

# Surgical Site Infection Prevention

## A Review

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**IMPORTANCE** Approximately 0.5% to 3% of patients undergoing surgery will experience infection at or adjacent to the surgical incision site. Compared with patients undergoing surgery who do not have a surgical site infection, those with a surgical site infection are hospitalized approximately 7 to 11 days longer.

**OBSERVATIONS** Most surgical site infections can be prevented if appropriate strategies are implemented. These infections are typically caused when bacteria from the patient's endogenous flora are inoculated into the surgical site at the time of surgery. Development of an infection depends on various factors such as the health of the patient's immune system, presence of foreign material, degree of bacterial wound contamination, and use of antibiotic prophylaxis. Although numerous strategies are recommended by international organizations to decrease surgical site infection, only 6 general strategies are supported by randomized trials. Interventions that are associated with lower rates of infection include avoiding razors for hair removal (4.4% with razors vs 2.5% with clippers); decolonization with intranasal antistaphylococcal agents and antistaphylococcal skin antiseptics for high-risk procedures (0.8% with decolonization vs 2% without); use of chlorhexidine gluconate and alcohol-based skin preparation (4.0% with chlorhexidine gluconate plus alcohol vs 6.5% with povidone iodine plus alcohol); maintaining normothermia with active warming such as warmed intravenous fluids, skin warming, and warm forced air to keep the body temperature warmer than 36 °C (4.7% with active warming vs 13% without); perioperative glycemic control (9.4% with glucose <150 mg/dL vs 16% with glucose >150 mg/dL); and use of negative pressure wound therapy (9.7% with vs 15% without). Guidelines recommend appropriate dosing, timing, and choice of preoperative parenteral antimicrobial prophylaxis.

**CONCLUSIONS AND RELEVANCE** Surgical site infections affect approximately 0.5% to 3% of patients undergoing surgery and are associated with longer hospital stays than patients with no surgical site infections. Avoiding razors for hair removal, maintaining normothermia, use of chlorhexidine gluconate plus alcohol-based skin preparation agents, decolonization with intranasal antistaphylococcal agents and antistaphylococcal skin antiseptics for high-risk procedures, controlling for perioperative glucose concentrations, and using negative pressure wound therapy can reduce the rate of surgical site infections.

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**A** surgical site infection is defined as infection following an operation at an incision site or adjacent to the surgical incision.<sup>1</sup> Infections occur in approximately 0.5% to 3% of patients undergoing surgery<sup>2-4</sup> and are among the most prevalent health care-acquired infections.<sup>5-7</sup> Surgical site infections are responsible for approximately \$3.5 billion to \$10 billion in US health care costs annually.<sup>8,9</sup> Compared with patients without surgical site infections, those with them remain in the hospital approximately 7 to 11 days longer<sup>7,10</sup>; 1 study involving 177 706 postsurgical patients reported that 78% were readmitted as a result of the infection.<sup>11</sup> This review summarizes current evidence-based interventions for prevention of surgical site infection that are applicable to the majority of operations (Box).

## Methods

We searched PubMed, Google Scholar, and the Cochrane database for English-language studies of pathogenesis, clinical presentation, and prevention of surgical site infections published from January 1, 2016, when guidelines were most recently published by the World Health Organization, to September 15, 2022. In addition, we manually searched the references of selected articles for additional relevant publications. We prioritized randomized trials, systematic reviews, meta-analyses, clinical practice guidelines, and articles pertinent to general medical readership. Of 94 studies identified, 69 were included, consisting of 14 randomized trials, 19

systematic reviews, 12 meta-analyses, 4 clinical practice guidelines, 17 cohort studies, and 3 cross-sectional studies.

## Discussion and Observations

### Pathophysiology

Surgical site infection acquisition depends on several factors, namely, exposure to bacteria and the host's ability to control the inevitable bacterial contamination of the incision. They are typically caused by bacteria inoculated into the surgical site at the time of surgery. Approximately 70% to 95% are caused by the patient's endogenous flora.<sup>12</sup> The most common organisms are *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, and *Escherichia coli*.<sup>13</sup> In some patients, introduction of only 100 colony-forming units of bacteria into the surgical site can cause infection.<sup>14</sup> However, exogenous sources of contamination during surgery such as bacteria transmitted from surgical personnel or heater-cooler units can also lead to infections.

Pathogens that cause infection vary by surgical location. The most common pathogens are components of skin flora such as *S aureus* and *Streptococcus* species. In contrast, infections following gastrointestinal procedures are typically associated with enteric organisms such as *Enterococcus* species and *E coli*.<sup>15</sup> Overall, *S aureus* is the most common cause of infection; for example, *S aureus* was associated with 24% of nonsuperficial surgical site infections in a cohort study including 32 community hospitals in the southeastern US.<sup>4</sup> Although methicillin-resistant *S aureus* (MRSA) was previously more likely to cause surgical site infections than methicillin-sensitive *S aureus* (MSSA), the rate of MSSA-derived infections from 2013 to 2018 was higher (0.07 per 100 procedures) than the rate of MRSA infections during the same period (0.05 per 100 procedures).<sup>4</sup> MRSA surgical site infections lead to worse clinical outcomes than those caused by less resistant pathogens.<sup>10</sup> Specifically, compared with MSSA surgical site infections, those due to MRSA were independently associated with 5.5 additional hospital days (95% CI, 1.97-9.11).<sup>10</sup> *E coli* and *Enterococcus* species respectively cause approximately 9.5% and 5.1% of all surgical site infections.<sup>13</sup>

### Factors Associated With Surgical Site Infection

Factors associated with surgical site infection include older age, presence of immunosuppression, obesity, diabetes, effectiveness of antimicrobial prophylaxis, surgical site tissue condition (such as the presence of foreign material), and degree of wound contamination (Table 1 and Table 2). For example, a national study of more than 387 000 patients found that for most surgery types, rates of surgical site infection were increased in patients with obesity.<sup>21</sup> The rates of surgical site infection following mastectomy among 16 473 patients increased with body mass index (BMI), calculated as weight in kilograms divided by height in meters squared. Those with a BMI of 20 to 25 had a surgical site infection rate of 4.66%; BMI of more than 30 to 40, 7.06%; and BMI of more than 40, 10.58%. Similarly, after 29 603 laparoscopic cholecystectomy procedures (urgency not specified), the infection rate increased with BMI: 8.57% with a BMI of 20 to 25; 10.62% with a BMI of 30 to 40; and 17.11% with a BMI of more than 40.

### Box. Commonly Asked Questions

#### How can the generalist clinician help in preventing surgical site infections?

The generalist can help patients improve modifiable characteristics associated with increased risk of surgical site infections, such as helping obese patients lose weight, assisting patients who have diabetes with optimal glucose control, and assisting with smoking cessation.

#### Is there a threshold hemoglobinA<sub>1c</sub> value above which surgical site infections are more common and surgery should be delayed?

Perioperative hyperglycemia in patients with or without diabetes is associated with surgical site infections, and randomized clinical trials support perioperative glucose control as an evidence-based practice to decrease risk of surgical site infection. In contrast, there are no randomized clinical trials that have found a clear association between a specific hemoglobin A<sub>1c</sub> cutoff value and surgical site infections. However, patients with higher hemoglobin A<sub>1c</sub> levels will likely have higher perioperative glucose values and glucose levels that are harder to control.

#### What therapies can prevent a surgical site infection?

Numerous strategies are currently recommended as outlined in this review. Six are supported by randomized clinical trials:

- (1) do not remove hair at the surgical site unless necessary;
- (2) decolonization with intranasal antistaphylococcal agent and antistaphylococcal skin antiseptic prior to high-risk procedures (eg, cardiothoracic, orthopedic);
- (3) use a chlorhexidine gluconate-alcohol antiseptic agent for skin preparation;
- (4) maintain normothermia intraoperatively;
- (5) control perioperative glucose values between 110 and 150 mg/dL;
- and (6) use incisional negative pressure wound dressings.

Some of these risk factors associated with surgical site infection are modifiable, such as hyperglycemia, obesity, and tobacco use. Other factors are nonmodifiable, such as age, which must be considered when deciding on the surgical intervention for the patient.<sup>26,49</sup>

### Clinical Presentation

The median time to diagnosis of surgical site infection varies by procedure.<sup>50</sup> For example, *S aureus* infection is typically diagnosed a median of 14 days after plastic surgery, 24 days after general orthopedic surgery, and 28 days after orthopedic surgery where a prosthetic device was inserted. A surgical site infection is suspected when purulent drainage is present at the incision site or when there is evidence of an abscess involving the surgical bed. Physical examination findings such as systemic signs of infection (eg, fevers, rigors), local erythema, wound dehiscence, pain, nonpurulent drainage, or induration are the most common. However, the presence or absence of these symptoms varies depending on factors such as surgical site, host, and time from surgery to presentation. For example, fevers can be present in 14% of patients with a chronic prosthetic joint infection but up to 75.5% of patients if the etiology of the prosthetic joint infection is hematogenous.<sup>51</sup> Articular effusion and swelling may be present in 29% to 75% of prosthetic joint infections of the knee,<sup>52</sup> and delayed wound healing, wound dehiscence, or wound drainage

Table 1. Modifiable and Nonmodifiable Patient-Related Factors Associated With Surgical Site Infections

Factor	Pathophysiology
<b>Patient-related, modifiable</b>	
Diabetes	Hyperglycemia impairs the innate immune system and promotes glycosylation of proteins, which compromises wound healing. <sup>16</sup> Diabetes can lead to higher perioperative glucose levels and hyperglycemia that is more difficult to treat. <sup>17</sup>
Immunosuppressive medications and conditions	Immunosuppressive clinical conditions or medications diminish the inflammatory phase of wound healing. <sup>18,19</sup>
Malnutrition	Malnutrition can decrease collagen synthesis, granulation formation in surgical wounds, and result in poor tissue healing. Hypoalbuminemia weakens innate immunity by prompting macrophage apoptosis and diminishing macrophage activation. Low albumin also accelerates the seepage of interstitial fluid into the surgical wound and promotes general tissue edema. <sup>20</sup>
Obesity	Adipose tissue has less blood flow, which inhibits the delivery of oxygen and antibiotics. <sup>21-23</sup>
Preoperative infections	Prior to elective surgery, recognize and treat all infections (even if they are distant from the surgical site). <sup>24</sup>
Tobacco use	Tobacco use causes vasoconstriction, which can progress to alterations in collagen metabolism, decreased inflammatory response, and relative ischemia. <sup>25</sup>
<b>Patient-related, nonmodifiable</b>	
Age	The skin's basement membrane and dermis thin with increasing age, and the skin loses its reserve of cutaneous blood vessels and nerves that diminish wound healing. <sup>26,27</sup>
History of prior skin and soft tissue infections	A history of skin and soft tissue infections may be indicative of issues with inherent immunity and propensity for infection. <sup>28</sup>
History of radiation therapy	Treatment with radiation induces underlying tissue injury and inhibits wound healing.

Table 2. Modifiable Operation-Related Factors Associated With Surgical Site Infections

Factor	Pathophysiology
Airborne contamination	Raising the amount of microorganisms in the operating room environment provides additional opportunity for surgical site infection. Most of the airborne pathogens are generated by persons in the operating room and their movements. <sup>29,30</sup>
Anticoagulation	Anticoagulants may generate continual oozing of the incision and slow wound healing. <sup>31</sup>
Blood transfusions	Blood transfusions impair macrophage activity and influence infection risk. <sup>32</sup>
Decreased tissue oxygenation	Diminished tissue oxygenation lends itself to decreased oxidative killing by neutrophils and impaired tissue healing from depleted epithelialization, neovascularization, and collagen formation. Low oxygen settings can curtail the efficacy of perioperative antibiotics. <sup>33,34</sup>
Foreign material	Foreign material stimulates inflammation at the surgical site and raises the risk of surgical site infection. <sup>35,36</sup>
Operation length	Longer operative time is associated with higher damage to wound cells, wound contamination, and exposure to the outside environment. <sup>37</sup>
Perioperative hypothermia	Perioperative hypothermia weakens immune system protection against surgical wound contamination: vasoconstriction leads to impaired tissue perfusion and less access for key immune cells, less motility of key immune cells, and decreased scar formation. <sup>38</sup>
Postoperative hyperglycemia	Cellular functions of bactericidal activity, leukocyte adherence chemotaxis, and phagocytosis are enhanced by insulin and glycemic control, suggesting a direct relation between elevated blood glucose and cellular function deficits. <sup>39</sup> This relationship is observed in patients with and without a diagnosis of diabetes.
Surgical technique	Wound healing is decreased by leaving behind devitalized tissues, inadvertent entry into hollow viscera, inadequate blood supply maintenance, rough manipulation of tissue, misplaced drains and sutures, and unsuitable postoperative wound care. <sup>40</sup>
Wound care	Wounds that remain uncovered following surgery can be contaminated, or uncontrolled drainage can diminish the integrity of the surrounding skin. <sup>41,42</sup>
Wound contamination from patient's own flora	Wound classification delineates the degree of contamination of a surgical wound at the time of the operation. <sup>43</sup> Skin preparation and perioperative antibiotic administration reduce but do not eliminate the introduction of microorganisms at the surgical site. <sup>44,45</sup> Shaving leads to microscopic cuts in the skin that can become niduses for bacteria to multiply. <sup>40</sup> Without appropriate drapes and barrier devices, bacteria from hair follicles and deeper skin layers can recolonize the surgical site.
Wound contamination from operating room personnel	Transition of microorganisms from the surgical personnel's shoes, mouths, or body can contaminate surgical wounds. <sup>14</sup> Microorganisms from the hands of health care workers in the operating room can move onto the patient and operating field if personnel do not perform appropriate handwashing or gloving. <sup>14,46,47</sup>
Wound contamination from surgical instruments	Sterilization eliminates all microorganisms on the surfaces of surgical instruments. Using insufficiently sterilized tools can lead to pathogen transmission. <sup>48</sup>

may accompany up to 44% of prosthetic joint infections.<sup>53,54</sup> The presence of a sinus tract or purulent drainage has a specificity of between 97% and 100% and a positive predictive value of

100%.<sup>55</sup> Joint stiffness has a reported sensitivity of 20.5% and specificity of 99% in patients with a hematogenous source of prosthetic joint infection.<sup>56</sup> Many of the aforementioned

Table 3. Surgical Site Infection Prevention Strategies From Prospective Studies

Intervention	Type of studies	Absolute or median value	RR or OR (P value)
<b>Preoperative</b>			
Do not remove hair at the surgical site unless the presence of hair will affect the procedure <sup>a</sup>	Meta-analysis of 19 RCTs and 6 quasi-randomized trials <sup>59</sup>	<ul style="list-style-type: none"> <li>Razor vs clippers: 4.4% (84 of 1889) vs 2.5% (46 of 1834)</li> <li>Razor vs depilatory cream: 7.8% (68 of 868) vs 3.6% (26 of 725)</li> <li>Razor vs none: 4.2% (34 of 819) vs 2.1% (19 of 887)</li> </ul>	<ul style="list-style-type: none"> <li>RR, 1.64 (.005)</li> <li>RR, 2.28 (.02)</li> <li>RR, 1.82 (.03)</li> </ul>
Decolonize surgical patients with intranasal antistaphylococcal agent and antistaphylococcal skin antiseptic for high-risk procedures (eg, cardiothoracic, orthopedic) <sup>b</sup>	Meta-analysis of 5 RCTs and 12 observational studies <sup>60</sup>	Decolonization vs none: 0.8% (52 of 19 940) vs 2.0% (253 of 12 790)	RR, 0.41 (<.001)
Antimicrobial prophylaxis within 1 h of incision with weight-based antimicrobial agents selected based on most common pathogens for specific procedure <sup>61,62c</sup>	Cohort <sup>61</sup>	<ul style="list-style-type: none"> <li>Administration within 30 min before incision vs 30-60 min before incision: 1.6% (22 of 1339) vs 2.4% (38 of 1558)</li> <li>Administration within 30 min before incision vs after incision: 1.6% (22 of 1339) vs 5.2% (9 of 174)</li> </ul>	<ul style="list-style-type: none"> <li>OR, 0.67 (.13)</li> <li>OR, 3.27 (.003)</li> </ul>
Use a checklist based on the World Health Organization 19-item surgical checklist to ensure adherence to best practices <sup>63,64</sup>	Multicenter, quasi-experimental study <sup>65</sup>	Without vs with checklist: 6.2% vs 3.4%	RR, 0.55 (<.001)
<b>Intraoperative</b>			
Using chlorhexidine gluconate and alcohol-containing skin preparatory agent in combination <sup>d</sup>	Meta-analysis of 4 RCTs <sup>66</sup>	Chlorhexidine gluconate + alcohol vs povidone iodine + alcohol: 4.0% (54 of 1337) vs 6.5% (86 of 1326)	RR, 0.62 (.005)
Maintain normothermia during the surgical procedure	Systematic review of 3 RCTs <sup>67</sup>	Hypothermia vs normothermia: 4.7% (14 of 299) vs 13% (37 of 290)	RR, 3.67 (.008)
<b>Postoperative</b>			
Maintain and monitor blood glucose levels regardless of diabetes status Maintain blood glucose values between 110 and 150 mg/dL	Meta-analysis of 15 RCTs <sup>68</sup>	Glycemic control (<150 mg/dL) vs conventional control (>150 mg/dL): 9.4% (231 of 2464) vs 16% (392 of 2488)	RR, 0.59 (<.001)
Application of incisional negative pressure wound dressings	Meta-analysis of 23 RCTs <sup>69</sup>	Incisional negative pressure wound therapy vs standard dressings: 9.7% (124 of 1279) vs 15% (191 of 1268)	RR, 0.67 (<.001)

Abbreviations: OR, odds ratio; RCT, randomized clinical trial; RR, relative risk.

SI conversion factor: To convert glucose from mg/dL to mmol/L, multiply by 0.0555.

<sup>a</sup> If hair removal is necessary, remove outside of the operating room. For male genitalia, 1 RCT suggested that preoperative hair removal on scrotal skin using a razor as opposed to clippers resulted in less skin trauma without an increased risk in surgical site infection.<sup>70</sup>

<sup>b</sup> Antistaphylococcal skin antiseptic agents include chlorhexidine gluconate baths or wipes or dilute bleach baths.

<sup>c</sup> Two hours are allowed for vancomycin and fluoroquinolones; redose antimicrobials for procedures with excessive blood loss and lengthy surgeries.

<sup>d</sup> Alcohol containing skin preparation products are contraindicated for some procedures (eg, mucosa, cornea, or ear).

presentations may overlap with noninfectious conditions, such as a hematoma, seroma, or stitch abscess at points of suture penetration.

### Classification of Surgical Site Infection

Despite variable presentations of surgical site infections, the US Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) and the National Surgical Quality Improvement Program (NSQIP) provide specific surgical site infection definitions for surveillance and epidemiological purposes.<sup>57,58</sup> Surveillance consists of systematic monitoring of patients following surgery to detect variance in surgical site infection rates and to develop quality improvement initiatives to lower infection rates. The goal of these definitions is to be simple and objective but flexible enough to encompass clinically relevant

infections. Both NHSN and NSQIP categorize surgical site infections into 3 groups: superficial-incisional (involving the skin or subcutaneous tissue layers of the incision), deep-incisional (involving muscle or connective tissue layers of the incision), and organs/spaces deep to the incision. Surveillance for surgical site infections continues for 30 days for most procedures and 90 days for specific procedures involving implanted materials. The NHSN collects data on all NHSN-eligible procedures, and NSQIP analyzes a subsample of 20% of cases for analysis via an 8-day systematic sampling cycle.

### Prevention

#### Preoperative Period

A recent meta-analysis including 19 randomized and 6 quasi-randomized trials involving 8919 patients evaluated various ap-

proaches to preoperative hair removal for reducing surgical site infection (Table 3).<sup>59</sup> Across 7 randomized clinical trials (RCTs), hair removal with a razor was associated with a higher rate of surgical site infection: 4.4% (84 of 1889) patients whose hair was removed with a razor experienced an infection vs 2.5% (46 of 1834) whose hair was removed with clippers experienced an infection (relative risk [RR], 1.64 [95% CI, 1.16-2.33],  $P = .005$ ). Across 9 RCTs, hair removal with a razor was associated with a higher rate of surgical site infection: 7.8% (68 of 868) patients vs 3.6% (26 of 725) patients whose hair was removed with a depilatory cream (RR, 2.28 [95% CI, 1.12-4.65];  $P = .02$ ). Seven RCTs demonstrated that removing hair with a razor was associated with an increased risk of surgical site infection: 4.2% (34 of 819) patients vs 2.1% (19 of 887) patients whose hair was not removed at all (RR, 1.82 [95% CI, 1.05-3.14];  $P = .03$ ).<sup>59</sup> Three RCTs reported that hair removal with clippers did not increase the risk of surgical site infection: 5.7% (49 of 863) patients vs 6.0% (52 of 870) patients whose hair was not removed (RR, 0.95 [95% CI, 0.65-1.39];  $P = .80$ ). If hair removal is necessary, it should be removed in the preoperative holding area and not in the operating room.

One method used to reduce surgical site infections is decolonization, in which patients are treated with an intranasal antimicrobial, skin antiseptic agent, or both to eliminate or temporarily reduce *S aureus* colonization prior to surgery. Evidence to support this recommendation is strongest for high-risk surgical procedures such as cardiothoracic surgeries and prosthetic joint replacement. This process typically includes an intranasal treatment with an antistaphylococcal agent (eg, mupirocin ointment or povidone iodine) and/or application of an antistaphylococcal skin antiseptic agent (eg, chlorhexidine gluconate solution or wipes) for 5 days. However, the precise timing, agent, and frequency of application are unclear because trials addressing this issue have used different strategies. The decolonization strategy should be completed as close to the surgical procedure as possible. A meta-analysis that included 5 RCTs and 12 observational studies showed that nasal decolonization was associated with lower rates of surgical site infections caused by gram-positive bacteria than no decolonization: 0.8% (152 of 19 940) vs 2.0% (253 of 12 790; RR, 0.41 [95% CI, 0.30-0.55];  $P < .001$ ).<sup>60</sup>

This association persisted among the 11 studies in which patients were decolonized regardless of *S aureus* colonization status (RR, 0.40; 95% CI, 0.29-0.55) and among the 6 studies in which nasal decolonization was combined with skin antiseptics (RR, 0.29; 95% CI, 0.19-0.44, primary data not provided).<sup>60</sup> In contrast, other trials that included a more heterogeneous group of surgeries did not find a difference in surgical site infection incidence with decolonization.<sup>71</sup> For example, a prospective cohort study that included 8 surgical categories (abdominal, orthopedic, urological, neurological, cardiovascular, thoracic, and plastic surgery and solid organ transplant) found that decolonization strategies did not reduce MRSA surgical site infections.<sup>72</sup> The authors identified 60 MRSA infections (0.55%) among 10 910 procedures in the control group compared with 70 MRSA infections (0.65%) among 10 844 procedures during the intervention period ( $P = .29$ ). As a result, decolonization is typically focused on orthopedic, cardiothoracic, or high-risk procedures such as spine and brain surgeries.

The intervention requires a significant amount of coordination to perform the appropriate test prior to surgery, have the result reviewed, and ensure the appropriate decolonization

approach was applied. Given the number of steps required, some hospitals perform decolonization on all patients undergoing high-risk surgical procedures, an approach that may ultimately be cost-effective (estimated \$153 per person) based on modeling studies.<sup>73</sup> In contrast, widespread use of antistaphylococcal antibiotics such as mupirocin may ultimately increase rates of resistant *S aureus* infections.<sup>74,75</sup>

Conducting RCTs for surgical site infection prevention is challenging given the relatively low incidence of the outcome of interest. Thus, additional prevention strategies in the preoperative setting exist, but lack high-quality evidence. As a result, these interventions are predicated on expert opinion and results from retrospective cohort studies. For example, in contrast to postoperative glucose control, no RCTs have found a clear association between a specific hemoglobin A<sub>1c</sub> cutoff and surgical site infections.

The administration of antibiotic prophylaxis is recommended in all surgical site infection prevention guidelines, despite the absence of RCTs.<sup>14,17,76,77</sup> One multicenter cohort study involving 4186 patients found that risk of infection increased as the time from antibiotic infusion to incision increased, although the trend was not statistically significant: administration within 30 minutes prior to incision was associated with a risk of 1.6% (22 of 1339) vs 2.4% (38 of 1558) with administration of antibiotic between 31 and 60 minutes before surgery ( $P = .13$ ).<sup>61</sup> In the absence of trial data, guideline consensus is that antibiotics should be given within 60 minutes of the incision to maximize tissue concentration of the antibiotic. Additional recommendations include dosing antibiotics according to the patient's weight to ensure that adequate tissue concentrations are achieved and administering subsequent doses of antibiotics for lengthy procedures if excessive bleeding occurs. For example, cefazolin, the most commonly used agent for antimicrobial prophylaxis, should be redosed every 4 hours until completion of the procedure. These recommendations are mainly based on older cohort studies and evaluation of secondary outcomes (eg, tissue concentrations of antibiotics).<sup>62</sup> Although the optimal duration of prophylactic antibiotics is not known, prolonged antimicrobial prophylaxis is increasingly associated with patient harm, such as acute kidney injury.<sup>78</sup> Authors of a systematic review of 28 randomized trials involving 9478 patients receiving either a single dose for prophylaxis or multiple doses concluded that additional doses did not reduce the risk of infection 6.2% (278 of 4499) vs 5.9% (261 of 4440; OR, 1.06 [95% CI, 0.89-1.25]).<sup>79</sup> Thus, guidelines recommend stopping antibiotic prophylactic antibiotics when the surgical wound is closed.

The WHO's surgical safety checklist is a 19-item list to improve adherence with best practice and decrease surgical site infection incidence. WHO developed this safety checklist to promote more consistent implementation of best practices. This 19-item checklist included surgical site infection (eg, antimicrobial prophylaxis) and non-surgical site infection components (eg, surgical time-out). A multicenter, quasi-experimental study of 8 sites and 3733 patients showed that the infection rate prior to the implementation of the checklist was 6.2% compared with 3.4% after implementation of the checklist ( $P$  value  $< .001$  for the risk difference).<sup>65</sup> These results have been supported by subsequent multi- and single-center prospective studies.<sup>63,64</sup> However, the exact mechanism of improvement is unclear and most likely multifactorial.



### Intraoperative

Topical alcohol is highly bactericidal but does not have persistent activity when used as monotherapy for skin antisepsis (Table 3). Multiple guidelines recommend that surgical site antisepsis should be performed with a product that contains alcohol and another antiseptic agent (eg, chlorhexidine gluconate or povidone iodine).<sup>17,76,80</sup> Products that combine alcohol and antiseptic agents are available in the US. Chlorhexidine gluconate plus alcohol appears to be superior to povidone iodine plus alcohol for the prevention of surgical site infections.<sup>81</sup> In a meta-analysis of data from 4 RCTs involving 6916 women who had cesarean deliveries, the authors concluded that surgical site preparation with chlorhexidine gluconate plus alcohol was associated with lower rates of infection than preparation with povidone iodine plus alcohol: 4.0% (54 of 1337) vs 6.5% (86 of 1326; RR, 0.62 [95% CI, 0.45-0.87];  $P = .005$ ).<sup>66</sup> Similarly, a meta-analysis of 20 RCTs and 5 prospective, 4 retrospective, and 1 ambispective studies, including more than 29 000 participants found that skin preparation with chlorhexidine gluconate was associated with fewer surgical site infections than povidone iodine: 4.8% (725 of 15 263) vs 6.7% (925 of 13 743; RR, 0.65 [95% CI, 0.55-0.77];  $P < .001$ ).<sup>82</sup>

Normothermia to keep core body temperatures from dropping during surgery is maintained by combinations of forced warm air, skin warming, and warmed intravenous fluids (Table 2). Targets for core temperatures vary: more than 35.5 °C and more than 36 °C. A systematic review of 3 RCTs examining active body surfacing warm systems for preventing complications of inadvertent perioperative hypothermia in adults found that using a forced air warming device was associated with lower rates of the risk of surgical site infection than no forced air warming: 4.7% (14 of 299) vs 13% (37 of 290; RR, 0.36 [95% CI, 0.20-0.66];  $P = .008$ ; Table 3).<sup>67</sup>

### Postoperative

Although there are no RCTs that have evaluated intensive glucose control to lower the preoperative average glucose (hemoglobin A<sub>1c</sub>) vs usual care before surgery, postoperative hyperglycemia was associated with an increased risk of surgical site infections in patients with and without diabetes (Table 3).<sup>48,83,84</sup> As a result, strategies to prevent hyperglycemia to prevent surgical site infection are recommended in all major guidelines. Most data to support this strategy are from RCTs involving patients with diabetes. In a meta-analysis of 15 RCTs comparing the use of tight glycemic control (<150 mg/dL; 8.32 mmol/L) with conventional control (>150 mg/dL), tight control was associated with lower rates of surgical site infection: 9.4% (231 of 2464) vs 16% (392 of 2488; RR, 0.59 [95% CI, 0.50-0.68];  $P < .001$ ).<sup>68</sup>

Incisional negative pressure wound therapy, defined as wound dressing systems that continuously or intermittently apply subatmospheric pressure to the system, can reduce the risk of surgical site infection by promoting reducing fluid accumulation in the wounds, thereby accelerating primary wound healing. Authors of a meta-analysis of 23 RCTs involving 2547 patients undergoing various surgical procedures (eg, abdominal, cesarean delivery, orthopedic, vascular) concluded that use of incisional negative pressure wound therapy for primary wound closure was associated with lower rates of surgical site infection than use of standard dressings: 9.7% (124 of 1279) vs 15% (191 of 1268; RR, 0.67 [95% CI, 0.53-0.85];  $P < .001$ ); however, the effect varied by procedure type.<sup>69</sup> The authors indi-

cated that they did not find evidence for substantial differences between the different types of surgery. Similarly, authors of a recent meta-analysis of 28 RCTs concluded that incisional negative pressure wound therapy was associated with lower rates of surgical site infection than standard dressing: 8.8% (194 of 2193) vs 14% (315 of 2205; RR, 0.61 [95% CI, 0.49-0.76];  $P < .001$ ).<sup>85</sup> The authors specified that when stratified by surgical discipline, the greatest benefits for surgical site infection reduction occurred in vascular surgery (RR, 0.45; 95% CI, 0.32-0.65;  $P < .001$ ) and cardiac surgery (RR, 0.17; 95% CI, 0.03-0.96;  $P = .05$ ), whereas the intervention was not associated with statistically significant benefit for abdominal surgery (RR, 0.56; 95% CI, 0.30-1.03), obstetric surgery (RR, 0.73; 95% CI, 0.44-1.20), orthopedic or trauma-derived surgery (RR, 0.68; 95% CI, 0.43-1.08), and plastic surgery (RR, 0.82; 95% CI, 0.26-2.63). The broader CIs for these later 4 subgroups suggest the possibility that they were underpowered to find a significant difference.

### Hospital-Wide Surveillance

As one of the original surgical site infection prevention investigations, data from the Study on the Efficacy of Nosocomial Infection Control (SENIC)<sup>86</sup> supported the use of routine surveillance and feedback to reduce infections. The multicenter, 1985 SENIC study, evaluated infection prevention practices and found that the use of standardized surgical site infection surveillance by trained infection prevention personnel and routine feedback to surgeons was associated with an estimated reduction in infections in US hospitals from 586 000 to 510 000 compared with when no surveillance and feedback were given. Current recommendations advise health care institutions to identify high-volume, high-risk procedures and implement a system for collecting and storing data. Periodic reports should be prepared and given to key stakeholders to provide feedback on infection rates. Surveillance and feedback, along with several other quality improvement strategies (eg, education of surgeons, surgical staff, and patients) are endorsed by all surgical site infection prevention guidelines.<sup>14,17,77,80</sup>

### Limitations

This review has several limitations. First, this review focused on prevention of surgical site infection following general, commonly performed surgical procedures. Second, not all recommendations in previously published guidelines were summarized herein given the lack of available RCT data. Third, some interventions had been studied in only a small number of RCTs. Fourth, in some cases, the only available studies were older. Fifth, quality of included literature was not assessed. Sixth, some relevant studies may have been missed.

### Conclusions

Surgical site infections affect approximately 0.5% to 3% of patients undergoing surgery and are associated with longer hospital stays than patients with no surgical site infections. Avoiding razors for hair removal, maintaining normothermia, use of chlorhexidine gluconate plus alcohol-based skin preparation agents, decolonization with intranasal antistaphylococcal agents and antistaphylococcal skin antiseptics for high-risk procedures, controlling for perioperative glucose concentrations, and using negative pressure wound therapy can reduce the rate of surgical site infections.

## ARTICLE INFORMATION

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**Submissions:** We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at [mdm608@northwestern.edu](mailto:mdm608@northwestern.edu).

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