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PROSTHETIC JOINT INFECTION (S NODZO AND N FRISCH, SECTION EDITORS)

Centers for Disease Control and Prevention 2017 Guidelines for Prevention of Surgical Site Infections: Review and Relevant Recommendations

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Abstract

Purpose of Review The associated patient morbidity and resource-intensive nature of managing surgical site infections (SSI) has focused attention toward not only improving treatment protocols but also enhancing preventative measures. The purpose of this review was to summarize the relevant updated CDC guidelines for the prevention of SSI that were released in 2017. The CDC recommends the integration of the guidelines for improvement in quality metrics, reportable outcomes, and patient safety.

Recent Findings The updated guidelines include generalized recommendations for parenteral antimicrobial prophylaxis, non-parenteral antimicrobial prophylaxis, glycemic control, normothermia, oxygenation, and antiseptic prophylaxis. The arthroplasty section includes recommendations for blood transfusion, systemic immunosuppressive therapy, and antibiotics during drain use. There was low-quality evidence precluding recommendations for preoperative intra-articular corticosteroid injections, orthopedic surgical space suits, and biofilm management.

Summary The recommendations provided throughout this review, including more recent guidelines from other organizations such as the AAOS and ACR, should assist clinicians in developing and/or refining surgical site prevention protocols for their patients undergoing total joint arthroplasty procedures.

Keywords Centers for Disease Control and Prevention · Surgical site infection · Total joint arthroplasty · Prosthetic joint arthroplasty · Guidelines

Introduction

Surgical site infections (SSIs) are infections of the incision, organ, or operative space that occur after surgery and are a common type of healthcare-associated infection (HAI) as defined by the Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Between 2006 and 2009, approximately 1.9% of all surgical procedures in the USA were complicated by SSIs [1]. Infection after orthopedic procedures is an especially devastating complication that has a significant clinical and financial impact on the patient, treating surgeon as well as the healthcare system. The prevalence of SSI for all orthopedic procedures is reported to be between 0.6 and 2.55% [2, 3].

There has been an exponential increase in the number of orthopedic procedures performed over the past decade, with a substantial percentage of that increase stemming from arthroplasty procedures. Total joint arthroplasties (TJA) are among the most successful procedures that lead to improvement in pain, function, and quality of life with expected rise in growth of 673% for total knee arthroplasties (TKA), 174% for total hip arthroplasties (THA), and 150% for total shoulder arthroplasties (TSA) [4, 5]. TJAs are projected to increase to 3.8 million procedures annually by the year 2030 [5, 6]. Periprosthetic joint infection (PJI) is one of the leading causes of failure for TKA and THA, and is one of the most common

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reasons for revision shoulder and elbow arthroplasty [7•, 8••, 9]. The costs associated with periprosthetic joint infection (PJI) have been shown to exceed $90,000 per case of infection with a projected cost of $1.62 billion by the year 2030 [5, 10]. Direct and indirect costs include increased readmissions, hospital length of stay, emergency department visits, outpatient visits, use of ancillary services, intravenous (IV) and other antibiotics, loss of productivity, and temporary or permanent disability [11, 12]. As such, there is substantial concern surrounding the current and predicted prevalence and economic burden accompanied by TJAs complicated by SSI. The associated patient morbidity and resource-intensive nature of managing SSIs has focused attention toward not only improving treatment protocols but also enhancing preventative measures.

Infection prevention strategies are multifaceted, with focused efforts on patient-specific modifiable risk factors, host optimization, operative environment, and reduction of bacterial burden. With the advent of bundle care payment models and the movement toward value-based medicine, concentrated efforts have shifted toward the preoperative setting, and critically evaluating the patient and their potential risks for postoperative complications. Identifying both modifiable and non-modifiable patient risk factors is essential for guiding the approach to optimal patient care and setting appropriate expectations. Commonly employed techniques of infection prevention include reduction of bacterial burden by introducing decolonization methods, targeted perioperative antibiotics, and skin preparation as well as perioperative medical optimization of patient comorbidities prior to TJA. Previous reports have noted that approximately half of SSIs may be preventable by implementing evidence-based strategies [13]. In 2017, the CDC released updated guidelines for the prevention of SSI after surgical procedures and recommends the integration of the guidelines for improvement in quality metrics, reportable outcomes, and patient safety [14••].

CDC Guidelines for the Prevention of Surgical Site Infection (2017)

The CDC and Centers for Medicare and Medicaid Services (CMS) instituted the Surgical Infection Prevention (SIP) project in 2002 to develop quality improvement measures to standardize processes to help decrease the morbidity and mortality associated with postoperative SSIs. In 2006, this project was expanded to the Surgical Care Improvement Project (SCIP), a national quality partnership of organizations, which provided an infrastructure for robust national data collection and quality improvement measures for hospitals. Since 2012, hospitals have been required by the CMS Hospital Inpatient Quality Reporting Program to report SSI outcome data with payments being adjusted downwards for healthcare-associated infections (HAIs) through the Deficit Reduction Act of 2005 [14••, 15]. In 2009, the United States Department of Health and Human Services (HHS) developed the *National Action Plan to Prevent Healthcare-Associated Infections: Road Map to Elimination* to set SSI reduction goals. The HAI Action Plan Reduction target was a 25% reduction in admission and readmission SSI for SCIP procedures from 2008 to 2013, with a revised metric proposed of another 30% reduction by 2020 [16, 17]. Primary TKA and THA are included within the ten designated SCIP procedures for the action plan. SSIs must occur within 30 days of the procedure if no implant is left in place or within 1 year of the procedure if an implant was left in place. The following inclusion metrics are also evaluated for decisions on reportable data, deep incisional and organ/space infections based on clinical symptoms, laboratory reports, diagnostic imaging results, and surgeon diagnosis. The prevetion of SSI is becoming increasingly important, especially in the orthopedic community with the public reporting process, performance and outcome driven incentives, and concern for the reduction or denial of reimbursements for treating SSIs [14••].

The recent CDC Guidelines for the Prevention of SSI focused on select areas that were considered important by clinical experts and the HICPAC. Targeted systematic reviews of the literature were conducted using large databases from 1998 through April 2014. The strength of recommendations for each core section was provided through a GRADE (modified Grading of Recommendations, Assessment, Development, and Evaluation) approach. An overview and brief summary of the core topics analyzed in the evidence-based review and relevant recommendations can be found in Table 1. The core sections evaluated a broad range of data and provided recommendations that are generalizable to many surgical specialties. The prosthetic joint arthroplasty evidence-based recommendations are specified in Table 2 and have been described in further detail below. Table 3 outlines the areas of re-emphasis of select 1999 CDC and HICPAC recommendations for prevention of SSIs. This review outlines the current recommendations found in the 2017 CDC guidelines along with pertinent recommendations from associated governing bodies.

Specific Considerations for Prosthetic Joint Arthroplasty

Blood Transfusion

CDC Recommendation

- Available evidence suggests uncertain tradeoffs between the benefits and harms of blood transfusions on the risk of SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*). Please see organization specific recommendations below.

Table 1 Summary Centers for Disease Control 2017 Evidence-Based Review Recommendations for Prevention of Surgical Site Infection: Core Sections

Core Section Evidence Review	Relevant recommendations
Parenteral Antimicrobial Prophylaxis	• Antimicrobial prophylaxis should be administered only when indicated based on published clinical practice guidelines
	• Antimicrobial prophylaxis should be timed such that bactericidal concentrations of the agent are established in the serum of respective surgical site tissues when the incision is made
	• For clean and clean-contaminated procedures, additional prophylactic antimicrobial agents doses should not be administered after the surgical incision is closed
Non-Parenteral Antimicrobial Prophylaxis	• Do not apply antimicrobial agents (i.e., ointments, solutions, powders) to surgical incision for prevention of SSI
	• Antimicrobial dressings applied to surgical incision following primary closure is an unresolved issue with no current recommendations
Glycemic Control	• Implement intraoperative and perioperative glycemic control and use blood glucose target < 200 mg/dL in diabetic and non-diabetic patients
	• Optimal HbA1C target level for the prevention of SSI in patients with and without diabetes remains and unresolved issue with current recommendations
Normothermia	• Maintain perioperative normothermia
Oxygenation	• For patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased fraction of inspired oxygen intraoperatively and post-extubation in the immediate postoperative period
	• To optimize tissue oxygen delivery, maintain perioperative normothermia and adequate volume replacement
Antiseptic Prophylaxis	• Advise patients to shower or bathe (full body) with soap (antimicrobial or non-antimicrobial) or an antiseptic agent on at least the night before the operative day
	• Perform intraoperative skin preparation with an alcohol-based antiseptic agent, unless contraindicated

All recommendations were Category IA (a strong recommendation supported by high-to-moderate-quality evidence suggesting net clinical benefits or harms) or Category IB (a strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice supported by low-to-very low-quality evidence), unless otherwise specified with "unresolved issue"

HbA1C Hemoglobin A1C

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

The outcome measure of SSI was utilized when evaluating how perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients. There were six studies reviewed, two randomized controlled trials (RCTs) and four observational studies (OBS) that assessed European transfusion practices between 1999 and 2007 with transfusion thresholds ranging from 8 to 11 g/dL. The blood products were variable from autologous, allogeneic, and combined autologous and allogeneic. In one meta-analysis ($N = 8493$) of all six studies and in another meta-analysis of the four OBS studies, blood transfusions were found to increase the risk of SSI [18–23]. When a meta-analysis was completed critically looking at the two RCTs ($N = 1009$), the findings did not suggest an increased risk of SSI with autologous and autologous plus additional allogeneic blood transfusion [14••].

When comparing specific blood products with a risk of SSI, the critical outcomes were determined to be SSI, PJI, reoperation due to wound infection, and wound disturbance. There were nine studies used to evaluate this question, two RCTs and seven OBS, which were considered to be low-quality evidence and had significant variations between studies including surgical procedures, definition of SSI, hemoglobin transfusion thresholds, conflicts of interest, and follow-up. In a meta-analysis ($N = 5737$) looking at allogeneic blood versus no transfusion in four OBS studies of primary and revision TKA and THA, the risk of SSI was shown to increase with allogeneic blood transfusions, although there was no difference in reoperation due to wound infection noted in a separate observational study [19–22, 24]. In comparison, autologous blood transfusion did not increase the risk of SSI when compared to no transfusion in one large RCT, showing no

Table 2 Summary Centers for Disease Control 2017 Evidence-Based Review Recommendations for Prevention of Surgical Site Infection: Prosthetic Joint Arthroplasty Sections

Prosthetic Joint Arthroplasty Section	Relevant recommendations
Blood Transfusion	• Transfusion of blood products should not be withheld from surgical patients as a means to prevent SSI
Systemic Immunosuppressive Therapy	• For prosthetic joint arthroplasty patients on systemic corticosteroid or other immunosuppressive therapy—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
Preoperative Intra-articular Corticosteroid Injections	• Available evidence suggests uncertain tradeoffs between the benefits and harms of preoperative intra-articular corticosteroid infection the incidence of SSI in prosthetic joint arthroplasty
Anticoagulation	• Available evidence suggests uncertain tradeoffs between the benefits and harms of venous thromboembolism prophylaxis on the incidence of SSI in prosthetic joint arthroplasty
Orthopedic Surgical Space Suit	• Available evidence suggests uncertain tradeoffs between the benefits and harms of orthopedic surgical space suits or the health care personnel who should wear them for the prevention of SSI in prosthetic joint arthroplasty
Drain Use	• Do not administer additional antibiotics after surgical incision is closed in presence of a drain
Biofilm	• Available evidence suggests uncertain tradeoffs between the benefits and harms regarding cement modifications and the prevention of biofilm formation or SSI in prosthetic joint arthroplasty

All recommendations were Category IA (a strong recommendation supported by high-to-moderate-quality evidence suggesting net clinical benefits or harms) or Category IB (a strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice supported by low-to-very low-quality evidence), unless otherwise specified with "unresolved issue"

difference in SSI at 90 days in patients who had undergone a THA [23].

When comparing allogeneic blood versus autologous blood, moderate-quality evidence was found after a meta-analysis of three OBS ($N = 2592$) that allogeneic blood transfusions increased the risk of SSI by fourfold when compared with autologous transfusions [19, 21, 25]. Lastly, there was moderate-quality evidence suggesting that combined autologous and additional allogeneic blood transfusions did not increase the risk of SSI after a thorough sub-analysis was completed in one of the RCTs ($N = 470$) and two OBS ($N = 1632$) [19, 21, 23]. There were no associations found between the complexity of cases, increasing blood transfusion requirements, or volume of transfused blood on the risk of SSI.

Other Recommendations: Blood Management

The transfusion algorithms recommended in recent practice guidelines are more stringent than those evaluated in the studies mentioned previously. The practice guidelines note that in adult and pediatric intensive care (ICU) patients, the recommended hemoglobin level for transfusion is 7 g/dL or less. Transfusion is recommended for a hemoglobin level of 8 g/dL or less in hemodynamically stable patients presenting with symptoms classified as those with chest pain, orthostatic hypotension, tachycardia unresponsive to fluid resuscitation, or congestive heart failure [26].

Systemic Immunosuppressive Therapy

CDC Recommendations

- Available evidence suggests uncertain tradeoffs between the benefits and harms of systemic corticosteroid or other immunosuppressive therapy on the risk of SSI in prosthetic joint arthroplasty. (*No recommendations/unresolved issue*). Please see organization-specific recommendations below.
- For prosthetic joint arthroplasty patients on systemic corticosteroid or other immunosuppressive therapy, 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*).

Patients with rheumatoid arthritis (RA) are commonly treated with systemic corticosteroid therapy and/or immunosuppressive agents. These agents are typically classified into disease-modifying antirheumatic drugs (DMARDs) and

Table 3 Accepted practices: Re-emphasis of Select 1999 CDC and HICPAC Recommendations for Prevention of SSI

CDC Guideline 1999	Relevant recommendations
Preparation of the Patient	• Identify and treat all infections remote to the surgical site before elective operations and postpone elective operations on patients with remote site infections until the infection has resolved
	• *Hair Removal*: Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation. If hair removal is necessary, remove immediately before the operation with clippers
	• *Skin Preparation*: Ensure skin around the incision site is free of gross contamination before performing antiseptic skin preparation
	• *Tobacco Cessation*: Encourage tobacco cessation for a minimum of at least 30 days before elective operations
Hand/Forearm Antisepsis for Surgical Team	• Perform preoperative surgical hand/forearm antisepsis according to manufacturer's recommendations for the product being used prior to every procedure
Operating Room Ventilation	• Maintain positive pressure ventilation in the operating room and adjoining spaces
	• Maintain number of air exchanges, airflow patterns, temperature, humidity, location of vents, and use of filters in accordance with recommendations from the most recent version (2014) of the Facilities Guidelines Institute— Guidelines for Design and Construction of Hospitals and Outpatient Facilities
Cleaning and Disinfection of Environmental Surfaces	• Do not perform special cleaning or closing of operating rooms after contaminated or dirty operations
Reprocessing of Surgical Instruments	• Sterilize all surgical instruments according to published guidelines and manufacturer's recommendations
	• Immediate-use steam sterilization should never be used for reasons of convenience, as an alternative to purchasing additional instrument sets or to save time. This practice should only be reserved for patients care items that will be used immediately in emergency situations when no other options are available
Surgical Attire and Drapes	• Wear a surgical mask that fully covers the mouth and nose when entering the operating room if an operation is about to begin or already underway, or if sterile instruments are exposed, wear mask throughout the operation
	• Wear a new, disposable, or hospital-laundered head covering for each case, when entering the operating room. Ensure it fully covers all hair on the head and all facial hair not covered by the surgical mask
	• Change scrub suits that are visibly soiled, contaminated and/or penetrated by blood or other potentially infectious materials
Sterile and Surgical Technique	• If drainage is necessary, used a closed suction drain, through separate incision distant from operative incision, remove drain as soon as possible
Postoperative Incision Care	• Protect primarily closed incisions with a sterile dressing for 24–48 h postoperatively

All recommendations were Category IA (a strong recommendation supported by high-to-moderate-quality evidence suggesting net clinical benefits or harms) or Category IB (a strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice supported by low-to-very low-quality evidence), unless otherwise specified with "unresolved issue"

biologic agents. There are numerous DMARDs with the most commonly used being methotrexate or methotrexate-based, which is thought to inhibit enzymes involved in purine metabolism, and through a sequence of pathways, deactivate enzyme activity relevant to immune system function in RA patients [27]. Biologic agents are targeted for immunotherapy and are used to suppress patient's immune systems for disease such as RA and psoriatic arthritis. These agents can be subdivided into non-tumor necrosis factor (TNF) agents and anti-TNF agents (Table 4).

Systemic corticosteroids and immunosuppressive therapy medications were evaluated for their effect on the risk of SSI in prosthetic joint arthroplasty patients in the most recent CDC guidelines. The outcomes measured were SSI, PJI, superficial SSI, deep wound abscess, infected hematoma, surgical wound necrotic eschar, and serous drainage. Additionally, wound dehiscence as defined by the wound being not completely healed 14 days after surgery or needing secondary closure. Continued discharge and culture-positive infection were compiled into an "adverse events of the surgical wound" variable. There were four OBS reviewed in RA patients, with the first question looking at biologic agents versus DMARDs. The quality of evidence was rated as very low in two of the OBS ($N = 528$) where biologic agents and years of disease duration were shown to increase the risk of SSI and superficial SSI through multivariate regression analyses, but not increase the risk of

Table 4 ACR and AAHKS 2017 Systemic Immunosuppressive Therapy Medications Guidelines

Class	Medication	Recommendation
Systemic Corticosteroid	Glucocorticoid (Prednisone—oral)	Continue current dose through surgery; stress dosing not usually recommended
DMARD	Methotrexate	Continue through surgery
	Hydroxychloriquine	Continue through surgery
	Leflunomide	Continue through surgery
	Doxycycline	Continue through surgery
	Sulfasazaline	Continue through surgery
	Azathioprine	Withhold for 1 week prior and 14 days after surgery if not severe disease
	Cyclosporine	Withhold for 1 week prior and 14 days after surgery if not severe disease
Biologic Agents		
Non-TNF Agents	Anakinra (Kineret)	Hold 2 days prior to surgery
	Abatacept (Orencia)	Hold 5 weeks prior to surgery if monthly dosing and 2 weeks prior to surgery if weekly dosing
	Rituximab (Rituxan)	Hold 7 months prior to surgery
	Tocilizumab (Actemra)	Hold 5 weeks prior to surgery if monthly dosing and 2 weeks prior to surgery if weekly dosing
Anti-TNF Agents	Adalimumab (Humira)	Hold 2 weeks prior to surgery
	Etanercept (Enbrel)	Hold 2 weeks prior to surgery
	Infliximab (Remicade)	Hold 5–9 weeks prior to surgery depending on dosing pattern
	Certolizumab pegol (Cimzia)	Hold 3 to 5 weeks prior to surgery depending on dosing pattern
	Golimumab (Simponi)	Hold 5 weeks prior to surgery if monthly dosing and 9 weeks prior to surgery if bimonthly dosing

Recommendations for discontinuation of biological agents are based on the half-life of the drug and dosing pattern. Biologic antirheumatic drugs can be restarted after the wound has healed which is usually around 14 days postoperatively

PJI [28, 29]. The larger of these studies evaluated primary and revision TKA and THA in RA patients and noted a superficial SSI rate of 18.8% with an increased risk of SSI when biologic agents were used compared to DMARD therapy [28]. The patients on biologic therapy (anti-TNFs and non-TNFs) were concomitantly taking prednisone (average 5 mg/day) and 88% were receiving methotrexate. The DMARD patients were on daily prednisone (average 3 mg/day), as well as single or multiple DMARD therapy. In contrast, a smaller study found no difference in adverse events of the surgical wound in patients receiving biologic therapy who underwent total hip, knee, shoulder, and elbow arthroplasty [30].

There were two OBS studies that provided very low-quality evidence when comparing patients on methotrexate therapy to patients who have never taken methotrexate and the risk of SSI. One study from 1991 found no difference in PJI, infected hematoma, deep wound abscess, necrotic eschar, or serous drainage at 6 months of follow-up with patients on an average weekly methotrexate dose of 8.7 mg (range 7.5–12.5 mg) [31]. There are a few limitations to this study, the first of which is the patients in the methotrexate group contained patients who had continued their methotrexate therapy throughout the perioperative period as well as patients who had stopped their methotrexate therapy 4 weeks prior to surgery. The patients in the no methotrexate group had never taken methotrexate, but some were taking daily prednisone therapy. Secondly, the utilization of this study for providing current recommendations in our total joint arthroplasty patients is limited as the dosing of methotrexate may be subtherapeutic based on more recent practice guidelines [32]. The study may be underpowered due to the smaller sample size and limited total number of events/infections. Lastly, the relevance of this study should be taken into consideration as the study results were published approximately 27 years prior.

Other Recommendations: 2017 ACR and AAHKS Guide to Managing Systemic Corticosteroid and Immunosuppressive Therapies Perioperatively

In 2017, a workgroup of The American College of Rheumatology (ACR) and American Academy of Hip and Knee Surgeons (AAHKS) released specific recommendations for perioperative management of biologic and DMARD agents in patients undergoing total joint arthroplasty (Table 4) [33••]. Their review of the literature included recommendations based on severity of the disease process and dosing of the agent. They concluded, in general, all biologic agents should be discontinued prior to surgery at a length of time based off the half-life of the agent, and restarted approximately 14 days after surgery when the wound has healed.

Additionally, DMARD agents can be safely continued throughout the surgical period (Table 4).

Intra-articular Corticosteroid Injections and SSI: Preoperative Injections

CDC Recommendations

- Available evidence suggests uncertain tradeoffs between the benefits and harms of preoperative intra-articular corticosteroid injection on the incidence of SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*). Please see organization specific recommendations below.

Intra-articular corticosteroid injections for both the knee and hip are used for both diagnostic as well as therapeutic options for the management of osteoarthritis as well as rheumatoid arthritis in clinical practice [34, 35]. The injections are usually composed of a short-acting and long-acting anesthetic to enhance diagnostic acumen as well as the corticosteroid, which provides an anti-inflammatory affect within the joint [36]. To evaluate the risk of SSI in patients undergoing total joint arthroplasty procedures who had prior intra-articular corticosteroid injections, two OBS in TKA and three OBS in THA were reviewed with 1-year follow-up [37–41]. One of the studies looking at patients ($N = 144$) who received a steroid injection in the 11 months prior to undergoing a TKA compared to those who had not, found an increased risk of PJI in the injection group, although the incidence of superficial infection was not significantly different between the two groups [38]. The authors concluded that careful thought should be placed into the decision to administer intra-articular corticosteroid injections in patients that may be undergoing TKA within the year. In contrast, the other study of 270 TKAs revealed no difference in the incidence of PJI between groups [41]. When a meta-analysis ($N = 414$) was conducted of the two OBS, intra-articular injections did not increase the risk of SSI, PJI, or superficial SSI after TKA [38, 41]. Along with other limitations, critical differences between these studies included the environment and techniques in which the intra-articular steroid injections were given, and the CDC subsequently rated the evidence as very low quality.

The three individual OBS and meta-analyses completed demonstrated no significant difference in SSI, superficial SSI, or PJI for patients undergoing intra-articular corticosteroid injections prior to THA. One study evaluated was a retrospective matched cohort study looking at 224 primary THAs implanted within 1 year of intra-articular corticosteroid injection compared with 224 primary THAs in patients who had not received an injection. There were 3 deep and 11 superficial infections noted in the injection group compared with 1 deep and 8 superficial in the no injection group, with mean time from steroid injection to THA of 44 days in the patients who had a deep infection develop. Although the authors concluded that intra-articular steroid injection within 1 year of THA did not affect postoperative rates of infection, they did caution the use of steroid injections within 2 months of THA. The mean time from steroid injection to THA was 44 days in the patients who had a deep infection, prompting the cautionary use within the 2 month timeframe [39].

Other Recommendations: AAOS and ACR Guidelines for Preoperative Injections Prior to Total Joint Arthroplasty

Current clinical practice guidelines, including American Academy of OrthopaedicSurgeons (AAOS) and ACR, consider the use of intra-articular corticosteroids as a nonsurgical treatment option for the management of osteoarthritis and RA [42, 43]. Although these guidelines do not outline specific recommendations for prevention of SSI, the CDC and HICPAC endorse safe injection practices for administration of intra-articular corticosteroid injections [44]. The AAOS 2013 clinical practice guideline strongly recommended against the use of hyaluronic acid injections and did not recommend for or against growth factor or platelet-rich plasma (PRP) injections in patients with symptomatic knee OA. A recent prospective multicenter cohort study of 100 patients with radiographic evidence and symptoms consistent with osteoarthritis (OA) received an intra-articular corticosteroid injection were found to have improved pain and function at all time points (3 weeks, 6 weeks, 3 months, 6 months) [45••]. Obesity and severity of OA affected the efficacy of the injection, leading the authors to conclude that clinicians can expect less improvement in patients with obesity and/or advanced OA.

A recent large database review demonstrated injection before TKA was associated with a higher risk of postoperative infection and is time-dependent with closer proximity between injection and TKA having increased odds of infection [46, 47]. There is also evidence suggesting an increased risk of PJI when THA is performed within 3 months of an intra-articular hip injection or when multiple injections are utilized preoperatively [48]. This information is useful when counseling patients about non-operative symptom management options prior to elective THA and TKA.

Anticoagulation

CDC Recommendations

- Available evidence suggests uncertain tradeoffs between the benefits and harms of venous thromboembolism prophylaxis on the incidence of SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*). Please see organization specific recommendations below.

The CDC and HICPAC asked the following questions to address management strategies for perioperative venous thromboembolism (VTE) prophylaxis in the context of reducing SSI in prosthetic joint arthroplasty patients:

- Does the risk of SSI differ by individual VTE prophylaxis agent? (Agents reviewed: enoxaparin, fondaparinux, rivaroxaban, aspirin, bemiparin, fraxiparin, low molecular weight heparin, warfarin, and mechanical prophylaxis.)
- What is the optimal timing and duration of perioperative VTE prophylaxis for the reduction of SSI in prosthetic joint arthroplasty patients?
- How safe and effective is modifying the dose of perioperative VTE prophylaxis agent to reduce the risk of SSI?

The primary outcomes measured in four RCTs, five OBS, and one systematic review of unilateral, primary, and revision TKA, THA, and hip fracture procedures were SSI and PJI, where secondary outcomes also evaluated included drug-related adverse events, hemorrhagic wound complications, wound hematoma, and persistent wound drainage [49–58]. For elective primary or revision TKA and THA, there was no difference in the risk of SSI, hemorrhagic wound complications, or drug-related adverse events found between enoxaparin and rivaroxaban in a large meta-analysis (N = 12,383) of four RCTs [51–54]. Although, the evidence in these large, international, multicenter studies was determined to be high quality, the dosing and duration of anticoagulation varied between groups with the primary outcome being postoperative VTE. There is very low-quality evidence showing no significant difference in the risk of SSI when comparing enoxaparin or fondaparinux to aspirin with or without the use of mechanical prophylaxis [50, 56]. In two large retrospective studies, there was no difference in the risk of SSI between perioperative warfarin (starting day of surgery; target INR = 2 in one study, no target INR reported in the other study) and ASA (with or without mechanical prophylaxis devices) [50, 56]. One study analyzed 93,840 patients (warfarin = 55%, 40% = injectable agents, 5% = aspirin) who underwent primary TKA at 307 hospitals in the USA over a 24-month period and found after adjustment for patient and hospital factors; there were no differences in risk of bleeding, infection, or mortality [56]. The authors of this study concluded that aspirin, when used in conjunction with other clinical care protocols, may be an effective VTE prophylaxis option for specific TKA patients.

One case control study, classified as very low-quality evidence, of 5496 consecutive patients who underwent TKA from 2005 to 2006 in 13 orthopedic centers suggested that administration of injectable LMWHs or fondaparinux at close proximity to surgery did not increase risk of SSI [55]. There were 50 patients who developed PJI within the 6-month follow-up period, in which 44 were matched to 106 controls. This study did find that the case patients had received the first LMWH dose at approximately 12 h from the start of surgery more often than their matched controls, although after adjusting for risk factors, there was no statistical association between timing of LMWH and risk of infection. Notably, data was not identified evaluating optimal timing in THA or for patients using oral VTE prophylaxis agents. Also, there was not sufficient data to evaluate the safety and effectiveness of modifying the dose of perioperative VTE prophylaxis agent and the subsequent impact of SSI [14••].

Other Recommendations: AAOS and ACCP Recommendations for VTE Prophylaxis After Total Joint Arthroplasty

In 2012, the American College of Chest Physicians released recommendations for VTE prophylaxis for orthopedic surgery procedures, which highlighted a compromise between safety and efficacy for chosen regimens [59]. The ACCP and AAOS recommendations have become increasingly similar, although the AAOS guidelines do not endorse any specific anticoagulation agent [60]. The ACCP guidelines provide the following relevant recommendations for patients undergoing TKA and THA:

- VTE prophylaxis for ≥ 10–14 days, rather than no prophylaxis. May be extended up to 35 days
- Recommends against screening with duplex ultrasonography before hospital discharge
- LMWH be started 12 h before or 12 h after surgery to limit postoperative bleeding
- Acceptable anticoagulants: LWMH, fondaparinux, dabigatran, apixaban, rivaroxaban, low-dose unfractionated heparin, adjusted-dose vitamin K antagonist (warfarin), aspirin, and portable mechanical compression

The following suggestions were also included in the ACCP 2012 guidelines:

- Use of LMWH for chemoprophylaxis due to extensive data supporting safety and efficacy
- Use chemoprophylaxis and mechanical compression during hospital stay
- Using mechanical compression or no prophylaxis in patients at high risk for bleeding

In a recent review article, emphasis was placed on the importance of deciding upon a safe and effective VTE prophylaxis algorithm that is tailored to the patient's specific risk profile [61•]. Multiple studies have evaluated risk factors associated with VTE-related complications including, previous VTE, advanced age, obesity, immobility, estrogen therapy,

cancer, thrombophilias, molecular risk factors, atrial fibrillation, chronic obstructive pulmonary disease, depression, and higher Charlson Comorbidity Indices [62, 63•, 64]. There have also been multiple risk stratification protocols developed utilizing these various assigned risk factors, with no consensus on one specific validated risk strategy [64–66]. The surgeon should understand the VTE risk factors, be knowledgeable of the available agents and associated published guidelines when deciding on an appropriate patient specific regimen [61•].

Orthopedic Surgical Space Suit

CDC Recommendations

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

The outcomes measured to evaluate the safety, efficacy, and personnel allocation of an orthopedic surgical space suit in reducing the risk of SSI were deep SSI, deep SSI requiring reoperation, and superficial SSI. There was no benefit noted to wearing an orthopedic space suit to reduce the risk of SSI when three OBS were critically analyzed when the above outcomes were used [67–69]. The quality of evidence was graded as very low-quality, as some sample sizes were small and event rates were low with varying individuals wearing the space suit and notable environmental differences including laminar flow.

Prevention of Biofilm Formation

CDC Recommendations

- Available evidence suggests uncertain tradeoffs between the benefits and harms regarding cement modifications and the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*).
- 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*).
- The search did not identify studies evaluating vaccines for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*).
- The search did not identify studies evaluating biofilm control agents such as biofilm dispersants, quorum-sensing inhibitors, or novel antimicrobial agents for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. (*No recommendation/unresolved issue*).

The most effective strategies to reduce the risk of biofilm formation and SSI in prosthetic joint arthroplasty patients continue to be investigated by the orthopedic community with no current consensus on optimal protocols. The CDC and HICPAC sought to evaluate the available literature based on the following: effectiveness of cement modification, effectiveness of prosthesis modifications (i.e., antimicrobial coating, printing technologies, and nanotechnology), use of vaccines, and effectiveness of biofilm control agents (i.e., dispersants, quorum-sensing inhibitors, novel antimicrobial agents). There were two RCTs identified as moderate-quality evidence that examined cefuroxime-loaded cement compared to plain cement in primary TKAs who received perioperative antibiotics. A meta-analysis of these studies ($N = 428$) showed a benefit to using cefuroxime-loaded cement (2 g in 40 g of polymethylmethacrylate) in both diabetic and patients without diabetes when deep SSI was used at the outcome measure [70, 71].

There were no in vivo studies acknowledged that evaluated the other questions posed regarding the safety and effectiveness of prosthesis modifications, vaccines, or biofilm control agents and their influence on biofilm formation and subsequent risk of SSI [14••].

Other Recommendations: Intraoperative Irrigation in Prosthetic Joint Arthroplasty

There are multiple types of irrigation solutions available including detergents, antibiotic-infused irrigation, and antiseptic agents. Detergents have been shown to be superior to saline and antibiotic solution for bacterial removal in vitro largely due to their ability to inhibit bacterial adherence properties [72]. Adding antibiotics to irrigation is controversial as earlier reports suggested topical antibiotics were more efficacious than normal saline and in vitro studies proved that topical antibiotics decreased bacterial inoculum in clean wounds. These methods have not proven to be as effective as IV prophylactic antibiotics with regard to decreasing the incidence of SSI. Studies have demonstrated that the use of antibiotic irrigation can be associated with higher rate of wound complications, dermatitis, and hypersensitivity reactions, and an increased concern for bacterial resistance [73–75].

Antiseptic agents for wound irrigation reduces bacterial load without creating resistance and there is supporting evidence for their effectiveness in SSI prevention [76]. Cytotoxicity is a concern with antiseptic agents, which potentially could impair wound healing and lead to development of necrotic tissue.

Five antiseptic agents were evaluated in a recent study assessing the cytotoxicity against human fibroblasts and stromal progenitor cells while maintaining a bacterial load reduction of 99.9%. When tested against *Staphylococcus aureus* and *Staphylococcus epidermidis*, all agents, except

polyhexanide were bactericidal and cytotoxic at commercially available levels. Diluted povidone-iodine to 1.3 g/L was bactericidal at concentrations in which some cells remained viable [77]. This study and other prior reports have evaluated the optimal dilution, cytotoxicity, and reduction of bacterial burden in wound irrigation with various antiseptic agents prior to closure during elective TJA procedures and have found that dilute povidone-iodine solution (0.35%) has been shown to decrease the risk of SSI and PJI [76, 77].

There are numerous newer antiseptic agents and wound lavage systems available for use for intraoperative wound irrigation including a jet lavage system containing low-dose chlorhexidine gluconate 0.05% in sterile water (Irrisept, IrriMax Corp, Lawrenceville, GA, USA). A recent study demonstrated that there was no discernable difference in infection rates between chlorhexidine irrigation and dilute Betadine for THA and 0.9% saline for TKA [78]. There are also systems with proposed mechanisms that remove debris, microorganisms, and biofilms through their chemical structural composition, including a wound lavage system consisting of ethanol (solvent), acetic acid (pH modifier), sodium acetate (buffer), benzalkonium chloride (detergent/surface agent), and water (Bactisure; Zimmer Biomet, Warsaw, IN, USA). Future research will be directed at assessing the efficacy of reducing the bacterial burden while minimizing wound complications and potentially preventing SSI, especially in high-risk patients.

Conclusion

There are a multitude of factors contributing to a patient's potential risk for developing surgical site infection. The authors recognize that this is a comprehensive review dedicated to the 2017 CDC recommendations and does not incorporate some of the most important aspects of clinical assessment and perioperative medical host optimization of modifiable and non-modifiable risk factors. The recommendations provided throughout this review, including more recent guidelines from other organizations such as the AAOS and ACR, should assist clinicians in developing and/or refining surgical site prevention protocols for their patients undergoing total joint arthroplasty procedures. There are numerous areas where low-quality evidence precluded recommendations, as such, future research should focus on expansion of the existing evidence and further defining strategies for SSI prevention.

Compliance with ethical standards

Conflict of Interest The authors have nothing relevant to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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