

# Evidence-based Prevention of Surgical Site Infection



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## KEYWORDS

• Surgical site infection • SSI • Enhanced recovery after surgery • SSI bundles

## KEY POINTS

- Despite significant progress in reducing the incidence of surgical site infection, infectious complications remain a challenging and costly complication of surgery.
- There is strong evidence to support the use of mechanical and oral antibiotic bowel preparation in colorectal surgery, smoking cessation before elective surgery, prophylactic antibiotics, chlorhexidine-based skin antisepsis, and maintenance of normothermia throughout the perioperative period. These measures should be strongly considered during development of local surgical site infection reduction bundles.
- Interventions such as surgical caps, use of surgical jackets, preoperative bathing with antibiotic-containing soaps, adhesive surgical barriers, iodine-impregnated adhesive drapes, hyperoxia, and hair removal before surgery have inconsistent levels of evidence to provide strong recommendations for or against their use. Decisions regarding these practices should be deferred to institution and/or surgeon preference using a common-sense approach.

## INTRODUCTION

Surgical site infection (SSI) remains a frequent and challenging complication of surgery. SSI accounts for greater than 20% of all health care–associated infections, rivaling pneumonia as the most common nosocomial infection.<sup>1</sup> SSI affects an estimated 160,000 to 300,000 individuals annually with an associated financial cost that may exceed \$3.5 billion.<sup>2–6</sup> The high morbidity and costs associated with SSI have resulted in a concerted effort to precisely define and study SSI in order to limit infectious complications after surgery.<sup>2</sup>

There has been significant progress in reducing the incidence of SSI through a variety of local and national programs, including the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP).<sup>7–10</sup> Despite this, SSI continues to affect 2% to 5% of all surgical patients.<sup>4</sup> The medical and surgical community

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has responded with high-quality SSI-reduction research, clinical practice guidelines, and development of multifaceted SSI-prevention bundles with encouraging results.<sup>6,9–16</sup> In addition, surgeons have looked to the past and reincorporated older practices as new data have provided insight into the benefits of their use.<sup>7,15–17</sup> With the wide range of available strategies to reduce the risk of SSI, familiarity with the evidence behind their use is desirable.

This article reviews common SSI-reduction strategies and provides an evaluation of the data for their use. It highlights high-quality interventions that are easily incorporated into practice and have been shown to reduce SSI. It also discusses practices that have limited evidence to strongly support or refute their use and encourages these practices to be left to the discretion of the operating surgeon or hospital system.

## DEFINING SURGICAL SITE INFECTION AND WOUND CLASSIFICATIONS

The United States Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) has provided precise criteria and definitions for SSI.<sup>2,18</sup> For the purposes of this article, SSI is defined according to CDC NHSN definitions as infection occurring within or around the surgical site within 30 days of the index procedure or within 90 days of a procedure with implantation of prosthetic material.<sup>2</sup> Further, SSI is subcategorized by the location of infection, including superficial SSI, deep SSI, and organ/space SSI (Table 1).

Wound classification continues to be used to categorize surgical wounds in the literature, although there is some debate regarding its ability to predict development of SSI. Surgical wounds are classified into clean, clean contaminated, contaminated, or dirty/infected, with a presumed higher risk of SSI as the degree of contamination increases. This article focuses primarily on data relating to elective clean and clean-contaminated cases.

## EVIDENCE-BASED REDUCTION OF SURGICAL SITE INFECTION

### *Smoking Cessation*

Up to 50.6 million US adults are actively using tobacco products.<sup>19</sup> Current and former smokers are at increased risk for poor wound healing and development of postoperative complications.<sup>20–24</sup> A meta-analysis of 140 studies comparing smokers with non-smokers in elective surgery showed that the risk of SSI was nearly doubled in active smokers.<sup>20</sup> These findings were similarly shown in patients undergoing elective colorectal surgeries using the ACS-NSQIP database.<sup>21</sup> After adjusting for a variety of SSI risk factors, both current and former smoking was independently associated with an increased risk of SSI (odds ratio [OR], 1.32 and 1.27 respectively). For this reason, smoking cessation before elective surgery is recommended by multiple societies.<sup>6,11,12</sup>

The optimal duration of smoking cessation before elective surgery is unclear. Sorensen and colleagues<sup>22</sup> reported a randomized trial investigating the effect of smoking cessation on the development of SSI after creation of a series of identical wounds. Smokers were compared with a cohort of never-smokers. Active smokers developed wound infections at a rate of 12%. Both never-smokers and smokers who had abstained for 4 weeks had significantly lower rates of SSI compared with active smokers (2% and 1% respectively). The investigators concluded that 1 month of smoking cessation may be sufficient to reduce the development of SSIs.<sup>22</sup>

Another widely cited study has suggested that a 6-week to 8-week time frame preoperatively is desirable.<sup>23</sup> However, smoking cessation on the day of surgery alone may reduce the rate of SSI.<sup>24</sup> When possible, smoking cessation should occur at least

**Table 1**  
**United States Centers for Disease Control and Prevention National Healthcare Safety Network classification of surgical site infection<sup>2</sup>**

Superficial Incisional SSI	<p>The date of event occurs within 30 d after any NHSN operative procedure</p> <p>And</p> <p>Involves only skin and subcutaneous tissue of the incision</p> <p>And</p> <p>The patient has at least 1 of the following:</p> <ol style="list-style-type: none"> <li>1. Purulent drainage from the superficial incision</li> <li>2. An organism is identified from an aseptically obtained specimen from the superficial incision or subcutaneous tissue by a culture-based or non-culture-based microbiological testing method that is performed for purposes of clinical diagnosis or treatment</li> <li>3. Superficial incision that is deliberately opened by a surgeon, physician, or physician designee and culture-based or non-culture-based testing of the superficial incision or subcutaneous tissue is not performed, and the patient has at least 1 of the following signs or symptoms: localized pain or tenderness, localized swelling, erythema, or heat.</li> <li>4. Diagnosis of a superficial incisional SSI by a physician or physician designee</li> </ol>
Deep Incisional SSI	<p>The date of event occurs within 30 or 90 d after the NHSN operative procedure</p> <p>And</p> <p>Involves deep soft tissues of the incision (eg, fascial and muscle layers)</p> <p>And</p> <p>The patient has at least 1 of the following:</p> <ol style="list-style-type: none"> <li>1. Purulent drainage from the deep incision</li> <li>2. Deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, physician, or physician designee</li> </ol> <p>And</p> <p>An organism is identified from the deep soft tissues of the incision by a culture-based or non-culture-based microbiologic testing method that is performed for purposes of clinical diagnosis or treatment</p> <p>And</p> <p>The patient has at least 1 of the following signs or symptoms:</p> <ol style="list-style-type: none"> <li>1. Fever(&gt;38°C); localized pain or tenderness</li> <li>2. An abscess or other evidence of infection involving the deep incision that is detected on gross anatomic or histopathologic examination, or imaging test</li> </ol>
Organ Space SSI	<p>Date of event occurs within 30 or 90 d after the NHSN operative procedure</p> <p>And</p> <p>Involves any part of the body deeper than the fascial/muscle layers that is opened or manipulated during the operative procedure</p> <p>And</p> <p>The patient has at least 1 of the following:</p> <ol style="list-style-type: none"> <li>1. Purulent drainage from a drain that is placed into the organ/space (eg, closed suction drainage system, open drain, T-tube drain, computed tomography-guided drainage)</li> <li>2. An organism identified from fluid or tissue in the organ/space by a culture-based or non-culture-based microbiologic detecting method that is performed for purposes of clinical diagnosis or treatment</li> <li>3. An abscess or other evidence of infection involving the organ/space that is detected on gross anatomic or histopathologic examination, or imaging test evidence suggestive of infection</li> </ol> <p>And</p> <p>Meets at least 1 criterion for a specific organ/space infection site as defined by CDC/NHSN</p>

4 weeks before an elective operation. Given the evidence for SSI reduction and the associated health benefits, smoking cessation should be pursued in all patients before elective surgery.

### ***Perioperative Showering/Bathing***

In an effort to further reduce the incidence of SSI, investigators have evaluated the utility of perioperative bathing/showering with chlorhexidine-based products in an effort to maximally decolonize skin before surgery. In theory, reduction of bacterial colonization would be anticipated to decrease SSI development. However, the effect on SSIs has been variable, with some studies suggesting potential harm.<sup>25–27</sup>

A 2015 meta-analysis of randomized controlled trials (RCTs) showed no significant benefit to preoperative washing with chlorhexidine compared with placebo (relative risk [RR], 0.91; confidence interval [CI], 0.80–1.04).<sup>25</sup> Similarly, compared with bar soap, washing with chlorhexidine did not significantly reduce the incidence of SSI (RR, 1.02; CI, 0.57–1.84). However, data were limited for the comparison with bar soap, and these findings should be interpreted with caution because the largest individual study included in the meta-analysis did find a reduction in SSI.<sup>26</sup> In the trials reporting adverse skin and allergic reactions, the incidence was low (0.0%–0.5%) and was comparable with placebo (0.6%). The meta-analysis advised that there was no clear benefit to the use of preoperative chlorhexidine washing compared with other wash products.

Prabhu and colleagues<sup>27</sup> reviewed 3924 patients undergoing ventral hernia repair in the Americas Hernia Society Quality Collaborative data registry from 2013 to 2016. Patients who received a prehospital chlorhexidine gluconate (CHG) scrub were compared with those who did not receive prehospital CHG scrub. Results of the multivariate regression modeling showed prehospital CHG was associated with an increased risk of SSI (OR, 1.49; CI, 1.05–2.11). These findings persisted after propensity score modeling. The investigators acknowledged that the administration of CHG scrub was not standardized, but suggested that their findings may approximate real-world use of CHG scrub before surgery. The investigators cautioned against indiscriminate use of CHG scrub before surgery without proven benefit, especially in the setting of concern for development of antibiotic-resistant organisms.

These data do not suggest that perioperative hygiene is not an important component of preparation for surgery. Patients should shower/bathe before surgery, as is generally recommended. However, with the current limitations in available data, and no clear benefit to preoperative showering/bathing with chlorhexidine-based products, the authors do not routinely use these products as part of our preoperative preparation of patients.

### ***Bowel Preparation in Elective Colorectal Surgery***

Data regarding the benefits of combined oral antibiotic and mechanical bowel preparation (CBP) in colorectal surgery were in part brought to light by Nichols and colleagues<sup>17</sup> in 1972, who reported a reduction in wound infections with the addition of neomycin-erythromycin base to mechanical bowel preparation (MBP). In the years following, various studies have reported conflicting results regarding the benefits of bowel preparation before colorectal surgery.<sup>7,15,16,28–31</sup> This culminated in a Cochrane Review that reported no significant benefit to MBP in 2011, and resulted in an overall movement away from preoperative bowel preparation.<sup>31</sup> However, through strong evidence provided by large statewide and national datasets, full mechanical and oral antibiotic bowel preparation before elective colorectal surgery has again entered the

mainstream and is currently recommended in clinical practice guidelines by multiple surgical societies.<sup>6,7,13,15,16</sup>

Englesbe and colleagues<sup>7</sup> reported the results of the multi-institution Michigan Surgical Quality Collaborative investigation of bowel preparation in elective open and laparoscopic colectomy. After propensity score matching, CBP was associated with fewer SSIs overall, superficial SSI, and organ space SSI (4.6% vs 12.4%, 2.4% vs 8.6%, and 1.6% vs 4.3% respectively). The rate of *Clostridioides difficile* colitis was similar (1.9% vs 3.0%) in CBP versus MBP. The investigators concluded that there was a strong association with CBP and reduction in SSI, although a causal relationship was unable to be determined given the observational study design.

In 2017, Ohman and colleagues<sup>15</sup> reported the results of implementation of an infection prevention bundle. Use of this bundle decreased the rate of SSI from 19.7% to 8.2%. Patients who received an MBP, plus oral neomycin and Flagyl, had a lower rate of SSI compared with all other forms of bowel preparation (2.7% vs 15.8%). MBP and oral antibiotic-only bowel preparation resulted in similar rates of SSI compared with no bowel preparation. Only CBP was independently associated with a reduction in SSI, which persisted after multivariate analysis (adjusted OR, 0.2; CI, 0.1–0.6).

Similarly, Klinger and colleagues<sup>16</sup> evaluated the effect of bowel preparation on development of SSI in elective colorectal surgery using the 2012 to 2015 ACS-NSQIP data. Use of CBP resulted in a lower proportion of patients developing both superficial and organ space SSI compared with no bowel preparation within 30 days of surgery (OR, 0.39 and OR, 0.56 respectively). Further, MBP was compared with CBP. MBP was associated with an increased proportion of patients developing superficial and organ space SSI compared with CBP (ORs, 2.25 and 1.64 respectively). Anastomotic complications were less frequent in the CBP cohort, with similar rates of *C difficile* colitis between the two groups. Although SSI-prevention bundles and bowel preparation formulations before surgery were not standardized, the investigators concluded with a recommendation in favor of CBP.<sup>16</sup>

The optimal combination of oral antibiotic and mechanical preparation remains unknown. Additional studies are needed to delineate the optimal CBP before elective colorectal surgery. Further, to date there has been no RCT directly comparing CBP with oral antibiotic-only preparation. This omission will be evaluated in the upcoming ORALEV2 study, which is anticipated to be completed in 2022.

With the preponderance of data supporting the use of CBP, the authors are in favor of a combined mechanical and oral antibiotic preparation for all elective colorectal surgery in patients in whom it is safe and feasible.

### Perioperative Surgical Attire

Perioperative surgical attire is an important component of patient and surgical staff safety. However, there are limited data to suggest optimal surgical dress, leaving much of operating room policy regarding surgical attire to be decided by expert consensus.<sup>32</sup> Definitions of appropriate surgical attire have become particularly relevant during periods of personal protective equipment shortage. Surgical attire standards have been tested by the scarcity of resources during the coronavirus disease 2019 (COVID-19) pandemic, causing some investigators to reevaluate the data behind former practices.

The use of disposable bouffant caps versus scrub caps as a way to reduce SSI has been an area of controversy, with strong proponents on either side of the issue. Despite limited data to show benefit to more stringent surgical attire, major medical centers have enacted large-scale changes to surgical attire policy in an effort to reduce SSI.<sup>33,34</sup>

Wills and colleagues<sup>33</sup> completed a retrospective cohort study of all inpatient cases at a single institution comparing no requirement for either bouffant or surgical jacket, the use of surgical jackets only, and mandatory use of both surgical jackets and bouffant with the primary end point of incidence of SSI. There was no significant difference in SSI risk between these 3 groups (1.01% vs 0.99% vs 0.83% respectively) and no significant difference in the secondary outcomes of mortality, postoperative sepsis, or wound dehiscence. These findings suggest that use of bouffant caps and surgical jackets is unlikely to have a meaningful impact on SSI development compared with other high-quality SSI-reduction interventions.

Similarly, Farach and colleagues<sup>34</sup> published the results of a series of strict surgical attire regulations in 2 teaching hospitals across the United States. In total, 6517 patients were analyzed across the 9 months before and after implementation. They reported no difference in the overall rate of SSI in clean and clean-contaminated cases between the two time periods (0.7% vs 0.8%). Multivariate analysis did not find these policies to be independently associated with the risk of SSI. The investigators then calculated that a sample size of 485,154 patients would be needed to appropriately power a future study to detect a 10% decrease in SSI in clean-contaminated cases at their institution, showing the impracticality of attempting to perform a large RCT. This hypothetical study would be associated with a number needed to treat of 1429 patients.

The choice of surgical headwear and its effect on incidence of SSI and contamination of the surgical field have been evaluated in multiple studies.<sup>35–37</sup> A retrospective review of the Americas Hernia Society Quality Collaborative Database performed by Haskins and colleagues<sup>35</sup> evaluated the relationship between the type of surgical hat worn and the development of SSI after hernia repair. Surgeons who had submitted at least 10 patients into the database were surveyed regarding their choice of surgical hat (disposable skull cap, cloth skull cap, cloth bouffant, disposable bouffant with ears exposed, disposable bouffant with ears covered, or other surgical headgear). Sixty-eight surgeons (79.1% of those surveyed) responded, resulting in 6210 cases being available for analysis. Surgeons most commonly wore a disposable skull cap (55.3%) or disposable bouffant (34.8%). The overall incidence of SSI was 4.0% (251 patients). There was no significant difference in the distribution of surgical headwear between cases with and without SSI on univariate analysis. In addition, multivariate logistic regression found that, compared with disposable bouffant with ears covered, surgeon choice of headwear was not independently associated with development of SSI. The investigators concluded that there was no association between the type of surgical hat and the incidence of postoperative wound events following ventral hernia repair and that surgical hats may be chosen at surgeon discretion.

Using data from a previously published prospective RCT, Kothari and colleagues<sup>36</sup> investigated the effect of bouffant and skull caps on SSI rates. A total of 1543 patients were included, encompassing a variety of surgery types, including colorectal, hernia, biliary, and foregut surgery. Sixty-one percent of surgeons wore skull caps and 39% wore bouffant. SSIs occurred more frequently in cases where a bouffant was worn (8.1% with bouffant vs 5.0% with skull cap). When adjusting for type of operation and surgical approach, multivariate modeling did not show skull caps to be an independent risk factor for SSI. Again, surgeon preference was recommended when deciding the optimal headwear for surgery.

Material and microbial analysis of bouffant-style caps has brought into question the presumed benefits of over-the-ear bouffant caps.<sup>37</sup> Markel and colleagues<sup>37</sup> performed a 1-hour mock surgical procedure using both bouffant hats and skull caps, hypothesizing that bouffant-style hats would have similar permeability, particle

transmission, and pore size. Bouffant hats had a significantly higher microbial shed rate, as measured by passive settle plate analysis. Interestingly, no human hair was detected on any of the settle plates following the procedures. Further, bouffant hats had significantly higher median permeability compared with both disposable and cloth skull caps. These findings may in part be explained by the porosity of bouffant caps. Both average pore diameter and maximum pore diameter were significantly larger in bouffant caps compared with skull caps as measured by electron microscopy. The results of this study run contrary to the assumption that disposable bouffant hats provide optimal protection against microbial contamination and provide a mechanistic explanation as to why disposable or cloth skull caps are an acceptable alternative to bouffant caps.

Given the impracticality of performing a definitive RCT regarding these matters and some data to suggest skull caps may provide enhanced protection, the authors recommend using a common-sense approach when creating surgical attire guidelines because flexibility in surgical caps or other surgical attire does not seem to have significant impact on perioperative outcomes. The data suggest that the focus on enforcing specific types of surgical headwear does not play a significant role in SSI. Resources are better used to focus on interventions that have been shown to reduce SSI.

### ***Perioperative Hyperoxia and Supplemental Oxygen***

Increased fraction of inspired oxygenation ( $\text{FiO}_2$ ) has been studied as a method to reduce SSI and is included in many perioperative bundles and organizational guidelines.<sup>6,11,38–41</sup> Hypoxemia is thought to lead to impaired wound healing and may increase the risk of infection. Wound hypoxia can be caused by decreased systemic oxygen delivery or local wound trauma, resulting in interruption of blood flow to the wound. By increasing  $\text{FiO}_2$ , systemic oxygen delivery is increased and may prevent wound hypoxia, thereby reducing the incidence of SSI.

Belda and colleagues<sup>38</sup> randomized 300 patients undergoing elective, open colorectal resection to either 30% or 80%  $\text{FiO}_2$  intraoperatively and for 6 hours postoperatively. Patients underwent similar bowel preparation and antibiotic prophylaxis before surgery. The rate of SSI was 24.4% in the 30%  $\text{FiO}_2$  arm and 14.9% in the 80%  $\text{FiO}_2$  arm. After adjustment for covariates, the use of 80%  $\text{FiO}_2$  remained independently associated with a reduction in SSI (RR, 0.46; CI, 0.22–0.95). The investigators recommended, given the low cost and few risks to the patients, that higher  $\text{FiO}_2$  supplemental oxygen be considered as part of ongoing quality improvement activities.

A meta-analysis of 5 RCTs performed by Qadan and colleagues<sup>39</sup> affirmed the benefits of higher  $\text{FiO}_2$  in the perioperative period. Hyperoxia was associated with an overall reduction in the rate of infection from 12.0% to 9.0%, with a number needed to treat of 33. Considering colorectal procedures specifically, hyperoxia resulted in a larger reduction in SSI (RR, 0.556; CI, 0.383–0.808). Hyperoxia was not associated with a significant increase in pulmonary complications in the included trials. These findings provided further evidence that supplemental oxygenation plays an important role in reducing SSIs and, again, suggested that these effects are particularly noticeable in colorectal procedures.

However, not all studies have shown benefit of hyperoxia. The PROXI trial assessed the effects of hyperoxia on development of SSI as well as pulmonary complications.<sup>40</sup> Meyhoff and colleagues<sup>40</sup> randomized patients undergoing laparotomy to either 80% or 30%  $\text{FiO}_2$  during surgery and for 2 hours postoperatively. Their findings showed no significant difference in SSI rates between the two groups (19.1% in the 80%  $\text{FiO}_2$  arm and 20.1% in 30%  $\text{FiO}_2$  arm; OR, 0.94; CI, 0.72–1.22). Although hyperoxia did not



seem to reduce SSI, it notably did not lead to an increased rate of pulmonary complications. Specifically, atelectasis was identified in 7.9% of high  $\text{FiO}_2$  versus 7.1% of low  $\text{FiO}_2$ , pneumonia in 6% versus 6.3, respiratory failure in 5.5% versus 4.4% (4.4%), and 30-day mortality in 4.4% versus 2.9%.

Although the data regarding the effect of perioperative hyperoxia on SSI have been controversial, it does not seem to cause significant harm to patients.<sup>40,41</sup> As with other measures taken to reduce SSI, it does seem to have more effect on subsets of populations, particularly patients undergoing colorectal surgeries. With the low cost and limited risks to patients, the authors agree with major societies in recommending use of supplemental oxygen in the perioperative period.<sup>6,11,12</sup>

### ***Skin Preparation Before Elective Surgery***

Antiseptic preparation of the skin is foundational to SSI prevention and is routinely performed before elective surgery. There are many commercially available preparations; however, most exist as a combination of povidone-iodine or chlorhexidine and a solubilizing agent. Both the antiseptic and solubilizing agent play an important role in SSI reduction.

Darouiche and colleagues<sup>42</sup> reported a multicenter RCT on the effect of chlorhexidine-alcohol-based versus povidone-iodine-based skin preparation in clean-contaminated cases. All patients received appropriate preoperative intravenous antibiotics and similar proportions received preoperative showering. The overall rate of SSI was significantly lower in the chlorhexidine-alcohol group versus the povidone-iodine cohort (9.5% vs 16.1%, respectively). Specifically, superficial SSI (RR, 0.48) and deep SSI (RR, 0.33) saw a significant reduction; however, there was no difference in organ space infection or sepsis relating to SSI. These differences in overall rate of SSI persisted in a subgroup analysis specifically evaluating intra-abdominal surgery (12.5% vs 20.5% respectively).

A recent meta-analysis comparing chlorhexidine-based versus povidone-iodine-based skin preparation for surgical skin antisepsis has shown similar findings.<sup>43</sup> Specifically, chlorhexidine-based skin preparation was found to be associated with a significant reduction in SSI in clean-contaminated patients (RR, 0.58). Chlorhexidine-based preparation was also superior to povidone-iodine in clean patients (RR, 0.81). Adverse skin reactions occurred at a similar rate between the two skin preparations. The investigators cautiously concluded by suggesting chlorhexidine-based skin antisepsis is superior to povidone-iodine but acknowledged current limitations in the surgical literature and recommended further high-quality studies.

Tuuli and colleagues<sup>44</sup> evaluated the effect of chlorhexidine-alcohol and iodine-alcohol preoperative skin preparation before cesarean delivery on the incidence of wound-related complications. This RCT was performed at a single center with the primary outcome of superficial and deep SSI within 30 days of delivery. A total of 1147 patients were included in the intention-to-treat analysis. Among those with complete follow-up (94.3% of patients), SSI was diagnosed in 23 patients (4.3%) within the chlorhexidine-alcohol group and in 42 patients (7.7%) within the iodine-alcohol group (RR, 0.55). There was no significant difference in hospital readmissions for infection-related complications or hospital length of stay, but patients treated with chlorhexidine-alcohol preparations had significantly fewer office visits for wound complications. These data suggest that chlorhexidine provided a modest improvement in SSI-related outcomes compared with iodine antisepsis even when both skin preparations were alcohol based.

The finding of improved SSI rates in chlorhexidine-based skin preparations has not been replicated in all studies.<sup>45</sup> A nonrandomized, prospective study was performed



by Swenson and colleagues<sup>45</sup> that compared the use of povidone-iodine scrub paint, 2% chlorhexidine/70% isopropyl alcohol, and iodine povacrylex/isopropyl alcohol skin preparations before surgery. The primary outcome was development of SSI at 6 months following the index operation. Each of these preparations was used as the preferred skin preparation modality for all general surgery procedures for a set period of time during the study. A total of 3209 operations were included. SSI rates were the lowest when DuraPrep was the preferred agent (3.9%) compared with Betadine (6.4%) and ChlorPrep (7.1%). Furthermore, their results showed significantly decreased SSI rates when either Betadine or DuraPrep was used (4.8%) compared with ChlorPrep (8.2%). The investigators suggested that iodophor-based compounds may be superior to chlorhexidine in the general surgery population.

Given the preponderance of data suggesting improvement in rates of SSI when chlorhexidine is used, the authors recommend preoperative skin antisepsis with a chlorhexidine-based product as directed by manufacturer instructions in all patients without sensitivity or allergy to chlorhexidine. In addition, we recommend use of an alcohol-based solubilizing agent when available because use of alcohol-based skin preparations may independently improve the overall rate of SSI.<sup>44,45</sup>

In the past, it has been recommended that skin preparations be applied in concentric circles radiating outward from the site of incision.<sup>46</sup> However, some guidelines more recently have suggested that a back-and-forth application may be preferable. At present, there are no compelling data to suggest a superior method of delivering skin antisepsis, whether that is a circular or back-and-forth application. Either preference is acceptable if a complete preparation of the operative site is ensured.

### ***Hair Clipping Before Elective Surgery***

Hair removal before surgery is widely practiced despite recommendations against routine removal. Results of a 2015 meta-analysis and a 2011 Cochrane Review have shown no benefit to hair removal (by clipping or chemical depilation), with preoperative shaving noted to increase the rate of SSI.<sup>47,48</sup> However, because practice patterns regarding hair removal before surgery are unlikely to change, recent studies have attempted to establish noninferiority of clipping.<sup>49</sup>

Kowalski and colleagues<sup>49</sup> reported the results of a noninferiority study comparing clipping with no hair clipping in 1678 elective general surgery operations. In line with previous studies, in the per-protocol analysis, the overall rate of SSI was 6.1% versus 6.3% in the clipped and nonclipped cohorts respectively. Although hair clipping did not reach the prespecified noninferiority limit, the investigators concluded that there is unlikely to be any clinically significant difference in SSI rate with clipping and that the decision to remove hair should be up to surgeon discretion.

An important consideration in the discussion of hair removal is the use of alcohol-based skin preparations. Manufacturers recommend a 3-minute dry time for hairless areas, but up to an hour's dry time for areas with hair. With evidence suggesting that chlorhexidine-alcohol skin antisepsis is superior to povidone-iodine preparations for reducing SSI, hair clipping is likely to remain widely practiced.

If hair removal is desired before surgery, hair should be removed by hair clippers rather than shaving. Care should be taken to avoid unnecessary injury to the surrounding skin, and clipping limited to the potential areas of interest.

### ***Maintenance of Normothermia***

Maintenance of intraoperative normothermia is routinely included in measures to reduce SSI.<sup>6,11,12</sup> It is thought that hypothermia leads to a higher incidence of SSI by way of vasoconstriction, reduced oxygen delivery, as well as impaired tissue

immunity.<sup>50</sup> Early studies in patients undergoing colorectal surgery provided strong evidence for the benefits of maintaining normothermia.<sup>50</sup>

Kurz and colleagues<sup>50</sup> showed the benefits of normothermia in their double-blinded study of colorectal patients who underwent a standardized anesthesia and antibiotic administration and were placed into either the hypothermia (mean temperature, 34.7°C) or normothermia (mean temperature, 36.6°C) groups.<sup>50</sup> Within the hypothermic group, 19% developed SSI, whereas only 6% of normothermia group developed infection. Likewise, the hypothermic group's hospitalization was increased by 2.6 days.

Building on the evidence in favor of normothermia for colorectal patients, other specialties have also sought to identify whether temperature regulation can improve SSI rates universally. Seamon and colleagues<sup>51</sup> performed a retrospective study of all patients with trauma having laparotomy at a level 1 trauma center who survived at least 4 days postoperatively. The primary outcome was diagnosis of SSI within 30 days of surgery. Overall, 36.1% of these patients developed an SSI during the study. Patients who developed infection were found to have a lower mean intraoperative temperature nadir. The investigators determined that a temperature of 35°C was most predictive of SSI development. They also found that a single temperature measurement less than 35°C was an independent risk factor for SSI. These data suggest that the trauma population also benefits from tight temperature control as a means to reduce SSI.

However, temperature regulation and avoidance of intraoperative hypothermia do not seem to affect all populations equally. SSI data and temperature data for ventral hernia repairs were collected between 2005 and 2012 at a single institution.<sup>52</sup> The investigators found the mean temperature nadir to be 35.7°C and this was not associated with SSI (OR, 0.93; CI, 0.778–1.131). Likewise, they found the length of time spent at the temperature nadir did not increase the risk of SSI (OR, 1.471; CI, 0.983–2.203).

Maintenance of normothermia has variable benefit in differing surgical populations; however, it is an easy measure to implement. The authors advocate maintenance of normothermia in all surgical procedures, in agreement with other societies.<sup>6,11,12</sup>

### ***Use of Adhesive Dressings After Skin Preparation***

After appropriate skin cleansing, use of adhesive drapes or iodine-impregnated drapes after skin antisepsis has been theorized to reduce the risk of SSI by preventing wound contamination and bacterial migration. A recent study in patients undergoing open joint-preservation procedures showed a significant reduction in the incidence of bacterial colonization of the surgical incision at the conclusion of the operation when an iodine-impregnated dressing was applied before surgery compared with standard draping (12% vs 27.5% respectively).<sup>53</sup> The investigators did not go on to evaluate subsequent development of SSI, but suggested that reduction of bacterial colonization is desirable in patients undergoing operations with implantable prosthetic joints.

Adhesive drapes have also been investigated in clean and clean-contaminated abdominal surgery. Moores and colleagues<sup>54</sup> reported a nonrandomized comparison of a single surgeon's experience comparing the use of loban (3M, Maplewood, MN) before complex ventral hernia repair with mesh. All patients underwent a standardized perioperative regimen to optimize patient risk factors and received similar preoperative antibiotics. All patients underwent an open retrorectus and/or preperitoneal placement of large-pore polypropylene mesh. The incidence of SSI was 4% and 1% in the draped and nondraped cohorts respectively. The investigators concluded that there was no additional benefit of an iodine-impregnated drape and advised against routine

use of iodine-impregnated drapes in open ventral hernia repairs in the setting of a clean wound.

Similarly, use of the microbial sealant InteguSeal (Kimberly-Clark, Irving, TX) did not reduce the incidence of SSI in elective colorectal surgery.<sup>55</sup> Patients undergoing open or laparoscopic colorectal procedures were randomized to use of a microbial sealant versus standard draping. Preoperative bowel preparation and perioperative care were the same between groups. The overall incidence of SSI was similar with or without microbial sealant (11% vs 16% respectively). No significant differences were noted in the open or laparoscopic subgroups. The investigators concluded that InteguSeal did not show additional SSI-reduction benefit in clean-contaminated colorectal procedures.

A 2015 meta-analysis of 7 RCTs including 4195 patients comparing the use of adhesive drapes concluded that there was added benefit to their use.<sup>56</sup> Specifically, in the 5 RCTs evaluating adhesive drapes without iodine impregnation, the SSIs were increased 13.7% versus 11.2% (RR, 1.23; CI, 1.02–1.48). Two RCTs involving 1113 patients investigating iodine-impregnated adhesive drapes showed no significant difference in SSI rate on pooled analysis (RR, 1.03; CI, 0.66–1.60). The investigator concluded that the available evidence suggests adhesive drapes are unlikely to reduce the rate of SSI and may in some instances increase their risk.

Given the limited evidence for their use in abdominal surgery, the authors do not use adhesive drapes, whether plain or iodine impregnated, as part of our SSI-reduction strategy and therefore recommend that the use of adhesive drapes be left to surgeon preference.

### ***Preoperative Intravenous Antibiotics***

Surgical antibiotic prophylaxis (SAP) is an effective and strongly evidence-supported practice.<sup>57</sup> Parenteral antibiotics should be tailored to the operation performed, and, in all cases, coverage for skin and viscus-specific flora should be considered. Comprehensive guidelines for antibiotic selection before surgery have been provided by multiple societies, including the Infectious Diseases Society of America.<sup>58</sup> Administration of a first-generation or second-generation cephalosporin is generally recommended for patients without allergy or adverse reaction that prohibits use. However, in select cases, specific SAP regimens may be more effective.<sup>58</sup>

Whenever possible, antibiotics should be administered before incision, should take into consideration the patient's weight, and should be redosed to achieve adequate tissue concentrations for prophylaxis.<sup>6,11,58,59</sup> Antibiotic administration within 1 hour of incision is most commonly recommended. This window should be extended in antibiotics such as vancomycin because of prolonged administration times. However, there are conflicting data on the exact time within the 60-minute window during which antibiotics should be given, or whether extending the window to 120 minutes before surgery influences SSI-related outcomes.<sup>57,60–62</sup>

In a prospective observational study of visceral, vascular, and trauma surgeries Weber and colleagues<sup>60</sup> investigated the effect of timing of antibiotic administration on subsequent development of SSI. The investigators reviewed 3836 cases that were predominantly class I wounds. Incisions were followed for a minimum of 30 days. After adjusting for SSI-related risk factors, antibiotic administration within the final 30 minutes before surgery was associated with significant increase in SSI compared with administration between 2 hours and 30 minutes before surgery (OR, 1.66; CI, 1.2–2.3). When subdivided into 15-minute intervals, administration 59 to 45 minutes before surgery was associated with the lowest incidence of SSI. From the results of this study, the investigators suggested prophylaxis be administered between 30 to 60 minutes before surgery.

In a later study, Weber and colleagues<sup>61</sup> randomized 5580 patients undergoing surgery to early versus late administration of antibiotic prophylaxis (in anesthesia room vs in operating room respectively). Median administration time was 42 minutes (interquartile range [IQR], 30–55 minutes) and 16 minutes (IQR, 10–25 minutes) in the early and late administration arms. Overall rate of SSI at 30 days with 88.8% of patients completing follow-up was similar in the 2 groups at 4.9% versus 5.3%. The investigators concluded that their study did not support narrowing the antibiotic administration window.

Multiple additional studies have provided conflicting results on the best timing of antibiotic administration, with each study possessing limitations that prohibit generalized recommendations.<sup>57,60–62</sup> At present, there is no compelling evidence to suggest that any specific time within the 1-hour window is superior to another. The authors continue to recommend antibiotic administration with a 1-hour window as recommended by a variety of medical and surgical societies.

Many surgeons continue antibiotics for 24 hours after clean-contaminated surgeries. However, there is level 1a evidence that prophylactic intravenous antibiotics do not need to be continued after wound closure, because it does not affect subsequent SSI.<sup>63</sup>

## SUMMARY

SSIs continue to be a major source of postoperative morbidity and remain a costly complication of surgery. Accordingly, significant effort has been placed into identifying methods to reduce their incidence. There is strong evidence that oral antibiotics and MBP before colorectal surgery, smoking cessation before any elective surgery, prophylactic intravenous antibiotics, maintenance of normothermia, and chlorhexidine-based skin preparation are effective measures to help reduce SSI and should be strongly considered during development of SSI-reduction strategies. Other interventions, including choice of surgical attire (cap, jackets), hyperoxia, preoperative bathing, hair removal, surgical barriers, and iodine-impregnated drapes, have variable levels of evidence to promote their use or have differing efficacy in specific surgical populations, limiting their generalized use. With regard to these measures, discretion should be left up to individual surgeons or hospital systems when creating local guidelines.

## CLINICS CARE POINT

- There is strong evidence that a mechanical bowel prep with oral antibiotics before colorectal surgery, smoking cessation before any elective surgery, prophylactic intravenous antibiotics, maintenance of normothermia, and alcohol/chlorhexidine based skin preparation are effective measures to prevent SSI.

## DISCLOSURE

The authors have nothing to disclose.

## REFERENCES

1. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014;370(13):1198–208.

2. Centers for Disease Control and Prevention. National healthcare safety network patient safety component manual chapter 9: surgical site infection (SSI) event. Available at: [https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual\\_current.pdf](https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf). Accessed February 26, 2021.
3. Magill SS, O'Leary E, Janelle SJ, et al. Changes in prevalence of health care-associated infections in U.S. hospitals. *N Engl J Med* 2018;379(18):1732–44.
4. Anderson DJ, Podgorny K, Berríos-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35(6):605–27.
5. Scott RD. The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention. Atlanta: Centers for Disease Control and Prevention; 2009. Available at: [http://www.cdc.gov/hai/pdfs/hai/scott\\_costpaper.pdf](http://www.cdc.gov/hai/pdfs/hai/scott_costpaper.pdf). Accessed February 26, 2021.
6. Ban KA, Minei JP, Laronga C, et al. American college of surgeons and surgical infection society: surgical site infection guidelines, 2016 update. *J Am Coll Surg* 2017;224(1):59–74.
7. Englesbe MJ, Brooks L, Kubus J, et al. A statewide assessment of surgical site infection following colectomy: the role of oral antibiotics. *Ann Surg* 2010;252(3):514–9 [discussion: 519–20].
8. Cohen ME, Liu Y, Ko CY, et al. Improved surgical outcomes for ACS NSQIP hospitals over time: evaluation of hospital cohorts with up to 8 years of participation. *Ann Surg* 2016;263(2):267–73.
9. Cima R, Dankbar E, Lovely J, et al. Colorectal surgery surgical site infection reduction program: a national surgical quality improvement program–driven multidisciplinary single-institution experience. *J Am Coll Surg* 2013;216(1):23–33.
10. Weiser MR, Gonen M, Usiak S, et al. Effectiveness of a multidisciplinary patient care bundle for reducing surgical-site infections. *Br J Surg* 2018;105(12):1680–7.
11. Leaper DJ, Edmiston CE. World Health Organization: global guidelines for the prevention of surgical site infection. *J Hosp Infect* 2016;95(2):135–6.
12. Carmichael JC, Keller DS, Baldini G, et al. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American society of colon and rectal surgeons and society of American gastrointestinal and endoscopic surgeons. *Dis Colon Rectum* 2017;60(8):761–84.
13. Migaly J, Bafford AC, Francone TD, et al. The American society of colon and rectal surgeons clinical practice guidelines for the use of bowel preparation in elective colon and rectal surgery. *Dis Colon Rectum* 2019;62(1):3–8.
14. Hoang SC, Klipfel AA, Roth LA, et al. Colon and rectal surgery surgical site infection reduction bundle: to improve is to change. *Am J Surg* 2019;217(1):40–5.
15. Ohman KA, Wan L, Guthrie T, et al. Combination of oral antibiotics and mechanical bowel preparation reduces surgical site infection in colorectal surgery. *J Am Coll Surg* 2017;225(4):465–71.
16. Klinger AL, Green H, Monlezun DJ, et al. The role of bowel preparation in colorectal surgery: results of the 2012–2015 ACS-NSQIP data. *Ann Surg* 2019;269(4):671–7.
17. Nichols RL, Broido P, Condon RE, et al. Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. *Ann Surg* 1973;178(4):453–62.
18. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg* 2017;152(8):784–91.

19. Cornelius ME, Wang TW, Jamal A, et al. Tobacco product use among adults — United States, 2019. *MMWR Morb Mortal Wkly Rep* 2020;69:1736–42.
20. Sorensen LT. Wound healing and infection in surgery, the clinical impact of smoking and smoking cessation: a systematic review and meta-analysis. *Arch Surg* 2012;147(4):373–83.
21. Sharma A, Deeb AP, Iannuzzi JC, et al. Tobacco smoking and postoperative outcomes after colorectal surgery. *Ann Surg* 2013;258(2):296–300.
22. Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. *Ann Surg* 2003;238(1):1–5.
23. Møller AM, Villebro N, Pedersen T, et al. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. *Lancet* 2002;359(9301):114–7.
24. Nolan MB, Martin DP, Thompson R, et al. Association between smoking status, preoperative exhaled carbon monoxide levels, and postoperative surgical site infection in patients undergoing elective surgery. *JAMA Surg* 2017;152(5):476–83.
25. Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. *Cochrane Database Syst Rev* 2015;(2):CD004985.
26. Hayek LJ, Emerson JM. Preoperative whole body disinfection—a controlled clinical study. *J Hosp Infect* 1988;11(Suppl B):15–9.
27. Prabhu AS, Krpata DM, Phillips S, et al. Preoperative chlorhexidine gluconate use can increase risk for surgical site infections after ventral hernia repair. *J Am Coll Surg* 2017;224(3):334–40.
28. Cao F, Li J, Li F. Mechanical bowel preparation for elective colorectal surgery: Updated systematic review and meta-analysis. *Int J Colorectal Dis* 2012;27(6):803–10.
29. Nicholson GA, Finlay IG, Diamant RH, et al. Mechanical bowel preparation does not influence outcomes following colonic cancer resection. *Br J Surg* 2011;98(6):866–71.
30. Hata H, Yamaguchi T, Hasegawa S, et al. Oral and parenteral versus parenteral antibiotic prophylaxis in elective laparoscopic colorectal surgery (JMTO PREV 07-01): a phase 3, multicenter, open-label, randomized trial. *Ann Surg* 2016;263(6):1085–91.
31. Güenaga KF, Matos D, Wille-Jørgensen P. Mechanical bowel preparation for elective colorectal surgery. *Cochrane Database Syst Rev* 2011;2011(9):CD001544.
32. Link T. Guidelines in practice: surgical attire. *AORN J* 2020;111(4):425–39.
33. Wills BW, Smith WR, Arguello AM, et al. Association of surgical jacket and bouffant use with surgical site infection risk. *JAMA Surg* 2020;155(4):323–8.
34. Farach SM, Kelly KN, Farkas RL, et al. Have recent modifications of operating room attire policies decreased surgical site infections? an american college of surgeons NSQIP review of 6,517 patients. *J Am Coll Surg* 2018;226(5):804–13.
35. Haskins IN, Prabhu AS, Krpata DM, et al. Is there an association between surgeon hat type and 30-day wound events following ventral hernia repair? *Hernia* 2017;21(4):495–503.
36. Kothari SN, Anderson MJ, Borgert AJ, et al. Bouffant vs skull cap and impact on surgical site infection: does operating room headwear really matter? *J Am Coll Surg* 2018;227(2):198–202.
37. Markel TA, Gormley T, Greeley D, et al. Hats off: a study of different operating room headgear assessed by environmental quality indicators. *J Am Coll Surg* 2017;225(5):573–81.



38. Belda FJ, Aguilera L, García de la Asunción J, et al. Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. *JAMA* 2005;294(16):2035–42.
39. Qadan M, Akça O, Mahid SS, et al. Perioperative supplemental oxygen therapy and surgical site infection: A meta-analysis of randomized controlled trials. *Arch Surg* 2009;144(4):359–66 [discussion: 366–7].
40. Meyhoff CS, Wetterslev J, Jorgensen LN, et al. Effect of high perioperative oxygen fraction on surgical site infection and pulmonary complications after abdominal surgery: the PROXI randomized clinical trial. *JAMA* 2009;302(14):1543–50.
41. Mattishent K, Thavarajah M, Sinha A, et al. Safety of 80% vs 30–35% fraction of inspired oxygen in patients undergoing surgery: a systematic review and meta-analysis. *Br J Anaesth* 2019;122(3):311–24.
42. 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.
43. Chen S, Chen JW, Guo B, et al. Preoperative antisepsis with chlorhexidine versus povidone-iodine for the prevention of surgical site infection: a systematic review and meta-analysis. *World J Surg* 2020;44(5):1412–24.
44. 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.
45. Swenson BR, Hedrick TL, Metzger R, et al. Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. *Infect Control Hosp Epidemiol* 2009;30(10):964–71.
46. Stonecypher K. Going around in circles: is this the best practice for preparing the skin? *Crit Care Nurs Q* 2009;32(2):94–8.
47. Lefebvre A, Saliou P, Lucet JC, et al. Preoperative hair removal and surgical site infections: Network meta-analysis of randomized controlled trials. *J Hosp Infect* 2015;91(2):100–8.
48. Tanner J, Norrie P, Melen K. Preoperative hair removal to reduce surgical site infection. *Cochrane Database Syst Rev* 2011;11:CD004122.
49. Kowalski TJ, Kothari SN, Mathiason MA, et al. Impact of hair removal on surgical site infection rates: A prospective randomized noninferiority trial. *J Am Coll Surg* 2016;223(5):704–11.
50. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of wound infection and temperature group. *N Engl J Med* 1996;334(19):1209–15.
51. Seamon MJ, Wobb J, Gaughan JP, et al. The effects of intraoperative hypothermia on surgical site infection: an analysis of 524 trauma laparotomies. *Ann Surg* 2012;255(4):789–95.
52. Baucom RB, Phillips SE, Ehrenfeld JM, et al. Association of perioperative hypothermia during colectomy with surgical site infection. *JAMA Surg* 2015;150(6):570–5.
53. Rezapoor M, Tan TL, Maltenfort MG, et al. Incise draping reduces the rate of contamination of the surgical site during hip surgery: a prospective, randomized trial. *J Arthroplasty* 2018;33(6):1891–5.
54. Moores N, Rosenblatt S, Prabhu A, et al. Do iodine-impregnated adhesive surgical drapes reduce surgical site infections during open ventral hernia repair? A comparative analysis. *Am Surg* 2017;83(6):617–22.
55. Doorly M, Choi J, Floyd A, et al. Microbial sealants do not decrease surgical site infection for clean-contaminated colorectal procedures. *Tech Coloproctol* 2015;19(5):281–5.



56. Webster J, Alghamdi A. Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev* 2015;2015(4):CD006353.
57. Bowater RJ, Stirling SA, Lilford RJ. Is antibiotic prophylaxis in surgery a generally effective intervention? Testing a generic hypothesis over a set of meta-analyses. *Ann Surg* 2009;249(4):551–6.
58. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt)* 2013;14(1):73–156.
59. Deierhoi RJ, Dawes LG, Vick C, et al. Choice of intravenous antibiotic prophylaxis for colorectal surgery does matter. *J Am Coll Surg* 2013;217(5):763–9.
60. Weber WP, Marti WR, Zwahlen M, et al. The timing of surgical antimicrobial prophylaxis. *Ann Surg* 2008;247(6):918–26.
61. Weber WP, Mujagic E, Zwahlen M, et al. Timing of surgical antimicrobial prophylaxis: a phase 3 randomised controlled trial. *Lancet Infect Dis* 2017;17(6):605–14.
62. Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992;326(5):281–6.
63. Berrios-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. Erratum in: *JAMA Surg*. 2017 Aug 1;152(8):803. PMID: 28467526.