also included the period after hospital discharge, collected data from 2011-2012 from 16 European states. It found that the highest rate of SSIs 30 days post-operation occurs in colorectal surgery (9.5%; episodes per 100 operations), followed by heart surgery (3.5%), whereas the incidence is 2.9% after delivery by Caesarean section, 1.4% after cholecystectomy, 1% in the case of hip arthroplasty, 0.8% after laminectomy and 0.75% after knee arthroplasty. This study also highlighted a decrease in SSI incidence after certain kinds of surgery, such as Caesarean delivery, hip arthroplasty and laminectomy **(Figure 1)** (1).

A 30-days post-surgery surveillance study on 4,665 surgical operations carried out in 48 Italian hospitals registered a 5.2% SSI incidence, which ranged between 18.9% after colorectal surgery, 13.6% after gastric surgery, 8.6% after appendectomy and 2.6% after a Caesarean delivery (6). In Italy, the data collected by the Sistema di Sorveglianza Nazionale delle Infezioni del Sito Chirurgico [National System for the Surveillance of SSIs] in 355 surgery departments between 2009 and 2011 highlighted that the incidence of SSIs was equal to 2.6% (1,628 cases out of 60,460 surgical procedures). A third of the cases were deep incisional or organ/space SSIs. On average, 60% of SSIs were diagnosed in the 30 days of post-discharge surveillance. SSI incidence appeared higher after colon (9.0%) and rectal (7.0%) surgery, whereas it was 3.1% after laparotomy and 2.1% after appendectomy. A long surgical procedure, an ASA (American Society of Anaesthesiologists) score ≥3, at least two days of pre-operative hospitalisation and emergency surgery were found to be the factors most strongly associated with an increase in SSI risk. Minimally invasive laparoscopy procedures had a lower incidence of SSIs (7).

Many factors can affect the risk of developing SSIs. Some of them are linked to the patient (age, ASA score, comorbidities) or the type of surgery (contaminated, urgent, laparoscopic), while others are linked to correct operative procedures (8). Some intrinsic variables (such as age) cannot be changed for obvious reasons, but many risk determiners can be effectively corrected or at least improved, regardless of whether they are linked to the patient (e.g. nutritional status, smoking) or to the surgical procedure, e.g. by using appropriate antibiotic prophylaxis measures, sterilisation, disinfection, hair removal

Figure 1. Cumulative incidence of SSIs per year and per type of procedure in the countries of the European Union and the European Economic Area in the 2008-2011 period. *Modified from (3). Data source: (1).*



CABG: *Coronary Artery Bypass Graft*; **CHOL:** *Cholecystectomy*; ***COLO:*** colon; **CSEC:** *Caesarean Section*; **HPRO:** *Hip Prosthesis*; **KPRO:** *Knee Prosthesis*; **LAM:** laminectomy;
SSI: *Surgical Site Infection.*

and skin antisepsis (3).

Most SSIs are acquired in the operating theatre, as shown by a number of studies in which the microorganisms responsible for the infection were found to be identical to those detected in the operating theatre or on the surgeon's fingers. Some studies have shown that the bacterial load of the surgical site at the time of incision plays a major role and that preventive environmental measures (i.e. the ones that aim at fighting the access of microbes to the incision site) can reduce the risk of SSI (9).

According to the European point prevalence survey conducted by the ECDC in the 2011-2012 period in 947 hospitals in 30 European countries, the aetiological agents of SSIs were Gram-positive bacteria in 46.3% of cases (*Staphylococcus aureus*: 17.9%, coagulase-negative staphylococci: 9.6%, *Enterococcus* spp.: 14.5%, *Streptococcus* spp.: 3.6%, other bacteria: 0.6%), followed by Enterobacteriaceae in 32.5% of cases (*Escherichia coli*: 14%, *Klebsiella spp.*: 6%, *Enterobacter spp.*: 5.4%, *Proteus spp.*: 3.6%) and non-fermenting Gram-negative bacteria (12.8%; *Pseudomonas aeruginosa*: 7.6%, *Acinetobacter spp.*: 2.9%) (5).

SSIs are increasingly caused by multidrug-resistant bacteria; the proportion of methicillin-resistant *Staphylococcus aureus* isolated from SSIs varies in Europe between 24 and 43%, depending on the type of surgery, and is 44% in the USA. In the USA, the proportion of *Escherichia coli* strains resistant to third-generation cephalosporins is 11%, whereas it is 25% in the case of resistance fluoroquinolones (5,10). Compared to other SSIs, infections caused by drug-resistant microorganisms are associated with greater problems in healing and worse outcomes, which means longer hospitalisation periods and additional costs.

Clinical impact of SSIs

SSIs have a considerable clinical impact because they are associated with a significant increase in mortality, morbidity and long-term disability, which translates into considerable social and economic implications for patients, their families and for the healthcare system. Patients with SSIs require extended hospitalisation periods and undergo more tests and treatments than what is normal for the surgery they have had. In some cases, they have to be hospitalised again or have more surgery, which considerably increases the burden of pain and personal distress of individual patients and their families, as a result of being absent from home and from work. The delayed healing of surgical wounds can expose patients to secondary complications such as bacteraemia and cause clinically permanent outcomes such as disfiguring scars, pain, persistent paraesthesia and reduced joint mobility. As a result, developing a SSI can severely compromise a patient's health-related quality of life (HRQoL). The studies that have specifically addressed this parameter are very few. Additionally, the quantification of this parameter is difficult because there is so much variability in relation to the affected body area and the severity of the infection (superficial, deep, organ/space involvement). It is often at risk of being underestimated, because data related to the post-discharge period are rarely collected. Despite this, all the papers published on this issue document the negative effect of SSIs on QoL (11,12).

A systematic review of 26 studies conducted in 6 European countries (including Italy) has highlighted that SSIs are constantly associated with longer hospitalisation times (between 2.1 and 54 days), with a certain amount of variability dependent on the severity of the SSIs, the country considered and the specialty unit. The greatest increase in hospitalisation times was observed in orthopaedic surgery and traumatology (13). Other data (also related to Europe) specify that hospitalisation periods for patients developing SSIs are on average 2 times longer than those of uninfected patients (14,15).

In England, 77% of deaths among patients with SSIs are estimated to be directly attributable to the infection itself (16). SSI-associated excess mortality is reported constantly in all studies. The increase in the risk of death in patients with SSIs varies depending on the type of surgery and is 2 to 11 times higher compared to operated patients who do not develop an infection (17, 18).

A recent systematic review of the literature considered 28 studies that quantified (using a number of methods) the decrease in Health Utility Values associated with the development of SSIs (19). Health Utility Values are a broad range of values that estimate health state and the quality of life; they include patient perceptions, mobility, ambulation and pain. The decrease varied between 0.04 and 0.48, with 19 out of 28 studies reporting values between 0.1 and 0.3, i.e. the same order of the ones estimated for pathological conditions such as major depression, beta-thalassemia, schizophrenia and hepatocellular carcinoma (20).

A recent ECDC study assessed the overall impact of HAIs in terms of DALYs (*Disability-Adjusted Life Years*), a composite measurement unit that takes into account the number of cases, the associated mortality and the short-term and long-term disability caused by a disease. Although the population examined for the risk of HAIs was limited to hospitalised patients, the estimated total impact was 501 DALYs every 100,000 among the general population in EU and EEA countries, which is significantly higher than that of all 32 major transmissible diseases (including 'flu, tuberculosis and HIV) assessed for the same parameters. This stresses the need to apply prevention and control measures to deal with SSIs (21).

Economic impact of SSIs

Considering the high incidence that still characterises SSIs, combined with the clinical impact associated with them, it is easy to understand how such events are a considerable economic burden for national health systems and, of course, for patients and their families. With regard to direct costs (attributable to the increased morbidity and mortality associated with SSIs) the greatest economic impact derives from the longer hospitalisation periods, with everything that that implies in terms of care provided by hospital staff, additional tests and therapies and, if required, more surgery (13). Additionally, SSIs represent a loss of opportunities for hospitals, because the management of patients with SSIs requires the use of hospital resources that could have been used for other activities. It also means beds are not available for other hospitalisations, which delays planned operations and slows activities in the surgery unit. After discharge from hospital, other healthcare services can assist patients with SSIs, but

the management of these outpatients still contributes to the overall costs incurred by the national health system for the treatment of SSIs (13).

The direct costs associated with SSI development must be added to indirect costs, such as loss of income and productivity caused by the inability to work and the need for support to be provided by relatives and healthcare assistants. There are also various other, intangible costs incurred by the patient in relation to physical pain, psychological distress and reduction of the quality of life. Although these costs are difficult to quantify, they represent a social and personal cost that has a considerable impact on the patient (22). The direct and indirect costs arising from the development of SSIs are shown in **Table 1**.

In European hospitals, the economic burden of patients with SSIs is approximately double that of surgery patients who do not develop SSIs, in relation of hospitalisation periods that can last more than twice as long (23). Overall, the economic impact associated with HAIs in Europe is estimated to be about 7 billion euro, considering the direct costs associated with 16 million days of additional hospitalisation alone. Similarly, in the US the costs associated with HAIs are estimated to be about 6.5 billion dollars (24). In Europe, with an estimated cost of €10,000-20,000 and over for each case, SSIs are the most important infection related to healthcare assistance in terms of economic impact (8).

In Italy, the overall management of HAIs is estimated to cost the national health service approximately one billion euro. These costs (mainly linked to longer hospitalisation periods) can vary depending on the specialty involved, ranging between €4,000 for Medicine units to €28,000 for Intensive Care Units, which are actually the hospital units with the highest frequency of hospital-acquired infections (25). A recent Italian study reported that the management of SSIs in orthopaedic surgery and traumatology comes with an additional cost of approximately €32,000, which corresponds to an additional average cost of €9,560 per patient compared to patients without infections (26).

All the studies contained in the international literature and that address the economic impact focus on what is considered the major indicator of SSI costs, i.e. longer hos-

Table 1. Direct and indirect costs linked to the development of SSIs

DIRECT COSTS		INDIRECT COSTS	
Healthcare assistance	**Non-healthcare assistance**	**Loss of productivity**	**Human cost (intangible)**
• Hospitalisation (inpatient stay) • Medicines • Laboratory tests • Diagnostic procedures • Outpatient medical appointments • Support rehabilitation therapies • Home care services provided by nurses	• Home care services provided by family members when not at work • Domestic support (meals, household cleaning) • Transport (e.g. going to doctor's appointments)	• Days of work lost by patient because of hospitalisation/ healthcare assistance and temporary disability • Days of work lost by family members to assist the patient	• Physical pain • Psychological distress • Lower quality of life • Social isolation

pitalisation periods. Despite the common base, the results are very heterogeneous, probably because it is difficult to quantify hospitalisation costs in a standardised manner. The various papers show great variability in terms of the considered cost determiners (assistance provided by doctors and nurses, pharmacological therapies, laboratory and instrument tests, more surgery, etc.), as well as variability in terms of type and severity of the infections, the specialties considered, the methods and costs of the therapies and the refunds provided by the various national health systems.

According to an Australian review, 31% of the total cost of SSIs (>AU$53 million) comes from hospitalisation, 14% from post-discharge healthcare assistance and the remaining 55% from the patient's loss of productivity (20%) and the activity of caregivers (35%) (27). There is therefore the risk that studies greatly underestimate the real cost associated with SSIs. The reason lies in the difficulty of assessing all the elements involved after hospital discharge (costs related to healthcare and non-healthcare assistance) and of considering all the indirect cost determiners, in terms of loss of productivity and in human terms (i.e. the physical and psychological distress caused by SSIs, which are more difficult to quantify).

Prevention and safety of treatments and of patients

Greater knowledge regarding transmission mechanisms and infection prevention strategies and the availability of innovative medical and technological devices mean SSIs can today be considered an avoidable complication of surgical procedures. Although it is acknowledged that not all SSIs can be prevented, evidence suggests that the current incidence can be considerably reduced - and so can most of the costs associated with these infections. According to some estimates, up to 65-70% of SSIs can be prevented. Overall, the studies that evaluated the proportion of reasonably avoidable SSIs have concluded that the current, evidence-based prophylaxis strategies do not allow 100% prevention. However, the systematic implementation of those strategies would prevent hundreds of thousands of HAIs and save tens of thousands of lives, saving billions of dollars as well (28).

It is likely that SSIs will be included more and more among "never events", i.e. healthcare-related events that should never occur because they are clearly identifiable and preventable with suitable procedures, and that the SSI-associated costs will be included in avoidable healthcare costs (29). In light of the considerable clinical impact of SSIs in terms of morbidity and mortality (and the substantial economic burden associated with them), it is necessary to use all the tools available to reduce their incidence. This can be achieved by implementing prevention programmes that use standardised procedures characterised by proven effectiveness and sustainable costs.

Although international guidelines (GL) are available, the implementation of these measures has not yet been globally standardised. The GL produced in European countries and in North America reveal inconsistencies in the interpretation of scientific evidence, leading to different recommendations among countries and increasing differences between instructions and clinical practice (3). As a result, SSI rates have not fallen appreciably, despite probably being the most preventable among hospital-acquired infections (30).

In the last ten years, more and more attention has been given internationally to patient safety and the prevention of infections. In terms of patient safety, the large-scale interventions that have had a significant impact on outcomes have been focused on the reduction of infections associated with healthcare procedures, such as measures to reduce infections linked to central venous catheters and the introduction of a checklist for the operating theatre (31,32). Among healthcare-related infections and because of their considerable clinical and economic impact, SSIs have been the subject of considerable interest among the professionals and the health authorities tasked with controlling infection complications. Additionally, the awareness that many SSIs are preventable has led these infections to being perceived as indicators of the low quality of treatment (21).

Improvements in the quality and safety of healthcare assistance is currently one of the foundations of the management approach used by health systems in the perspective of Clinical Integrated Governance. This governance identifies planning and service management policies by putting people's needs at the heart of them and basing them on clinical choices that valorise the role and responsibility of doctors and healthcare staff (33). In this perspective, Law no. 24 of 8 March 2017 (Gelli-Bianco) on the re-

sponsibilities of health professionals and on the safety of treatment shows how there is greater sensitivity for the safety of patients in Italy at a public and legislative level. After Denmark in 2004, Italy was the second country to enact a comprehensive law on the safety of patients (34), which gives responsibility to all the healthcare professionals involved in patient care and encourages the application of GL and evidence-based good practices. The law establishes that risk management should not take into account only clinical activities in a broad sense - it must also apply to all the activities related to providing healthcare assistance, including technological-environmental and organisational aspects and aspects related to treatment suitability and sustainability. This means that the clinical and organisational suitability of healthcare assistance and the principles of clinical risk management are now an integral part of the skill set that doctors and healthcare professionals are expected to have. The enactment of this provision requires that all healthcare units commit, at all levels, to activating monitoring, prevention and risk management strategies and to promoting the implementation of specific protocols to improve adherence to GL (35). The Gelli-Bianco Law also changes the way in which treatment safety management is organised, because it focuses on the capacity to manage risk and on the application of evidence-based practices by the entire network of healthcare professionals and not by the individual alone. SSIs are assistance-related infections and, as such, are considered adverse events, i.e. unexpected events related to healthcare and that cause unintentional and undesirable harm to the patient. Adverse events can be preventable or non-preventable. An adverse event caused by a mistake is a "preventable adverse event". Italian data show that 56% of adverse events are preventable (36). The approach that so far has achieved the best results in terms of adverse event containment and reduction follows the principle of ergonomics and human factor (37).

All the facts in the premise above have created the need for a document that, starting from the recommendations in the most recent international GL, can, in Italy, call to action all the professional roles involved in the prevention of SSIs. The aim is for them to provide evidence-based, univocal and updated instructions that are specifically tailored to Italian settings.

Italian Consensus Document: objectives and recipients

This document aims to be an educational tool for healthcare professionals, which allows them to transpose into Italian clinical practice the recommendations on the interventions that most effectively reduce the risk of infection in the perioperative phase. To that end, we have examined the recommendations contained in the most recent and reliable international GL published by the WHO and CDCs (Centers for Disease Control and Prevention) (3,38), with the aim of defining a care bundle that supplies a synthesis of the most appropriate preventive measures according to the available scientific evidence and to cost-effectiveness tests. Thanks to a section on application, this document aims at supplying the operational tool to implement the bundle (i.e. the procedure checklist) combined with some practical suggestions and possible strategies for applying it. Our intention is that the above strategies, albeit tailored to conditions in Italy and as part of the current laws, will help implement the prevention measures listed here. The aim is obviously to improve compliance among healthcare professionals, overcoming the organisational barriers and cultural objections that often hinder the execution of new procedures and recommendations. It is not by chance that this document is aimed at all members in surgery teams (surgeons, anaesthetists, nurses, technicians and the other staff in an operating theatre). The objective is also to reach hospital workers who have an organisational role and are decision-makers (staff in the hospital administration offices and quality offices, heads of surgery departments, anaesthesia and resuscitation units, head nurses and the managers responsible for pharmacies and for the organisation and management of operating theatres). The purpose is to make them understand the importance of standardised procedures for patient safety and the cost-effectiveness of some the current behavioural procedures.

Among all the evidence-based recommendations contained in the international GL for SSI prevention, this document aims at examining more in detail the ones considered essential in terms of strong scientific evidence, with special attention on the ones regarding the perioperative phase (the required cultural and organisational transition seems most delicate in this phase, because it involves

changes in operator habits, procedural organisation and on the supply of devices needed in the operating theatre). Historically, SSI-prevention measures have concentrated on the asepsis of the healthcare workers and of the environment. However, it is today a well-known fact that one of the main sources of pathogens responsible for SSIs is the patient's skin, as a result of the direct contamination of the surgical wound by skin bacteria, which enter after the surgical incision causes the loss of the skin barrier's integrity (39,40). The recent updates in international GL stress the importance of skin asepsis practices, in order to reduce, as much as possible, the microbial load on the patient's skin before the surgical incision. Acting as the spokesperson for all the most recent information in the GL, this document identifies preoperative skin antisepsis and hair removal as two of the subjects that should be discussed in detail. There are two reasons for this - the recommendations on them have recently been updated as a result of new evidence and because the new recommendations are very different from the current clinical practice in Italy, which means a greater effort is needed for their implementation.

Proposal for a bundle for SSI prevention applicable in Italy

As explained extensively above, many patient- and process-related factors can contribute to increasing the risk of SSIs. Preventing these complications is therefore a complex matter which requires the integration of a series of measures to implement before, during and after surgery. Only a multi-modal strategy, with the integrated and systematic application of multiple practices aimed at reducing the risk of bacterial contamination and at improving the patient's defences, will manage to effectively reduce SSI incidence. Therefore, to contain the risk of infection and improve safety in the operating theatre, it is deemed necessary to propose a care bundle, which is defined as a relatively small set of evidence-based interventions, behaviours and/or practices that, executed jointly and appropriately, improve the quality and the outcome of the processes with an effect that is greater than the effect achieved if each is performed separately (41). Although evidence-based guidelines are the crucial reference documents, they do not always have an effective and truly appreciable impact on the behaviour of healthcare staff at the bedside. The very same recommendations, if simplified and set out clearly in a specific bundle, can really change behaviours, as they appear as a new procedure to be applied in a systematic, standardised, multi-disciplinary manner that is coordinated and previously shared, driven by results and verified by the outcome (41).

The evidence available from the literature unanimously suggests that adopting therapeutic programmes based on care-bundles improves the efficacy of prevention measures and significantly lowers the risk of SSIs in surgery units (42,43).

Recommendations for the perioperative prevention of SSIs

Below is a detailed examination, using the most respected international GL published by the WHO and CDCs as references, of the evidence-based recommendations that the authors of this document identify as crucial for the perioperative prevention of SSIs, according to the consistency of the scientific evidence that supports them, the emergence of new data, cost-effectiveness tests and the strength of the recommendations. These recommendations deserve to be brought to the attention of Italian surgeons because they contain new elements and because of their difference compared to current clinical practice in Italy. The various recommendations will be presented according to a logical and temporal order based on the phases of a surgical procedure. Each will have a category of strength and evidence assigned by the GL, which reflects the level of the effectiveness tests (evidence) currently available according to the grading system used **(Table 2)**.

Table 2. Grading system of the examined GL
Data elaborated from (3,38)

WHO		CDC
Strength	**Quality of the evidence** (level of evidence/cost-benefit ratio)	**Category**
Strong: intervention in which the benefits are certain to outweigh the risks	**High**: we are very sure the actual effect of the intervention is close to the estimated effect.	**IA:** strongly recommended for implementation and strongly supported by well-designed experimental, clinical or epidemiologic studies.
Conditional: intervention in which the benefits probably outweigh the risks	**Moderate:** we are moderately sure of the estimated effect; the actual effect of the intervention is probably close to the estimated effect, but it may possibly be very different.	**IB:** strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale; or an accepted practice (e.g., aseptic technique) supported by limited evidence.
Suggested	**Low:** our confidence in the estimated effect is low; the actual effect of the intervention could be very different from the estimated effect.	**IC:** required for implementation as mandated by federal or state regulation or standard. **II:** suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.
	Very low: our confidence in the estimated effect is very low; the actual effect of the intervention is probably very different from the estimated effect.	**UI** (No recommendation/ Unresolved issue): practices for which insufficient evidence or no consensus regarding efficacy exists, or no efficacy test published on the clinical outcome considered critical to weigh the risks and benefits of a given course of action.

• *SCREENING AND SANITISATION FOR STAPHYLOCOCCUS AUREUS*

RECOMMENDATIONS

- **Perform the preoperative decolonisation of nasal carriers of *S. aureus* in all cases of cardiothoracic and orthopaedic surgery (WHO 2016, strong/moderate).**
- **For all other operations, individual hospitals can evaluate if decolonisation is needed (WHO 2016, conditional/moderate).**
- **According to WHO GL, the decolonisation should be performed with intranasal applications of 2% mupirocin ointment and can be associated (always in the presence of methicillin-resistant *S. aureus*) or not with chlorhexidine gluconate bodywash (WHO 2016, strong/moderate). Alternatively, decolonisation can be executed with another cost-effective pharmacological strategy.**

The decolonisation of S. aureus carriers has been the subject of numerous studies, as this bacterium is the main pathogen associated with healthcare in hospitals around the world. S. aureus infections are an important cause of morbidity and mortality and are increasing because methicillin-resistant strains are spreading, which has a considerable economic impact on healthcare resources (WHO, 2016). Up to 2016, the GL suggested screening for methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) *S. aureus* only before orthopaedic surgery, vascular and cardiac surgery with the implantation of prosthesis. The 2016 WHO GL extend the recommendation of nasal decolonisation with mupirocin to all patients positive for *S. aureus* and who are undergoing cardiothoracic and orthopaedic surgery (8). Other factors must be taken into account in the case of other types of surgery, such as the local rate of MSSA and MRSA and patient-related factors, such as previous *S. aureus* infection, status as known carrier of community-acquired MRSA and *S. aureus* colonisation in sites other than the nose (WHO, 2016).

In the studies that led to recommending nasal decolonisation with mupirocin (2 applications per nostril for 5 days) with or without a combination of chlorhexidine bodywash, the chlorhexidine was in a 4% solution (2% in one study).

In these studies, *S. aureus* screening was not considered an integral part of the procedure, so no recommendation can be made on its role in the population of surgery patients. However, an approach based on the indiscriminate treatment of all patients (regardless of their "carrier" status) is not considered advisable because of the risk of inducing mupirocin resistance. Although screening these patients for *S. aureus* is important to avoid useless treatment and the induction of resistance, the decision to screen should be governed by national recommendations, based on local epidemiology, the presence of risk factors for the patient resulting from exposure to *S. aureus* and the actual local feasibility, based on the availability of funding and of microbiology laboratories. Each healthcare centre should therefore assess the benefit of a screening programme based on the local incidence of *S. aureus*-caused SSIs and/or MRSA infections, also considering the programme's feasibility in organisational and cost-benefit terms (WHO, 2016).

• *PREOPERATIVE SHOWERING*

RECOMMENDATIONS

- **Patients should bathe or shower (and wash their hair) on the evening before or on the day of surgery, using normal or antiseptic soap (WHO 2016, conditional/moderate; CDC 2017, IB).**
- **The optimal time for a preoperative bath or shower, the total number of soap or antiseptic applications or the effectiveness of chlorhexidine-soaked pads in the prevention of SSIs is not known (CDC 2017, no recommendation/unresolved issue).**

Preoperative baths or showers are to be considered good clinical practice for cleansing the skin as much as possible and reducing the bacterial load, especially in the incision site, because microorganisms on the patient's skin are the primary source of infection (WHO, 2016).
An antimicrobial soap is used (generally 4% chlorhexidine gluconate, combined with a triclosan preparation or detergent) in settings in which this product is available at affordable prices. However, it has not been proven to be more effective than normal soap in reducing the incidence of SSIs, despite the greater risk of (albeit rare) allergic reactions (WHO, 2016).
The importance of bathing or showering the evening before or on the day of the surgery must be included in the information given to the patient as part of the "instructions for preparing for surgery". The information for patients, provided during the preoperative assessment, must be included in an information leaflet and explain the reason for washing, i.e. reducing infection complications, and must provide details on essential areas to wash (e.g. the need to wash hair, moustache and beard as well). The information must be provided in a clear, understandable format and must be appropriate for the patient's age, education and language skills (8).
If the patient has prepared for surgery at home, upon entering the hospital, nurses must check preparation has been carried out appropriately. If preparation is poor or the patient is already in hospital, bathing or showering (or bed bathing, in the case of bed-ridden patients) must be carried out in hospital, before surgery, with the help of ward staff (8).

• *HAIR REMOVAL*

RECOMMENDATIONS

- **The routine preoperative removal of hair is to be avoided. Hair should be removed only when necessary, i.e. if the hairs, on or around the surgical site, interferes with the procedure (WHO 2016, strong/moderate; CDC 2017 stresses recommendation of CDC 1999).**
- **When necessary, it should be removed on the day of the procedure and only with an electric clipper (WHO 2016, strong/moderate; CDC 2017 stresses recommendation of CDC 1999).**
- **The safest time for hair removal is currently considered to be just before surgery (WHO 2016; CDC 2017 stresses recommendation of CDC 1999).**
- **It is not possible to recommend depilatory creams because of contradicting indications (WHO 2016).**
- **The WHO strongly advises against the use of razors with traditional blades in the preoperative phase and in the operating theatre (WHO 2016, strong/moderate).**

Routine hair removal, even when hairs do not interfere with the surgical incision, is a legacy of the past, when it was erroneously believed that extensive hair removal guaranteed cleanliness. It was considered a preventive strategy against the risk of infection. On the contrary, the current scientific evidence suggests that it is a risk factor for SSIs, because it can cause skin abrasions and microtrauma that favour colonisation by bacteria in the site of surgery (WHO, 2016). Specifically, the literature shows that removing hair with a traditional razor is associated with a significantly higher level of infection compared to shaving with an electric razor or not shaving at all. Traditional razors use a sharp blade that is drawn across the skin's surface, while clippers cut hairs at their base, without touching the skin (WHO 2016). Hospitals must replace traditional razors with electric clippers with single-use or reusable blades. The clippers must be appropriately sterilised between patients and, therefore, it is advisable to use devices that can be left to soak in disinfectant solutions for long periods of time (with the highest IPX rating possible, i.e. with the highest level of resistance against the entry of liquids) (Box 1). Operators must be trained on how to choose, use and decontaminate clippers and on maintenance procedures. Posters with that information in strategic positions can be used (8).

Reducing the time between hair removal and surgery reduces the chances of contamination in the site of surgery, so hair removal with clippers should be carried out no earlier than two hours before surgery, either in the ward or in the pre-operative area, i.e. immediately before taking the patient to the surgery unit or the room in which pre-operative procedures are completed before the surgical operation (8). Patients must be told not to shave before surgery and this information must be included in the information leaflets given to them.

Box 1.

Clippers for hair removal before surgery

Modified from (44)

Clippers for preoperative hair removal are recommended by the guidelines instead of traditional razors with blades, because using clippers reduces the risk of SSIs, protecting the surgical site from microlesions and the related colonisation by bacteria. Clippers (electric or with rechargeable batteries) are electric razors that are easy to use and allow to shave hair (wet or dry) near the skin (2-3 mm above) without causing microtrauma or irritating the skin. They allow to rapidly remove hair in one glide, painlessly and quickly, and they do not require additional materials such as soaps, softening foams or gauzes. The clippers currently available on the market, although more expensive than traditional razors, are technologically reliable and long-lasting, intuitive to use and hygienically safe, because they can be fully disassembled and are made with materials suitable for full immersion in solutions, so they can be thoroughly cleaned and disinfected. Technological evolution has also improved the devices' performance, with long-lasting batteries and charge indicators that warn if the device needs recharging.

• *PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS (PAP)*

RECOMMENDATIONS

- **PAP must be administered only when appropriate, depending on the type of surgery (WHO 2016, strong/low; CDC 2017, IB).**
- **It must be administered within 120 minutes before the incision, taking the antibiotic's half-life into account (WHO 2016, strong/moderate), i.e. timing administration in order to achieve an effective antibiotic concentration in the serum and in tissues at the time of incision (WHO 2016; CDC 2017, IB).**
- **In the case of delivery by Caesarean section, PAP should be given before performing the skin incision (CDC 2017, IA).**
- **PAP should not be continued after the surgical incision has been sutured (WHO 2016, strong/moderate), not even in the presence of drainage (WHO 2016, conditional/low; CDC 2017, IA).**

PAP is advised only for the operations listed in the national GL in which the expected benefit (prevention of SSI and its potential severity) outweighs the risk (severe side effects, *Clostridium difficile* infections, spreading of resistance) (45). PAP plays an important role in fighting the effects of site contamination at the time of surgery, but to be effective it must be administered at the right time. When deciding, it is important to consider the pharmacokinetic properties of the antibiotic used: the administration must be nearer the time of incision (<60 minutes) for antibiotics with a short half-life (such as cefazolin, cefoxitin and penicillins in general), whereas antibiotics with long infusion times, such as vancomycin and fluoroquinolones, should be administered 120 minutes before the incision (WHO 2016). Evidence also shows that a low antibiotic concentration in tissues at the time of wound suturing is associated with higher SSI rates, which means that the antibiotic's pharmacokinetic properties must be taken into account, in order to achieve a suitable blood and tissue concentration during the entire surgical procedure (WHO 2016). A single dose of antibiotic with a sufficiently long half-life can usually ensure effective prophylaxis during the entire operation (45).

Although it seems reasonable to administer an additional intraoperative dose of antibiotic in the case of operations that last double the antibiotic's half-life or if there is considerable blood loss during surgery (>1500 ml in adults) (45,46), the currently available evidence is not enough to determine practice on that regard (WHO 2016; CDC 2017, no recommendation/unresolved issue).

A recent systematic review shows that it is preferable to administer PAP to women undergoing a Caesarean delivery before the incision, rather than after clamping the umbilical cord, in order to reduce maternal infection complications (47).

• *ORAL ANTIBIOTIC PROPHYLAXIS*

RECOMMENDATIONS

- **The preoperative administration of antibiotics via the oral route, combined with mechanical bowel preparation (MBP) is recommended to reduce the risk of SSIs in adult patients undergoing elective colorectal surgery (WHO 2016, conditional/moderate).**
- **MBP alone (without the administration of oral antibiotic prophylaxis) must not be used to reduce SSIs in adult patients undergoing elective colorectal surgery (WHO 2016, strong/moderate).**

MBP consists in the preoperative administration of solutions containing glycol polyethylene or sodium phosphate in order to induce bowel evacuation. Overall, moderate quality tests suggest that the oral administration of antibiotics combined with MBP significantly reduces SSI incidence compared to MBP alone. Therefore, if mechanical preparation is performed, prophylaxis with oral antibiotics should be given as well, both in addition to intravenous antibiotic prophylaxis when appropriate (WHO 2016).

• *PREPARATION OF THE SKIN OF THE SURGICAL TEAM*

RECOMMENDATIONS

- **Before entering the operating theatre, wash hands with non-medicated soap, to remove organic material and reduce the skin's bacterial load (for correct hand hygiene in healthcare settings, please read the specific GL on this topic) (48,49).**
- **Before putting on sterile gloves, perform the surgical preparation of the healthcare staff's hands and forearms by washing with antiseptic soap or by applying hydroalcoholic gel (WHO 2016, strong/moderate).**

The surgical preparation of the hands is crucially important to maintain the contamination of the surgical field at low levels, preventing the entry into the surgical incision of bacteria released from the skin of the surgical team in the case of punctured sterile gloves during surgery (WHO 2016). Moderate quality tests, from randomised controlled trials (RCTs) that were appropriately designed to assess the reduction of SSI risk, show that the two methods recommended above for surgical hand preparation are essentially equivalent, although hydroalcoholic gels proved to be more effective in reducing the formation of new bacterial colonies after putting on the gloves compared to normal or medicated soaps (50).
If an antiseptic soap is used, the time of washing must comply with the manufacturer's instructions (generally 2-5 minutes). If using a hydroalcoholic gel, a product with prolonged action is recommended (e.g. containing chlorhexidine). The manufacturer's instructions for application must be followed, using enough product to scrub the skin of the arms and forearms up to the elbow. The effectiveness of an alcohol-based gel can be reduced if the product is applied onto skin that is not perfectly dry, so washing with antiseptic soap and with hydroalcoholic gel must not be consecutive (WHO 2009). Skin irritation, dermatitis and (rarely) allergic reactions may occur as a result of frequently using products for surgical skin preparation. They are more common when using iodine-based products (WHO 2016).

• *PATIENT SKIN ANTISEPSIS*

RECOMMENDATIONS

- **Before proceeding with the antisepsis of the surgical site, thoroughly cleanse the skin around the incision area to remove coarse contamination (CDC 2017).**
- **The antisepsis of the patient's skin must be achieved with an antiseptic solution containing chlorhexidine gluconate. In subjects allergic to chlorhexidine, the use of alcoholic povidone-iodine for antiseptic preparation is an alternative, on condition it is applied correctly and, possibly, in a 10% alcohol solution.**
- **The use of dye-containing products is recommended in order to check the product has been correctly applied.**
- **Using a single-use applicator (compared to the traditional method with gauzes and multiple-use containers) improves the safety (risk of fire and contamination) and standardisation (correct dose of antiseptic) of the procedure and is more practical (application time).**
- **There is currently no evidence in favour of repeating antisepsis before suturing the surgical incision (CDC 2017, no recommendation/unresolved issue).**

Moderate quality evidence shows that alcohol-based antiseptic solutions are more effective in reducing SSI risk compared to aqueous solutions (WHO 2016). In most studies, the application of chlorhexidine-alcohol reduced the risk of SSI by over 40% compared to aqueous povidone-iodine solutions (51).

Chlorhexidine-alcohol has proven to be significantly better than aqueous povidone-iodine solutions in preventing superficial and deep incisional infections (52).

Additional studies in which both preparations in alcoholic solutions were directly compared showed that, for the surgical site antisepsis of the patient's skin, chlorhexidine alcohol is more effective than povidone-iodine alcohol (WHO 2016). In two RCTs, preoperative skin antisepsis with chlorhexidine alcohol, compared to povidone-iodine alcohol, was associated with a significantly lower SSI risk after Caesarean section or after the insertion of an intravascular catheter (53,54).

A systematic review of data from 19 international studies, conducted by Italian authors, showed a 30% reduction in SSI incidence among patients undergoing preoperative antisepsis with chlorhexidine alcohol, compared to povidone-iodine alcohol, with moderate-quality evidence supporting the greater effectiveness of chlorhexidine in SSI prevention and with high-quality evidence supporting chlorhexidine's greater reduction of skin colonisation by bacteria, as shown by the significantly lower number of positive skin cultures after its application (55).

A recent meta-analysis that included 13 RCTs (totalling approximately 7,000 patients undergoing clean and clean-contaminated surgery) confirmed that, compared to povidone-iodine alcohol, preoperative antisepsis with chlorhexidine alcohol was significantly more effective in reducing SSIs (RR, 0.70, IC 95%, 0.60-0.83, I2 = 0) (56).

The two antiseptic preparations are similar in terms of broad-spectrum antimicrobial activity. However, the greater protection provided by chlorhexidine alcohol is probably

linked to its more rapid action, longer activity and greater residual effect despite being exposed to body fluids because (unlike povidone-iodine) it is not inactivated by contact with organic substances (57).
Additionally, in Italy, the povidone-iodine alcohol solution available on the market is 1% - not 10%, which is recognised as the effective concentration for antiseptic purposes. This is an additional reason for considering chlorhexidine alcohol (2% in a 70% isopropyl alcohol solution) as the first-choice product for surgical antisepsis, unless there are specific reasons for not using it (e.g. eye, middle ear and meninx surgery) (8)
However, chlorhexidine is more expensive than povidone-iodine and its use is potentially related to allergic reactions, although the incidence of allergic events in clinical studies is, overall, low (53).
Although allergies to iodine are more frequent than allergies to chlorhexidine, in subjects who are allergic to chlorhexidine, antisepsis with povidone-iodine alcohol is a valid second-choice alternative, on condition that it is applied correctly and, possibly, as a 10% alcohol solution.
Chlorhexidine alcohol is more expensive but, according to an economic analysis of the studies in which chlorhexidine alcohol and povidone-iodine alcohol for surgical site antisepsis were compared, the former was up to 36% more cost-effective than povidone-iodine alcohol solution (58).
Povidone-iodine in aqueous solution requires longer contact times, whereas alcoholic solutions have the advantage of drying rapidly after application onto the skin, which reduces the surgical site preparation time (55). However, alcohol is flammable and soaked fabric or droplets on the skin that have not dried are a fire risk in the operating theatre, especially if electrosurgical and laser instruments are used. This event must be prevented by not allowing the antiseptic to overflow and spread, checking that it has completely dried (after waiting at least 3 minutes after the application) or using single-use applicators (8).
Another element to consider when choosing an antiseptic is the presence (or absence) of a colouring agent. This is particularly important for surgeons and staff in the operating theatre, because a colourless antiseptic - no matter how effective - cannot guarantee antisepsis is complete in the surgical field, while coloured antiseptics can (59). Only a few of the currently marketed (aqueous and alcoholic) antiseptics contain colouring agents and any new colouring agent requires studies to assess effectiveness and tolerability. However, the use of colour-containing products, although not included in GL recommendations, must be considered a useful opportunity to check the product has been applied correctly onto the patient's skin. It should be recommended (WHO 2016).

Surgical antisepsis and application method

Most GL focus on the type of antiseptic agent without considering the method of application. Spanish GL are an exception, as they explicitly recommend a single-use applicator and a 30-second "back-and-forth" application method (60).
Traditionally, antiseptics are applied in concentric circles in a centrifugal direction, although this method is not supported by any scientific proof. There is some sense in this method when using aqueous products, which require additional drying time, to prevent the reintroduction of contaminants in previously cleaned areas (61).
Approximately 20% of bacteria live in the skin's deepest layers, among necrotic skin cells, sweat glands and hair follicles, which makes suitable skin decontamination difficult (62). The back-and-forth skin friction method has been suggested to reach a greater number of skin layers, penetrating more deeply into the epidermal layer and reducing the bacterial load more effectively (61).
To date, there are relatively few studies that have assessed the effectiveness of applicators for skin antisepsis. In a study that compared the various application techniques (chlorhexidine alcohol via an applicator and povidone-iodine alcohol applied with a gauze using the standard method), the compliance of healthcare staff with the protocol for the correct application of the antiseptic was considerably greater for chlorhexidine in an applicator, in terms of completing all the steps recommended by the manufacturer ($p = 0.027$). All the essential steps in the application method were carried out 90% of times for chlorhexidine and 33.3% for povidone-iodine ($p = 0.0001$) (63).
In another study, chlorhexidine in single-use applicators was found to be the safest and most effective method of antisepsis to avoid the contamination of donor blood bags, compared to povidone-iodine alcohol applied according to standard operating methods (64).
Until further studies allow to define the best application method, sterile applicators in single-use containers - preferably rated as medicines - seem to have clear advantages

compared to standard application with gauze and multi-use vials. This is based on empirical considerations and on a few preliminary studies, which all agree in this sense (65) (Appendix I).
It can be said that adopting single-use applicators (compared to the traditional application with gauze and multi-use containers) improves the safety of the patient's antisepsis, reducing the risk of fire and of solution contamination. It also increases standardisation and makes the procedure more practical by dispensing the right dose of antiseptic and reducing, at the same time, operator-linked risks, the risk of cross-contamination and the time of application (65).

• *NUTRITIONAL SUPPORT*

RECOMMENDATION

- **Consider the administration of nutritional supplements via the oral or enteral route, to prevent SSIs in malnourished patients undergoing major surgery (WHO 2016, conditional/ very low).**

Literature data on the role of nutritional support for the prevention of SSIs are limited, but a meta-analysis conducted by the WHO 2016 GL work group has highlighted the benefits of supplementation with multiple nutritional preparations (compared to a standard nutritional support) in malnourished patients undergoing major surgery (oncological and cardiac surgery in particular), although the quality of the evidence was very low. Patients are classified as malnourished if their body mass index is below 18.5 and/or their body weight is 15-20% lower than normal for their age and height (WHO 2016).

• *TISSUE OXYGENATION*

RECOMMENDATIONS

- **Patients who have general anaesthesia with tracheal intubation and mechanical ventilation must receive oxygen supplementation during surgery and, if possible, immediately after the operation (for 2-6 hours) in order to reduce the risk of SSI (WHO 2016, strong/moderate; CDC 2017, IA).**
- **According to WHO GL, the value of the fraction of inspired oxygen (FiO2) should be equal to 80% (WHO 2016, strong/moderate).**

The purpose of the supplementation of oxygen above the 30% standard is to improve tissue oxygenation in the surgical area and to improve the patient's defences, by increasing the oxidative capacity of neutrophils (WHO 2016).
A metanalysis of 11 RCTs, conducted by WHO GL experts, provided moderate-quality evidence of the superiority of perioperative 80% FiO2 in SSI reduction in patients undergoing surgery under general anaesthesia with tracheal intubation, compared to standard FiO2 (30-35%) (WHO 2016). The benefits of this intervention are observed only when O_2 supplementation is administered via intubation during surgery and via a high-flow mask immediately after the operation (WHO 2016).
To maximise the benefits of hyperoxygenation, perioperative normothermia and normovolemia should be maintained (WHO 2016; CDC 2017, IA).

• *NORMOTHERMIA*

RECOMMENDATIONS

- **Patient normothermia should be maintained for the entire perioperative period (WHO 2016, conditional/moderate; CDC 2017, IA).**
- **The use of heating devices in the operating theatre and during surgery for the purpose of preventing patient hypothermia is recommended in order to reduce the risk of SSI and other major complications (myocardial events, extensive bleeding that requires blood transfusion) (WHO 2016, conditional/moderate).**
- **No recommendation can be given regarding the best systems to obtain and maintain normothermia, on the minimum temperature to achieve, on the best time to start warming and on the optimal duration of the heating period (CDC 2017, no recommendation/ unresolved issue).**

A fall in body temperature is common during surgery and leads to reduced function in neutrophil granulocytes and hypoxia as a result of vasoconstriction, which are both associated with an increased risk of SSI (8). Moderate-quality evidence suggests that maintaining normothermia has significant benefits on the reduction of SSI risk compared to standard treatments (WHO 2016).

No RCTs have specifically assessed the different strategies to reach and maintain normothermia and the GL do not provide any advice on that regard (WHO 2016; CDC 2017, no recommendation/unresolved issue). Normothermia maintenance should follow an internal protocol, which includes the identification of patients at risk of hypothermia (ASA from 2 to 4, body temperature <36°C before an urgent operation, combined locoregional and general anaesthesia, intermediate or major surgery, risk of cardiovascular complications) (8).

• *NORMOGLYCAEMIA*

RECOMMENDATIONS

- **Adequate glycaemia controls should be performed on all surgical patients (diabetic and non-diabetic), in order to reduce the risk of SSI (WHO 2016, conditional/low; CDC 2017, IA).**
- **The benefits of a glycaemia target <200 mg/dl have been proven (CDC 2017, IA).**
- **Low-quality evidence supports that additional benefits are associated with tight control of glycaemia values (<110-150 mg/dl) (WHO 2016, conditional/low).**
- **If the established glycaemia target is <110 mg/dl, the risk of hypoglycaemia must be checked (WHO 2016).**

Surgical stress causes an increase in glucose blood levels during and after the operation. A number of observational studies have shown that this hyperglycaemia is associated with a higher risk of SSIs in diabetic and non-diabetic patients undergoing various kinds of surgery (66).
The clearest advantages provided by a tight control on hyperglycaemia emerged from studies that applied this approach in both intra- and postoperative phases (WHO 2016).
The currently available evidence is not enough to provide precise advice on the optimal timing, duration or method for the perioperative control of glycaemia for the purpose of preventing SSIs (WHO 2016; CDC 2017, no recommendation/unresolved issue).

• *NORMOVOLEMIA*

RECOMMENDATIONS

- **The patient's blood volume must be monitored for the entire intraoperative period and body fluids must be suitably replenished (WHO 2016, conditional/low; CDC 2017, IA).**
- **The intraoperative application of the Goal Direct Fluid Therapy (GDFT) protocol is recommended in order to reduce the risk of SSI (WHO 2016, conditional/low).**

The GDFT protocol allows to standardise the hemodynamic monitoring of the patient, assessing volemia on volumetric parameters, such as the Stroke Volume (SV) or the Stroke Volume Variation (SVV), instead of pressure parameters, in order to restore a suitable level of hydration and maximise the release of oxygen in the tissues (67). Low-quality evidence shows that intraoperative GDFT has a significant benefit in terms of reducing the rate of SSIs compared to standard fluid management. This effect has been shown for the postoperative period as well (WHO 2016).

Table 3 contains a summary of the recommendations explained above. The strength and quality of the evidence for each category are shown.

Table 3. Recommendations for the main procedures for the perioperative prevention of SSIs

PROCEDURE	RECOMMENDATIONS	STRENGTH/QUALITY
Screening for and sanitisation of *Staphylococcus aureus*	The preoperative decolonisation with 2% mupirocin nasal ointment, with or without chlorhexidine gluconate bodywash solutions, must be performed in all nasal carriers of *Staphylococcus aureus* undergoing cardiothoracic and orthopaedic surgery.	WHO 2016, strong/moderate; ACS-SIS 2016
	A different cost-effective pharmacological strategy can be considered as an alternative to mupirocin.	*Expert opinion*
	Hospitals can, for every other kind of surgery, assess if it is appropriate (in terms of organisational aspects and cost-effectiveness ratio) to perform screening and decolonisation.	WHO 2016, conditional/ moderate
Preoperative showering	Surgical patients should bathe or shower (and wash their hair) on the evening before or on the day of surgery, using normal or antiseptic soap	WHO 2016, conditional/ moderate; CDC 2017, IB.

PROCEDURE	RECOMMENDATIONS	STRENGTH/QUALITY
Hair removal	Hair removal must not be a routine procedure. Hair should be removed only if the hairs, in or around the surgical site, interfere with the surgical procedure. Only electric clippers must be used and hair must be removed only on the day of and immediately before surgery	WHO 2016, strong/ moderate; CDC 2017 confirms CDC 1999 recommendation
Perioperative antibiotic prophylaxis (PAP)	PAP must be administered only when appropriate, depending on the type of surgery	WHO 2016, strong/low; CDC 2017, IB
	It must be performed within 120 minutes before the incision, taking the antibiotic's half-life into account	WHO 2016, strong/moderate
	The time frame must allow to reach an effective concentration in the serum and tissues at the time of the incision	WHO 2016; CDC 2017, IB
	PAP should not be continued after suturing the surgical incision	WHO 2016, strong/moderate
	This recommendation also applies in the case of drainage	WHO 2016, conditional/low; CDC 2017, IA
Oral antibiotic prophylaxis	The preoperative administration of antibiotics via the oral route, combined with mechanical bowel preparation (MBP), is recommended to reduce the risk of SSIs in adult patients undergoing elective colorectal surgery	WHO 2016, conditional/ moderate
	MBP alone (without the administration of oral antibiotic prophylaxis) must not be used to reduce SSIs in adult patients undergoing elective colorectal surgery	WHO 2016, strong/moderate
Preparation of the skin of the surgical team	Before sterile gloves are put on, the healthcare staff's hands and forearms must be prepared for surgery by washing with antiseptic soap or by applying hydroalcoholic gel	WHO 2016, strong/moderate

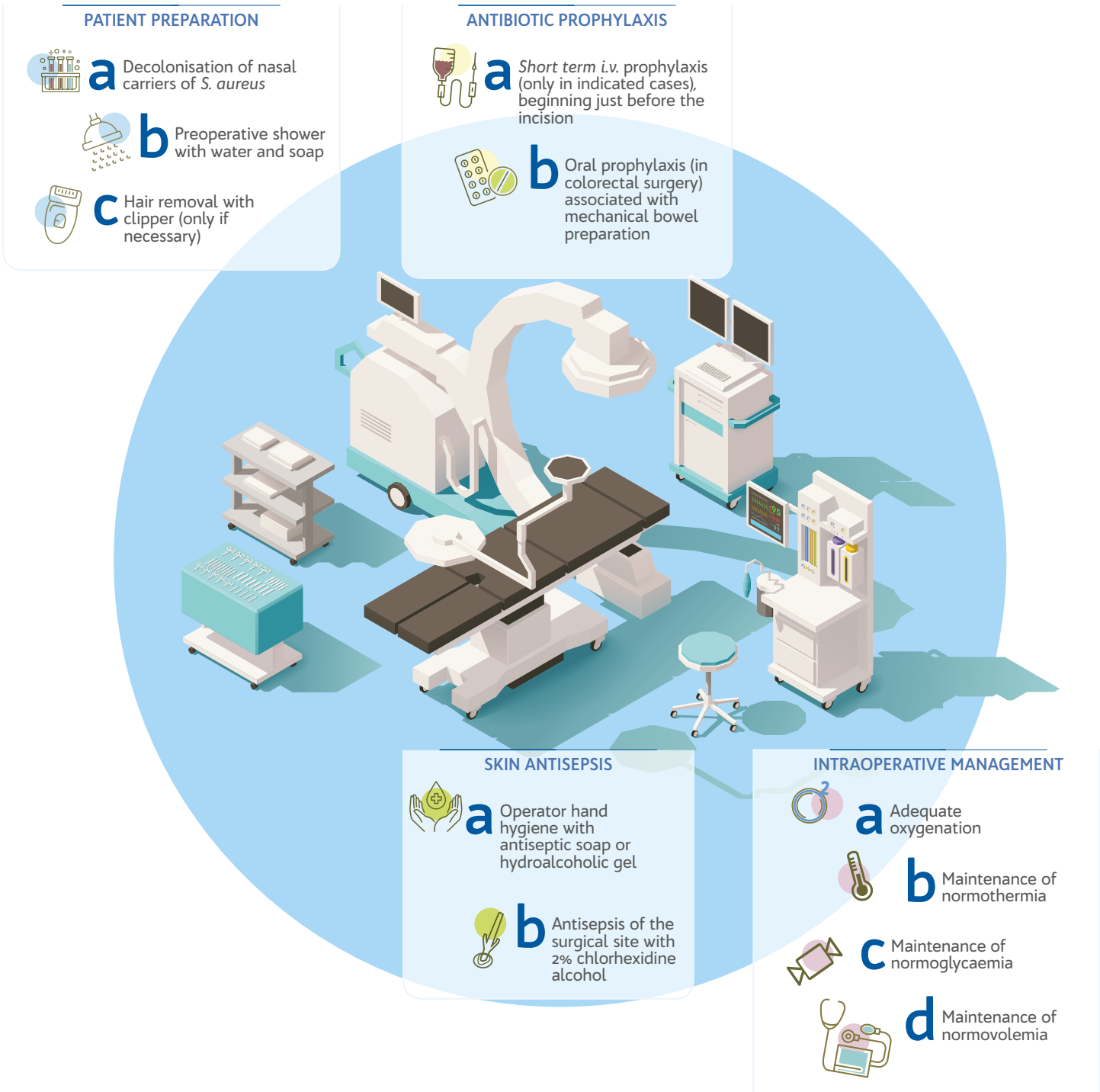
PROCEDURE	RECOMMENDATIONS	STRENGTH/QUALITY
Antisepsis in the surgical site	The patient's skin antisepsis must be performed with an antiseptic solution containing chlorhexidine gluconate	WHO 2016, strong/from low to moderate
	In subjects allergic to chlorhexidine, the use of povidone-iodine alcohol for antiseptic preparation is an alternative, on condition it is applied correctly and, possibly, in a 10% alcohol solution	CDC 2017
	The use of dye-containing products is recommended in order to check the product has been correctly applied	*Expert opinion*
	The use of a single-use applicator (compared to the traditional method with gauzes and multiple-use containers) improves the safety (risk of fire and of contamination) and standardisation (correct dose of antiseptic) of the procedure and is more practical (application time)	*Expert opinion*
Patient skin antisepsis	Before proceeding with the antisepsis of the surgical site, thoroughly cleanse the skin around the incision area to remove coarse contamination	CDC 2017
	Preoperative antisepsis of the surgical site must be completed with an alcohol-based antiseptic unless contraindicated, e.g. in the case of procedures involving the mucosae or the eye	CDC 2017, IA, WHO 2016
	The antiseptic in alcoholic solution for the antisepsis of the skin in the surgical site should contain chlorhexidine gluconate	WHO 2016, strong/from low to moderate
	There is currently no evidence in favour of repeating antisepsis before suturing the surgical incision	CDC 2017, no recommendation/ unresolved issue
Nutritional support	Consider the administration via the oral or enteral route of multiple nutritional supplements to prevent SSIs in malnourished patients undergoing major surgery	WHO 2016, conditional/very low

PROCEDURE	RECOMMENDATIONS	STRENGTH/QUALITY
Tissue oxygenation	Patients who have general anaesthesia with tracheal intubation and mechanical ventilation must receive oxygen supplementation during surgery and, if possible, immediately after the operation (for 2-6 hours) in order to reduce the risk of SSI	WHO 2016, strong/ moderate; CDC 2017, IA
	According to WHO GL, the value of the fraction of inspired oxygen (FiO_2) should be equal to 80%	WHO 2016, strong/ moderate
Normothermia	The patient's normothermia must be maintained for the entire perioperative period, in order to reduce the risk of SSI and other major complications	WHO 2016, conditional/ moderate; CDC 2017, IA
Normoglycaemia	Adequate glycaemia controls should be performed on all surgical patients (diabetic and non-diabetic), in order to reduce the risk of SSI	WHO 2016, conditional/ low; CDC 2017, IA
	The benefits of a glycaemia target <200 mg/dl have been proven	CDC 2017, IA
	Low-quality evidence supports that additional benefits are associated with tight control of glycaemia values (<110-150 mg/dl)	WHO 2016, conditional/low
	If the established glycaemia target is <110 mg/dl, the risk of hypoglycaemia must be checked	WHO 2016
Normovolemia	The patient's blood volume must be monitored for the entire intraoperative period and body fluids suitably replenished	WHO 2016, conditional/ low; CDC 2017, IA
	The intraoperative application of the Goal Direct Fluid Therapy (GDFT) protocol is recommended in order to reduce the risk of SSI	WHO 2016, conditional/low

Proposal of an Italian bundle for the perioperative prevention of SSIs

With the conviction that the winning strategy to translate the most important evidence-based practices into clinical practice is a strategy based on care-bundles, this document proposes a bundle of interventions (listed below) that must be performed together for the perioperative prevention of SSIs. These interventions are supported by strong scientific evidence that is undeniable in clinical terms, even taking Italian clinical practice into account. They are also realistically feasible and applicable and can be easily checked via adequate controls **(Table 4)**.

Table 4. Proposal of an Italian bundle for the perioperative prevention of SSIs



The role of human factors in the prevention of SSIs

The proposed actions are recommended with the aim of reducing the impact of surgical site infections in terms of morbidity and mortality. The approach based on the human factor has the potential to support actions through ergonomic healthcare designs. Action efficacy does not depend solely on the correct execution of the actions - it also relies on the capacity to include them in a real context. The context, i.e. the healthcare organisation, pre-dates the introduction of actions to fight SSIs and its past history does not necessarily make it easier to introduce such actions. Additionally, the implementation of activities against SSIs is not limited to surgery itself because it involves the system as a whole. A conceptual model that describes the system can help understand how the organisational structure reacts to the introduction of actions. Viewing the organisation according to a systemic approach (i.e. based on the human factor) means viewing it as hinged on three dimensions: human resources, hardware resources and software resources **(Table 5)**.

Table 5. Components of the system and of human activity

HUMAN RESOURCES (LIVEWARE)	HARDWARE RESOURCES	SOFTWARE RESOURCES
The human part of the system, the bearers of skills and of a personal communicative-relational, cognitive and emotional style. It is the flexible element that adjusts by interacting with the other parts of the system.	**The machines, tools, equipment and materials, i.e. the physical parts of the system.**	**The culture of the organisation, intended as the declared values and as implicit culture, including the rules and procedures, symbols and habits, working plans and adjustment strategies used in the field to manage the organisation of work and activities.**

Experts in ergonomics and human factors see healthcare operators as an integral part of the healthcare system. They believe that efforts to optimise the system must take into account the skills and limitations of operators in a systemic view.

Let us consider the provision of some specialties such as microbiology. If a simple "greater efficiency" vision is applied, the tendency to concentrate only on supplying a service quickly in response to requests for diagnostic tests, without considering skill growth and gaining new knowledge, does not reduce the chances of mistakes occurring, despite increasing the system's efficiency. To make the system safer, it is necessary to increase the capacity to identify the risks patients may be exposed to, such as healthcare-related infections. Seen through a human factor perspective, the individual service (such as a microbiology report) becomes part of treatment course and, above all, it is an opportunity to establish a professional relationship between the microbiologist and the other healthcare professionals, in a vision of patient treatment safety.

So now knowledge of microbiology becomes a growth opportunity for clinical competences such as surgery and internal medicine in the management of infections. In the specific case of microbiology, the diagnostic response according to a systemic approach changes from "bug-oriented" to "patient-oriented". It becomes greater, with a relationship stemming from a service. Seeing things from a human factor angle creates the need to study the interactions between people and the elements of the system they work in (physical environment, duties, tools/technologies and organisation, conditions) and to re-design the systems to successfully achieve the joint optimisation of a system's social and

technical elements. This means that human factors and ergonomics are a useful landmark to consider when changing a system, e.g. by creating a system for the surveillance of surgical site infections.

Let us now consider the elements of the bundle, in order to define a systemic design model to apply to the implementation of practices for SSI reduction.

There is no doubt that, to create an organisational context that supports the above, the cultural introduction of the fight against HAIs and Patient Safety are important. At an operational level, moving among software resources, it is necessary to have an in-depth knowledge of the pharmacokinetic and pharmacodynamics of the molecules suitable for interacting with the organic and human physiology element on which surgery is to be performed. Knowledge of the main risk factors in an individual patient (which could affect the molecule's action) is also required. It is also necessary for the sequence of activity phases in the surgical procedure to be scheduled and structured, from the preoperative to the intraoperative phase. The sequence pattern must not be limited to the surgery team alone; it must be shared with the anaesthesiologists, infectious disease specialists and pharmacists, the nurses in the operating theatre and the ward and the other specialty consultants who treat the patient. It is also crucial that the steps from one phase to the next are well known. On that regard, it is important to consider which information has been generated in each step of the process and how and to whom this information is communicated, to ensure that the activity is coordinated and managed without interruptions. Other dimensions are at this point involved, such as hardware or human resources ("liveware"). The first dimension leads to assessing which antibiotic molecule to use. If it has been correctly identified, the next step is to understand where it is physically located in the operational unit, how it can be requested, if it is available to the surgery department, its accessibility status, if it can be prescribed and administered and how (i.e. with which device and in which form). Additionally, from a human resources point of view, it is necessary that the aims of individual operators are coherent and aligned with the ones of the group and of the organisation as a whole. It is important to consider how operators communicate, if they are motivated, incentivized or if they consider the activity routine or overtime. It is also important to define governance, team building and incentivising mechanisms. It is necessary to understand if, to carry out the action (administering the right antibiotic at the right time), specific strategies are used, i.e. if a new activity is identified (which creates other operating roles and functions) or if the action is carried out by the same organisational chart with a variation in the tasks of individual actors.

In a more defined manner, the evidence-based actions, included in the bundle this document is proposing, can be sub-structured according to a systemic approach. This approach must consider the operators' cultural resources, as well as technological and structural resources, using the planning grid below.

PATIENT PREPARATION

RECOMMENDATION

Patients should bathe or shower (and wash their hair) on the evening before or on the day of surgery, using normal or antiseptic soap (WHO 2016, conditional/moderate; CDC 2017, IB).

Communication with the patient

SOFTWARE	HARDWARE	LIVEWARE
• The culture of "communication with patients" is favoured through specific training initiatives that consider all direct interactions with the patients and their families as an opportunity to spread information and to change behaviours	• Preparation of information material (brochure to give to patients and their families) • Printing of handbooks and paper tutorials for the various types of healthcare professionals (e.g. pre-hospitalisation nurses, GPs) • Preparation of the sheets in various formats (paper, digital) and available on different media	• Activation of a multidisciplinary and multi-professional work group and linking of the group with existing functions and roles, including territorial districts, GPs and primary care paediatricians, public relations office and pharmacies in the area • Creation of a new "evangelist" function in the structures • Involvement of patient associations • Organisation of the information campaign launch • Identification of a testimonial for the promotion
• Different communication strategies are used according to the types of patients in the various areas of surgery	• Providing antiseptics in the main points of contact between patients and the healthcare system	• Involvement of communication agencies and press offices
• Profiling patients according to social-economic and demographic determiners		
• Planning of a communication strategy on the various media		

ANTIBIOTIC PROPHYLAXIS

RECOMMENDATION

PAP must be administered only when appropriate, depending on the type of surgery (WHO 2016, strong/low; CDC 2017, IB)

Therapy sheets

SOFTWARE	HARDWARE	LIVEWARE
• Planning of antibiotic therapy sheets coherent with the guidelines accredited by sector-specific international literature. The sheets should be structured according to the type of surgery and the MIC and adjusted to the individual phases of the process and to the various professionals involved	• Graphic design of the sheets so that they can modified and integrated • Preparation of the sheets in various formats (paper, digital) and available on different media	• Activation of a multidisciplinary and multi-professional work team and linking to the existing functions and roles • Definition of governance of the work group • Organisation of a consensus for launching the therapy sheets
• The therapy sheets are formalised into algorithms that can be implemented in the currently used application software and integrated with the main administrative flows	• Availability of mobile application software	• Involvement of the ICT sector and its integration • Activation of specific training on the use of the functions/ application software
• The therapy sheets take patient risk factors into account		
• The therapy sheets can be adjusted to individual patient cases		

SKIN ANTISEPSIS

RECOMMENDATION

1. Operator hand hygiene with antiseptic soap or hydroalcoholic gel. Before entering the operating theatre, wash hands with non-medicated soap to remove organic material and reduce the skin's bacterial load. Before sterile gloves are put on, the healthcare staff's hands and forearms must be prepared for surgery by washing with antiseptic soap or by applying hydroalcoholic gel (WHO 2016, strong/moderate).

Training for operators and improvement projects

SOFTWARE	HARDWARE	LIVEWARE
• Infection prevention and control (IPC) initiatives are activated in the hospital in line with international standards (WHO framework) • The culture of infection prevention is encouraged through training initiatives in university syllabuses and in specific, on-the-job training activities • Clear instructions are given regarding the removal of jewellery • Periodical feedback is provided on improvement and on results	• Picture and video tutorials and posters displayed near basins/ cleaning stations for hand hygiene and surgery preparation are used to provide instructions on when and how to carry out the sanitising and preparation activities • The cleaning stations for hand hygiene and surgery preparation are constantly supplied with all the material needed for surgery preparation • Sterile towels and wipes are available	• Operators are periodically involved in the identification, analysis and solving of the critical issues arising in IPC activities, hand hygiene and surgery preparation activities • A responsibility matrix assigns roles in the surveillance activities to individual operators

SKIN ANTISEPSIS

RECOMMENDATION

2. Before proceeding with the antisepsis of the surgical site, thoroughly cleanse the skin around the incision area to remove coarse contamination (CDC 2017).
The antiseptic in alcoholic solution for the antisepsis of the skin in the surgical site should contain chlorhexidine gluconate (WHO 2016, strong/from low to moderate).

Preoperative antisepsis

SOFTWARE	HARDWARE	LIVEWARE
• Infection prevention and control (IPC) initiatives are activated in line with international standards • Meetings aimed at raising awareness among healthcare operators of the importance of skin antisepsis and of the risk and harm caused by HAIs are planned and held • Periodical feedback is provided on the obtained improvement (days without infection) and on the achieved and to-be-achieved planned objectives	• Posters on how to achieve correct skin antisepsis are printed and displayed in the surgical area, so that they are visible to operators • Tutorial videos showing the correct procedure are produced. • The supply of the needed material is guaranteed • The required material is provided and made available in the operating theatre. It is stored in visible, clearly marked cabinets	• A multidisciplinary and multisector work group has been created for the definition, monitoring and actions related to IPC • Skin antisepsis procedures are monitored by organising periodical audits • A responsibility matrix assigns to operators the maintenance of the devices and of the material for skin antisepsis and the antisepsis of the perioperative process
• The skills required for skin antisepsis are maintained and updated with specific courses • Training courses are organised and include a simulation on how to achieve correct skin antisepsis in patients	• All protection devices (mask, gloves, etc.) are available in the work areas • The integrity of medicines for skin antisepsis is checked before use • The patient's clinical history (including any implanted venous accesses) is known and shared among healthcare operators	• Patients who are allergic to chlorhexidine are identified and the information is supplied at every staff change

INTRAOPERATIVE MANAGEMENT

RECOMMENDATION

Patients who have general anaesthesia with tracheal intubation and mechanical ventilation must receive oxygen supplementation during surgery and, if possible, immediately after the operation (for 2-6 hours) in order to reduce the risk of SSI (WHO 2016, strong/moderate; CDC 2017, IA). Patient normothermia should be maintained for the entire perioperative period (WHO 2016, conditional/moderate; CDC 2017, IA). Adequate glycaemia controls should be performed on all surgical patients (diabetic and non-diabetic), in order to reduce the risk of SSI (WHO 2016, conditional/low; CDC 2017, IA). The patient's volemia should be monitored for the entire intraoperative period and body fluids must be suitably restored (WHO 2016, conditional/low; CDC 2017, IA).

Organisation of the activities of the operating theatre's team and of the surgery pathway

SOFTWARE	HARDWARE	LIVEWARE
• Training activities on non-technical skills are organised and executed, in order to improve teamwork abilities		• A multidisciplinary group is identified to maintain and deal with inter-professional relations during the surgery process, following a multi-professional and multi-sector approach in order to increase staff motivation • The operating theatre team and the ward staff are familiar with the bundle and with the scientific rationale underlying the intraoperative management of infection risk • In the operating theatre team and the process team, roles and responsibilities for the intraoperative management of infection risk are identified
• Reference values are identified for the type of patient; if values are exceeded it is necessary to carry out specific procedures to maintain normal values and to reduce the risk of infection	• All the devices located along the surgery pathway (operating theatre and recovery room) and required for checking metabolic and vital signs and/or needed to maintain normothermia and normovolemia are identified and maintained. • Graphic materials (included in the existing documentation) are prepared to trace values and to visually recognise deviations from the normal trend or the evolution of values towards situations in which the patient is at risk of infection. • Malfunctioning or faulty devices are maintained and replaced after reporting them to the competent functions	

Strategies for the application of the bundle: the 4 E model

There is considerable evidence showing that a bundle-based approach is effective in improving treatment safety. However, suitable strategies must be adopted to ensure it is implemented. For the recommendations in the bundle to be correctly put into practice, it is necessary to make them well-known and checks are required to see if they can really induce changes in behaviour (68).

To ensure the effective application of the bundle, it is best to follow a validated method such as the 4E model (*Engage, Educate, Execute, Evaluate*). This model is a set of strategies aimed at convincing, actively involving and educating staff, at ensuring the adopted measures can be implemented and at assessing the results obtained at system level (68).

In the bundle application process, the 4E model translates into actions aimed at redefining work processes, guaranteeing specific communication strategies, favouring training, encouraging the cooperation of healthcare professionals in a multidisciplinary team, ensuring appropriate infrastructure and technological devices and monitoring outcomes through surveillance programmes. Taken together, these actions contribute to increasing the effectiveness of the implemented measures, providing safer care in the patients' interest (68).

The process for introducing a bundle requires planning from a number of decision-makers and organisation departments (hospital administration, quality office, risk management unit, department heads). These professionals must promote the project in the work group by committing to sharing the bundle's practices and putting them into context, validating the operating and educational tools (checklist, posters, reminders), analysing the starting situation, defining aims and the indicators to monitor, standardising the level of knowledge and of bundle-related skills through structured training interventions (69).

Engage: promoting compliance with the bundle

The introduction of a care-bundle implies changing previously learnt behaviours which are often deeply rooted and well-established. This means that healthcare operators must take on the responsibility of working to achieve improvement. Promoting the culture of high-quality healthcare assistance as a common aim of the clinical team and convincing that the care bundle is an effective strategy for process improvement (stressing the importance of individual contributions in team work) are essential steps to motivate the surgical team and obtain high compliance with the bundle. This is crucial if the application of the bundle is to translate into a lower SSI incidence (43).

The active involvement of the managers mentioned above is crucial in all these actions. Their motivation and conviction can be a great support in the operating team's engagement process (69).

Educate: training on the bundle's practices

The surgical team's full compliance stems from the staff having correct information and training on the practices included in the bundle. This means that a structured phase of training must be planned, with the aim of explaining why the bundle was designed as it is, of showing how the interventions included in the bundle are feasible, of helping memorise them, checking they are correctly executed and proving that positive outcomes are achieved by implementing the bundle's actions. As stated numerous times above, adopting a care bundle requires the cooperation of all the professional staff involved in the pre-, intra- and postoperative management of surgical patients. In consequence of this, the training programme must involve all the people in the multidisciplinary team acting in the operating theatre (surgeons, nurses, scrub nurses, OT technicians, anaesthetists, staff dealing with sterilisation) and the people who are not in the OT but are crucial for the process (infectious disease specialists, pharmacists, staff dealing with quality control and risk management) (20).

After the initial phase of supplying information, the training programme must include periodical refresher classes, with

supporting educational interventions and programmes for audits and feedback, which must include results and the trends highlighted by the surveillance activities (69).
Specific educational tools help with training and include original scientific literature (which supports the indications included in the bundle) and materials providing summaries and greater visibility to the indications (checklists, posters, pocket handbooks, reminders, alert notifications) (70).

Educational tools for bundle visibility and summary of contents: the poster

Appendix II contains the picture representation of the bundle proposed in this document in the form of a poster, which sums up the main interventions for educational purposes.

The bundle's operating tool: the checklist

The activity in an operating theatre stands out for the intrinsic complexity that characterises surgical procedures, even the simplest. The complexity is linked to the number of professional figures involved, the acute conditions of the patients, the considerable load of information to manage, the urgent nature of the processes to execute, the management of highly complex technologies and multiple critical points in the process which may harm patients. In this complex scenario, safety in the operating theatre requires increasingly structured communication among the operating team and the use of all the tools that can aid the coordinated collaboration of the various professionals, knowledge sharing and the standardisation and control of operating procedures (33).
By providing a summary of the most important evidence and translating it into specific behaviours, checklists are an important tool to spread updated information into clinical practice, to standardise work processes and to create systematic controls in key processes (71).
In the current state, the checklist used in Italy is the one contained in the *Manuale per la Sicurezza in sala operatoria: Raccomandazioni e Checklist* [Manual for safety in the operating theatre: Recommendations and Checklist], issued by the Ministero del Lavoro, della Salute e delle Politiche Sociali [Ministry of Labour, Health and Social Policies], which was taken from the 2009 WHO guidelines (33). Over time, this checklist has been adjusted in various ways in Italy's regions, but the various versions and local adjustments do not include (with the exception of perioperative antibiotic prophylaxis) any of the strong recommendations (confirmed by the recent updates from the WHO and CDC GL) on the prevention of SSIs, such as those on skin antisepsis and hair removal.
In this logic, the preparation of a bundle dedicated to SSI prevention could suitably integrate/complete the checklist for safety in the operating theatre, repeating important recommendations to guarantee they are actually applied. Therefore, the authors of this document suggest a checklist for the perioperative prevention of SSIs **(Table 6)** that fully represents the operating tool of the bundle described above.
As with previous versions, this checklist also identifies three phases of use during surgical operations **(Box 2)**.

Box 2.

The three phases of checklist use

Modified from (33)

PHASE I, Sign in: before the induction of anaesthesia; it requires the presence of all members of the surgical team.

PHASE II, Time out: between the induction of anaesthesia and before the skin incision; it requires the involvement of all the team's members.

PHASE III, Sign out: its aim is to transfer information to the staff tasked with assisting patients after surgery. It must be completed before the patient and surgeon leave the operating theatre.

THE CHECKLIST FOR THE PERIOPERATIVE PREVENTION OF SSIS

BOX FOR PATIENT LABEL

Operational unit: _____

Date: _____

Operation: _____

PATIENT PREPARATION

a 

Nasal decolonisation of a nasal carrier of S. aureus performed

☐ YES ☐ NO

b 

The patient showered/ bathed on the morning of surgery or no more than 24 h before the operation

☐ YES ☐ NO

c 

Hair removal (when necessary) performed with electric clipper on the day of surgery

☐ YES ☐ NO

ANTIBIOTIC PROPHYLAXIS

a 

Antibiotic prophylaxis has been administered via the i.v. route (indicated cases only)

☐ YES ☐ NO

and ended no more than 30 min. before the incision, according to the duration of the action of the used antibiotic

☐ YES ☐ NO

b 

Oral prophylaxis (in colorectal surgery), associated with mechanical bowel preparation, has been administered

☐ YES ☐ NO

SKIN ANTISEPSIS

a 

Skin (hands and forearms) of the surgical team have been prepared with antiseptic soap or hydroalcoholic gel

☐ YES ☐ NO

b 

Antisepsis of the surgical site has been performed with 2% chlorhexidine gluconate in 70% alcohol solution or, in the case of allergy to chlorhexidine, with povidone iodine in 10% alcohol solution

☐ YES ☐ NO

INTRAOPERATIVE MANAGEMENT

a 

The patient's oxygenation in general anaesthesia with tracheal intubation is adequate (FiO_2 80%)

☐ YES ☐ NO

b 

The patient's body temperature is adequately controlled (patient normothermia)

☐ YES ☐ NO

☐ NOT CONTROLLABLE

c 

The patient's glycaemic control is adequate (<200 mg/dl)

☐ YES ☐ NO

d 

The patient's volemia has been monitored and body fluids have been suitably replenished

☐ YES ☐ NO

Signature of the Nurse/Midwife:

_____

Signature of the OT Nurse/Midwife:

_____

Signature of the Operating Surgeon

_____

To help use the checklist correctly, it is advisable to appoint a coordinator, chosen among the members of the surgical team. This person could be the circulating nurse, as suggested by the WHO. The coordinator will be responsible for checking that the various members of the operating team have checked the key points of the operative process and have ticked the box of the checked item.

Execute: the supply of the materials listed in the bundle

The application of the new bundle may require replacing some products and devices available in the hospital. The administrative and organisational offices that manage the healthcare centre (department heads, pharmacies, technical office) will have to be involved to deal with the logistics of providing new materials and authorise additional costs. Adjusting the materials needed for the bundle's application may imply some organisational issues linked to distribution and to training staff to use previously unused products. It may also require overcoming a certain amount of "cultural resistance" by professionals who have to change their clinical practice habits (20).

Thanks to research and technological advancement, there are now a number of innovative solutions that can significantly contribute to containing the risk of infection, improving the safety and efficacy of the measures taken to prevent SSIs. To use the currently available technological tools in an intelligent manner, it is important to identify the products that, at a sustainable cost, offer the greatest efficacy, suitability for the situation and safety according to production and storage characteristics (quality, sterility, tracking and tracing guarantees) and to application methods (ease of use, repeatability, standardisation) (59).

In this sense, there is broad recognition of the safety benefits arising from using single-use sterile materials, starting from surgical linens, gloves and gowns and including clipper heads and single-use applicators for skin antisepsis (65). Many of the technological adjustments that can support the evidence-based practices recommended in the bundle may be implemented at no additional expense. However, there is evidence that the extra costs for adjustments that require initial investments higher than the previous ones can be offset in economic terms by a lower incidence of SSIs (and the associated costs). The so-called "spend-to-save" approach can have positive economic results because it allows the optimal execution of practices that have been amply proven to be very cost-effective (20).

Evaluate: monitoring and checking results

Evidence shows that the monitoring and feedback processes increase awareness among healthcare operators of the importance of SSI prevention and makes them more aware of their role in ensuring patient safety (72).

The audit programmes are useful because they help understand if, when implementing the prevention programme, the defined procedures are followed, if roles and duties are fully understood and if the established objectives are correctly managed and pursued (69).

SSI surveillance programmes

Surveillance and disclosing the results to surgical teams has proven to be effective in reducing the risk of SSIs. It was found to be an integral part of the strategies of a programme for the prevention of hospital-acquired infections and a priority in all healthcare systems (73,74).

Surveillance systems, by executing one of the elements (Evaluate) of the change model described above, contribute to motivating staff to apply the bundle and achieve the result (Engage), as they are themselves able to improve the outcome (surveillance effect). In Italy, the implementation of a Programma Nazionale di Sorveglianza [National Surveillance Programme] has allowed to reduce the incidence of SSIs by 29% in 2 years (7).

SSI surveillance systems can be divided into patient-oriented systems, surveillance of the microorganisms responsible for infections and environment-oriented systems. This specific class of systems focuses on the role of the environment (and of the operating theatre in particular) and of surgical tools in the risk of infection, and studies the improvements deriving from disinfection/sterilisation procedures and the use of new kinds of materials, such as single-use products (75).

Surveillance is a circular process in which the first objective is the collection of data on SSI incidence, in order to have a measure of the extent of the problem in a specific healthcare setting and to identify the areas for intervention (Figure 2). These data must be analysed and interpreted, in order to identify needs and guide the implementation of prevention measures. Next, the surveillance system must

investigate trends after the implementation of the prevention activities, with the purpose of assessing effects and identifying further areas in need of improvement. Sharing the data with all the professionals in interdisciplinary teams is an essential step in every phase of the bundle's application, in order to convince staff of the need to change, obtain active participation, persuade staff that the adopted measures are effective and encourage improvement actions (75).

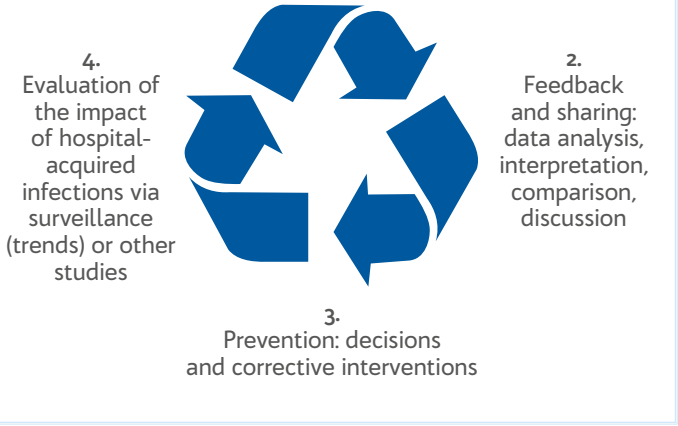
In addition to outcome indicators (i.e. the rate of SSIs), the other dimension that needs assessing in the SSI surveillance programme is that of process indicators, which include the rate of compliance among operators with 90% of the items in the checklist. Periodically monitoring these indicators means checking the results, in order to understand if the changes made by applying the bundle are actually leading to improvement.

Without prejudice to the ultimate objective, i.e. the reduction of hospital-acquired infections and the considerable cost associated with them, the validity of a SSI surveillance system is defined by characteristics such as simplicity (in order to minimise costs and working load), flexibility (to carry out appropriate changes), acceptability (expressed as the level of participation), coherence (by using standardised methods) and the sensitivity and specificity of the collected data (thanks to accurate methods and expert operators).

Additionally, an ideal surveillance programme should, in order to avoid underestimating real incidence data, extend the collection to include data on surgical patients after discharge from hospital (WHO 2016).

Figure 2. Surveillance as a "circular" process

Modified from (75)



Conclusions

SSIs are the most common hospital-acquired infections in low- and middle-income countries and affect about one third of the patients undergoing surgery. In high-income countries, they are the second most common HAI. SSIs are therefore a considerable problem and are associated with several risk factors. Some of the factors depend on the patient whereas others on the environmental context, the kind of surgery and even the way healthcare professionals behave. Many risk determiners can be effectively corrected or at least improved, e.g. the ones dependant on the individual patient (such as nutritional status or smoking), or the ones linked to the operative procedures surgical patients undergo, including measures such as antibiotic prophylaxis, sterilisation, disinfection, hair removal and skin antisepsis. Patient management procedures, such as maintaining normoglycaemia, normothermia and adequate tissue oxygenation, currently represent important standards for SSI prevention.

SSIs have a considerable impact on the physical and mental health of patients and on their quality of life. The significant increase in mortality, morbidity and long-term disability associated with these complications translates into a considerable expense for the national health system. Although not easy to quantify, this cost is certainly very high, considering the high incidence that still characterises this phenomenon.

150 years after Ignaz Semmelweis's crucial observations on puerperal fever and their reduction through hand antisepsis among obstetricians, SSIs are once again the focus of renewed interest because, with more and more increasingly complex operations often performed on older individuals with multiple risk factors, they can be considered a perfectly avoidable complication of surgical procedures. The percentage of preventable SSIs, while not 100%, is growing over the years in proportion with the prophylaxis measures that change the surgical team's habits, environmental hygiene and patient preparation. The most reliable estimates set the reduction of SSI incidence to up to 70% if specific prevention measures are applied. The publication of no fewer than two international guidelines in the last two years is an incentive to implement, in clinical practice, measures supported by solid scientific evidence and, at the same time, to design strategies aimed at improving those measures, such as the procedures and indications for hair removal, skin antisepsis and perioperative prophylaxis. Although these interventions are supported by evidence, they are still not standard healthcare practices in many parts of Italy.

Considering that patients undergoing surgery are becoming increasingly complex cases, with a risk of contracting infections much higher than in the past (subjects who are severely debilitated, undergoing multiple therapies, on average older than in the past), it is essential to start from a clinical assessment that is as detailed as possible. The aim of this is to stratify the risk and give the correct value to the adoption of all the recommendations that are to be applied next.

In light of the above, a multidisciplinary approach is crucial. "Multidisciplinary" must be intended as the greatest connection among the various healthcare professionals and disciplines in the team that operates on the patient. Inter-professional and multidisciplinary integration can be pursued by using, in addition to the so-called "non-technical skills", methods and tools that favour increasingly structured communication, such as briefings, debriefings and checklists, which become a valid support in improving daily clinical practice.

The best strategy for the actual application of effective measures is consensus on multi-modal approaches, which involve the various actors of the surgical operation process and that regard individual interventions in synergy with each other, as occurs when the care bundle is applied.

This Italian document wants to provide a practical and operational contribution to address, in a systematic and standardised manner, the issue of SSIs, for which there is a very good potential for reduction. The union of good healthcare practices, technological and scientific progress and the improvement of organisational measures (all elements of the "new Medicine") represent a safe and tested tool for successfully dealing with the issue. The main ob-

jective of this document is incentivising the adoption of evidence-based practices for the prevention of SSIs, which have a truly deep impact on the postoperative conditions of the patients and on the costs associated with treating such complications. The operational tools suggested here must therefore be considered changeable and adjustable to local conditions and the needs of the individual health-care centres that wish to use them.

Appendix I - Medicines vs biocides

Relevant context

The market of antiseptics and disinfectants is broad and quite varied, especially when considering the regulatory frameworks for production and marketing.

The European Chemicals Agency (ECHA) has prepared a guide for the application of the EU Biocidal Product Regulation (BPR-Regulation [EU] No. 528/2012). This regulation specifies very clearly that products for the antisepsis of injured skin (e.g. the antisepsis of surgical wounds) or the antisepsis of undamaged skin before an invasive medical treatment (e.g. preoperative antisepsis of the skin before surgery or before the application of vascular access devices) must always be medicinal products, which are regulated by Directive 2001/83/EC. A number of European countries, such as Belgium, Germany, the Netherlands and the UK, have acknowledged the importance of skin antisepsis to ensure patient safety and have classified the antiseptics used on the skin before surgery as medicinal products before ECHA established it (76).

According to the current laws, in Italy antiseptics to be used on undamaged skin and on mucosae must be registered as "medicinal products". As such, they must comply with Lgs.D. No. 219/2006 and s.a.i. (implementation of Directive 83/2001), undergo production controls and obtain a marketing authorisation. Antiseptics to be used on undamaged skin (e.g. for washing staff's hands and for the preparation of the surgical site) and disinfectants for the environment can be registered as "medico-surgical devices" with the Ministry of Health. Lastly, disinfectants for medical devices and/or equipment are registered as "medical devices" and must have the mark of compliance with Council Directive 93/42/EEC and s.a.i. (on 26 May 2020 this directive will be withdrawn and replaced by Regulation [EU] 2017/745 on Medical Devices).

Definitions

- **Antiseptic:** organic or inorganic substance used on living tissue to prevent or stop the action and the growth of pathogenic microorganisms.
- **Disinfectant:** chemical agent with antimicrobial activity intended for use on inanimate objects or surfaces (tools or environmental).

There are, however, essential differences in a number of aspects between a medicine and a biocide (77) (Table 7).

In skin antisepsis, the sterility of the solution is an important aspect to consider. In the EU, the Directive relating to medicinal products and the existing provisions on sterilisation guarantee that all medicinal products are sterile (78). However, non-sterile antiseptic solutions may be contaminated by bacteria or spores during the production process (intrinsic contamination), as extensively documented in scientific literature (79-83). In 2007, in the United States alone, over 40 epidemics and pseudo-epidemics caused by contaminated antiseptics were reported (82). In Spain, batches of antiseptic solutions (classified as biocides) had to be withdrawn from the market due to contamination (83).

Table 7. Medicines and biocides, main differences
Modified from (2)

MEDICINES		BIOCIDES
• Clinical trials are conducted in a regulated way in healthy subjects and in patients. • The efficacy, safety and quality of every single product are tested by a competent licensing body. • Evidence must be provided during the marketing authorisation procedure, in view of the benefits and potential risks of the product. • EMA's scientific guidelines on the clinical efficacy and the safety of medicinal products for human use help applicants prepare marketing authorisation applications.	Evidence of quality, safety and efficacy	• Experiments or tests for research or development involving an unauthorised biocide or a non-approved active substance intended exclusively for use in a biocidal product are carried out under the conditions laid down in the BPR (Biocide Regulation).
• Legislation requires medicinal products for human use, manufactured in or imported into the EU, to comply with the guidelines of good manufacturing practice (GMP). • Strict legislative requirements on the quality management system, the pharmaceutical quality assurance system, etc. • Production of medicinal products subject to constant official supervision and to a pharmacovigilance system. • Production of sterile products subject to special requirements that minimise the risks of microbiological contamination.	Manufac-turing and sterility	• No specific requirements for the manufacturing process. • No sterility or microbiological controls required.
• Suppliers subject to control and audits under the GMPs to verify compliance with the specifications of the supplied raw material and compliance with GMPs. • Suppliers are defined in the register and subject to approval and control in case of changes; they must inform the competent Authority and customers who purchase the product of any change.	Distribution chain	• No control of suppliers of the raw material required. • For co-formulants there is no specific indication and any co-formulant can be used; however, the active substance must be purchased from suppliers listed in art. 95 of the BPR.
• The EU Register lists all medicinal products for human and veterinary use as well as orphan medicinal products that have received a marketing authorisation through the centralised procedure. • Some Member States have established registers of nationally-authorised medicinal products.	Register	• EU Register for Biocidal Products

Implications

The use of biocides for medical purposes contradicts the aims of the provisions on biocidal and medicinal products. It is also a concern for other reasons, such as patient and occupational safety, environmental pollution and antimicrobial resistance.

For these reasons, it would be appropriate in the EU to have a harmonised approach on the classification of skin disinfectants before surgery or a medical procedure.

Regulatory framework governing the use of antiseptics and disinfectants

The implementation of Directive 98/8/EC concerning the placing of biocidal products on the market, implemented in Italy with Lgs.D. no. 174/2000 and later replaced by the Regulation directly applied in all member states (Regulation [EU] 528/2012, effective since September 2013), will, in the near future, lead to the standardisation of the procedures for the authorisation of such products in the European Union. In It-

Patient safety

Biocides and medicines are subject to very different regulatory routes, which confer very different standards in terms of safety, efficacy and quality. As a result, the use of biocidal products as medicines may jeopardise the patient's safety, because biocides do not have a marketing authorisation under the strict rules that apply to medicinal products.

As highlighted by the Medicines and Healthcare products Regulatory Agency (MHRA), the above practice is associated with risks and "Using the appropriately authorised product for its specific intended use, in accordance with the manufacturer's instructions for use, is the best way of minimising harm." (84) Studies have shown that biocides may have toxic and carcinogenic properties and disrupt the endocrine system (85).

Antimicrobial resistance

The former European Commission Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) stressed that, to preserve the role of biocides in the control of infection and in hygiene, it is essential to prevent the emergence of bacterial resistance and cross-resistance by using biocidal products appropriately and prudently (86).

The Committee also added that *"the need for proper use of disinfectants and antiseptics should be stressed and health care workers should be trained to comply with clear and agreed policies and practices, avoiding unnecessary and incorrect use of biocides."* (86)

In other words: in the specific case of skin antisepsis before medical treatment, the use of biocides should be limited to the cases in which it is strictly necessary and a more suitable alternative (such as a medicine) is not available.

Furthermore, as explained in this paper's introductory section, the misuse of antibiotics following false positive blood cultures does not just expose patients to the risk of serious adverse events with no clinical benefit - it also contributes to increased antimicrobial resistance.

Occupational safety

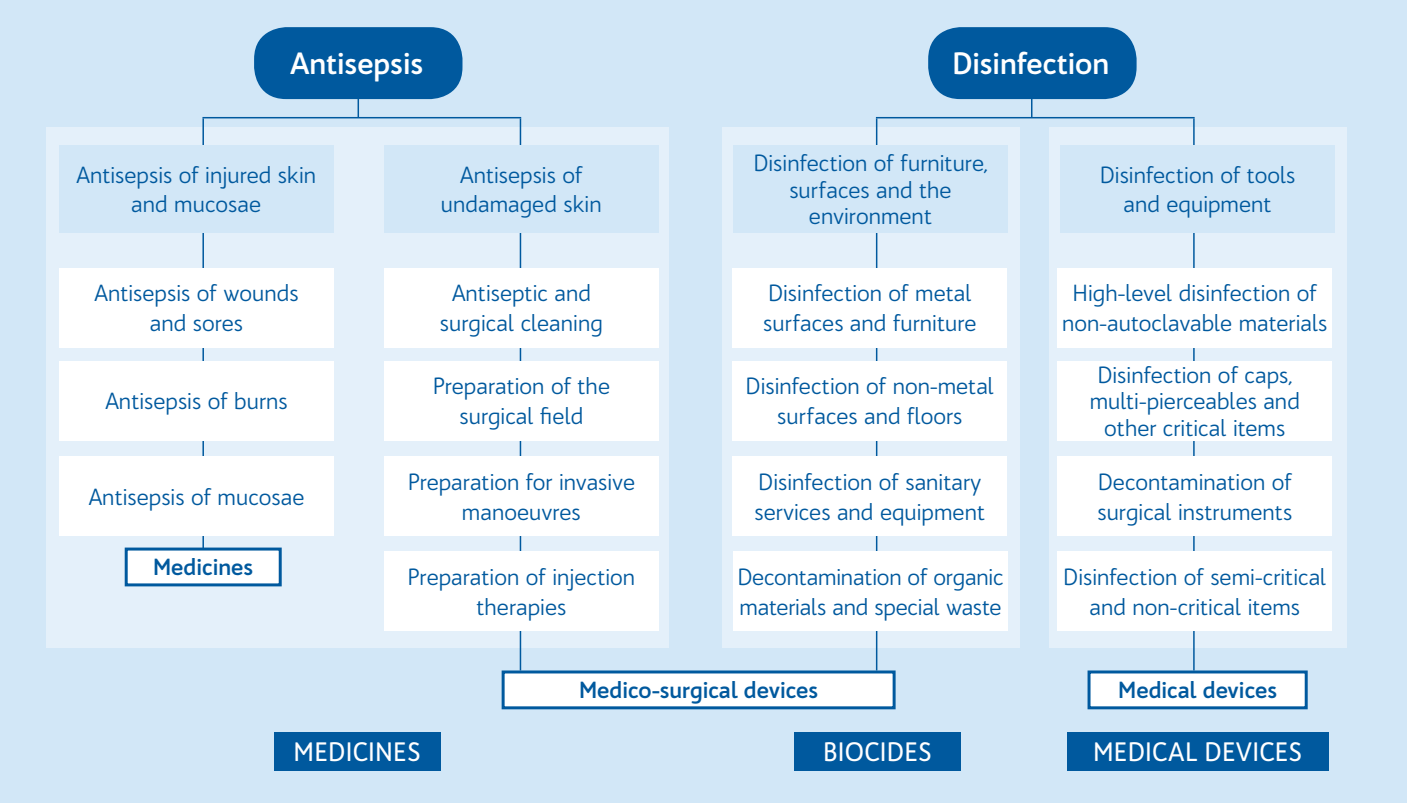
Healthcare workers can be exposed to biocides either directly or indirectly. In the former case (primary exposure), the worker/operator actively uses the biocidal product. In the latter (secondary exposure) workers are exposed after the actual use or application of biocidal products. As mentioned above, biocides may have toxic, carcinogenic and endocrine-disrupting properties, which may not be detectable, especially in the case of workers.
The Carcinogens and Mutagens Directive 2004/37/EC requires employers to ensure that the risk to workers' health and safety from dangerous substances is eliminated or reduced to a minimum (first level in the hierarchy of risk control). To fulfil this obligation, the first priority for employers is to replace or eliminate the risk of biocides, which can be done by using alternative disinfectants or replacing them with less hazardous procedures, substances, preparations or products.
The various existing European and national guidelines provide instructions for protecting workers during disinfection procedures, but the EU has no harmonised specific guidelines on the safe use of biocides in the healthcare sector. The EU Directorate-General for Employment, Social Affairs and Inclusion guidelines have provided a general description of good practice on safe working in disinfection activities (87) which does not dwell on biocides and their use in the healthcare sector.

Environmental impact

The use of biocides can have a considerable environmental impact. In the healthcare sector, the disposal of unused biocides or of biocide residues must be managed with great caution to avoid causing serious (and potentially long-lasting) environmental damage.

aly the transition will involve the current medico-surgical devices that are now governed by the DPR no. 392 (6 October 1998) and many other products that, despite having an intended use as biocides, are currently on the market without a Marketing Authorisation.
During this transition phase, many institutions are debating on whether or not to take a position in line with the position of other European countries on the directives related to the use of disinfectants and antiseptics for the skin antisepsis of patients. Unlike the situation in Italy, in many European countries such as Germany, France, Belgium, the Netherlands and the UK, the laws on disinfectants and antiseptics specify that surgical patient antisepsis (including on undamaged skin) must be performed with a product classified as a medicine, as a guarantee of the safety, quality, sterility, tracking and tracing (see text box on page 56) of the used product (Figure 3). This concept also applies to the so-called "borderline products" i.e. the products that, by their very nature, do not clearly belong to a specific sector with a single legal classification. Chlorhexidine is a typical example of this kind of product.

Figure 3. The market of antiseptics and disinfectants according to biocide legislation
Modified from (59)



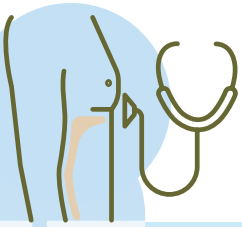
Tracking and tracing of products

Product tracking is the possibility of identifying and following a product through all phases of production, transformation and distribution, right up to its use. Tracking can be on two levels - batch tracking and unit tracking. Traceability is the ability to identify the "history" of the product by going through the tracking process in reverse. Tracking is a control activity established by the Ministry of Health and AIFA [Italian Medicine and Healthcare Products Agency] as a public health protection measure, to guarantee the integrity and the suitability for prescription of products for human use. Its aim is to fight fraud, counterfeiting and smuggling. Tracking and tracing allow to link a healthcare product to a patient, guaranteeing high levels of safety (88).

Article 40 of Law no. 39 (1 March 2002) required the Ministry of Health to create a central data bank that records the movements of individual packages of medicinal specialties, which are unequivocally identified via a unique label, pursuant to the Decree of the Ministry of Health (30 May 2014), which contains the marketing authorisation number ("autorizzazione all'immissione in commercio", AIC code) and a progressive number on each individual package, which guarantee full tracking and traceability.

The Decree of 11 June 2010 required the creation of a data bank for monitoring medical devices but the tracking system, although similar to that of medicines, does not include the tracking of individual packages because the items are not identified with a numbered label.

There are no legislative criteria that guarantee the traceability of medico-surgical devices and biocides.



1 PATIENT PREPARATION

a Preoperative shower with water and soap

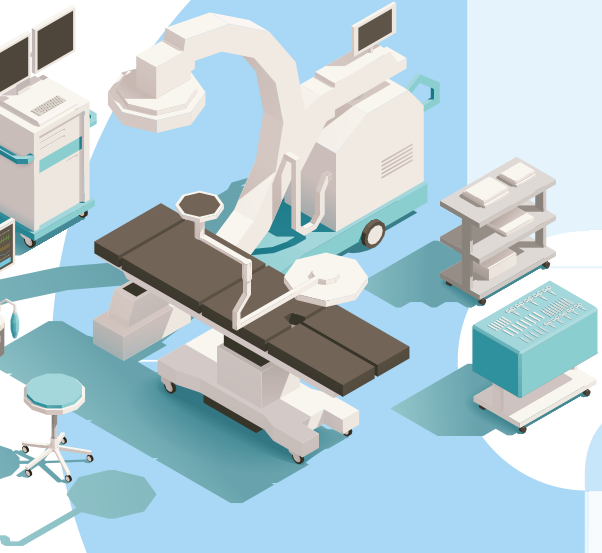
Surgical patients should bathe or shower (and wash their hair) on the evening before or on the day of surgery, using normal or antiseptic soap.

b Decolonisation of nasal carriers of *S. aureus*

The preoperative decolonisation with 2% mupirocin nasal ointment, with or without chlorhexidine gluconate bodywash solutions, must be performed in all nasal carriers of *Staphylococcus aureus* undergoing cardiothoracic and orthopaedic surgery. Hospitals can, for every other kind of surgery, assess if it is appropriate, in terms of organisation and cost-effectiveness ratio, to perform screening and decolonisation.

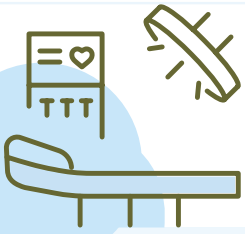
c Hair removal with clipper (only if necessary)

Hair removal must not be a routine procedure. Hair should be removed only if the hairs, in or around the surgical site, interfere with the surgical procedure. Only electric clippers must be used and hair must be removed only on the day of and immediately before surgery.



b Antisepsis of the surgical site with 2% chlorhexidine alcohol

The antiseptic preparation of the patient's skin must be performed with an antiseptic solution containing chlorhexidine gluconate. In subjects allergic to chlorhexidine, the use of alcoholic povidone-iodine for antiseptic preparation is an alternative, on condition it is applied correctly and, possibly, in a 10% alcohol solution. The use of dye-containing products is recommended in order to check the product has been correctly applied. The use of a single-use applicator (compared to the traditional method with gauzes and multiple-use containers) improves the safety (risk of fire and of contamination) and standardisation (correct dose of antiseptic) of the procedure and is more practical (application time).



4 INTRAOPERATIVE MANAGEMENT

a Adequate oxygenation

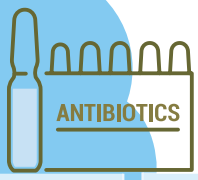
Patients who have general anaesthesia with tracheal intubation and mechanical ventilation must receive oxygen supplementation during surgery and, if possible, immediately after the operation (for 2-6 hours) in order to reduce the risk of infections in the surgical site. The value of the fraction of inspired oxygen (FiO_2) should be equal to 80%.

b Maintenance of normothermia

The patient's normothermia must be maintained for the entire perioperative period, in order to reduce the risk of SSI and other major complications.

APPENDIX II POSTER: THE ITALIAN BUNDLE FOR THE PERIOPERATIVE PREVENTION OF SSIS

2 ANTIBIOTIC PROPHYLAXIS



a Short-term i.v. prophylaxis (only in indicated cases), beginning just before the incision

PAP must be administered only when appropriate, depending on the type of surgery. It must be performed within 120 minutes before the incision, taking the antibiotic's half-life into account. The time frame must allow to reach an effective concentration in the serum and tissues at the time of the incision. PAP should not be continued after the surgical incision is sutured. This recommendation also applies in the case of drainage.

b Oral prophylaxis (in colorectal surgery) associated with mechanical bowel preparation

The preoperative administration of antibiotics via the oral route, combined with mechanical bowel preparation (MBP), is recommended to reduce the risk of SSI in adult patients undergoing elective colorectal surgery. MBP alone (without the administration of oral antibiotic prophylaxis) must not be used to reduce SSIs in adult patients undergoing elective colorectal surgery.

3 SKIN ANTISEPSIS

a Operator hand hygiene with antiseptic soap or hydroalcoholic gel

Before putting on sterile gloves, the healthcare staff's hands and forearms must be prepared for surgery by washing with antiseptic soap or by applying hydroalcoholic gel.

c Maintenance of normoglycaemia

Adequate glycaemia controls should be performed on all surgical patients (diabetic and non-diabetic), in order to reduce the risk of SSI. The benefits of a <200 mg/dl glycaemia target have been proven. Low-quality evidence supports that additional benefits are associated with tight control of glycaemia values (<110-150 mg/dl). If the established glycaemia target is <110 mg/dl, pay attention to the risk of hypoglycaemia.

d Maintenance of normovolemia

The patient's blood volume must be monitored for the entire intraoperative period and body fluids must be suitably replenished. The intraoperative application of the Goal Direct Fluid Therapy (GDFT) protocol is recommended in order to reduce the risk of SSI.

References

1. European Centre for Disease Prevention and Control. Surveillance of surgical site infections in Europe 2010-2011. Stockholm: ECDC; 2013.
2. Mangram AJ, Horan TC, Pearson ML, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999;20(4):250-78; quiz 279-80.
3. Global Guidelines for the Prevention of Surgical Site Infection. Geneva: World Health Organization (WHO); 2016.
4. Centers for Disease Control and Prevention. Surgical site infection (SSI) event. Atlanta (GA): CDC; gennaio 2017. www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (ultimo accesso: 15/10/2018).
5. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.
6. Petrosillo N, Drapeau CM, Nicastri E, et al.; ANIPIO. Surgical site infections in Italian Hospitals: a prospective multicenter study. BMC Infect Dis 2008;8:34.
7. Marchi M, Pan A, Gagliotti C, et al.; Sorveglianza Nazionale Infezioni in Chirurgia (SNICh) Study Group. The Italian national surgical site infection surveillance programme and its positive impact, 2009 to 2011. Euro Surveill 2014;19(21).
8. Moro ML, Pan A, Parenti M, Marcelli E; ASSR Regione Emilia-Romagna. Prevenzione delle infezioni del sito chirurgico. Dossier n. 261/2017. http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/dossier/doss261 (ultimo accesso: 15/10/2018).
9. Uçkay I, Harbarth S, Peter R, et al. Preventing surgical site infections. Expert Rev Anti Infect Ther 2010;8(6):657-70.
10. Sievert DM, Ricks P, Edwards JR, et al.; National Healthcare Safety Network (NHSN) Team and Participating NHSN Facilities. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infect Control Hosp Epidemiol 2013;34(1):1-14.
11. Perencevich EN, Sands KE, Cosgrove SE, et al. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis 2003;9(2):196-203.
12. Andersson AE, Bergh I, Karlsson J, Nilsson K. Patients' experiences of acquiring a deep surgical site infection: an interview study. Am J Infect Control 2010;38(9):711-7.
13. Badia JM, Casey AL, Petrosillo N, et al. Impact of surgical site infection on healthcare costs and patient outcomes: a systematic review in six European countries. J Hosp Infect 2017;96(1):1-15.
14. Jenks PJ, Laurent M, McQuarry S. Clinical and economic burden of surgical site infection (SSI) and predicted financial consequences of elimination of SSI from an English hospital. J Hosp Infect 2014 Jan;86(1):24-33.
15. Cossin S, Malavaud S, Jarno P, et al. Surgical site infection after valvular or coronary artery bypass surgery: 2008e2011 French SSI national ISO-RAISIN surveillance. J Hosp Infect 2015;91:225-30.
16. Harrington P. Surgical Site Infection. NICE Quality Standards. www.healthcareconferencesuk.co.uk/news/newsfiles/pauline-harrington_513.pdf (ultimo accesso: 15/10/2018).
17. Lamarsalle L, Hunt B, Schauf M, et al. Evaluating the clinical and economic burden of healthcare-associated infections during hospitalization for surgery in France. Epidemiol Infect 2013;141(12):2473-82.
18. Anderson DJ, Podgorny K, Berríos-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 Update. Infection Control 2014;35:605-27.
19. Gheorghe A, Moran G, Duffy H, et al. Health utility values associated with surgical site infection: a systematic review. Value Health 2015;18(8):1126-37.
20. Petrosillo N, Pittiruti M, et al. Impatto e prevenzione delle infezioni del sito chirurgico: una proposta di lavoro sulle linee guida. QIJPH 2017, vol 6, n 8. www.ijph.it/pdf/2017-v6-n8.pdf (ultimo accesso: 15/10/2018).
21. Cassini A, Plachouras D, Eckmanns T, et al. Burden of six healthcare-associated infections on european population health: estimating incidence-based disability-adjusted life years through a population prevalence-based modelling study. PLoS Med 2016;13(10):e1002150.
22. Drummond MF, O'Brien J, Stoddart GL, Torrance W. Metodi per la valutazione economica dei programmi sanitari. Il

Pensiero Scientifico Editore, terza edizione italiana: novembre 2010
23. Broex EC, van Asselt AD, Bruggeman CA, van Tiel FH. Surgical site infections: how high are the costs? J Hosp Infect 2009;72(3):193-201.
24. Health care-associated infections FACT SHEET WHO. www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf (ultimo accesso: 15/10/2018).
25. Privitera G; Assobiomedica. Controllo delle infezioni ospedaliere Giugno, 2011. Università degli Studi di Pisa, Dpt Patologia Sperimentale www.assobiomedica.it/static/upload/_con/controllo-delle-infezioni-opsedaliere.pdf (ultimo accesso: 15/10/2018).
26. Nobile M, Navone P, Orzella A, et al. Developing a model for analysis the extra costs associated with surgical site infections (SSIs): an orthopaedic and traumatological study run by the Gaetano Pini Orthopaedic Institute. Antimicrob Res Infect Control 2015;4(Suppl 1):P68.
27. Coleman K, Tan JT, Norris S et al. Surgical site infection in Australia: a systematic review of the incidence and economic burden. https://www.valueinhealthjournal.com/article/S1098-3015(11)73284-3/pdf
28. Umscheid CA, Mitchell MD, Doshi JA, et al. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. Infect Control Hosp Epidemiol 2011;32(2):101-14.
29. Department of Health and Human Services. Eliminating serious, preventable, and costly medical errors—never events. https://downloads.cms.gov/cmsgov/archived-downloads/smdl/downloads/smd073108.pdf (ultimo accesso: 15/10/2018).
30. Leaper DJ, Tanner J, Kiernan M, et al. Surgical site infection: poor compliance with guidelines and care bundles. Int Wound J 2015;12(3):357-62.
31. Pronovost P, Needham D, Berenholtz S, et al. Aninterventionto decrease catheter-related bloodstream infections in the ICU. N Engl J Med 2006;355(26):2725-32.
32. Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med 2009;360(5):491-9.
33. Ministero del Lavoro, della Salute e delle Politiche Sociali. Manuale per la Sicurezza in sala operatoria: Raccomandazioni e Checklist. Aggiornamento 16 maggio 2013. www.salastampa.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id=1119 (ultimo accesso: 15/10/2018).
34. Bellandi T, Tartaglia R, Sheikh A, Donaldson L. Italy recognises patient safety as a fundamental right. BMJ 2017;357:j2277.
35. Legge 8 marzo 2017, n. 24. Disposizioni in materia di sicurezza delle cure e della persona assistita, nonché in materia di responsabilità professionale degli esercenti le professioni sanitarie. (17G00041). GU Serie Generale n. 64 del 17-03-2017. www.gazzettaufficiale.it/eli/id/2017/03/17/17G00041/sg (ultimo accesso: 15/10/2018).
36. Tartaglia R, Albolino S, Bellandi T, et al. Eventi avversi e conseguenze prevenibili: studio retrospettivo in cinque grandi ospedali italiani. Epidemiol Prev 2012;36:151-61.
37. Gurses, AP, Ozok AA, Pronovost PJ. Time to accelerate integration of human factors and ergonomics in patient safety. BMJ Qual Saf 2012;21(4):347-51.
38. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al.; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg 2017;152(8):784-91.
39. Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. J Hosp Infect 2008;70 Suppl 2:3-10.
40. Weaving P, Cox F, Milton S. Infection prevention and control in the operating theatre: reducing the risk of surgical site infections (SSIs). J Perioper Pract 2008;18(5):199-204.
41. Resar R, Griffin FA, Haraden C, Nolan TW; Institute for Healthcare Improvement (IHI). Using Care Bundles to Improve Health Care Quality. IHI Innovation Series white paper 2012. www.ihi.org/resources/Pages/IHIWhitePapers/UsingCareBundles.aspx (ultimo accesso: 15/10/2018).
42. Carter EB, Temming LA, Fowler S, et al. Evidence-based bundles and cesarean delivery surgical site infections: a systematic review and meta-analysis. Obstet Gynecol 2017;130(4):735-46.
43. Koek MBG, Hopmans TEM, Soetens LC, et al. Adhering to a national surgical care bundle reduces the risk of surgical site infections. PLoS One 2017;12(9):e0184200.
44. IPASVI AQ. Tricotomia preoperatoria. Procedura assistenziale; 2009. www.ipasviaq.it/allegati/protocollo-tricotomia-avezzano-2009-2.pdf (ultimo accesso: 15/10/2018).
45. Sistema Nazionale Linee Guida; SNLG 17. Antibioticoprofilassi perioperatoria nell'adulto. 2011 www.anmdo.org/wp-content/uploads/2016/10/Linee-guida-Antibioticoprofilassi-perioperatoria-nelladulto.pdf (ultimo accesso: 15/10/2018).

46. Bratzler DW, Dellinger EP, Olsen KM, et al.; American Society of Health-System Pharmacists (ASHSP). Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013;14(1);73-156.
47. Mackeen AD, Packard RE, Ota E, et al. Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean delivery. Cochrane Database Syst Rev 2014;12:CD009516.
48. WHO guidelines on hand hygiene in health care. Geneva: World Health Organization; 2009.
49. Centers for Disease Control and Prevention. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR 2002;51
50. Tanner J, Dumville JC, Norman G, Fortnam M. Surgical hand antisepsis to reduce surgical site infection. Cochrane Database Syst Rev 2016;1:CD004288.
51. National Institute for Health and Care Excellence (NICE). A summary of selected new evidence relevant to NICE clinical guideline 74 "Prevention and treatment of surgical site infection" (2008). Evidence update 43. June 2013. www.nice.org.uk/guidance/cg74/evidence (ultimo accesso: 15/10/2018).
52. Darouiche RO, Wall MJ Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. N Engl J Med 2010;362(1):18-26.
53. Tuuli MG, Liu J, Stout MJ, et al. A Randomized trial comparing skin antiseptic agents at cesarean delivery. N Engl J Med 2016;374(7):647-55.
54. Mimoz O, Lucet JC, Kerforne T, et al. Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. Lancet 2015;386(10008):2069-77.
55. Privitera GP, Costa AL, Brusaferro S, et al. Skin antisepsis with chlorhexidine versus iodine for the prevention of surgical site infection: A systematic review and meta-analysis. Am J Infect Control 2017;45(2):180-9.
56. Zhang D, Wang XC, Yang ZX, et al. Preoperative chlorhexidine versus povidone-iodine antisepsis for preventing surgical site infection: A meta-analysis and trial sequential analysis of randomized controlled trials. Int J Surg 2017;44:176-84.
57. Denton GW. Chlorhexidine. In: Block SS, ed. Disinfection, sterilization, and preservation. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2001:321-36.
58. Lee I, Agarwal RK, Lee BY, et al. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol 2010;31(12):1219-29.
59. De Rosa M, et al; SIFACT. Documento di scenario. Prodotti antisettici e disinfettanti. Pharmadocument, giugno 2017.
60. Sociedad Espanola de Medicina Preventiva, Salud Publica e Higiene. Proyecto Infeccion Quirurgica Zero, gennaio 2017 http://infeccionquirurgicazero.es/images/stories/recursos/protocolo/2017/3-1-17-documento-Protocolo-IQZ.pdf (ultimo accesso: 15/10/2018).
61. Stonecypher K. Going around in circles: is this the best practice for preparing the skin? Crit Care Nurs Q 2009;32(2):94-8.
62. Stohl S, Benenson S, Sviri S, et al. Blood cultures at central line insertion in the intensive care unit: comparison with peripheral venipuncture. J Clin Microbiol 2011;49(7):2398-403.
63. Lundberg PW, Smith AA, Heaney JB, et al. Pre-operative antisepsis protocol compliance and the effect on bacterial load reduction. Surg Infect (Larchmt) 2016;17(1):32-7.
64. So BK, Chu CC, Ho PL, et al. Evaluation of two chlorhexidine-alcohol-based skin disinfectants in blood donation setting. Vox Sang 2014;106(4):316-21.
65. Casey AL, Badia JM, Higgins A, et al. Skin antisepsis: it's not only what you use, it's the way that you use it. J Hosp Infect 2017;96(3):221-2.
66. Kotagal M, Symons RG, Hirsch IB, et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. Ann Surg 2015;261(1):97-103.
67. Alta Scuola Di Economia E Management Del Sistemi Sanitari (ALTEMS), Ministero della Salute. Mini-HTA report. Protocollo di ottimizzazione emodinamica del paziente in fase perioperatoria. 2015
68. Pronovost PJ, Berenholtz SM, Goeschel CA, et al. Creating high reliability in health care organizations. Health Serv Res 2006;41(4 Pt 2):1599-617.
69. Azienda Sanitaria della Regione Emilia-Romagna. Linee di indirizzo alle Aziende per la gestione del rischio infettivo: infezioni correlate all'assistenza e uso responsabile di antibiotici. DGR n. 318/2013 http://assr.regione.emilia-romagna.it/it/ricerca-innovazione/prevenzione-antibioticoresistenza-infezioni/sorveglianza-controllo/sorveglianza-rischio-infettivo/linee-indirizzo-antibiotici-infezioni (ultimo accesso: 15/10/2018).

70. Wu AW, WHO. Translating Evidence to Safer Care. Patient Safety Research Introductory Course Session 7. www.who.int/patientsafety/research/ps_online_course_session7_intro_2in1_english_2010_en.pdf (ultimo accesso: 15/10/2018).
71. Winters BD, Gurses AP, Lehmann H, et al. Clinical review: Checklists - translating evidence into practice. Critical Care 2009;13(6):210.
72. Tanner J, Padley W, Assadian O, et al. Do surgical care bundles reduce the risk of surgical site infections in patients undergoing colorectal surgery? A systematic review and cohort meta-analysis of 8,515 patients. Surgery 2015;158(1):66-77.
73. Zingg W, Holmes A, Dettenkofer M, et al. Hospital organisation, management, and structure for prevention of health-care-associated infection: a systematic review and expert consensus. Lancet Infect Dis 2015;15(2):212-24.
74. Core components for infection prevention and control programmes. Geneva: World Health Organization; 2009.
75. WHO/CDS/CSR/EPH/2002/12. Prevention of hospital-acquired infections. A practical guide – 2nd edition. www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_EPH_2002_12/en/ (ultimo accesso: 15/10/2018).
76. ECHA. Guidance on the biocidal products regulation. Volume II Efficacy – Assessment and Evaluation (Parts B+C). Version 3.0 April 2018.
77. European Policy Recommendations. Optimising skin antisepsis for an enhanced prevention of healthcare-associated infections in the EU.
78. EMA. Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container. www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/04/WC500204724.pdf (ultimo accesso: 27/04/2018).
79. Burdon DW, Whitby JL. Contamination of hospital disinfectants with Pseudomonas species. Br Med J 1967;2:153-5.
80. Heo ST, Kim SJ, Jeong YG et al. Hospital outbreak of Burkholderia stabilis bacteraemia related to contaminated chlorhexidine in haematological malignancy patients with indwelling catheters. J Hosp Infect 2008;70:241-5.
81. Kiedrowski LM, Perisetti A, Loock MH, et al. Disinfection of iPad to reduce contamination with Clostridium difficile and methicillin-resistant Staphylococcus aureus. Am J Infect Control 2013;41:1136-7.
82. Weber DJ, Rutala WA, Sickbert-Bennett EE. Outbreaks associated with contaminated antiseptics and disinfectants. Antimicrob Agents Chemother 2007;51:4217-24.
83. Agencia Española de Medicamentos y Productos Sanitarios (AEMPS). Retirada del mercado del antiséptico de piel sana Bohmclorh solución acuosa 2% de clorhexidina, 250 ml. Notas informativas 2014. www.aemps.gob.es/en/informa/notasInformativas/cosmeticosHigiene/seguridad/2014/COS_02-2014-Bohmclorh.htm (ultimo accesso: 27/04/2018).
84. Royal College of Surgeons. Joint RCS/MHRA Statement on use of topical chlorhexidine for skin preparation prior to surgery. www.rcseng.ac.uk/about-the-rcs/government-relations-and-consultation/joint-rcs-mhra-statement-on-use-of-tropical-chlorhexidine-for-skin-prep (ultimo accesso: 27/04/2018).
85. PAN Germany. Biocides – risks and alternatives. Challenges and perspectives regarding the handling of biocides in the EU, febbraio 2010.
86. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Assessment of the Antibiotic Resistance Effects of Biocides, 2009. http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_021.pdf (ultimo accesso: 27/04/2018).
87. EU-Directorate-General for Employment, Social Affairs and Inclusion. Occupational health and safety risks in the healthcare sector, 2014. https://publications.europa.eu/en/publication-detail/-/publication/b29abboa-f41e-4cb4-b787-4538ac5f0238/language-en (last accessed: 27/04/2018).
88. AIFA. La tracciabilità del farmaco. www.agenziafarmaco.gov.it/content/la-tracciabilità-del-farmaco (latest access: 27/04/2018).