IMPORTANCE The human and financial costs of treating surgical site infections (SSIs) are increasing. The number of surgical procedures performed in the United States continues to rise, and surgical patients are initially seen with increasingly complex comorbidities. It is estimated that approximately half of SSIs are deemed preventable using evidence-based strategies.

OBJECTIVE To provide new and updated evidence-based recommendations for the prevention of SSI.

EVIDENCE REVIEW A targeted systematic review of the literature was conducted in MEDLINE, EMBASE, CINAHL, and the Cochrane Library from 1998 through April 2014. A modified Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess the quality of evidence and the strength of the resulting recommendation and to provide explicit links between them. Of 5759 titles and abstracts screened, 896 underwent full-text review by 2 independent reviewers. After exclusions, 170 studies were extracted into evidence tables, appraised, and synthesized.

FINDINGS Before surgery, patients should shower or bathe (full body) with soap (antimicrobial or nonantimicrobial) or an antiseptic agent on at least the night before the operative day. Antimicrobial prophylaxis should be administered only when indicated based on published clinical practice guidelines and timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made. In cesarean section procedures, antimicrobial prophylaxis should be administered before skin incision. Skin preparation in the operating room should be performed using an alcohol-based agent unless contraindicated. For clean and clean-contaminated procedures, additional prophylactic antimicrobial agent doses should not be administered after the surgical incision is closed in the operating room, even in the presence of a drain. Topical antimicrobial agents should not be applied to the surgical incision. During surgery, glycemic control should be implemented using blood glucose target levels less than 200 mg/dL, and normothermia should be maintained in all patients. Increased fraction of inspired oxygen should be administered during surgery and after extubation in the immediate postoperative period for patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation. Transfusion of blood products should not be withheld from surgical patients as a means to prevent SSI.

CONCLUSIONS AND RELEVANCE This guideline is intended to provide new and updated evidence-based recommendations for the prevention of SSI and should be incorporated into comprehensive surgical quality improvement programs to improve patient safety.
Surgical site infections (SSIs) are infections of the incision or organ or space that occur after surgery.¹ Surgical patients initially seen with more complex comorbidities² and the emergence of antimicrobial-resistant pathogens increase the cost and challenge of treating SSIs.³-⁵ The prevention of SSI is increasingly important as the number of surgical procedures performed in the United States continues to rise.⁶,⁷ Public reporting of process, outcome, and other quality improvement measures is now required,⁸,⁹ and reimbursements¹⁰ for treating SSIs are being reduced or denied. It has been estimated that approximately half of SSIs are preventable by application of evidence-based strategies.¹¹

Methods

This guideline focuses on select areas for the prevention of SSI deemed important to undergo evidence assessment for the advancement of the field. These areas of focus were informed by feedback received from clinical experts and input from the Healthcare Infection Control Practices Advisory Committee (HICPAC), a federal advisory committee to the Centers for Disease Control and Prevention (CDC). This guideline was a systematic review of the literature. No institutional review board approval or participant informed consent was necessary.

This guideline’s recommendations were developed based on a targeted systematic review of the best available evidence on SSI prevention conducted in MEDLINE, EMBASE, CINAHL, and the Cochrane Library from 1998 through April 2014. To provide explicit links between the evidence and recommendations, a modified Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used for evaluating the quality of evidence and determining the strength of recommendations.¹²-¹⁵ The methods and structure of this guideline were adopted in 2009 by CDC and HICPAC.¹⁶,¹⁷ The present guideline does not reevaluate several strong recommendations offered by CDC’s 1999 Guideline for Prevention of Surgical Site Infection¹⁸ that are now considered to be accepted practice for the prevention of SSI. These recommendations are found in eAppendix 1 of the Supplement. A detailed description of the Guideline Questions, Scope and Purpose, and Methods, as well as the Evidence Summaries supporting the evidence-based recommendations, can also be found in eAppendix 1 of the Supplement.

The detailed literature search strategies, GRADE Tables, and Evidence Tables supporting each section can be found in eAppendix 2 of the Supplement. Results of the entire study selection process are shown in the Figure. Of 5759 titles and abstracts screened, 896 underwent full-text review by 2 independent reviewers. Full-text articles were excluded if: 1) SSI was not reported as an outcome; 2) all patients included had “dirty” surgical procedures (except for Q2
addressing the use of aqueous iodophor irrigation); 3) the study only included oral or dental health procedures; 4) the surgical procedures did not include primary closure of the incision in the operating room (eg, orthopedic pin sites, thoracotomies, or percutaneous endoscopic gastrostomy [PEG] procedures, or wounds healing by secondary intention); or 5) the study evaluated wound protectors used postincision. Evidence-based recommendations in this guideline were cross-checked with those from other guidelines identified in a systematic search.

CDC completed a draft of the guideline and shared it with the expert panel for in-depth review and then with HICPAC and members of the public at committee meetings (June 2010 to July 2015). CDC posted notice in the Federal Register for the following 2 periods of public comment: from January 29 to February 28, 2014, and from April 8 to May 8, 2014. Comments were aggregated and reviewed with the writing group and at another HICPAC meeting. Based on the comments received, the literature search was updated, and new data were incorporated into a revised draft. Further input was provided by HICPAC during a public teleconference in May 2015. Final HICPAC input was provided via a vote by majority rule in July 2015. After final HICPAC input, CDC updated the draft document and obtained final CDC clearance and coauthor approval.

Recommendation Categories

Recommendations were categorized using the following standard system that reflects the level of supporting evidence or regulations:

• Category IA: A strong recommendation supported by high to moderate- quality evidence suggesting net clinical benefits or harms.
• Category IB: A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms or an accepted practice (eg, aseptic technique) supported by low to very low-quality evidence.
• Category IC: A strong recommendation required by state or federal regulation.
• Category II: A weak recommendation supported by any quality evidence suggesting a trade-off between clinical benefits and harms.
• No recommendation/unresolved issue: An issue for which there is low to very low-quality evidence with uncertain trade-offs between the benefits and harms or no published evidence on outcomes deemed critical to weighing the risks and benefits of a given intervention.

Recommendations

Core Section

In 2006, approximately 80 million surgical procedures were performed in the United States at inpatient hospitals (46 million)7 and ambulatory hospital-affiliated or freestanding (32 million) settings.8 Between 2006 and 2009, SSIs complicated approximately 1.9% of surgical procedures in the United States.9,10 However, the number of SSIs is likely to be underestimated given that approximately 50% of SSIs become evident after discharge.11 Estimated mean attributable costs of SSIs range from $10 443 in 2005 US dollars to $25 546 in 2002 US dollars per infection.3,5,11 Costs can exceed $90 000 per infection when the SSI involves a prosthetic joint implant12,13 or an antimicrobial-resistant organism.23 The Core Section of this guideline (eAppendix 1 of the Supplement) includes recommendations for the prevention of SSI that are generalizable across surgical procedures, with some exceptions as mentioned below.

Parenteral Antimicrobial Prophylaxis

1A. Administer preoperative antimicrobial agents only when indicated based on published clinical practice guidelines and timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made. (Category IB–strong recommendation; accepted practice.)

1A.2. No further refinement of timing can be made for preoperative antimicrobial agents based on clinical outcomes. (No recommendation/unresolved issue.)

1B. Administer the appropriate parenteral prophylactic antimicrobial agents before skin incision in all cesarean section procedures. (Category IA–strong recommendation; high-quality evidence.)

1C. The literature search did not identify randomized controlled trials that evaluated the benefits and harms of weight-adjusted parenteral antimicrobial prophylaxis dosing and its effect on the risk of SSI. Other organizations have made recommendations based on observational and pharmacokinetic data, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

1D. The search did not identify sufficient randomized controlled trial evidence to evaluate the benefits and harms of intraoperative redosing of parenteral prophylactic antimicrobial agents for the prevention of SSI. Other organizations have made recommendations based on observational and pharmacokinetic data, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

1E. In clean and clean-contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room, even in the presence of a drain. (Category IA–strong recommendation; high-quality evidence.)

Nonparenteral Antimicrobial Prophylaxis

2A.1. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding intraoperative antimicrobial irrigation (eg, intra-abdominal, deep, or subcutaneous tissues) for the prevention of SSI. Other organizations have made recommendations based on the existing evidence, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

2A.2. The search did not identify randomized controlled trials that evaluated soaking prosthetic devices in antimicrobial solutions before implantation for the prevention of SSI. (No recommendation/unresolved issue.)
2B.1. Do not apply antimicrobial agents (ie, ointments, solutions, or powders) to the surgical incision for the prevention of SSI. (Category IB–strong recommendation; low-quality evidence.)

2B.2. Application of autologous platelet-rich plasma is not necessary for the prevention of SSI. (Category II–weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)

2C. Consider the use of triclosan-coated sutures for the prevention of SSI. (Category II–weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)

2D. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding antimicrobial dressings applied to surgical incisions after primary closure in the operating room for the prevention of SSI. (No recommendation/unresolved issue.)

Glycemic Control

3A. Implement perioperative glycemic control and use blood glucose target levels less than 200 mg/dL in patients with and without diabetes. (Category IA–strong recommendation; high to moderate-quality evidence.)

3A.2. The search did not identify randomized controlled trials that evaluated lower (<200 mg/dL) or narrower blood glucose target levels than recommended in this guideline nor the optimal timing, duration, or delivery method of perioperative glycemic control for the prevention of SSI. Other organizations have made recommendations based on observational evidence, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

3B. The search did not identify randomized controlled trials that evaluated the optimal hemoglobin A1C target levels for the prevention of SSI in patients with and without diabetes. (No recommendation/unresolved issue.)

Normothermia

4. Maintain perioperative normothermia. (Category IA–strong recommendation; high to moderate-quality evidence.)

5. The search did not identify randomized controlled trials that evaluated strategies to achieve and maintain normothermia, the lower limit of normothermia, or the optimal timing and duration of normothermia for the prevention of SSI. Other organizations have made recommendations based on observational evidence, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

Oxygenation

6A. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding the administration of increased fraction of inspired oxygen (FIO2) via endotracheal intubation during only the intraoperative period in patients with normal pulmonary function undergoing general anesthesia for the prevention of SSI. (No recommendation/unresolved issue.)

6B. For patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased FIO2 during surgery and after extubation in the immediate postoperative period. To optimize tissue oxygen delivery, maintain perioperative normothermia and adequate volume replacement. (Category IA–strong recommendation; moderate-quality evidence.)

6C. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding the administration of increased FIO2 via face mask during the perioperative period in patients with normal pulmonary function undergoing general anesthesia without endotracheal intubation or neuraxial anesthesia (ie, spinal, epidural, or local nerve blocks) for the prevention of SSI. (No recommendation/unresolved issue.)

6D. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding the administration of increased FIO2 via face mask or nasal cannula during only the postoperative period in patients with normal pulmonary function for the prevention of SSI. (No recommendation/unresolved issue.)

7. The search did not identify randomized controlled trials that evaluated the optimal target level, duration, and delivery method of FIO2 for the prevention of SSI. Other organizations have made recommendations based on observational studies, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

Antiseptic Prophylaxis

8A.1. Advise patients to shower or bathe (full body) with soap (antimicrobial or nonantimicrobial) or an antiseptic agent on at least the night before the operative day. (Category IB–strong recommendation; accepted practice.)

8A.2. Randomized controlled trial evidence suggested uncertain trade-offs between the benefits and harms regarding the optimal timing of the preoperative shower or bath, the total number of soap or antiseptic agent applications, or the use of chlorhexidine gluconate washcloths for the prevention of SSI. (No recommendation/unresolved issue.)

8B. Perform intraoperative skin preparation with an alcohol-based antiseptic agent unless contraindicated. (Category IA–strong recommendation; high-quality evidence.)

8C. Application of a microbial sealant immediately after intraoperative skin preparation is not necessary for the prevention of SSI. (Category II–weak recommendation; low-quality evidence suggesting a trade-off between clinical benefits and harms.)

8D. The use of plastic adhesive drapes with or without antimicrobial properties is not necessary for the prevention of SSI. (Category II–weak recommendation; high to moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)

9A. Consider intraoperative irrigation of deep or subcutaneous tissues with aqueous iodophor solution for the prevention of SSI. Intraoperative lavage with aqueous iodophor solution in contaminated or dirty abdominal procedures is not necessary. (Category II–weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)
98. The search did not identify randomized controlled trials that evaluated soaking prosthetic devices in antiseptic solutions before implantation for the prevention of SSI. (No recommendation/unresolved issue.)

10. Randomized controlled trial evidence was insufficient to evaluate the trade-offs between the benefits and harms of repeat application of antiseptic agents to the patient’s skin immediately before closing the surgical incision for the prevention of SSI. (No recommendation/unresolved issue.)

**Prosthetic Joint Arthroplasty Section**

Prevention efforts should target all surgical procedures but especially those in which the human and financial burden is greatest. In 2011, primary total knee arthroplasty accounted for more than half of the 1.2 million prosthetic joint arthroplasty procedures (primary and revision) performed in the United States, followed by total hip arthroplasty and hip hemiarthroplasty.24 Primary shoulder, elbow, and ankle arthroplasties are much less common. By 2030, prosthetic joint arthroplasties are projected to increase to 3.8 million procedures per year.25-27

Infection is the most common indication for revision in total knee arthroplasty28 and the third most common indication in total hip arthroplasty.18 By 2030, the infection risk for hip and knee arthroplasty is expected to increase from 2.18%22 to 6.5% and 6.8%, respectively.25 In addition, owing to increasing risk and the number of individuals undergoing prosthetic joint arthroplasty procedures, the total number of hip and knee prosthetic joint infections is projected to increase to 221,500 cases per year by 2030, at a cost of more than $1.62 billion.22,25 The Prosthetic Joint Arthroplasty section contains recommendations that are applicable to these procedures (eAppendix 1 of the Supplement).

**Blood Transfusion**

11A. Available evidence suggested uncertain trade-offs between the benefits and harms of blood transfusions on the risk of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations on this topic, and a reference to these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

11B. Do not withhold transfusion of necessary blood products from surgical patients as a means to prevent SSI. (Category IB–strong recommendation; accepted practice.)

**Systemic Immunosuppressive Therapy**

12 and 13. Available evidence suggested uncertain trade-offs between the benefits and harms of systemic corticosteroid or other immunosuppressive therapies on the risk of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on the existing evidence, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

14. For prosthetic joint arthroplasty patients receiving systemic corticosteroid or other immunosuppressive therapy, recommendation 1E applies: in clean and clean-contaminated procedures, do not administer additional antimicrobial prophylaxis doses after the surgical incision is closed in the operating room, even in the presence of a drain. (Category IA–strong recommendation; high-quality evidence.)

**Intra-articular Corticosteroid Injection**

15 and 16. Available evidence suggested uncertain trade-offs between the benefits and harms of the use and timing of preoperative intra-articular corticosteroid injection on the incidence of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on observational studies, and a summary of these recommendations can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

**Anticoagulation**

17. Available evidence suggested uncertain trade-offs between the benefits and harms of venous thromboembolism prophylaxis on the incidence of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on the existing evidence, and these references can be found in the Other Guidelines section of the narrative summary for this question (eAppendix 1 of the Supplement). (No recommendation/unresolved issue.)

**Orthopedic Surgical Space Suit**

18. Available evidence suggested uncertain trade-offs between the benefits and harms of orthopedic space suits or the health care personnel who should wear them for the prevention of SSI in prosthetic joint arthroplasty. (No recommendation/unresolved issue.)

**Postoperative Antimicrobial Prophylaxis**

**Duration With Drain Use**

19. In prosthetic joint arthroplasty, recommendation 1E applies: in clean and clean-contaminated procedures, do not administer additional antimicrobial prophylaxis doses after the surgical incision is closed in the operating room, even in the presence of a drain. (Category IA–strong recommendation; high-quality evidence.)

**Biofilm**

20A. Available evidence suggested uncertain trade-offs between the benefits and harms regarding cement modifications and the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (No recommendation/unresolved issue.)

20B. The search did not identify studies evaluating prosthesis modifications for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (No recommendation/unresolved issue.)

20C. The search did not identify studies evaluating vaccines for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (No recommendation/unresolved issue.)
Surgical site infections are persistent and preventable health care-associated infections. There is increasing demand for evidence-based interventions for the prevention of SSI. The last version of the CDC Guideline for Prevention of Surgical Site Infection was published in 1999. While the guideline was evidence informed, most recommendations were based on expert opinion, in the era before evidence-based guideline methods. CDC updated that version of the guideline using GRADE as the evidence-based method that provides the foundation of the recommendations in this guideline.

New and updated recommendations are not only useful for health care professionals but also can be used as a resource for professional societies or organizations to develop more detailed implementation guidance or to identify future research priorities. The paucity of robust evidence across the entire guideline created challenges in formulating recommendations for the prevention of SSI. Nonetheless, the thoroughness and transparency achieved using a systematic review and the GRADE approach to address clinical questions of interest to stakeholders are critical to the validity of the clinical recommendations.

The number of unresolved issues in this guideline reveals substantial gaps that warrant future research. A select list of these unresolved issues may be prioritized to formulate a research agenda to advance the field. Adequately powered, well-designed studies that assess the effect of specific interventions on the incidence of SSI are needed to address these evidence gaps. Subsequent revisions to this guideline will be guided by new research and technological advancements for preventing SSIs.

Conclusions

Surgical site infections are persistent and preventable health care-associated infections. There is increasing demand for evidence-based interventions for the prevention of SSI. The last version of the CDC Guideline for Prevention of Surgical Site Infection was published in 1999. While the guideline was evidence informed, most recommendations were based on expert opinion, in the era before evidence-based guideline methods. CDC updated that version of the guideline using GRADE as the evidence-based method that provides the foundation of the recommendations in this guideline.

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management, analysis, and interpretation of the data; and preparation, review, and approval for submission of the manuscript. For review, Centers for Disease Control and Prevention staff members were responsible for the overall design and conduct of the guideline and preparation, review, and approval of the manuscript.

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Disclaimer: The opinions of the reviewers might not be reflected in all of the recommendations contained in this document.

Additional Information: Before July 2014, Dr Berrios-Torres was employed at Centers for Disease Control and Prevention. She has no affiliation since July 2014. Authors recused themselves from discussions if they had competing interests related to recommendations under discussion. For product-specific recommendation discussions (e.g., triclosan-coated sutures), a new declaration of conflicts specific to that topic was requested from each author before his or her input was considered in the formulation of the recommendation.

Additional Contributions: The Centers for Disease Control and Prevention thanks the many individuals and organizations who provided valuable feedback on the guideline during the development process, especially the following experts for their input throughout the process: Rajender Agarwal, MD, MPH (Center for Evidence-Based Practice, University of Pennsylvania Health System, Philadelphia); J. William Costerton, PhD (Center for Genomic Sciences, Allegheny-Singer Research Institute, Pittsburgh, Pennsylvania); Jeffrey C. Hageman, MHS (Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia); Thomas Hunt, MD (Department of Surgery, University of California at San Francisco); Bernard Morrey, MD (Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota); Lena M. Napolitano, MD (Division of Acute Care Surgery, University of Michigan Health Systems, Ann Arbor); Douglas Osmon, MD (Department of Infectious Diseases, Mayo Clinic, Rochester, Minnesota); Robin Patel, MD(CM), FRCP(C), IDSA (Infectious Diseases Research Laboratory, Mayo Clinic, Rochester, Minnesota); and Mark Shirriff, PhD (Department of Microbial Pathogenesis, University of Maryland, Baltimore). None received compensation outside of their usual salary.

REFERENCES
Surgical Site Infection Prevention—What We Know and What We Do Not Know

Pamela A. Lipsett, MD, MHPE, MCCM

Surgical site infections remain among the most common preventable infections today. Recently, the World Health Organization,1,3 and the American College of Surgeons and Surgical Infection Society3 published their guidelines for the prevention of surgical site infections. In this journal, the long-awaited update to the 1999 guidelines from the Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee (HICPAC) were unable to judge trade-offs between harms and benefits of the proposed intervention because of lack of outcomes. The authors ultimately provide 42 statements, including 8 Category 1A, 4 Category 1B, 5 Category II, and 25 areas for which they made no recommendation or considered the area unresolved. The fact that most statements were unresolved, especially regarding prosthetic joint surgery, shows our investigators where we should be putting forth our efforts in clinical trials. There is a lot of opportunity to learn how we can provide more effective care to our patients.

The 12 Category 1A and Category 1B recommendations are based on moderate or high-quality evidence, and we should be using these recommendations in our practice. These key areas include (but are not limited to) the use of antimicrobial prophylaxis to achieve bactericidal concentrations in serum and tissues, including before cesarean section, and are limited to during the operation. Furthermore, we should not be using antibiotics because the patient has a drain, whether or not a prosthetic joint is in place. These recommendations are likely to be the most difficult to operationalize because some surgeons and practices have had difficulty confining antibiotic use to just 24 hours after a clean or clean-contaminated procedure, let alone when a drain is in place. Glycemic control should be achieved in all patients, with a glucose target less than 200 mg/dL. Normothermia should be maintained, and a higher fraction of inspired oxygen should be used in patients with normal


