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# Surgical site infections – an updated review of guidelines in the light of new scientific data

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## ABSTRACT

Surgical site infections are important and still more growing burden in 2023. WHO estimated that SSIs are one of the most common and frequent healthcare associated infections (HAI), and in the world's perspective, it can occur up to 10% after surgeries [1]. The knowledge about preliminary and novel ways of diagnosis and treatment and prevention of this disease are important in improving outcomes. Reducing the amount of complications after surgeries is crucial in helping with the recovery and it is an outcome of both proper prehabilitation and safe surgical protocols. Especially focus on the preventive measures for SSI, early diagnosis and aggressive treatment can really improve overall survival, lower the incidence of further complications (including sepsis), and improve patients recovery. This paper summarizes the current guidelines indications as well as their reflection in novel published data.

**KEY WORDS:** surgical wound; postoperative complications; surgical site infection (SSI); surgical wound infection; infection; perioperative care; prehabilitation

## INTRODUCTION

Surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where surgery was performed (most commonly in involves the surgical wound area). SSIs are potential complications associated with any type of surgical procedure. In Europe and the USA, SSIs remain the second most frequent healthcare associated infections [1]. It is estimated that SSIs can correspond up to 20-33% of HAIs [1]. There are many processes, patient- and procedural-related variables that contribute to the development of an SSI. Moreover, there is a significant degree of variation with regard to definitions of SSI. Recently, systematic reviews conducted by the WHO and the CDC have contributed to formulating evidence-based guidelines that allow surgical teams, infection prevention teams as well as hospital and regional managers to devise and implement protocols and policies to effectively address the global problem of SSI. Although SSIs are among the **most preventable HAIs**, they still represent a significant burden in terms of patient morbidity and mortality and additional costs to health systems and service payers worldwide [2].

WHO updated its analysis of the incidence of SSI in low income countries based on published studies between 1995 and 2015, and reported average incidence rates of 5,9 per 100 surgical procedures and 11,2 per 100 surgical patients [3], [4]. In 2018, WHO published new guidelines, reporting pooled incidence of 5,6 per 100 surgical procedures and 11,8 per 100 surgical patients in low- and middle-income countries [1].

The incidence of SSIs is between 0,6-10% worldwide, and its prevalence is about 160 000-300 000/year in the USA [1], [5]–[7].

The most frequent pathogens are usually *Staphylococcus aureus* and *Escherichia coli* [7], [8]. The average methicillin resistance among *S. aureus* is 54,5%, which is of concern when trying to treat some types of SSI [8].

The source of the pathogens that cause most surgical site infections is the endogenous flora of the patient's skin, mucous membranes or hollow viscera [9]. When a mucous membrane or skin is incised, the exposed tissues are at risk for contamination. Microorganisms include: aerobic Gram(+) cocci (e.g. *Staphylococcus aureus*), but may include faecal flora (e.g. anaerobic bacteria and Gram(-) aerobes) when the incision is made near the perineum or groin, or in the colorectal procedures. When a intestine or stomach is opened during an operation, Gram(-) bacilli (e.g. *Escherichia coli*), Gram(+) organisms (e.g. enterococci) and sometimes anaerobes (e.g. *Bacteroides fragilis*) are the typical isolates.

Bacterial contaminants may also enter the wound from exogenous sources, including the air in the operating room, dirty or contaminated instruments, prostheses or other implantable materials, or the surgical team that comes into contact with the wound without proper aseptic measures [9]. The exogenous flora are primarily aerobes, especially Gram(+) organisms (e.g. staphylococci and streptococci). Fungi from endogenous and exogenous sources rarely cause SSI, and their pathogenesis is not yet well understood.

See below for list of common isolates and their antimicrobial resistance (Table 4).

**SYMPTOMS**

Most often and obvious symptoms of SSI include 5 signs of inflammation at the site of surgery:

| Symptom | Latin translation |
|---|---|
| Heat | Calor |
| Pain | Dolor |
| Redness | Rubor |
| Edema/ swelling | Tumor |
| Loss of function | Functio laesa |

Table 1. Five signs of inflammation

In this situation, the loss of function could be considered as delayed healing. Other classic symptoms include signs of cellulitis, palpable abscess in the layers of incision and purulent discharge from the drains or directly from the wound and unpleasant smell.

Most of the symptoms located in the near distance or directly over or under the surgical wound suggest surgical site infection and should be thereafter evaluated using diagnostic criteria (see below) [10]–[14].

**RISK FACTORS**

Patient characteristics and comorbidity play an important role in determining the likelihood of infection after surgery [9], [10], [15]. Length of stay in hospital is, however, probably a surrogate for severity of illness and comorbid conditions requiring adequate work-up or therapy before or after the operation. Minimizing the length of surgery is considered to be one of the **principle** means of preventing infections. Meticulous surgical technique is widely considered to reduce the risk of SSI and includes maintaining effective haemostasis while preserving an adequate blood supply, preventing hypothermia, handling tissues gently, avoiding inadvertent entries into a hollow viscus, removing devitalized tissue, using drains and suture material appropriately and eradicating dead space. Antibiotic prophylaxis has the most evidence to support its use in the prevention of surgical site infection. Appropriate postoperative management of the incision can reduce SSI risk.

Risk factors associated with surgical site infection are listed in Table 2 below.

| Patient-related (intrinsic) risk factors | | | Procedure-related (extrinsic) risk factors | | |
|---|---|---|---|---|---|
| Age | infants; patients > 65yo (i.e. extremes of age) | **Unmodifiable** | Hospital hygiene | Nonadherence to rules of hospital hygiene either patients of the personnel | **Preoperative** |
| History of radiation | | | Hair removal method | inappropriate preoperative shaving | |
| History of SSTIs | prior skin infection may be a marker for inherent differences in host immune function | | Antibiotic prophylaxis | inappropriate antibiotic choice, timing, and weight-based dosing and re-dosing (if necessary) | |
| Comorbidities | DM t.2 (2-3x risk), HF, neoplasm, CRF, obesity | **Modifiable** | Operating team hand hygiene | inadequate surgical team preoperative hand and forearm antisepsis | |
| Obesity | BMI≥30kg/m$^2$ | | Skin antisepsis | Inaccurate surgical site preparation | |
| Hyperglycemia (diabetic and non-diabetic) | Glucose control: Control serum blood glucose levels for **all surgical patients**, including patients without DM. For patients with DM, reduce HbA1c. | | OR environment | inappropriate ventilation (not laminar flow) and cleanliness of environmental surfaces, increased OR traffic | |
| Nutritional status | • Poor nutritional status (malnutrition) increases risk 2,3-4,2-fold<br>• Either cachexia or obesity (see below) | | Designated surgical attire | including masks, caps and shoe covers | **Intraoperative** |
| Cigarette smoking | smoking cessation encouraged within 30d of procedure | | Sterile drapes and scrub suits | inappropriate surgical attire and drapes | |
| Alcohol usage | | | Instruments sterilization | improper sterilization of instruments; non-sterile equipment | |
| ASA scale | >3 points | | Length of surgery | excessive duration of operation | |
| Active infection | coexisting infection at a remote body site | | Length of stay (LOS) | even prolonged preoperative stay | |
| Colonization and carrier status | in particular *S. aureus* colonization (especially MRSA) | | Surgical site contamination | CDC's Surgical wound classification | |
| Altered immune response | immunosupression, systemic steroids | | Glucose control | poor glycemic control | |
| Hypoalbuminemia | although a noted risk factor (<3,5mg/dl), do not delay surgery for use | | Blood loss | and perioperative blood transfusion (blood transfusions increase the risk | |

| | | | | | |
|---|---|---|---|---|---|
| | of total parenteral nutrition (TPN). | | | of SSI by decreasing macrophage function) | |
| Hyperbilirubinemia | total bilirubin >1mg/dl | | Characteristics of the operation | emergency surgery, complexity of the procedure | |
| | | | Operational technique | laparoscopic vs open; poor surgical technique: excessive blood loss, tissue trauma, entry into a hollow viscus, devitalized tissues, presence of surgical drains and suture material, dead space | |
| | | | Hypothermia | and other homeostatic disturbances | |
| Drains | | | | | **Postoperative** |
| | | | Wound surveillance | | |
| | | | Postoperative anaemia | | |
| | | | Postoperative hyperglycemia | glucose levels >200mg/dl in immediate postoperative period ≤48h | |

Table 2. SSI risk factors: patient- and procedure-related (derived and adapted from [5], [9], [10], [13], [16], [17])

Another helpful tool is the CDC surgical wound classification [13]. This guide helps clinicians describe the degree of bacterial contamination of various surgical wounds. Clinicians can use this classification to gauge the risk of potential complications such as SSI in surgical procedures.

Surgical wounds are divided in this classification into four classes based on their cleanliness:

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

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

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

4. Dirty or infected includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

The classification of wound based on their contamination is a prevalent method to predict the risk of SSI [3]. SSI incidence pooled mean (per 100 surgical procedures) according to the wound classification are:
• 5,8% for clean wounds
• 9,5% for clean-contaminated wounds
• 18,9% for contaminated wounds
• 32,7% for dirty wounds

## DIAGNOSIS

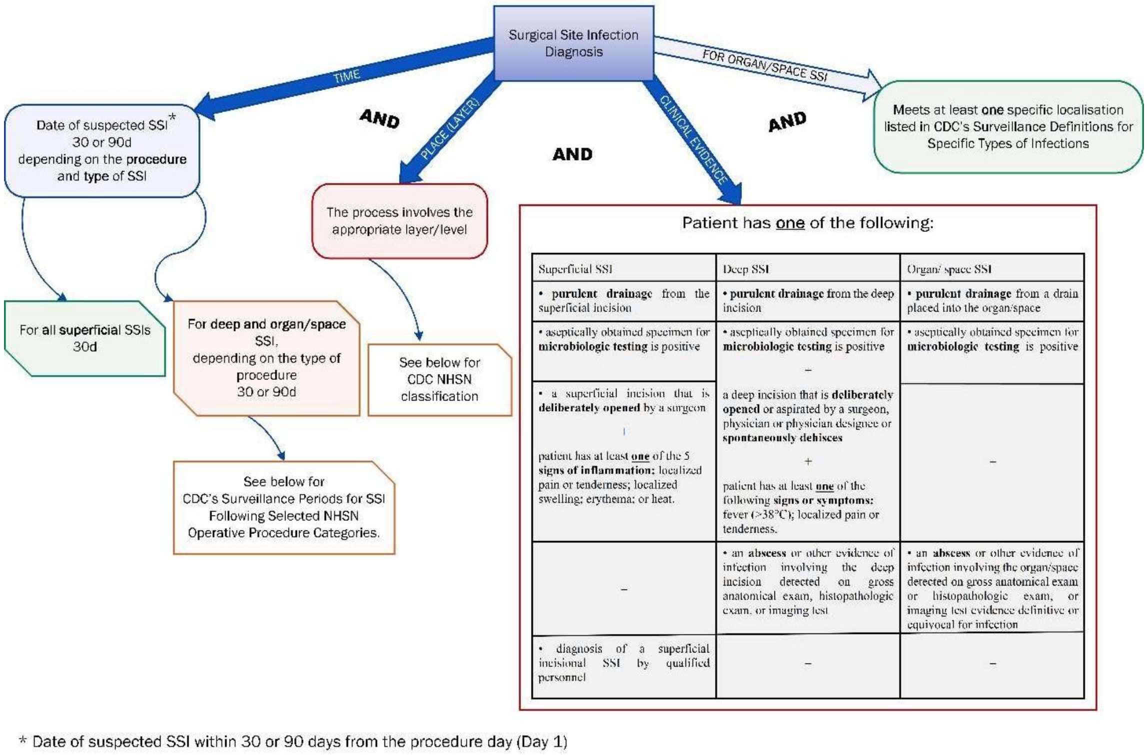


Figure 1. Diagnostic criteria of SSI (reproduced and derived from [11]–[13])

The diagnostic criteria for SSI include [11]–[14]:

• appropriate timing for the event (SSI) – it has to occur within 30 or 90d depending on the type of SSI and surgical procedure (see for CDC's Surveillance Periods for SSI Following Selected NHSN Operative Procedure Categories [12]),

• proper layer of tissues (= type of SSI) to further support the suspicion of an event with right clinical criteria (see below for CDC NHSN classification of SSIs,

• clinical evidence of infection and inflammation of the proper level of surgical wound:

| Superficial SSI | Deep SSI | Organ/ space SSI |
|---|---|---|
| • **purulent drainage** from the superficial incision | • **purulent drainage** from the deep incision | • **purulent drainage** from a drain placed into the organ/space |
| • aseptically obtained specimen for **microbiologic testing** is positive | • aseptically obtained specimen for **microbiologic testing** is positive<br>+ | • aseptically obtained specimen for **microbiologic testing** is positive |
| • a superficial incision that is **deliberately opened** by a surgeon<br>+<br>patient has at least **o ne** of the 5 **signs of inflammation:** localized pain or tenderness; localized swelling; erythema; or heat. | a deep incision that is **deliberately opened** or aspirated by a surgeon, physician or physician designee or **spontaneously dehisces**<br>+<br>patient has at least **o ne** of the following **signs or symptoms:** fever (>38°C); localized pain or tenderness. | – |

| | | |
|---|---|---|
| – | • an **abscess** or other evidence of infection involving the deep incision detected on gross anatomical exam, histopathologic exam, or imaging test | • an **abscess** or other evidence of infection involving the organ/space detected on gross anatomical exam or histopathologic exam, or imaging test evidence definitive or equivocal for infection |
| • diagnosis of a superficial incisional SSI by qualified personnel | – | – |

Table 3. Clinical signs and symptoms needed for diagnosis of SSI (adapted and reproduced from [11], [13])

• in the case of diagnosis of organ/space SSI it has to meets the specified definitions for a correct localized complication listed in CDC's Surveillance Definitions for Specific Types of Infections [12].

Additionally SSIs are stratified by the Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) classification which differentiates SSIs based on layer in which the infection is present [5]. The CDC NHSN classification states as follows [5], [13], [14]:

1. Superficial incisional (involving only skin or subcutaneous tissue of the incision).
2. Deep incisional (involving fascia and/or muscular layers).
   A. Deep incision primary (DIP) - SSI identified in a primary incision in a patient who has had an operation with 1 or more incisions.
   B. Deep incision secondary (DIS) - SSI identified in a secondary incision in a patient who has had an operation with more than 1 incision.
3. Organ/space (involving any part of the body opened or manipulated during the procedure, excluding skin incision, fascia, or muscle layers).

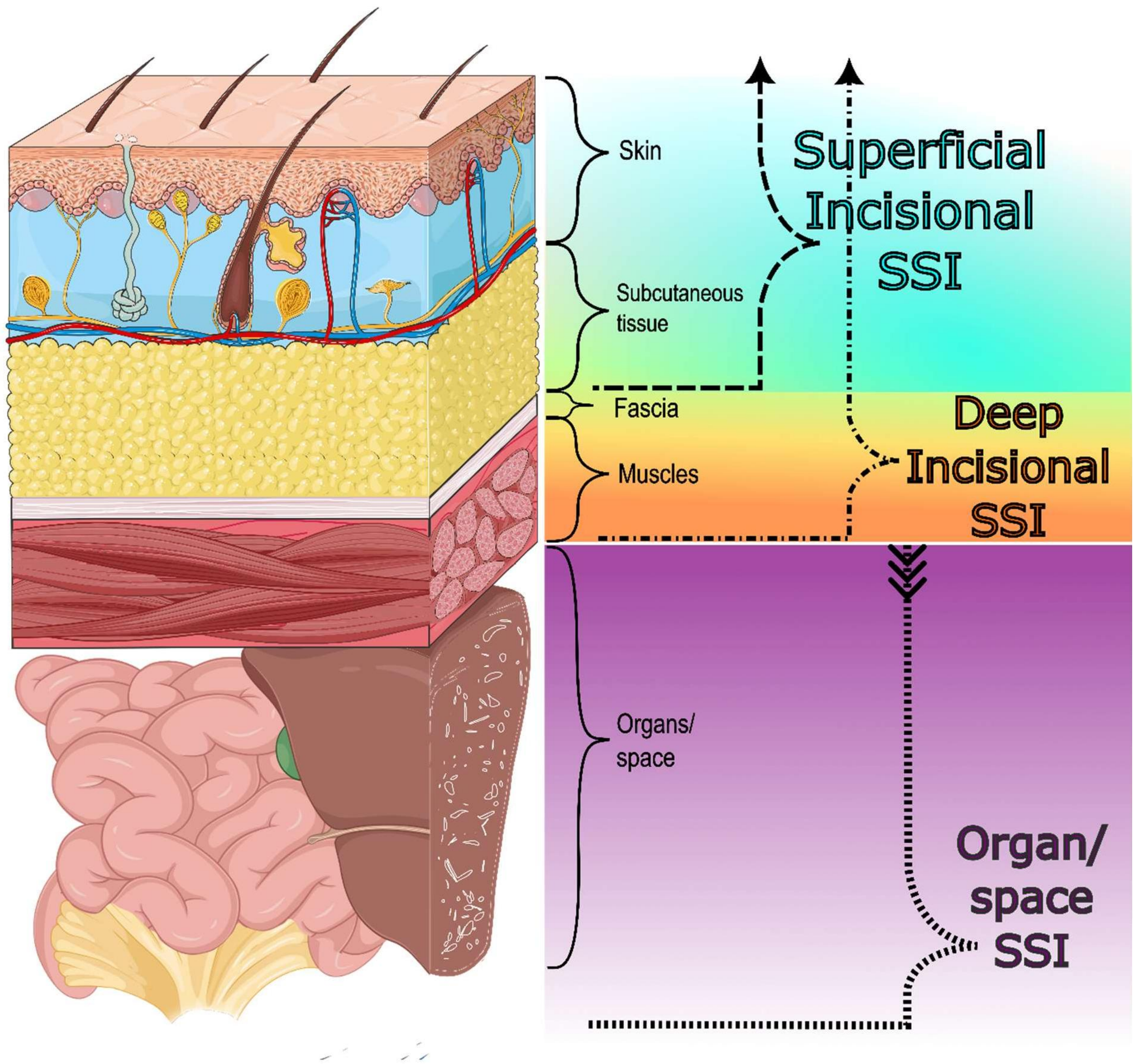


Figure 2. CDC NHSN classification for SSI (reproduced and adapted from [11], [13], [14]). This figure was created using the Servier Medical Art Commons Attribution 3.0 Unported Licence (http://smart.servier.com (accessed 15 January 2023)).

The diagnosis include also the microbial culture from the wound. The most common pathogens causing SSIs are:

| Pathogen | Percent of Occurrence | Antimicrobial agent(s) | resistance to antimicrobials |
|---|---|---|---|
| ***Staphylococcus aureus*** | 30,4% | oxacillin/methicillin | 43,7% |
| **Coagulase (-) *Staphylococci*** | 11,7% | n/a | n/a |
| ***Escherichia coli*** | 9,4% | extended spectrum cephalosporins (cefepime, cefotaxime, ceftazidime, ceftriaxone) | 10,9% |
| | | fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) | 25,3% |

| | | | |
|---|---|---|---|
| | | carbapenems (imipenem, meropenem) | 2% |
| | | multidrug resistance | 1,6% |
| ***Enterococcus faecalis*** | 5,9% | vancomycin | 6,2% |
| ***Pseudomonas aeruginosa*** | 5,5% | aminoglycosides (amikacin, gentamicin, tobramycin) | 6% |
| | | extended spectrum cephalosporins (cefepime, ceftazidime) | 10,2% |
| | | fluoroquinolones (ciprofloxacin, levofloxacin) | 16,9% |
| | | carbapenems (imipenem, meropenem) | 11% |
| | | piperacillin or piperacillin/tazobactam | 6,8% |
| | | multidrug resistance | 5,3% |
| ***Enterobacter* spp.** | 4,0% | extended spectrum cephalosporins (cefepime, cefotaxime, ceftazidime, ceftriaxone) | 27,7% |
| | | carbapenems (imipenem, meropenem) | 2,4% |
| | | multidrug resistance | 1,7% |
| ***Klebsiella* spp.** | 4,0% | extended spectrum cephalosporins (cefepime, cefotaxime, ceftazidime, ceftriaxone) | 13,2% |
| | | carbapenems (imipenem, meropenem) | 7,9% |
| | | multidrug resistance | 6,8% |

Table 4. SSIs etiology (reproduced from [1])

**TREATMENT**

The treatment of SSI consist mainly of antibiotic therapy, wound debridement and pus drainage [14], [18], [19]. The current guidelines (NICE) recommend, when SSI is suspected (presence of cellulitis, either by new infection or an infection caused by treatment failure), to start empirical antibiotic treatment covering the most likely microorganisms [18]. The local resistance patterns as well as antibiograms should be considered and reviewed when choosing an antibiotic. Local antimicrobial stewardship policies should be a valuable guidance [18]. All wounds with SSI should be cleaned, foreign materials removed and pus drained. Patient should be observed because septic shock can develop.

For wound debridement Eusol (chlorinated lime with boric acid) and gauze, dextranomer and enzymatic methods should **not be used** in the management of SSI [18].

**PREVENTION**

The most important measure taken to limit the occurrence of SSIs is perioperative optimization focused on lowering the incidence of risk factors and subsequently preventing the development of SSI. The objective of SSI prevention measures is reducing the cost and improving the quality of surgical care, as well as preventing avoidable deaths.

The methods used for SSI prevention can be divided into 3 groups regarding the period in which they should be administered/ performed:

• preoperative – measures applied to the patient in the time near the surgery, but just before the surgical incision takes place;

• intraoperative – all the methods which are used during the time of surgery;

• postoperative – interventions that focuses on the period after the surgery (it can last even longer than the length of stay after the surgery), it enhances the recovery state of the patient (therefore it's sometimes referred to as recovery period).

The point of many institutions (WHO, ACS, NICE, etc.) preparing and publishing guidelines on SSI and reducing complications of operations, is to improve perioperative care after patients, minimize the burden of HAIs (including one of the most common – which is SSI), reduce the economical and sociological cost of SSI treatment, provide best advice on surgical optimization and prehabilitation of patients and giving them best opportunities to enhance their recovery [1], [5]–[7], [9]–[11], [14], [15], [18], [20]–[24].

There should be sufficient access for both the patients and care-givers for relevant and consistent information regarding SSIs [18]. This should include informing and giving advice on clear and up-to-date methods how to care for the surgical wound after discharge (for patients alike the care-givers), the risks of SSIs, what is being done to reduce them and how they are managed, at last, how to recognize and diagnose SSI, providing contact persons in case of concerns about SSI might be developing. Patients should always be informed after their operation if they have been given antibiotics.

The general recommendations for preventing SSIs include, besides using and getting adequate and updated information, proper quality cleaning and disinfecting either OR equipment and furniture or decontamination and sterilization of instruments, and operative tools (such as wide variety of scope instruments) [1], [9].

1. Preoperative phase

The preoperative measures include reducing the preoperative and patient-related modifiable risk factors: malnutrition, microbial load and carriage, asepsis and antisepsis before incision.

Smoking cessation

ACS/SIS as the only professional society recommended frankly 4-6 weeks of smoking cessation preoperatively to reduce risk of SSI [10], [24]. Other societies incorporated those recommendations in guidelines regarding perioperative care in general (NICE) or safe surgery (WHO) [9], [23].

Recommendation proposed by ACS/SIS applies to all current smokers, especially those undergoing procedures with implantations of foreign bodies [10]. American College of Surgeons support the use of nicotine lozenges, gum, and medications to aid with smoking cessation [10], [24]. Appropriate patient education materials are provided by ACS.

Still more needs to be revealed in terms of evidence of marijuana and electronic cigarette cessation in preventing SSI events – on the experts consensus this should be advised [10].

Mechanical bowel preparation in colorectal surgery

Routine and solitary mechanical bowel preparation does not reduce the risk of SSI, therefore, as the only method it should not be used to prevent SSI events [1], [5], [18]. Combination of preoperative oral antibiotics with mechanical bowel preparation is to be considered a SSI preventive measure in adult patients undergoing elective colorectal surgery [1], [10]. There is evidence for this combination for lowering the rates of SSIs, anastomotic leaks, *Clostridium difficile* infections and postoperative ileus [10]. It reduces LOS and lowers the rate of readmission.

Enhanced nutritional support

World Health Organization guidelines emphasize considering the administration of oral or enteral **multiple nutrient-enhanced nutritional formulas** for preventing SSI events in **underweight** patients who undergo major surgical operations [1]. Quality of evidence for this recommendation is poor, however emerging prehabilitation movement actively encourages for using enhanced nutritional support, both in underweight and in **overweight undernourished** patients [15], [25]. Multiple nutrient-enhanced nutritional formulas contain any combination of arginine, glutamine, omega-3 fatty acids and nucleotides [26]. Malnutrition (in underweight as well as in overweight) reduces function [27]–[31]. Prehabilitation movements widely use enhanced nutritional support as well as immunonutrition to better prepare whole organism for the surgical stress induced by surgical maneuvers [15], [26], [32], [33].

Perioperative discontinuation of immunosuppressive agents WHO recommends to continue immunosuppressive medication prior to surgery, if it was initiated before the surgery as a method of SSI prevention [1]. The quality of evidence for this suggestion is very low, but it is known that surgical stress induces immunosuppression, as well as anaesthesia medications and common surgical states and complications, including hypothermia, hypotension, pain, or blood transfusion [5], [34].

### Nasal decolonization in *S. aureus* carriers

Decolonization with 2% mupirocin ointment whether or not with chlorhexidine gluconate body wash for the prevention of *Staphylococcus aureus* infection in nasal carriers [1], [10]. This recommendation is controversial from several perspectives. The nasal decolonization should be advised and locally determined depending on the type of operation, individual risk factors stratification and potential influence on patient's overall health as well as its microbial status and its effects of the infection itself, and being aware of increased risk of side effects of decolonization in preterm infants, as NICE recommends [18]. UK guidelines published by NICE takes an individual route to consider decolonizing the nasal carriers, however WHO guidelines strongly recommend decolonizing all patients undergoing cardiothoracic and orthopaedic surgery, justifying this recommendation by reminding that *Staphylococcus aureus* is the leading pathogen inducing HAIs (also the most common SSI etiologic factor) which is associated with substantial mortality, as well as the rise of methicillin-resistant strain of *S. aureus* (MRSA) [1], [5], [8], [18]. ACS/SIS guidelines follows same route as proposed by NICE – no standard decolonization protocol, decolonization should be considered individually [10], [24]. WHO besides advise to consider treating all nasal carriers, not only in the settings of cardiothoracic and orthopaedic surgery, who they believe could benefit significantly by this measure. NICE instead suggest decolonization before procedures in which *S. aureus* is a likely cause of a SSI.

NICE advise also to maintain surveillance on antimicrobial resistance for mupirocin and to include this information in antimicrobial stewardship programmes and local antibiotic policies [18]. WHO and ACS/SIS on the other hand emphasize the protocols for screening and isolation of *S. aureus* strains (especially antibiotic resistant ones), while guiding the screening of patients according to the prevalence of microorganisms in the local community, simultaneously WHO is not giving a clear recommendation for screening for *S. aureus* carriage due to the lack of evidence regarding screening as an intervention [1], [10], [24]. WHO suggest aligning these protocols with SSI prevention protocols. ACS/SIS advice to follow the clinical practice guidelines by the American Society of Health-System Pharmacists, who recommend standard screening before total joint replacement and cardiac procedures [10].

### Operation Room (OR) layout

WHO panel suggests that laminar airflow ventilation systems should not be used to reduce the risk of SSI for patients undergoing total arthroplasty surgery [1]. Whereas installation of these systems are mandatory by law in some countries, there is certain shortage of high quality evidence regarding this topic. It may be true, that laminar airflow ventilation reduces the antimicrobial load from the environment during the procedure [35].

### Hygiene of the surgical site

The preoperative measures include patients **bathing** and showering with plain soap or with antimicrobial soap the day before or on the day of surgery [1], [18], [20]. WHO and CDC are clear about this recommendation, NICE however recommends bathing just to reduce the microbial load, not necessarily to prevent SSI, and these UK guidelines suggest using of plain soap since evidence of using antiseptic soap is inconclusive.

NICE, WHO, SCIP, ACS/SIS and other societies recommend **not to remove** any hair from the planned operation site (at any time), but if it is an absolute necessary step, only the single-use electric clippers should be used (since shaving can disrupt the skin barrier, the use of razors increase therefore the risk of SSI) [1], [5], [10], [18], [24], [36]. Several studies have shown that preoperative hair removal by any means is associated with increased surgical site infection rates and have suggested that no hair be removed [9].

### Antibiotic prophylaxis

NICE gives a detailed list when to prescribe antibiotic prophylaxis: involving contaminated, clean-contaminated surgery, and clean surgery with a prosthesis implantation or other implant placed, however it is advised not to use antibiotic prophylaxis for routine clean non-prosthetic uncomplicated surgery [18]. WHO excludes from this list also low-risk elective laparoscopic procedures, which does not require prophylaxis [1].

If surgical antibiotic prophylaxis is indicated, it should be administered within 2 hours before the incision (with consideration of the specific antibiotic pharmacokinetics), WHO advises [1]. Surgical Care Improvement Project (SCIP) advised for up to 1h before incision takes place [5], [36]. NICE and CDC suggest administering the antibiotics intravenously in a **single dose** and disagree on the strict timing boundary proposed by WHO, taking into account specific antibiotic pharmacokinetics, local antibiotic formulary practices and antibiotic stewardship policy and proposes administrating antibiotics at the induction of anaesthesia instead [18], [20].

NICE recommends, if the operation last longer than the half-life of the antibiotic, there should be repeated doses given, according to the duration of the surgery [18]. Other evidence suggest however that antimicrobials should be redosed at intervals of 2 half-lives time from the initial dose in case of lengthy surgical case [5].

If surgery involves dealing with dirty or already infected wound, on the top of antibiotic prophylaxis, the antibiotic treatment should be initiated [18].

ACS/SIS guidelines give really complicated and precise overview on antibiotic prophylaxis of all of the guidelines [10]. ACS/SIS takes an in-between route over most of the guidelines. In short, the recommendations include administering antibiotics when prophylaxis is indicated only (WHO and CDC reminiscence) [1], [10], [20], [24]. Choice of agent should be determined by the type of procedure and possible SSI etiologic factors [5], [10], [24]. Prophylaxis in their view should be given 1h before incision (similarity to SCIP), with an exception of 2h for administering fluoroquinolones or vancomycin (reverberance with NICE and WHO guidelines) [1], [10], [18], [24], [36]. Most accentuation is put on **weight-adjusted dosing** of prophylactic antibiotics. **Re-dosing antibiotics** with update of adequate tissue levels based on agent half-life (resembling NICE suggestions) or **for every 1500ml of blood lost**.

Operation Room (OR) etiquette

UK guidelines suggest patients wear appropriate OR clothing for the procedure and clinical setting, which provides easy access for the operative field and places for other necessary devices. It also places emphasis on the comfort and dignity of such garments [18].

Medical staff should wear proper non-sterile OR clothing in all areas where surgery is performed [10], [18]. ACS/SIS guidelines focus also on usage of disposable bouffant hats and skull caps (if hair, jewelry on the head and neck is covered) [10]. Staff should keep their movements in and out operating area to a minimum (reducing the risk of turbulent airflow and mixing of contaminated and clean air over the surgical site) [18].

The operating team should remove all hand jewelry before operations as well as artificial nails and nail polish [9], [18], [37]. The operating team during the operation must wear sterile gowns in the OR [9], [18].

Operators hand hygiene

Team of operators should wash their hands using proper surgical scrubbing technique in an aqueous antiseptic surgical solution or antimicrobial soap, with single-use brush or pick for nails, until hands and nails are visually clean – before the first surgery of the day, or when hands become soiled [10], [18], [37]. Then, and before next operations hands should be washed by using alcoholic hand rub or antiseptic surgical solution [1], [18], [37]. There's a misunderstanding in using both surgical **handscrubbing** (using antimicrobial soap, or antiseptic solution, brush and/or picks for nails) and surgical **handrubbing** (using alcoholic product), which **should not be combined sequentially**, since the activity of alcohol-based handrubs may be impaired if hands has not completely dried before (usually by washing with water-based products = handscrubbing) [37]. The hands for handrubbing with alcohol should be perfectly clean and dry.

Antiseptic skin preparation

The skin of the surgical site should be prepared with the antiseptic just before the incision. Guidelines suggest for the first choice antiseptic **alcohol-based solutions of chlorhexidine gluconate** [1], [10], [18], [38]; if the surgical site is in the proximity of mucous membranes, aqueous solutions of chlorhexidine gluconate are advised to be used. If chlorhexidine is contraindicated (for example, due to the risk of severe chemical injuries after use of chlorhexidine in preterm babies) NICE recommends alcohol-based solutions of povidone-iodine. Last proposed instance in the guidelines takes in account a situation with both chlorhexidine gluconate and alcohol solutions are unsuitable, the aqueous solution of povidone-iodine is recommended [18].

Surgeon-related elements of preoperative prevention include disinfection of the skin of the patient, which should be performed with alcohol-based chlorhexidine gluconate solutions, with allowing to dry out fully (according to the manufacturers recommendations and indications), WHO as well as ACS/SIS guidelines suggest [1], [10], [24]. This recommendation, from ACS/SIS point-of-view is cautiously advised [10]. The panel of ACS/SIS and researchers of CDC group concluded that more effective solution are alcohol-based ones (as WHO, NICE, etc.) but the chlorhexidine superiority over iodine-containing preparations are not convincing to the researchers [5], [10], [20], [24]. However, the phrasing of recommendations remain the same of NICE suggest, the pressure is put on different points.

### Incise drapes

NICE in its guidelines states that non-iodophor-impregnated drapes may increase the risk of surgery, therefore if the incise drape is required, an iodophor-impregnated drape should be used. If the patient has a history of iodine allergy, the iodophor-impregnated drape is obviously contraindicated [18]. WHO in its guidelines argues that plastic adhesive incise drapes neither with antimicrobial properties nor without should be used for the purpose of preventing SSI (so does CDC) [1], [20]. Very limited knowledge of the topic in and the lack of available evidence caused this disagreement – still more research should be done in proving of concept of either opinions. Anderson et al. argues that incise drapes can be used, but not as a routine strategy of SSI prevention [5].

### Diathermy

If the diathermy is to be used during the case, there should be attention drawed to proper hazard reduction at the surgical site: therefore NICE suggest waiting for evaporating to dry of antiseptic skin preparations and solutions and taking measures to avoid pooling of alcohol-based solutions, since they could ignite after diathermy use [18]. Diathermy on its own doesn't reduce the risk of SSI, according to UK guidelines [18].

2. Intraoperative phase

### Maintaining patient homeostasis

• Most guideline groups agree on the recommendation of **maintaining normothermia** (body temperature>36°C) which is in line with NICE's guideline on hypothermia: prevention and management in adults having surgery [1], [5], [9], [10], [20], [36], [39], [40]. It is advised to use warming devices in the OR and during the surgical procedure for patient body warming for reduction of SSI incidence. This recommendation excludes cardiac surgery patients which can be put in state of refractory hypothermia during procedure [39].

• **Perioperative oxygenation**

WHO suggests that adult patients undergoing general anaesthesia with intubation for surgical procedures should receive an 80% **fraction of inspired oxygen** ($FiO_2$) intraoperatively and, if feasible, in the immediate postoperative period for 2-6h to reduce the risk of SSI [1]. This recommendation is controversial from the number of reasons [5], [36], [39], [41], [42]. WHO claims high $FiO_2$ (about 80%) can provide better oxygenation to already (probably) hypoperfused incision area, which can support some preventive mechanisms including molecular pathways activation and modulation, such as oxidative neutrophil killing [9], [41], [43], [44]. Normal standards for oxygenation include administering oxygen at $FiO_2$=30-35%, which is considered normoxic. Other professional societies and national authorities guidelines approach the problem from a different perspective. Although in the other research trials and meta-analyses this high oxygen concentration showed no increase in mortality and other adverse events, the toxicity of oxygen in high concentrations is known widely [36], [42], [45], [46].

Most UK guidelines (including NICE) suggest maintaining optimal oxygenation during surgery. In particular, giving patients sufficient oxygen during major surgery and in the recovery period to ensure that a **haemoglobin saturation** of more than 95% is maintained [1], [18], [39].

USA professional societies mostly represent the view presented by WHO. ACS and SIS give practically the same recommendations [10], [24]. The administration of supplemental oxygen (with $FiO_2$=80%) is advised **during surgery** and in the **immediate postoperative** period following surgery which was performed under general anaesthesia [10]. CDC however suggest administering increased $FiO_2$ during surgery and after extubation in the immediate postoperative period, **for patients with normal pulmonary function** undergoing general anaesthesia with intubation [20]. This is a strong recommendation with moderate quality of evidence.

There is no clear solution to this issue. From the anesthesiologic point-of-view the lower oxygen concentrations would be more beneficial for the patient, while maintaining oxygenation targeting saturation of $SpO_2$>95%.

• Maintain **adequate perfusion** during surgery. Most of the professional societies suggest the use of goal-directed fluid therapy intraoperatively in maintaining normovolemia (euvolemia) to reduce the risk of SSI [1], [20], [47]. Haemodynamic goals include titration of fluids and inotropic drugs to reach normal or supraoptimal physiological endpoints, such as cardiac output and oxygen delivery index (specially in major, complex or high-risk surgery) [18], [23], [47]. The exact recommendations on fluid therapy are beyond the scope of this article, it is advised to seek additional recommendations, e.g. NICE's guideline on Perioperative care in adults, NICE's guideline on intravenous fluids and cardiac monitoring for adults or NICE's guideline on perioperative care in adults [18], [23], [48].

• **Glucose management and insulin**

World Health Organization as well as NICE advises not to give insulin **routinely** to non-diabetic patients to optimize blood glucose **postoperatively** for prevention of SSI [1], [18]. However, the panel of WHO consultants suggests the use of protocols for **intensive perioperative blood glucose control** for both diabetic and non-diabetic adult patients undergoing surgical procedures in terms of reducing the risk of SSI. It would seem like WHO prepares for a statement with target levels of glucose control either in diabetic or non-diabetic patients, but due to the lack of evidence WHO decided not to formulate a recommendation on the topic of optimal perioperative glucose target levels in both diabetic and non-diabetic adults. In the rationale for the recommendations, it is pointed out that smaller scale studies adapted the protocols in which target glucose level ≤ 110mg/dl with an upper limit level of 110-150mg/dl.

American College of Surgeons working with Surgical Infection Society encourage optimal blood glucose control in all diabetic patient, with clear indication that no definitive evidence exist that lower HbA1c decreases SSI risk [10], [24]. ACS/SIS provide **perioperative target of 110-150mg/dl serum glucose level in all patient**, regardless of diabetic status. For patients undergoing cardiac surgery the target is <180mg/dl. ACS/SIS advise caution though, pointing out that serum glucose levels <110mg/dl are associated with adverse outcomes, episodes of hypoglycemia and do not lower SSI risk [5], [10].

CDC concluded that perioperative glucose control is recommended in all patients as well as indicating a target glycemia <200mg/dl [20].

The number of prehabilitation protocols wondered on proper glycemic perioperative optimization in DM patients and non-diabetics. Their recommendations include HbA1c levels <7,5% for elective procedures (with end-goal of <6,5%), **perioperative glucose level target of 120-160mg/dl**, and a recommendation of early involvement of inpatient glycemic counseling if blood glucose is poorly controlled by the patient [49]. The protocol is applicable for patients undergoing abdominal wall repair, however, more protocols in other types of procedures are developed.

The fact of surgery-induced insulin resistance, even in healthy patients is known for a long time [50]–[53]. It is postulated, that the extent of insulin resistance postoperatively corresponds to surgical stress induced in the procedure.

Wound protector devices

WHO, NICE and ACS/SIS carefully suggests considering the use of wound protector devices in clean-contaminated, contaminated and dirty abdominal surgical procedures for the purpose of reducing the rate of SSI (with very low quality of evidence, implying the need of further high quality studies) [1], [10], [18], [24]. ACS/SIS specifically suggest the usage in open abdominal surgery, with strongest evidence of lowering risk of SSI in elective colorectal and biliary tract procedures [5], [10], [24].

Wound irrigation and intracavity lavage

There have been sufficient evidence **against** the usage of wound irrigation and/or intracavity lavage as a mean to reduce SSI incidence [1], [18]. Some researchers on the other hand found contrary evidence to the topic of wound lavage, but the quality of this evidence is poor [5], [20]. The proposed method of wound lavage call for irrigation of subcutaneous or deep tissues with aequeous iodine preparation [20].

Elective colorectal surgery

In these specific circumstances, ACS/SIS recommends, before closure of the skin changing the gloves (rescrubbing is not recommended), and using new instruments for wound closure [10], [24]. According to this recommendation, ACS/SIS recommends using **double gloving technique**, not only to elective colorectal surgery, but to **all surgical procedures** [10], [24].

Wound closure

Before wound closure antiseptics or antibiotics should not be used in clinical situations [1], [18]. WHO panel agrees with above mentioned statement, but it gives a detailed case in which one antiseptic solution could be used: considering the use of irrigation of the incisional wound with an **aqueous povidone-iodine** solution before closure for the purpose of preventing SSI could be used particularly in clean and clean-contaminated wounds (quality of evidence of that recommendation is low) [1]. In cardiac surgery setting, the gentamicin-collagen implants can be considered to lower the risk of SSI [5], [18].

The sutures should be considered rather than staples in wound closure after cesarean section to reduce the risk of superficial wound dehiscence, which is a risk factor for SSI [18]. The antimicrobial triclosan-coated sutures can reduce risk of SSI, particularly in pediatric surgery [1], [10], [18], [20]. NICE carefully recommends that antimicrobial coated sutures may reduce SSI risk, but this effect could be specific to particular types of surgery, such as abdominal surgery [18]. ACS/SIS gives a strong recommendation in this case, specifying the use of triclosan-coated sutures in clean and clean-contaminated abdominal procedures [10], [24].

The surgical wound after approximation should be covered by an appropriate dressing at the end of operation using non-touch technique [18].

3. Postoperative phase

Antibiotic prophylaxis

The old SCIP guidelines tried to shorten the duration of antibiotic prophylaxis after surgery, which did not show any benefit in terms of reducing SSI incidence [36]. WHO recommend **against** the prolonged antibiotic prophylaxis postoperatively as SSI prevention [1]. The recommendation is strong, with moderate quality of evidence. World Health Organization and Centers for Disease Control and Prevention state also not to continue antibiotic prophylaxis in the presence of wound drains [1], [20].

Drain removal

The drain should be kept for such long time, as clinically indicated [1]. If indications for removing appear, the drain should be taken out. There are no specific recommendations regarding optimal timing in drain removal for the purpose of SSI prevention.

Wound dressing and cleansing

The aseptic non-touch technique is to be used when changing and removing wound dressings. The dressing should not be changed too frequently. The wound can be cleansed by using sterile 0,9% NaCl solution. This solution is advised to be used up to 48h after the surgery [18]. After 48h patients may shower and/or use tap water to cleanse the wound if the surgical wound split apart or has been surgically opened to drain pus [18]. Some articles disagree on changing frequency of the wound dressing, early or delayed wound showering and cleaning [10], [54]. There is however not much evidence on this topic, therefore any conclusions are uncertain.

In the recovery phase (as in the intraoperative period), topical antimicrobial agents should not be used to prevent SSI in wounds healing by primary intention [18], [20]. ACS/SIS give however a different recommendation – that mupirocin topic antibiotic application can decrease SSI risk in comparison with standard wound dressing [10], [24].

WHO suggests considering the use of prophylactic negative pressure wound therapy (pNPWT) in adult patients on primarily closed surgical incisions with high-risk wounds in the prevention of SSI, while taking resources into account [1]. ACS/SIS give a similar recommendation of usage of NPWT over stapled skin in open colorectal and vascular procedures [10], [24].

When a surgical incision is left open at the level of the skin for a few days before it is closed (delayed primary closure), the incision should be packed with sterile moist gauze and covered with a sterile dressing or a hydrofibre dressing [9].

Healing by secondary intention

Healing by secondary intention requires more attention and careful management on the other hand. There should be used an appropriate interactive dressing, for example NPWT dressings [18]. The professional and interdisciplinary counseling needs to be done regarding choosing proper dressings, which also is a recommended step in assisting with healing the wound [18]. In the management of these wounds additional substances are often unnecessary, and NICE guidelines support those statements suggesting not to use Eusol (chlorinated lime with boric acid solution – used for disinfecting wounds, ulcer cleaning), moist cotton gauze or normal gauze or mercuric antiseptic solutions [18].

4. Novel directions in prevention

In colorectal surgery the prophylactic antibiotics can be ineffective due to concerning increase in microbial antibiotic resistance, these microorganism also are responsible for increased rate of SSI [55]–[57]. From a different perspective using antibiotics can disrupt and disturb the delicate gut microbiota inducing harmful interactions [58]. The researchers found that modulating the gut flora using pro-, pre- and synbiotics, rather than "genocide" on the microbiota can impact better healing [59]–[61].

All the time spent in hospital while preparing for surgery increases the risk of falls and its complications, disorientation, infections (including SSI), therefore any shortening of the length of stay (LOS) implicate better prognosis [62].

Modern surgical dressing, including negative pressure wound therapy (NPWT) has gained increasing popularity over the last few years. A reflection of this popularity can be found in guidelines regarding prevention and treatment of SSI, for a reason – NPWT can be used as a complementary therapy to promote healing, or it can be a preventive method to facilitate better outcomes, especially in surgical wounds fraught with high risk of SSI [18], [63]–[67]. For now the value of pNPWT (preventive Negative Pressure Wound Therapy) after some surgical procedures still remains uncertain and more research needs to be done in this matter [66]–[69].

There is ongoing debate whether classic, open surgery is a risk factor for SSI more than laparoscopic and other minimally-invasive methods [70]–[78]. The conclusions are not yet clear above all due to the differences in the risk factors in open surgery patients versus laparoscopic method patients.

## SUMMARY

In conclusion, SSI is a complex surgical complication, and its burden is still a massive problem around the world. Much needs to be done in terms of ensure appropriate prevention. Many of the steps of preventing SSIs are contained within the perioperative medicine optimization programmes, specially prehabilitation strategies and recommendations [15], [49], [79], [80]. Fortunately, prehabilitation and perioperative medicine activities impact the surgical complications rate, including SSI, and their guidelines promote for intensive measures ensuring best recovery for the patients, apart from SSI and other complications. Many of the recommendations still needs to be disseminated and implemented. The most of the work is focused nowadays on preventing SSI rather than on its treatment due to antibiotic resistance emerging and rapidly increasing [81]–[83]. Therefore much effort needs to be focused on implementing abovementioned guidelines and recommendations to standard practice, while much data needs to be collected to provide better evidence for evolving future suggestions and stronger recommendations.

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## ABBREVIATIONS

(-) – negative (e.g. Gram (-) – Gram-negative)

(+) – positive (e.g. Gram(+) – Gram-positive)

ACS – American College of Surgeons

ACS/SIS – American College of Surgeons with Surgical Infection Society

ASA – American Society of Anesthesiologists

CDC – Centers for Disease Control and Prevention

CRF – chronic renal failure

d – day(s)

DM/ DM t.2 – diabetes mellitus/ diabetes mellitus type 2

h – hour(s)

HAI/ HAIs – Healthcare Associated Infection(s)

HbA1c – glycosylated hemoglobin A1c

HF – heart failure

LOS – length of stay

ml – mililiter(s)

MRSA – methicillin-resistant *Staphylococcus aureus*

n/a – not available

NHSN – National Healthcare Safety Network

NICE – National Institute for Health and Care Excellence

NPWT – negative wound pressure therapy

OR – Operation Room/ operating theatre

pNPWT – prophylactic negative wound pressure therapy

SCIP – Surgical Care Improvement Project

spp. – species

SSI/ SSIs – Surgical Site Infection(s)

SSTIs – skin and soft-tissue infections

UK – United Kingdom

USA – the United States of America

WHO – World Health Organization

yo – years old

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