Prevention

1.1. PREVENTION: HOST RELATED

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QUESTION 1: What are the absolute and relative contraindications to elective primary total joint arthroplasty (TJA), with respect to surgical site infection (SSI) and periprosthetic joint infection (PJI) risk?

RECOMMENDATION: Elective joint arthroplasty is contraindicated in patients with an infectious lesion in the ipsilateral extremity, until the infection is resolved. TJA needs to be deferred in patients with uncontrolled conditions such as diabetes, malnutrition, chronic kidney disease, as well as other diseases that are known to increase the risks of SSIs/PJIs.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 90%, Disagree: 7%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

Immunosuppression and Rheumatoid Arthritis (RA) (Relative Modifiable Risk Factors (MRF))

Evidence Strength: Moderate

Current studies evaluating the risks of PJIs in immunosuppressed patients have primarily been grounded in transplant patients (discussed in later sections), and those receiving biologics or non-biologic disease modifying anti-rheumatic drugs (DMARDs). In a Japanese study by Momohara et al., the risk for post-TJA SSI due to biologic DMARDs was compared against that of non-biologic DMARDs in RA patients [1]. Of note, non-biologic DMARDs were continued throughout the perioperative period, but biologic DMARDs were withheld in concordance with the British Society for Rheumatology and Japanese College of Rheumatology guidelines (~2 to 4 weeks based on half-life). The odds ratio (OR) for SSIs with biologic DMARDs was 5.69 (95% confidence interval (CI) 2.07-15.61). Furthermore, multiple logistic regression analysis found tumor necrosis factor-α blocker therapy to be the most potent of the biologics, with infliximab conferring a 9.8 greater odds (OR 2.41-39.82) and etanercept conferring 9.16 greater odds (95% CI 2.77-30.25) for SSIs. The only other significant risk factor for increased SSIs was RA disease duration (OR 14.5; 95% CI 8.9–21.0). A separate Japanese hospital surveillance study also demonstrated a smaller, but significant increase in SSIs with biologic DMARDs when compared to non-biologic DMARDs (OR 2.12; 95% CI 1.48–3.03) [2].

Conversely, a Danish database study comparing biologic versus non-biologic DMARD treated TJA candidates found no significant differences in PJI rates (adjusted hazards ratio 1.61; 95% CI 0.70-3.69) [3]. Furthermore, glucocorticoid exposure within 90-days of surgery was found to increase the 1-year risk for PJIs (OR 2.31; 95% CI 1.09 to 4.89). Lastly, one-year PJI risk was also elevated in RA patients when compared to osteoarthritis patients (OR 1.59; 95% CI 1.23-2.04).

The American College of Rheumatology (ACR) and American College of Hip and Knee Surgeons (AAHKS) have recently developed guidelines with regards to biologic and non-biologic drug management in the perioperative period [4]. Current guidelines indicate biologic DMARDs are to be discontinued in the perioperative period based on medication half-lifes. However, discontinuation may still not deter the risks conferred. In general, traditional, nonbiologic DMARDs can be continued throughout the perioperative period.

Intra-articular Injections (Modifiable)

Evidence Strength: Strong

In a matched cohort database study by Cancienne et al., patients receiving intra-articular corticosteroid injections of the knee were separated into three cohorts based on the last injection prior to surgery: 0 to 3 months, 3 to 6 months and 6 to 12 months. Matched controls were selected based on the absence of any previous intra-articular injections. Patients receiving intra-articular steroids 0 to 3 months before surgery demonstrated an increased risk for infection at 3 months (OR 2.0; 95% CI 1.6-2.5; 2.60% vs. 1.33%) and 6 months (OR 1.5; 95% CI 1.2-1.8; 3.41% vs. 2.34%) postoperatively. For patients receiving corticosteroids more than 3 months preoperatively, no increase in postoperative PJI was observed. A similar database study of 173,958 THAs by Schairer et al. showed intra-articular corticosteroid injections 0 to 3 months preoperatively increased the risk of infection 0 to 3 months (Hazard Ratio (HR) 1.52), 3 to 6 months (HR 1.46) and 6 to 12 months (HR 1.39) postoperatively [5]. Similar to the findings from Cacienne et al., it was reported that steroids injected greater than three months preoperatively did not increase postoperative PJI risks.

The quantity of intra-articular steroid injections within one year of surgery may also play a role in PJIs. Chambers et al. reported increased infection rates in patients who received two or more intra-articular steroid injections (OR 3.30; 2.0% vs. 6.6%) when compared to those who only received one. Like the studies performed by Cancienne et al. and Schairer et al., viscosupplementation patients were excluded from the study.

Current systematic reviews and meta-analyses have attempted to better define the effects of intra-articular injections, but a paucity of prospective studies, randomized-control trials and highly variable study designs have led to highly confounded and poorly defined results [6–9]. Moreover, with PJI rates of approximately 3% in total knee arthroplasty (TKA) [10] and 0.4-2.2% in total hip arthroplasty (THA) [11,12], current studies are reported to be too underpowered to detect the differences in PJI rates.

There is strong evidence that surgery should be absolutely delayed for a minimum of three months following intra-articular steroid injections. Surgeons may also consider intra-articular injections of the knee within three months to one year a potential relative contraindication. However, future large cohort or randomized control trials are required to assess the true risks. Evidence regarding viscosupplementation is unavailable.

Body Mass Index (BMI) ≤ 20 (Modifiable)

Evidence Strength: Moderate

In a case-control study of 27 patients by Manrique et al., underweight patients (BMI <18.5 kg/m^2) suffered from an increased risk for SSIs (11.1% vs. 0.0%). Conversely, in a database study of 4,665 TJAs by Anoushiravani et al., patients who are underweight (BMI ≤ 19 kg/m^2) were at reduced risks for PJIs (OR 0.23; 95% CI 0.09-0.61) [13]. Similarly, when underweight patients were compared to obese patients, no differences in infection rates were observed [14]. Current evidence for or against PJIs in underweight patients are equivocal; however, due to the multitude of complications associated with underweight patients, TJA is relatively contraindicated, and medical optimization should precede TJA.

Obesity (Modifiable)

Evidence Strength: Strong

In a retrospective database study by Werner et al., postoperative outcomes of 891,567 patients undergoing THA were stratified into four distinct cohorts: non-obese (BMI < 30 kg/m^2), obese (BMI 30-40 kg/m^2), morbidly obese (BMI 40-50 kg/m^2) and super-obese (BMI > 50 kg/m^2) [15]. The risks of SSIs increased with increasing BMI. SSI rates were noted to be 0.8% in the non-obese, 2.6% in the obese, 5.2% in the morbidly obese and 12.4% in the super-obese. In a study of 71,599 cases by Fu et al., wound complications (superficial infections, deep surgical site infections, organ space surgical site infections or wound dehiscences) were also observed to positively correlate with BMI, with 0.8% of non-obese patients experiencing wound complications, 0.9% in class 1 obesity, 1.0% in class 2 obesity and 1.7% in class 3 obesity [16]. In addition, patients diagnosed with malnutrition were two times more likely to have wound complications (2.0% vs. 1.0%). Hypothyroidism should also be evaluated in this population, as new studies indicate a potential causal link between the two disease states and PJI [17,18]. These findings of increased SSIs with obesity have been supported by several meta-analyses [19–21]. Current management guidelines indicate weight loss is helpful in reducing PJIs in this patient population. Hence, obesity is considered a relative contraindication while morbid obesity serves as an absolute contraindication. However, the current approach to weight loss protocols is highly controversial, with no absolute guidelines for which methodology (e.g., diet/exercise vs. medically prescribed very low-calorie diets vs. bariatric surgery) is superior.

Bariatric Surgery (Non-modifiable)

Evidence Strength: Strong

Studies regarding the effect of pre-TJA bariatric surgery remain equivocal. In a matched cohort study by Inacio et al., bariatric surgery did not result in significantly lower rates of 1-year deep or 30-day superficial infections when compared among patients with bariatric surgery > 2 years prior to TJA (superficial 0%; deep 1.5%), those with bariatric surgery within 2 years of TJA (superficial 2.0%; deep 1.0%) and obese patients without bariatric surgery (superficial 1.2%; deep 0.5%) [22]. In a study by Watts et al., bariatric patients experienced a non-significant trend towards lower infection rates compared to controls matched by BMI (HR 1.3; 95% CI 0.8-20.3) [23]. It is suspected that in patients undergoing bariatric surgery prior to TJA, the risks for PJIs are reduced due to decreasing BMIs, but is offset by the increased risk for malnutrition. Improved patient stratification (e.g., malnutrition workup) may allow for better risk appraisal of these patients preoperatively.

Malnutrition (Modifiable)

Evidence Strength: Strong

The estimated prevalence of malnutrition in TJA patients ranges from 27 to 50% [24–26]. Malnutrition patients can be described using a variety of markers including serum albumin < 3.5 g/dL, total lymphocyte count < 1,500/mm^3, and/or transferrin < 200 mg/dL [27,28]. Multiple reviews have supported the claims that the degree of malnutrition correlates with an increased risk of impaired wound healing, persistent wound drainage, PJI and low success rates of the initial irrigation and debridement (I&D) [29–35]. In a small cohort study by Lavernia et al., it was reported that 4.54% of patients with an albumin < 3.5 g/dL developed a deep infection versus 2.06% in controls [36]. Many other studies have confirmed malnutrition to be a significant risk factor for prolonged hospitalization and postoperative complications, particularly SSIs and PJIs [33,37]. In a prospective study of 779 primary TJA patients, Kamath et al. found the incidence of preoperative albumin < 3.5 g/dL to be 15% [38]. In a separate, matched cohort study, malnutrition (albumin < 3.5 g/dL) was determined to be an independent risk factor for PJIs (adjusted OR 3.00, 95% CI 1.56 to 5.75) [39]. In a propensity-matched, retrospective, American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database analysis of 34,800 TKA patients with preoperative albumin levels, Fu et al. reported that preoperative hypoalbuminemia was a strong predictor for multiple complications (OR 1.78, 95% CI 1.20 to 2.64) [16]. A retrospective cohort-control study of 49,603 TJAs reported the prevalence of hypoalbuminemia to be 4%, placing patients at a significantly higher risk of SSIs (risk rate (RR) 2.0, 95% CI 1.5 to 2.8) [40].

In a retrospective cohort, Jaberi et al. confirmed that malnutritioned TJA patients were more likely to develop a deep infection and require further treatment with I&D [28]. Of these I&D patients, 35% continued to fail. Bohl et al. found that patients with hypoalbuminemia were three times more likely to have an indication of sepsis for revision arthroplasty (RR 3.8, 95% CI 3.4 to 4.3), and twice as likely to develop PJIs within 30 days of revision for aseptic indications (RR 2.1, 95% CI 1.2 to 3.5) [41]. A retrospective cohort study of 501 revision TJAs for PJIs noted the incidence of at least one laboratory parameter suggestive of malnutrition was 51% (OR 2.3, 95% CI 1.5 to 3.5) [32]. After multivariate analysis, Yi et al. found that malnutrition was a significant risk factor for chronic septic failures (OR 2.131, 95% CI 1.294 to 3.512) and acute PJIs complicating aseptic revision arthroplasty (OR 5.858, 95% CI 1.317 to 26.057). Severely malnutritioned patients are at

a significantly increased risk of PJIs/SSIs after primary TJA, and experience even more dramatic rates of failure and infection in revision procedures.

Malnutrition is therefore a relative contraindication for TJA. However, current guidelines recommending which patient populations to screen are currently absent. Severe malnutrition (serum albumin < 3 g/dL), however, should be an absolute contraindication.

Diabetes Mellitus (Modifiable)

Evidence Strength: Strong

Outcomes regarding PJIs in diabetic patients have been controversial. In a retrospective cohort study of 56,216 knees, the diagnosis of diabetes was reported to confer a 1.28 (HR; 95% CI 1.03 to 1.60) greater risk for PJIs, when compared to non-diabetic controls [42]. In a Chinese study of 1,133 TKAs by Lee et al., diabetes was reported to be associated with a 6-fold (OR 6.07; 95% CI 1.43-25.75) increased risk for PJI when compared with unmatched controls [43]. In a separate study based on Chinese patients, Wu et al. showed an adjusted risk for PJIs of 5.47 (95% CI: 1.77 to 16.97) over controls. Several metanalyses have also reported a significantly elevated rate of PJIs within the diabetic population [19,42,44–48].

Conversely, in a high-quality study utilizing the Mayo Clinic Total Joint Registry, diabetes was reported not to be a risk factor for PJIs (HR 1.23; 95% CI 0.87 to 1.74) when confounding variables were appropriately adjusted for age, gender, BMI, type of surgery (THA vs. TKA), American Society of Anethesiolgists (ASA) score and operative time [49]. A separate high-quality retrospective database study by Martinez-Huedo et al. also demonstrated no substantial increases in PJIs in diabetic patients undergoing THAs (0.46 vs. 0.44%) or TKAs (0.24 vs. 0.24%) [50]. Similar to the Mayo Clinic Joint Registry report, this study extensively matched patient cohorts by variables including: year of surgery, age, sex and all of the comorbidities listed in the modified Elixhauser Comorbidity Index. Together, they indicate that diabetes may not be the primary driver of postoperative PJIs. Instead, confounding variables such as diabetic end-organ damage (e.g., chronic kidney disease, vascular disease, etc.), may be the underlying cause for PJIs in this population.

Studies regarding the utility of perioperative glucose and preoperative hemoglobin A1c (HbA1c) monitoring have also been highly heterogeneous [49,51–56]. In the Mayo Clinic Joint Registry study, after adjusting only for age and gender, perioperative glucose (+/-1 day/week) and preoperative HbA1c monitoring were not found to correlate with postoperative PJIs [49]. In a study by Iorio et al., HbA1c was not significantly different between infected diabetic (HbA1c mean 6.2%; range 5.1 to 11.1%) and nondiabetic (HbA1c mean 6.92%; range 4.7 to 15.1%) TJA patients. Chrastil et al. showed a significant increase in PJIs when evaluating maximum perioperative glucose, particularly with a cutoff of ≥ 194 mg/dL (HR 1.44; 95% CI 1.10 to 1.89), but reported no increase in PJIs for patients with HbA1c > 7% (HR 0.86; 95% CI 0.68 to 1.1) [53]. However, when graphed, an evident inflection point for increased PJIs appeared when HbA1c levels rose above approximately 8 to 9%. Similarly, serum glucose demonstrated an overt increase in infection rates when glucose levels rose above ~200 mg/dL. A meta-analysis study by Shohat et al. only showed non-significant trends for increased SSIs when correlating PJIs with HbA1c levels in a pooled OR of 1.49 (95% CI 0.94 to 2.37). The study reported significant heterogeneities between studies ($I^2 = 81.32\%$; $p < 0.0001$).

Diagnosis of diabetes, preoperative hyperglycemia and elevated HbA1c are not likely direct risk factors for PJIs, but more likely to be indirect markers of more serious comorbid conditions (e.g., chronic kidney disease (CKD), peripheral vascular disease (PVD), etc.). Patients, with a sole diagnosis of well-controlled diabetes, do not confer a clinically significant risk for PJIs. However, further evaluation and optimization are necessary for patients with uncontrolled diabetes, end-organ damage or other clinically relevant comorbid conditions. Elevated perioperative glucose and HbA1c are equivocal in predicting PJIs, but should still be optimized in the perioperative period. However, severely uncontrolled diabetes is an absolute contraindication for TJA (e.g., serum glucose ≥ 200 mg/dL). For those with HbA1c ≥ 8 to 9% or glucose levels between 180 to 200 mg/dL, optimization may be a consideration in the preoperative period.

Chronic Kidney Disease (CKD) (Modifiable)

Evidence Strength: Strong

In a retrospective database study by Cavanaugh et al., patients undergoing primary TJA with CKD/end-stage renal disease (ESRD) were associated with a significantly increased risk for SSIs when compared to matched, non-CKD/ESRD controls (OR 1.59; 95% CI 1.14 to 2.21) [57]. When stratified by a patient's dependence on hemodialysis, patients requiring dialysis were at significantly increased risk for SSIs compared to non-dialysis, CKD/ESRD controls (OR 2.44; 95% CI 1.27 to 4.70). When compared to CKD/ESRD patients who underwent renal transplant surgery, dialysis patients also fared significantly worse (OR 2.92; 95% CI 1.93 to 4.42).

The risks of SSIs/PJIs in patients that do not require dialysis is uncertain. In two large separate database studies by Kildow et al. and Erkocak et al., CKD versus non-CKD did not show elevated risks for SSIs or PJIs. However, it should be noted that patient-matching was more extensive in Cavanaugh's study, and that it is difficult to assess the severity of CKD progression in the large database studies.

In a Medicare database study, patients were divided into five cohorts: (1) diabetes mellitus (DM) and THA, (2) DM, THA, CKD, (3) DM, THA, Hemodialysis (HD), (4) DM, THA, Renal Transplant (RT) and (5) age/gender-matched controls. At 90-days, the risk for PJIs increased with worsening comorbidity status: DM/THA OR 2.85 (95% CI 2.54 to 3.19), DM/THA/CKD OR 4.19 (95% CI 3.58 to 4.91) and DM/THA/HD OR 6.61 (95% CI 4.25 to 10.27). DM/THA/RT demonstrated no significant increases in PJI risks over that of control (OR 1.12; 95% CI 0.60 to 2.07), but by 2 years DM/THA/RT became significant with an OR of 1.45 (95% CI 1.04 to 2.04). Compared to previous studies, the risk of PJIs due to diabetes may be synergistic with CKD. This risk is similar to that reported by Cavaughn et al. (OR 2.03, 95% CI 1.53 to 2.7) [57].

In summary, patients with CKD are at increased risks for postoperative SSIs, but require stratification to adequately assess their risk. Current evidence suggests that patients with ESRD requiring hemodialysis fare worse than non-hemodialysis CKD and renal transplant patients. With the reduced risks for postoperative SSIs/PJIs, patients on hemodialysis should be evaluated for renal transplant prior to TJAs.

Clotting Disorders (Non-modifiable)

Evidence Strength: Moderate

Comparative studies examining the effects of clotting disorders and risks for PJIs/SSIs are limited, with most studies reporting only on the natural history or incidence. In a study by Cancienne et al., the risk of PJIs in two cohorts undergoing primary TKAs, hemophiliacs and patients with von Willebrand's disease were compared against those of matched controls without a bleeding disorder [58]. At 3 months, hemophiliacs suffered from a 1.5 greater odds (95% CI 1.2 to 2.0) for PJIs, and patients with von Willebrand's disease trended towards 1.4 greater odds (95% CI 0.9 to 2.1) for PJIs. PJI rates were marked by six

months for both groups (hemophilia OR 1.6 (95% CI 1.4 to 2.0); von Willebrand's disease OR 1.5 (95% CI 1.1 to 2.0)). Large cohort database studies demonstrate inconsistent findings regarding coagulopathies [18,59–61]. However, these studies have failed to sub-analyze the underlying pathologies (e.g., Vitamin K deficiency, von Willebrand's disease, etc.) responsible for abnormal clotting, therefor potentially confounding results.

Currently, the study by Cancienne et al. is the largest, comparative study directly assessing patients with blood clotting disorders. Patients afflicted by clotting disorders are more likely to suffer from PJIs due to their increased risks for hemoarthropathies. Management of these patients, particularly with regards to venous thromboembolism (VTE) prophylaxis, remains challenging. Patients with clotting disorders are relative contraindications to TJA.

Previous Infection of the Operative Joint (Non-modifiable)

Evidence Strength - Strong

In a retrospective cohort study by Pugely et al., patients undergoing elective primary TJAs with a history of previous wound infection were reported to be at a 5.0 greater odds (95% CI 2.3 to 10.9) for SSIs when compared to patients without a history of joint infections [62]. Similarly, in a study of patients afflicted by RA, history of joint infections also resulted in increased risks for postoperative PJIs (OR 5.4; 95% CI 1.87 to 16.14) [63]. Patients reporting previous infections of the joint should be evaluated for active infections with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Surgery should be delayed for those with markers of active infections.

Active Infection (Modifiable)

Evidence Strength - Strong

Systemic or local tissue infections have also been associated with hematogenous or direct seeding of the prostheses after TJA [64–70]. Active infections of an arthritic joint have also been proven to increase the rates of PJIs after TJA substantially [71,72]. A retrospective case-control study found that active *Staphylococcus* septicemia was associated with an increased risk of SSI OR 4.87 (95% CI 1.44 to 15.35) [73]. More interestingly, Radtke et al. reported that preoperative systemic extended-spectrum beta-lactamase bacterial infections within 15 months of THAs significantly increased the risks for PJIs (OR 20.13) [74]. Grammatico-Guillon et al. reported that patients with active ulcers preoperatively had significantly higher rates of SSIs following TJA versus those without ulcers (HR 2.55; 95% CI 1.94 to 3.35) [75]. The authors also showed that patients with urologic inflammatory diseases have also been noted to have increased risks for SSIs after TJAs. However, randomized control trials and metanalyses have indicated that patients with asymptomatic bacteriuria do not appear to be at increased risks for PJIs [76,77]. Moreover, PJI cultures were never the same as the urologic cultures. Larger database studies and retrospective chart reviews have demonstrated no associations between urinary tract infections and PJIs [59,60,78].

In summary, to prevent the catastrophic sequelae of PJIs, active infections of the joint, bloodstream or local tissue are an absolute contraindication to surgery and should be managed prior to performing a TJA.

Human Immunodeficiency Virus (HIV) (Modifiable)

Evidence Strength: Moderate

In a cohort study utilizing the National Inpatient Sample (NIS) database between 1998 and 2010, HIV(+) patients demonstrated a significant 2.78 odds (95% CI: 1.15 to 6.72) of developing SSIs [79]. A similar study by Schairer et al. also reported a 2.06 (95% CI: 1.31 to 3.26) greater odds for PJIs in HIV/Aquired Immune Deficency Syndrome (AIDS) patients, but did not differentiate between the two cohorts. The effects became more evident in the study by Tan et al., which demonstrated 4.44 greater odds (95% CI: 2.47 to 7.99) for PJIs in the AIDS patient population. More recent cohort studies, such as those by Capogna et al. and Lin et al., reported only non-significant trends towards increased infections (OR 6.6 (95% CI 0.64 to 61.0) and OR 3.8 (95% CI 0.06 to 76.75), respectively) in cohorts with HIV [80–82]. Arguably, these discrepancies may be the result of improved HIV antiretroviral therapies and protocols.

Hepatitis co-infection should be investigated and addressed in all patients with HIV. The estimated incidence of hepatitis C co-infection is reported to be 23.2 to 37.0%, and co-infection with hepatitis B is 10.1 to 24.0% [80,83]. In a matched-cohort Medicare database study by Kildow et al., patients were stratified by concomitant hepatitis infections: (1) HIV, (2) hepatitis B virus (HBV), (3) hepatitis C virus (HCV), (4) HIV with HBV or HCV and (5) matched HIV(-) controls [84]. When examining HIV (+) patients only, PJI infections at 90-days post-TKA/THA and 2-years post-THA were not significantly different from HIV(-) controls. Conversely, PJI risks in HIV(+) with HBV(+) or HCV(+) patients were elevated at 90-days post-TKA (OR 2.32; 95% CI 1.27 to 4.25), 2-years post-TKA (OR 2.17 1.48 to 3.18) and 2-years post-THA (OR 2.67 1.59 to 4.47) when compared to matched HIV(-) and HBV(-) and HCV(-) controls.

Similarly, in a meta-analysis of PJIs in HIV only versus HIV with hemophilia patients, hemophilia conferred a 5.28 greater odd (95% CI 2.24 to 11.98) for PJI [85]. A separate analysis was also carried out examining the effects of HIV with and without highly active antiretrovial therapy (HAART) for PJI [85]. Patients receiving HAART were found to have a significantly reduced risk (OR 0.12; 95% CI 0.03 to 0.44) for PJIs [57].

Current recommendations regarding TJAs in patients with HIV indicate all patients undergoing TJA should be initiated on HAART therapy immediately, regardless of CD4+ counts and viral load. Untreated HIV patients are absolutely contraindicated for TJAs. However, due to the logistical nature of clinical studies, no studies to date have been developed to adequately correlate, stratify or control for CD4+ counts and HIV viral loads in relation to PJI outcomes. It is recommended that patients on HAART therapy maintain a preoperative CD4+ count of at least ≥ 200 or greater.

MRSA Colonization (Modifiable)

Evidence Strength: Strong

Outcomes regarding methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in TJA patients have primarily been studied in small sample sizes with highly variable outcomes. Kalmeijer et al. determined that high-level nasal carriage of *S. aureus* was a significant independent risk factor with a risk rate (RR) of 16.0 (95% CI 3.1 to 82.2) for developing an *S. aureus* SSI [86]. Subsequent studies have also demonstrated that THA patients colonized by MRSA have an elevated relative risk for SSIs of 4.46 (CI 95% 1.12 to 17.82; 5.26 vs. 1.17%) when compared to non-colonized cohorts [87]. Similarly, in TKA patients, the RR for SSIs was 5.61 (95% CI 1.81 to 17.38; 7.32 vs. 1.3%). A retrospective analysis of patients with PJI reported *S. aureus* colonization to have a 3.97 greater odds (95% CI 1.49 to 10.54) for PJI compared to control groups [88]. Furthermore, *S. aureus* colonization has been found to have an additive effect with active tobacco use, revision surgery, and/or BMI ≥ 30 kg/m^2, increasing the risk 3 to 12 times that of controls [89]. A number of prospective studies and systematic reviews in both the orthopaedic and general surgery literature

have reported rapid screening and decolonization of *S. aureus* nasal carriers on admission to be effective [90,91].

S. aureus screening and treatment are quick, inexpensive and simple and should be performed on all patients prior to surgery. A small number of patients do not respond to treatment and remain chronic carriers. Although their risk remains elevated for PJIs, continued *S. aureus* colonization is a relative contraindication to elective primary TJA, but may be managed with intraoperative, local vancomycin. However, the use of vancomycin must be balanced against the risk for acute kidney injury [92].

Bacterial Skin Colonization Other Than MRSA (Modifiable)

Evidence Strength: Strong

Preoperative chlorhexidine-based skin preparation has been proposed as a method of reducing SSIs. In a randomized control trial by Kapadia et al., use of chlorhexidine-impregnated clothes the night before or the morning of admission reduced the 1-year PJI rate by 2.5% (2.9 vs. 0.4%) when compared to the previous standard of care (OR 8.15; 95% CI 1.01 to 65.6) [93]. Similar results have been observed in a previous retrospective cohort study (in the same institution) [94,95], as well as in the general surgery patient population [96].

Hepatic Disease

Evidence Strength: Strong

Hepatitis (Modifiable)

A retrospective study by Kuo et al. looking at 3,435 TKA patients in the Taiwanese Longitudinal Health Insurance Database reported that males with HBV had a 4-fold, (OR; 4.32; 95% CI 1.85 to 10.09) increased risk of PJIs compared to those without HBV [97]. The PJI risk was highest 6 months to 1 year following TKA (HR 18.7; 95% CI 1.90 to 184) and decreased after the first year (HR 4.8; 95% CI 1.57 to 14.7). The authors reported no differences in PJI incidences between patients without HBV in the first month. The presence or absence of cirrhosis and HCV infection did not further influence PJI risks in these patients. Interestingly, HBV did not appear to significantly increase the risk of PJIs for females.

In a retrospective, matched control study of 77 HCV(+) TJAs, there were no differences in PJI incidences in HCV(+) versus HCV(-) patients [98]. However, of the two infections in the HCV(+) group, both were deep infections that required reoperation. Meanwhile, both infections in the control group only reported superficial infections that were treated with IV antibiotics. When the HCV cohort was further stratified by disease progression, the incidence of PJIs was noted to be markedly higher in patients whose disease progressed to fibrosis (21 vs. 0%). Kildow et al. reviewed 22,663 TJA patients using the PearlDiver Medicare database and found increased TJA PJI risks for HCV(+) patients at 90-days (OR 1.96; 95% CI 1.53 to 2.50) and 2 years (OR 1.93, 95% CI 1.66 to 2.25), as well as in HBV(+) patients at 2 years (OR 1.66; 1.06 to 2.59) [99]. Although not directly compared to one another, concomitant HIV infection appears to increase infection rates further. With new HCV treatments, it will be important to observe the effects of HCV resolution and PJI outcomes.

Liver Cirrhosis (Modifiable)

To better delineate the effects of cirrhosis versus hepatitis, Jian et al. performed a matched control cohort study using 880,786 TJA patients from the NIS database [82]. When compared to controls, HBV(+) patients without cirrhosis were found to be at no increased risk for PJIs (1.22 (HR; 95% CI 0.77 to 1.95), while HCV(+) patients without cirrhosis were at a 2-fold greater risk for PJI (HR 2.33; 95% CI 1.97 to 2.76), and patients with cirrhosis were at 2.42 greater odds for PJIs (95% CI 1.87 to 3.12). In a large Danish database study by Deleuran et al., deep infection at one year was higher in cirrhotic patients than matched controls (OR 1.65; 95% CI 0.61 to 3.56; 3.1 vs. 1.4%) [100].

Other small, retrospective studies regarding liver cirrhosis demonstrated mixed results. Seol et al. retrospectively compared 71 cirrhotic patients undergoing elective TJA against non-cirrhotic controls [101]. Only a non-significant trend towards increased PJIs (13.5 vs. 5.6%) and SSIs (17.6 vs. 2.8%) was found. It was also noted that most patients who experienced surgical complications were more likely to have chronic comorbidities (e.g., CKD, diabetes and hypertension). Other older studies have described increased rates of wound complications after elective TJAs in patients with asymptomatic liver disease and advanced cirrhosis [102,103]. Similarly, a small study by Cohen et al. has suggested that certain subgroups of cirrhotic patients, specifically Child-Pugh A and B, can safely undergo elective TJA with no increased risk of adverse events [104].

Transplant (Non-modifiable)

Regarding patients receiving a liver transplant, the relative risk of PJIs remains a debated topic, with many studies being only case series. Two case series reported an overall PJI rate of 3.2 to 3.6% [105,106]. A cohort study by Ledford and colleagues reported that organ transplants substantially increased the risks of SSIs or PJIs (3.2%), but there were no differences between groups [106]. One study, which utilized the NIS database, compared the outcomes of 4,493 TJA patients with a history of organ transplantion and revealed that liver transplantion had the greatest increased risks of wound infections and SSIs (OR 3.90, 95% CI: 1.4 to 3.9) compared to kidney, heart, lung and pancreas transplantions [57].

HBV, HCV, cirrhosis and hepatic transplant are relative contraindications to surgery. However, both HCV and cirrhosis present as potentially modifiable risk factors with the advent of HCV immunotherapies and transplant surgeries, respectively. Preliminary evidence points towards HCV treatment prior to TJA. Additionally, the degree of liver cirrhosis and potential risks can be assessed based on the efficacy of serum clotting factors. Due to the lack of conclusive evidence, no strong recommendations can be given at this time for or against HCV immunotherapy, cirrhosis optimization or hepatic transplant prior to TJA. Hepatic panels and coagulation panels should be assessed in patients with end-stage liver disease and surgery should delayed if any bleeding deficiencies are noted.

Chronic Anticoagulation (Non-modifiable)

Evidence Strength: Low

In a matched case-control study by Simpson et al., chronic preoperative warfarin therapy in TKA patients led to: substantially increased hematoma formations within 48 hours (26.8 vs. 7.3%), superficial infections (16.8 vs. 3.3%), deep infections (6.0 vs. 0%) and returns to the operating room (OR) for washout (4.7 vs. 0.7%) [107]. Subset analysis of patients who required heparin-bridging demonstrated markedly higher, deep infection rates when compared to patients who continued warfarin. A similar matched case-control study of THA patients also reported increased rates of deep infections (9 vs. 2.2%) and superficial infections (13.5 vs. 2.2%) [108].

Due to the absence of strong, conclusive evidence or management guidelines, it is recommended for patients on warfarin therapy to be evaluated for other risk factors and optimized appropriately to mitigate the risks of PJI. Bridging of patients on warfarin should be avoided and only performed if absolutely necessary. Future studies

are needed to examine the relationship of International Normalized Ratio (INR), as well as modern-day heparin analogues (e.g., factor Xa inhibitors), with infection.

Alcohol Consumption (Modifiable)

Evidence Strength: Strong

A recent meta-analysis found that alcohol use had a two-fold risk of PJI following TJA (OR 1.88, 95% CI 1.32 to 2.68) [44]. Wu et al. reported similar outcomes in a retrospective study of Chinese patients undergoing TJA (OR2.95; 95% CI, 1.06 to 8.23) [45]. A large, retrospective, matched-control study of 880,786 Statewide Inpatient Database patients illustrated that alcohol use significantly increased the PJI risk after TJA (HR 1.64, 95% CI 1.38 to 1.95) and represented an additive risk factor when present concomitant to cirrhosis [82]. Grammatico-Guillon et al. retrospectively analyzed 32,678 patients in the French Regional Hospital Discharge database and found that alcohol abuse was correlated with a significant increase in SSI risk (HR 2.47, 95% CI 1.67 to 3.63) [75]. The major impact of alcohol abuse on PJI rates was demonstrated by Radtke et al. [74]. After retrospectively reviewing 566 THAs, alcohol abuse was found to increase the odds of PJI by 5.59 (95% CI 95% CI 1.14 to 27.33) within 18 months of surgery. Alcohol consumption has therefore been clearly shown to increase the risk of PJIs for patients undergoing TJAs [18,59–61,109,110]. While there is no defined period of required alcohol cessation prior to TJA, at least four weeks of abstinence has been suggested to reverse physiologic abnormalities associated with excessive alcohol use that predispose patients to increased risk of postoperative morbidity [111].

Alcohol consumption must be assessed on a case-by-case basis. Excessive alcohol consumption is a modifiable risk factor that is a relative contraindication for elective TJA until patients remain abstinent for a minimum of four weeks. However, patients who remain functional in good socioeconomic standing may not require surgical delay.

Smoking (Modifiable)

Evidence Strength: Strong

A recent review reported that 18% of the U.S. population are smokers, placing them at an RR of deep infection after TJA 3.5 times higher than the average population [112]. Tobacco use is growing in the obese population and carries eight times the risk of infection compared to non-obese, non-smokers [88]. In a study by Maoz et al., tobacco use, *S. aureus* colonization and BMI ≥ 30 kg/m^2 were additive in their risks for PJIs (OR 12.76; 95% CI 2.47 to 66.16) [89]. A 2:1 matched-cohort study reported significantly higher surgical complication rates (3.6%) in smokers compared to nonsmokers (0%). Moreover, the majority of revision TJAs performed in the smoking cohort were secondary to infection [113]. In their ACS NSQIP database study, Duchman et al. described a significant increase in the risk of wound complications after TJA in tobacco users (OR 1.47, 95% CI 1.21 to 1.78) [114]. In a comparable large database study, Kremers et al. conveyed similar outcomes with an increased risk of SSI in smokers (HR 1.7, 95% CI 1.1 to 2.6) [115]. Although Singh et al. did not find a significant difference in the rate of SSI in smokers, the authors reported a substantial risk for PJIs when compared to a matched nonsmokers control group (HR 2.28, 95% CI 0.99 to 5.27) [116]. Sahota et al. performed a propensity, score-matched analysis of 12,588 TJA patients in the ACS NSQIP database to assess the effects of smoking on 30-day postoperative complications. The overall 30-day surgical complication rate was higher in current smokers at 2.5% compared to 1.4% in nonsmokers (OR 1.84, 95% CI 1.21 to 2.80). Smokers also exhibited a markedly higher rate of 30-day deep SSIs (1.1%) in a combined THA/TKA cohort. Upon subgroup analysis, active smokers experienced substantially higher incidences of 30-day deep SSIs after THAs (1.3%) and 30-day superficial SSIs following TKAs (1.8%) [117]. A prospective, hospital-registry-based cohort study by Gonzalez et al. found that current smokers had higher one-year postoperative PJI rates than former smokers, both of which were significantly higher than never-smokers (HR 1.8, 95% CI 1.04 to 3.2). Beyond the first year of surgery, the risks of PJIs decreased slightly but remained significantly elevated compared to a history of no smoking (HR 1.12, 95% CI 0.64 to 2.04) [118]. A meta-analysis of six randomized trials demonstrated that smoking cessation had a relative risk reduction of 41% of total postoperative complications. In the same study, the authors pooled data from 15 observational studies and found that patients who discontinued smoking prior to surgery had decreased wound healing complications (RR 0.73, 95% CI 0.61 to 0.87) [119]. On the other hand, Azodi et al. reported that patients partaking in smoking a higher number of packs per year resulted in a significant increased risk of postoperative complications [120]. Moreover, after adjusting the multivariate logistic analysis, the heaviest tobacco smoking group had a 121% increased risk of systemic complications (OR, 2.21; 95% CI 1.28 to 3.82). Smoking represents an independent, modifiable risk factor that significantly compounds the risks of SSIs/PJIs when present alongside other comorbidities. Therefore, active smoking, especially heavy tobacco use, represents a relative contraindication to TJA until enrolled in a smoking cessation program for at least four weeks.

Intravenous Drug Abuse (Modifiable)

Intravenous drug abusers (IVDA) can often present with HIV, creating a myriad of risks that are problematic to treat. Previous retrospective studies have described a four-fold increase in septic arthritis of native joints in IVDA versus non-IVDA patients [121,122]. A retrospective study by Lehman et al. reported higher rates of PJIs in IVDA and/or HIV(+) patients [123]. IVDA also carried almost twice as high PJI incidences (25%) compared to HIV(+) only patients(14%). When IVDA and HIV were both present, the rates of PJIs increased to 40%. More recent studies confirmed that IVDA was a significant risk factor for THAs and resulted in higher odds of PJIs in orthopaedic surgery [109,124]. The risks of PJIs continue well past the primary TJA, and substantially impacts ensuing revision procedures. Su et al. reported an estimated 25% survival, free of reinfection rates, for two years in IVDA patients compared to 96% in control revision THA patients [125]. Pitta et al. conducted a prospective cohort study of 405 failed primary TKAs [126]. Their study demonstrated that IVDA was a significant risk factor for TKA failure and correlated with a five-fold increase in risk for revision surgery. Two retrospective reviews of IVDA within 1 year of THA and TKA described failure rates as high as 50%, complicated revision procedures and a 17% amputation rate [127,128]. The unacceptable PJI rates, leading to complex salvage procedures and high failure rates after primary and revision surgeries, make TJA in active IVDAs futile and an absolute contraindication. Patients should be referred to appropriate drug counseling programs and be offered surgery only after remaining abstinent from drug use for a minimum of one year.

Osteonecrosis (Non-modifiable)

Evidence Strength: Moderate

Evidence regarding osteonecrosis and its relation to SSIs/PJIs is highly conflicting. Currently, the three identified studies in this systematic review were all derived from the Kaiser Permanente Total Joint Replacement Registry (TJRR). In two studies by Namba et al.,

similar methods were applied to evaluate the effects of osteonecrosis on SSIs/PJIs; one focused on THAs while the other focused on TKAs [42,129]. Both studies demonstrated an increased risk for SSIs/PJIs in TJA candidates with osteonecrosis. However, a third study by Singh et al. [130], which contained many overlapping authors from the Namba et al. studies and utilized the TJRR, extended the original 8-year database to 11 years, and found no increases in SSIs/PJIs in THA candidates with osteonecrosis. Due to the conflicting evidence and high potential for study bias, osteonecrosis of the hip is not a strong risk factor for SSIs/PJIs in TJA candidates.

Age (Non-modifiable)

Evidence Strength: Moderate

There is inconsistent evidence on whether age contributes to increased risks of PJIs. The meta-analysis by Chen and colleagues showed no associations between age and risk of infection [46]. In a pooled analysis of eight studies, age (as a continuous exposure) was not associated with the risks of PJI [19]. However, findings from two studies suggested that patients 75 years old and above had an increased risk of SSIs following primary THAs [131,132].

Gender (Non-modifiable)

Evidence Strength: Moderate

The effects of gender on the risks of PJIs have been mostly inconsistent. While some studies suggest males are at an increased risk of developing PJIs following joint arthroplasty, others suggest the contrary. In a pooled analysis of eight studies, Chen et al. demonstrated that males had a higher risk of infection after TKA than females [46]. Recent pooled multivariate analysis of 28 studies confirms the emerging evidence [19].

Race (Non-modifiable)

Evidence Strength: Strong

Pooled analysis shows that black and Hispanic populations have increased risks of developing PJIs/SSIs, when compared to white populations [42,61,133].

Location (Non-modifiable)

Evidence Strength: Limited

One study reported an increased risk of infections for patients residing in rural locations as opposed to urban locations in China [45]. However, this may be the result of a country's care system as opposed to geographic location.

Hip vs. Knee Arthroplasty (Non-modifiable)

Evidence Strength: Strong

Compared to THAs, TKAs were consistently associated with increased risk of PJIs/SSIs [73,134].

Underweight (Modifiable)

Evidence Strength: Strong

Three studies compared underweight (BMI < 18.5 kg/m^2) vs. normal vs. overweight BMI categories and found no associations with PJIs [13,14,129].

Hypertension (Modifiable)

Evidence Strength: Strong

Pooled analysis of four large database studies with matched controls showed no significant evidence of associations between hypertension and the risks of PJIs/SSIs [18,59,60,135].

Socioeconomic Status (Non-modifiable)

Evidence Strength: Strong

Consistent evidence showed that a low income was associated with increased risks of PJIs/SSIs [136–138].

Electrolytes (Modifiable)

Evidence Strength: Strong

There was no significant evidence of associations between electrolyte imbalances and risks of PJIs/SSIs [18,62].

Depression (Modifiable)

Evidence Strength: Strong

Evidence suggested histories of depression and psychosis to be associated with increased risks of PJIs following TJA [18,59,60].

Steroids (Modifiable)

Evidence Strength: Moderate

A previous meta-analysis of four studies suggested a history of steroid therapy to be associated with increased risks of PJIs following TKAs [46]. In a pooled analysis of five studies, Zhu et al. also demonstrated steroid therapy to be associated with increased risks of PJIs following TJA [48]. In the most recent pooled analysis of 10 studies, the findings were consistent with previous evidence [19].

Cardiovascular Disease (CVD) (Modifiable)

Evidence Strength: Strong

A pooled analysis of seven studies reporting inconsistent findings showed a history of CVD to be associated with increased risks of PJIs/SSIs following TJAs [59,60,78,139–143]. In a pooled analysis of studies that evaluated congestive heart failure (CHF) and cardiac arrhythmias as risk factors, significant associations were demonstrated [5,18,59,60,133].

Peripheral Vascular Disease (PVD) (Modifiable)

Evidence Strength: Strong

A pooled analysis of six studies should a history of PVD is associated with increased risks of PJIs/SSIs [5,18,59,60,82,144].

Lung Disease (Modifiable)

Evidence Strength: Strong

The presence of chronic pulmonary diseases remains equivocal. While pooled analysis of four studies evaluating the associations of chronic pulmonary disease with risk of PJIs showed no evidence of an association [5,59–61], two studies reported consistent associa-

tions. With regards to chronic obstructive pulmonary disease, specifically, an increased risk for PJIs/SSIs was noted in a pooled analysis of four studies [3,73,133,135].

Rheumatoid Arthritis (RA) (Modifiable)

Evidence Strength: Moderate

A pooled analysis of seven studies showed RA to be associated with increased risks of PJIs following TKAs [46]. In another pooled analysis of seven studies, Zhu et al. demonstrated RA to be associated with increased risks of PJI [48]. Findings of a recent pooled analysis of 13 studies confirms the accumulating evidence [19] .

Malignancy (Non-modifiable)

Evidence Strength: Strong

A history of cancer or malignancy was associated with increased risks of PJIs/SSIs following arthroplasty in a pooled analysis of seven studies [18,59–61,73,145,146]. However, evidence on the associations between metastatic tumors and risks of PJIs/SSIs was limited and inconsistent [5,18,59,60].

Previous Joint Surgery (Non-modifiable)

In a pooled analysis of five studies, a history of previous joint surgery (vs. no previous joint surgery) was associated with a threefold increased risk of PJIs [19]. When compared to primary arthroplasties, revision arthroplasties were associated with increased risks of PJIs in a pooled analysis of five studies [19]. Two studies reported a history of previous joint infections to be associated with increased risks of PJIs, but these findings were based on univariate analysis [3,63].

Frailty (Modifiable)

Evidence Strength: Moderate

A single, high-quality study reported increased risks of PJIs comparing frail patients with non-frail patients [147].

Anemia (Modifiable)

Evidence Strength: Strong

Consistent evidence showed that preoperative anemia was associated with increased risks of PJIs/SSIs following TJAs [5,59,60,148].

ASA (Non-modifiable)

Evidence Strength: Strong

An ASA grade of > 2 was associated with increased risks of PJIs/SSIs; this was consistent across all studies [42,89,129,131,133,134].

Charlson Comorbidity Index (Modifiable)

Evidence Strength: Strong

Though the exposures were not comparable, and therefore could not be pooled, there was consistent evidence showing a higher Charlson Comorbidity Index to be associated with an increased risk of PJIs/SSIs [136,137,149].

Osteoarthritis (Non-modifiable)

Evidence Strength: Strong

Pooled evidence from seven studies showed no significant associations of osteoarthritis with the risks of PJIs following joint arthroplasties [42,109,129,130,150,151].

Post-Traumatic Arthritis (Non-modifiable)

Evidence Strength: Strong

Pooled analysis of three studies showed no evidence of associations between post-traumatic arthritis and risks of PJIs/SSIs [42,129,152].

Dental Procedures (Non-modifiable)

Evidence Strength: Limited

In two studies that evaluated the associations of dental procedures with risks of PJIs, there was no evidence of any significant associations [45,145].

Neurologic (Modifiable)

Evidence Strength: Strong

A history of neurologic disease such as hemiplegia/paraplegia was associated with increased risks of PJIs/SSIs in a pooled analysis of four studies with inconsistence findings [59–61]. The results were the same for dementia and PJIs/SSIs [59,60,73].

Hypercholesterolemia (Modifiable)

Evidence Strength: Strong

None of the studies, which evaluated the associations of hypercholesterolemia and peptic ulcer disease with the risks of PJIs, showed any evidence of associations [18,59,60].

Valvular Disease (Non-modifiable)

Evidence Strength: Strong

Evidence regarding the associations between valvular diseases and risks of PJIs/SSIs was limited and inconsistent [18,59–61]. In the pooled analysis, there was no significant evidence of PJIs/SSIs being associated with a history of pulmonary circulatory disorders [5,59–61], a history of hypothyroidism [18,59,60,153], or a history of drug abuse [18,59,60].

Transfusion (Non-modifiable)

Evidence Strength: Strong

Patients who receive allogenic blood transfusions are at increased risks of SSIs/PJIs [5,134,154–156]; however, the evidence is limited for autogenic blood transfusions [5]. Prophylaxis with warfarin or low molecular weight heparin for venous thromboembolism was associated with increased risks of PJIs [157,158].

Methods and Materials: Manuscripts pertaining to host-related risk factors for PJIs were searched using PubMed, ScienceDirect, and Web of Science, with a date restriction of January 1, 2013 to February 23, 2018. The following search queries and their results are listed in the following chart:

Database	Search Term/Filter	Results
PubMed	("arthroplasty, replacement, hip"[MeSH Major Topic] OR "arthroplasty, replacement, knee"[MeSH Major Topic]) OR ("knee"[TITLE] OR "hip"[TITLE]) AND ("arthroplasty"[TITLE] OR "replacement"[TITLE]) AND ("infection"[MeSH Major Topic] OR "deep infection"[TITLE] OR "PJI"[TITLE] OR "Prosthetic Joint Infection"[TITLE] OR "Periprosthetic Joint Infection"[TITLE] OR "Surgical Site Infection"[TITLE] OR "SSI"[TITLE]) NOT ("autobiography"[Publication Type] OR "comment"[Publication Type] OR "congresses"[Publication Type] OR "dictionary"[Publication Type] OR "editorial"[Publication Type] OR "interview"[Publication Type] OR "lectures"[Publication Type] OR "legal cases"[Publication Type] OR "legislation"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type] OR "patient education handout"[Publication Type] OR "periodical index"[Publication Type] OR "personal narratives"[Publication Type] OR "technical report"[Publication Type] OR "webcasts"[Publication Type]) AND "last 5 years"[PDat] AND English[lang]	510
ScienceDirect	pub-date > 2012 and TITLE-ABSTR-KEY(((("hip arthroplasty" OR "hip replacement") OR ("knee arthroplasty" OR "knee replacement")) AND infection)	956
Web of Science	((TI=(("hip arthroplasty" OR "hip replacement" OR "knee replacement" OR "knee arthroplasty") AND (infection OR PJI OR SSI)))) AND LANGUAGE:(English) AND DOCUMENT TYPES: (Article OR Abstract of Published Item OR Data Paper OR Database Review OR Early Access OR Review)	246
	Total	1712

These results were subsequently imported into Mendeley Reference Management Software (Elsevier, Amsterdam, Netherlands) and 347 duplicates were removed. These abstracts were then imported into the Rayyan (Qatar Computing Research Institute, Doha, Qatar) for subsequent screening of titles and abstracts by authors J.E.F. and Z.C. Of the 1,365 abstracts collected, 1,126 were excluded due to incorrect study topic, foreign language, or low study quality (case reports and case series without comparative groups). Of the remaining abstracts, 239 remained for full-text article review with study quality assessment using the American Academy of Orthropaedic Surgeons (AAOS) Clinical Practice Guideline and Systematic Review Methodology guidelines [159]. The Relative Risk, Odds Ratios, and Hazard Ratios, as well as incidences and statistical significances, were used to assess outcomes of prosthetic joint-related infections.

A separate systematic review was performed by S.K. Data sources included Medline, Embase, Web of Science, Cochrane Library and reference lists of relevant studies from inception to February 15, 2018. Studies of interest were longitudinal studies (observational studies and randomized controlled trials (RCTs)) that have evaluated the associations of patient-related factors and the risk of SSIs and/or PJIs in patients undergoing orthopaedic procedures. Of 7,177 potentially relevant citations, 69 studies were finally included in this review. No RCTs relevant to the review topic were identified.

What modifiable and non-modifiable host factors contribute to an increased risk of SSI/PJI?

Modifiable host risk factors for PJI/SSI in TJA:

- Active Infection
- Alcoholism
- Cardiovascular Disease
  - Congestive Heart Failure
  - Cardiac Arrhythmia
- Chronic Kidney Disease
- Chronic Obstructive Pulmonary Disease
- Clotting Disorders
- Depression
- Diabetes Mellitus
  - HbA1c
  - Serum Glucose
- Drug Abuse
- End-stage Renal Disease
- Frailty
- HIV/AIDS
- Immunosuppression
- Intra-articular Steroid/Viscosupplement Injection
- Kidney Disease
- Malnutrition
- MRSA Colonization
- Obesity
- Peripheral Vascular Disease
- Psychosis
- Renal Disease
- Rheumatoid Arthritis
- Skin Colonization
  - MRSA/MSSA
- Smoking
- Untreated HCV

Non-modifiable host risk factors for PJI/SSI in TJA:

- Age
- ASA >2
- Bariatric Surgery
- Chronic Anticoagulation
- Gender
- Hemiplegia/Paraplegia
- HBV
- Osteonecrosis
- Previous Joint Surgery
- Previous Joint Infection
- Previous Infection
- Transplant

In addition to identifying pertinent risk factors for PJIs, what is the acceptable total risk for patients undergoing elective, primary

TABLE 1. Definitions

	Modifiable Risk Factor	Non-modifiable Risk Factor
Absolute Contraindication	**Absolute modifiable risk factor**: A risk factor that is associated with a preventable complication and delays surgery until it is appropriately evaluated and optimized.	**Absolute non-modifiable risk factor:** A risk factor that cannot be optimized and precludes the patient from receiving surgery. Alternative therapies for joint pain should be pursued.
Relative Contraindication	**Relative modifiable risk factor:** A risk factor that is modifiable but does not require surgical delay if no other risk factors are present. However, when the patient's risk for postoperative complications crosses the threshold of acceptability, this risk should be optimized.	**Relative non-modifiable risk factor:** A risk factor that is non-modifiable and does not require surgical delay. For patients with additional risk factors which cross the threshold of acceptability, other modifiable risk factors should be optimized prior to surgery.

TJAs? The Readmission Risk Assessment Tool (RRAT) was specifically developed to reduce the incidence of preventable hospital readmissions in patients undergoing elective TJA [160]. The RRAT includes eight distinct risk factors and uses a weighted score to quantify a patient's risk of readmission (e.g., MRSA colonization – 3 points, Smoking – 1 point, BMI ≥ 40 – 3 points, etc.). With nearly 45% of readmissions being due to SSIs, the RRAT is a powerful tool to identify and optimize patients at risk for PJIs. Despite the development of these powerful tools, a discussion regarding an ethically and financially acceptable risk cutoff for PJI is still required.

When does the accumulated relative risk of infection due to comorbidity burden (modifiable, non-modifiable or a combination) become unacceptable to proceed with TJA?

Examples:

- **Modifiable risk factors that are absolute contraindications (Absolute MRF):** Untreated HIV, serum glucose ≥ 200, active sepsis, active joint infection, intra-articular injections within three months, active intravenous drug use, super obesity (BMI ≥ 50 kg/m^2)
- **Modifiable risk factors that are relative contraindications (Relative MRF):** Obesity, elevated HbA1c, smoking, catastrophizers, high fall-risk patients, non-metastatic cancer, malnutrition, hepatitis C
- **Non-Modifiable risk factors that are absolute contraindications (Absolute Non-MRF):** Pulmonary hypertension
- **Non-modifiable risk factors that are relative contraindications (Relative Non-MRF):** Gender, age, hemiparesis, metastatic cancer, blood clotting disorders, hemophilia, von Willebrand's, previous infection of the operative joint, liver transplant, kidney transplant, hepatitis B

REFERENCES

[1] Momohara S, Kawakami K, Iwamoto T, Yano K, Sakuma Y, Hiroshima R, et al. Prosthetic joint infection after total hip or knee arthroplasty in rheumatoid arthritis patients treated with nonbiologic and biologic disease-modifying antirheumatic drugs. Mod Rheumatol. 2011;21:469–475. doi:10.1007/s10165-011-0423-x.

[2] Suzuki M, Nishida K, Soen S, Oda H, Kaneko A, Takagishi K, et al. Risk of postoperative complications in rheumatoid arthritis relevant to treatment with biologic agents: a report from the Committee on Arthritis of the Japanese Orthopaedic Association. J Orthop Sci. 2011;16:778–784. doi:10.1007/s00776-011-0142-3.

[3] Cordtz RL, Zobbe K, Højgaard P, Kristensen LE, Overgaard S, Odgaard A, et al. Predictors of revision, prosthetic joint infection and mortality following total hip or total knee arthroplasty in patients with rheumatoid arthritis: a nationwide cohort study using Danish healthcare registers. Ann Rheum Dis. 2017;77. doi:10.1136/annrheumdis-2017-212339.

[4] Goodman SM, Springer B, Guyatt G, Abdel MP, Dasa V, George M, et al. 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons guideline for the perioperative management of antirheumatic medication in patients with rheumatic diseases undergoing elective total hip or total knee arthroplasty. Arthritis Care. 2017;69:1111–1124. doi:10.1002/acr.23274.

[5] Schairer WW, Nwachukwu BU, Mayman DJ, Lyman S, Jerabek SA. Preoperative hip injections increase the rate of periprosthetic infection after total hip arthroplasty. J Arthroplasty. 2016;31:166–169.e1. doi:10.1016/j.arth.2016.04.008.

[6] Pereira LC, Kerr J, Jolles BM. Intra-articular steroid injection for osteoarthritis of the hip prior to total hip arthroplasty: is it safe? A systematic review. Bone Joint J. 2016;98-B:1027–1035. doi:10.1302/0301620X.98B8.37420.

[7] Charalambous CP, Prodromidis AD, Kwaees TA. Do intra-articular steroid injections increase infection rates in subsequent arthroplasty? A systematic review and meta-analysis of comparative studies. J Arthroplasty. 2014;29:2175–2180. doi:10.1016/j.arth.2014.07.013.

[8] Tian W. Does previous intra-articular steroid injection increase the risk of joint infection following total hip arthroplasty or total knee arthroplasty? A meta-analysis. Med Sci Monit. 2014;20:1878–1883. doi:10.12659/MSM.890750.

[9] McMahon SE, Leroux JA, Smith TO, Hing CB. Total joint arthroplasty following intra-articular steroid injection: a literature review. Acta Orthopaedica Belgica. 2013;79:672–679.

[10] Jämsen E, Varonen M, Huhtala H, Lehto MUK, Lumio J, Konttinen YT, et al. Incidence of prosthetic joint infections after primary knee arthroplasty. J Arthroplasty. 2010;25:87–92. doi:10.1016/j.arth.2008.10.013.

[11] Lindeque B, Hartman Z, Noshchenko A, Cruse M. Infection after primary total hip arthroplasty. Orthopedics. 2014;37:257–265. doi:10.3928/01477447-20140401-08.

[12] Gundtoft PH, Overgaard S, Schonheyder HC, Moller JK, Kjærsgaard-Andersen P, Pedersen AB. The "true" incidence of surgically treated deep prosthetic joint infection after 32,896 primary total hip arthroplasties. Acta Orthopaedica. 2015;86:326–334. doi:10.3109/17453674.2015.1011983.

[13] Anoushiravani AA, Sayeed Z, Chambers MC, Gilbert TJ, Scaife SL, El-Othmani MM, et al. Assessing in-hospital outcomes and resource utilization after primary total joint arthroplasty among underweight patients. J Arthroplasty. 2016;31:1407–1412. doi:10.1016/j.arth.2015.12.053.

[14] Sayeed Z, Anoushiravani AA, Chambers MC, Gilbert TJ, Scaife SL, El-Othmani MM, et al. Comparing in-hospital total joint arthroplasty outcomes and resource consumption among underweight and morbidly obese patients. J Arthroplasty. 2016;31:2085–2090. doi:10.1016/j.arth.2016.03.015.

[15] Werner BC, Higgins MD, Pehlivan HC, Carothers JT, Browne JA. Super obesity is an independent risk factor for complications after primary total hip arthroplasty. J Arthroplasty. 2017;32:402–406. doi:10.1016/j.arth.2016.08.001.

[16] Fu MC, McLawhorn AS, Padgett DE, Cross MB. Hypoalbuminemia is a better predictor than obesity of complications after total knee arthroplasty: a propensity score-adjusted observational analysis. HSS J. 2017;13:66–74. doi:10.1007/s11420-016-9518-4.

[17] Laurberg P, Knudsen N, Andersen S, Carlé A, Pedersen IB, Karmisholt J. Thyroid function and obesity. Eur Thyroid J. 2012;1:159–167. doi:10.1159/000342994.

[18] Tan TL, Rajeswaran H, Haddad S, Shahi A, Parvizi J. Increased risk of periprosthetic joint infections in patients with hypothyroidism undergoing total joint arthroplasty. J Arthroplasty. 2016;31:868–871. doi:10.1016/j.arth.2015.10.028.

[19] Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD. Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. PLoS ONE. 2016;11:e0150866. doi:10.1371/journal.pone.0150866.

[20] Yuan K, Chen HL. Obesity and surgical site infections risk in orthopedics: a meta-analysis. IJSU. 2013;11:383–388. doi:10.1016/j.ijsu.2013.02.018.

[21] Kerkhoffs GMMJ, Servien E, Dunn W, Dahm D, Bramer JAM, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty. J Bone Joint Surg. 2012;94:1839–1844. doi:10.2106/JBJS.K.00820.

[22] Inacio MCS, Paxton EW, Fisher D, Li RA, Barber TC, Singh JA, et al. Bariatric surgery prior to total joint arthroplasty may not provide dramatic improvements in post-arthroplasty surgical outcomes. J Arthroplasty. 2014;29:1359–1364. doi:10.1016/j.arth.2014.02.021.

[23] Watts CD, Wagner ER, Houdek MT, Osmon DR, Hanssen AD, Lewallen DG, et al. Morbid obesity: a significant risk factor for arthroplasty for infection. J Bone Joint Surg. 2014;96:1–7. doi:10.2106/JBJS.M.01289.

[24] Schwarzkopf R, Russell TA, Shea M, Slover JD. Correlation between nutritional status and Staphylococcus colonization in hip and knee replacement patients. Bull NYU Hosp Jt Dis. 2011;69:308–311.

[25] Jensen JE, Smith TK, Jensen TG, Dudrick SJ, Butler JE, Johnston DA. The Frank Stinchfield Award Paper. Nutritional assessment of orthopaedic patients undergoing total hip replacement surgery. Hip. 1981:123–135.

[26] Rai J, Gill SS, Kumar BRJS. The influence of preoperative nutritional status in wound healing after replacement arthroplasty. Orthopedics. 2002;25:417–421.

[27] Gherini S, Vaughn BK, Lombardi A V, Mallory TH. Delayed wound healing and nutritional deficiencies after total hip arthroplasty. Clin Orthop Relat Res. 1993:188–195.

[28] Jaberi FM, Parvizi J, Haytmanek CT, Joshi A, Purtill J. Procrastination of wound drainage and malnutrition affect the outcome of joint arthroplasty. Clin Orthop Relat Res. 2008;466:1368–1371. doi:10.1007/s11999-008-0214-7.

[29] Cross MB, Yi PH, Thomas CF, Garcia J, Della Valle CJ. Evaluation of malnutrition in orthopaedic surgery. J Am Acad Orthop Surg. 2014;22:193–199. doi:10.5435/JAAOS-22-03-193.

[30] Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr. 2008;27:5–15. doi:10.1016/J.CLNU.2007.10.007.

[31] Morey VM, Song YD, Whang JS, Kang YG, Kim TK. Can serum albumin level and total lymphocyte count be surrogates for malnutrition to predict wound complications after total knee arthroplasty? J Arthroplasty. 2016;31:1317–1321. doi:10.1016/j.arth.2015.12.004.

[32] Yi PH, Frank RM, Vann E, Sonn KA, Moric M, Della Valle CJ. Is potential malnutrition associated with septic failure and acute infection after revision total joint arthroplasty? Clin Orthop Relat Res. 2015;473:175–182. doi:10.1007/s11999-014-3685-8.

[33] Walls JD, Abraham D, Nelson CL, Kamath AF, Elkassabany NM, Liu J. Hypoalbuminemia more than morbid obesity is an independent predictor of complications after total hip arthroplasty. J Arthroplasty. 2015;30:2290–2295. doi:10.1016/j.arth.2015.06.003.

[34] Nelson CL, Elkassabany NM, Kamath AF, Liu J. Low albumin levels, more than morbid obesity, are associated with complications after TKA. Clin Orthop Relat Res. 2015;473:3163–3172. doi:10.1007/s11999-015-4333-7.

[35] Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, et al. Risk factors for prosthetic joint infection: case-control study. Clin Infect Dis. 1998;27:1247–1254.

[36] Lavernia CJ, Sierra RJ, Baerga L. Nutritional parameters and short term outcome in arthroplasty. J Am Coll Nutr. 1999;18:274–278. doi:10.1080/07315724.1999.10718863.

[37] Del Savio GC, Zelicof SB, Wexler LM, Byrne DW, Reddy PD, Fish D, et al. Preoperative nutritional status and outcome of elective total hip replacement. Clin Orthop Relat Res. 1996:153–161.

[38] Kamath AF, McAuliffe CL, Kosseim LM, Pio F, Hume E. malnutrition in joint arthroplasty: prospective study indicates risk of unplanned ICU admission. Arch Bone Joint Surg. 2016;4:128–131.

[39] Courtney PM, Rozell JC, Melnic CM, Sheth NP, Nelson CL. Effect of malnutrition and morbid obesity on complication rates following primary total joint arthroplasty. J Surg Orthop Adv. 2016;25:99–104.

[40] Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbuminemia independently predicts surgical site infection, pneumonia, length of stay, and readmission after total joint arthroplasty. J Arthroplasty. 2016;31:15–21. doi:10.1016/j.arth.2015.08.028.

[41] Bohl DD, Shen MR, Kayupov E, Cvetanovich GL, Della Valle CJ. Is Hypoalbuminemia associated with septic failure and acute infection after revision total joint arthroplasty? a study of 4517 patients from the National Surgical Quality Improvement Program. J Arthroplasty. 2016;31:963–967. doi:10.1016/j.arth.2015.11.025.

[42] Namba RS, Inacio MCSC s. S, Paxton EW. Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. J Bone Joint Surg Am. 2013;95:775–782. doi:10.2106/JBJS.L.00211.

[43] Lee QJ, Mak WP, Wong YC. Risk factors for periprosthetic joint infection in total knee arthroplasty. J Orthop Surg (Hong Kong). 2015;23:282–286. doi:10.1177/230949901502300303.

[44] Kong L, Cao J, Zhang Y, Ding W, Shen Y. Risk factors for periprosthetic joint infection following primary total hip or knee arthroplasty: a meta-analysis. Int Wound J. 2017;14:529–536. doi:10.1111/iwj.12640.

[45] Wu C, Qu X, Liu F, Li H, Mao Y, Zhu Z, et al. Risk factors for periprosthetic joint infection after total hip arthroplasty and total knee arthroplasty in Chinese patients. PLoS ONE. 2014;9:e95300. doi:10.1371/journal.pone.0095300.

[46] Chen J, Cui Y, Li X, Miao X, Wen Z, Xue Y, et al. Risk factors for deep infection after total knee arthroplasty: a meta-analysis. Arch Orthop Trauma Surg. 2013;133:675–687. doi:10.1007/s00402-013-1723-8.

[47] Yang Z, Liu H, Xie X, Tan Z, Qin T, Kang P. The influence of diabetes mellitus on the post-operative outcome of elective primary total knee replacement: a systematic review and meta-analysis. Bone Joint J. 2014;96B:1637–1643. doi:10.1302/0301-620X.96B12.34378.

[48] Zhu Y, Zhang F, Chen W, Liu S, Zhang Q, Zhang Y. Risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. J Hosp Infect. 2015;89:82–89. doi:10.1016/j.jhin.2014.10.008.

[49] Maradit Kremers H, Lewallen LW, Mabry TM, Berry DJ, Berbari EF, Osmon DR. Diabetes mellitus, hyperglycemia, hemoglobin A1C and the risk of prosthetic joint infections in total hip and knee arthroplasty. J Arthroplasty. 2015;30:439–443. doi:10.1016/j.arth.2014.10.009.

[50] Martínez-Huedo MA, Jiménez-García R, Jiménez-Trujillo I, Hernández-Barrera V, del Rio Lopez B, López-de-Andrés A. Effect of type 2 diabetes on in-hospital postoperative complications and mortality after primary total hip and knee arthroplasty. J Arthroplasty. 2017;32:3729–3734.e2. doi:10.1016/j.arth.2017.06.038.

[51] Shohat N, Muhsen K, Gilat R, Rondon AJ, Chen AF, Parvizi J. Inadequate glycemic control is associated with increased surgical site infection in total joint arthroplasty: a systematic review and meta-analysis. J Arthroplasty. 2018. doi:10.1016/j.arth.2018.02.020.

[52] Shohat N, Tarabichi M, Tischler EH, Jabbour S, Parvizi J. Serum fructosamine: a simple and inexpensive test for assessing preoperative glycemic control. J Bone Joint Surg Am. 2017;99:1900–1907. doi:10.2106/JBJS.17.00075.

[53] Chrastil J, Anderson MB, Stevens V, Anand R, Peters CL, Pelt CE. Is hemoglobin A1c or perioperative hyperglycemia predictive of periprosthetic joint infection or death following primary total joint arthroplasty? J Arthroplasty. 2015;30:1197–1202. doi:10.1016/j.arth.2015.01.040.

[54] Jamsen E, Nevalainen P, Kalliovalkama J, Moilanen T, Jämsen E, Nevalainen P, et al. Preoperative hyperglycemia predicts infected total knee replacement. Eur J Int Med. 2010;21:196–201. doi:https://doi.org/10.1016/j.ejim.2010.02.006.

[55] Cancienne JM, Werner BC, Browne JA. Is There an association between hemoglobin A1C and deep postoperative infection after TKA? Clin Orthop Relat Res. 2017;475:1642–1649. doi:10.1007/s11999-017-5246-4.

[56] Jämsen E, Nevalainen P, Eskelinen A, Huotari K, Kalliovalkama J, Moilanen T. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. J Bone Joint Surg Am. 2012;94:e101. doi:10.2106/JBJS.J.01935.

[57] Cavanaugh PK, Chen AF, Rasouli MR, Post ZD, Orozco FR, Ong AC. Total joint arthroplasty in transplant recipients: in-hospital adverse outcomes. J Arthroplasty. 2015;30:840–845. doi:10.1016/j.arth.2014.11.037.

[58] Cancienne JM, Werner BC, Browne JA. Complications after TKA in patients with hemophilia or Von Willebrand's disease. J Arthroplasty. 2015;30:2285–2289. doi:10.1016/j.arth.2015.06.015.

[59] Bozic KJ, Lau E, Kurtz S, Ong K, Berry DJ. Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. Clin Orthop Relat Res. 2012;470:130–137. doi:10.1007/s11999-011-2043-3.

[60] Bozic KJ, Lau E, Kurtz S, Ong K, Rubash H, Vail TP, et al. Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. J Bone Joint Surg Am. 2012;94:794–800. doi:10.2106/JBJS.K.00072.

[61] Poultsides LA, Ma Y, Della Valle AG, Chiu YL, Sculco TP, Memtsoudis SG. In-hospital surgical site infections after primary hip and knee arthroplasty - incidence and risk factors. J Arthroplasty. 2013;28:385–389. doi:10.1016/j.arth.2012.06.027.

[62] Pugely AJ, Martin CT, Gao Y, Schweizer ML, Callaghan JJ. The incidence of and risk factors for 30-day surgical site infections following primary and revision total joint arthroplasty. J Arthroplasty. 2015;30:47–50. doi:10.1016/j.arth.2015.01.063.

[63] Bongartz TIM, Halligan CS, Osmon DR, Reinalda MS, Bamlet WR, Crowson CS, et al. Incidence and risk factors of prosthetic joint infection after total hip or knee replacement in patients with rheumatoid arthritis. Arthritis Rheum. 2008;59:1713–1720. doi:10.1002/art.24060.

[64] Cruess RL, Bickel WS, vonKessler KL. Infections in total hips secondary to a primary source elsewhere. Clin Orthop Relat Res. 1975;106:99–101.

[65] del Sel HJ, Charnley J. Total hip replacement following infection in the opposite hip. Clin Orthop Relat Res. 1979:138–142.

[66] Fitzgerald RH, Nolan DR, Ilstrup DM, Van Scoy RE, Washington JA, Coventry MB. Deep wound sepsis following total hip arthroplasty. J Bone Joint Surg Am. 1977;59:847–855.

[67] Hanssen AD, Rand JA. Evaluation and treatment of infection at the site of a total hip or knee arthroplasty. Instr Course Lect. 1999;48:111–122.

[68] Schmalzried TP, Amstutz HC, Au MK, Dorey FJ. Etiology of deep sepsis in total hip arthroplasty. The significance of hematogenous and recurrent infections. Clin Orthop Relat Res. 1992:200–207.

[69] Stinchfield FE, Bigliani LU, Neu HC, Goss TP, Foster CR. Late hematogenous infection of total joint replacement. J Bone Joint Surg Am. 1980;62:1345–1350.

[70] Thomas BJ, Moreland JR, Amstutz HC. Infection after total joint arthroplasty from distal extremity sepsis. Clin Orthop Relat Res. 1983:121–125.

[71] Cherney DL, Amstutz HC. Total hip replacement in the previously septic hip. J Bone Joint Surg Am. 1983;65:1256–1265.

[72] Jupiter JB, Karchmer AW, Lowell JD, Harris WH. Total hip arthroplasty in the treatment of adult hips with current or quiescent sepsis. J Bone Joint Surg Am. 1981;63:194–200.

[73] Everhart JS, Andridge RR, Scharschmidt TJ, Mayerson JL, Glassman AH, Lemeshow S. Development and validation of a preoperative surgical site infection risk score for primary or revision knee and hip arthroplasty. J Bone Joint Surg. 2016;98:1522–1532. doi:10.2106/JBJS.15.00988.

[74] Radtke K, Tetzlaff T, Vaske B, Ettinger M, Claaßen L, Flörkemeier T, et al. Arthroplasty-center related retrospective analysis of risk factors for peri-

prosthetic joint infection after primary and after revision total hip arthroplasty. Technol Health Care. 2016;24:721–728. doi:10.3233/THC-161158.
[75] Grammatico-Guillon L, Baron S, Rosset P, Gaborit C, Bernard L, Rusch E, et al. Surgical site infection after primary hip and knee arthroplasty: a cohort study using a hospital database. Infect Control Hosp Epidemiol. 2015;36:1198–1207. doi:10.1017/ice.2015.148.
[76] Cordero-Ampuero J, González-Fernández E, Martínez-Vélez D, Esteban J. Are antibiotics necessary in hip arthroplasty with asymptomatic bacteriuria? Seeding risk with/without treatment. Clin Orthop Relat Res. 2013;471:3822–3829. doi:10.1007/s11999-013-2868-z.
[77] Mayne AIW, Davies PSE, Simpson JM. Antibiotic treatment of asymptomatic bacteriuria prior to hip and knee arthroplasty: a systematic review of the literature. Surgeon. 2017. doi:10.1016/j.surge.2017.08.007.
[78] Lai K, Bohm ER, Burnell C, Hedden DR. Presence of medical comorbidities in patients with infected primary hip or knee arthroplasties. J Arthroplasty. 2007;22:651–656. doi:10.1016/j.arth.2006.09.002.
[79] Boylan MR, Basu N, Naziri Q, Issa K, Maheshwari A V., Mont MA. Does HIV infection increase the risk of short-term adverse outcomes following total knee arthroplasty? J Arthroplasty. 2015;30:1629–1632. doi:10.1016/j.arth.2015.03.018.
[80] Capogna BM, Lovy A, Blum Y, Kim SJ, Felsen UR, Geller DS. Infection rate following total joint arthroplasty in the HIV population. J Arthroplasty. 2013;28:1254–1258. doi:10.1016/j.arth.2012.12.021.
[81] Lin CA, Takemoto S, Kandemir U, Kuo AC. Mid-term outcomes in HIV-positive patients after primary total hip or knee arthroplasty. J Arthroplasty. 2014;29:277–282. doi:10.1016/j.arth.2013.06.015.
[82] Jiang SL, Schairer WW, Bozic KJ. Increased rates of periprosthetic joint infection in patients with cirrhosis undergoing total joint arthroplasty. Clin Orthop Relat Res. 2014;472:2483–2491. doi:10.1007/s11999-014-3593-y.
[83] Snir N, Wolfson TS, Schwarzkopf R, Swensen S, Alvarado CM, Hamula M, et al. Outcomes of total hip arthroplasty in human immunodeficiency virus-positive patients 2014. doi:10.1016/j.arth.2013.04.023.
[84] Kildow BJ, Agaba P, Moore BF, Hallows RK, Bolognesi MP, Seyler TM. Postoperative impact of diabetes, chronic kidney disease, hemodialysis, and renal transplant after total hip arthroplasty. J Arthroplasty. 2017;32:S135–S140.e1. doi:10.1016/j.arth.2017.01.018.
[85] Enayatollahi MA, Murphy D, Maltenfort MG, Parvizi J. Human immunodeficiency virus and total joint arthroplasty: the risk for infection is reduced. J Arthroplasty. 2016;31:2146–2151. doi:10.1016/j.arth.2016.02.058.
[86] Kalmeijer MD, van Nieuwland-Bollen E, Bogaers-Hofman D, de Baere GA. Nasal carriage of Staphylococcus aureus is a major risk factor for surgical-site infections in orthopedic surgery. Infect Control Hosp Epidemiol. 2000;21:319–323. doi:10.1086/501763.
[87] Tandon T, Tadros BJ, Akehurst H, Avasthi A, Hill R, Rao M. Risk of surgical site infection in elective hip and knee replacements after confirmed eradication of mrsa in chronic carriers. J Arthroplasty. 2017;32:3711–3717. doi:10.1016/j.arth.2017.06.036.
[88] Crowe B, Payne A, Evangelista PJ, Stachel A, Phillips MS, Slover JD, et al. Risk factors for infection following total knee arthroplasty: a series of 3836 cases from one institution. J Arthroplasty. 2015;30:2275–2278. doi:10.1016/j.arth.2015.06.058.
[89] Maoz G, Phillips M, Bosco J, Slover J, Stachel A, Inneh I, et al. The Otto Aufranc Award: modifiable versus nonmodifiable risk factors for infection after hip arthroplasty. Clin Orthop Relat Res. 2014;473:453–459. doi:10.1007/s11999-014-3780-x.
[90] Hacek DM, Robb WJ, Paule SM, Kudrna JC, Stamos VP, Peterson LR. Staphylococcus aureus nasal decolonization in joint replacement surgery reduces infection. Clin Orthop Relat Res. 2008;466:1349–1355. doi:10.1007/s11999-008-0210-y.
[91] Schweizer M, Perencevich E, McDanel J, Carson J, Formanek M, Hafner J, et al. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. BMJ. 2013;346:f2743.
[92] Courtney PM, Melnic CM, Zimmer Z, Anari J, Lee G-C. Addition of vancomycin to cefazolin prophylaxis is associated with acute kidney injury after primary joint arthroplasty. Clin Orthop Relat Res. 2015;473:2197–2203. doi:10.1007/s11999-014-4062-3.
[93] Kapadia BH, Elmallah RK, Mont MA. A randomized, clinical trial of preadmission chlorhexidine skin preparation for lower extremity total joint arthroplasty. J Arthroplasty. 2016;31:2856–2861. doi:10.1016/j.arth.2016.05.043.
[94] Kapadia BH, Issa K, McElroy MJ, Pivec R, Daley JA, Mont MA. Advance preoperative chlorhexidine preparation reduces periprosthetic infections following total joint arthroplasty. Seminars Arthr. 2013;24:83–86. doi:https://doi.org/10.1053/j.sart.2013.07.006.
[95] Kapadia BH, Johnson AJ, Daley JA, Issa K, Mont MA. Pre-admission cutaneous chlorhexidine preparation reduces surgical site infections in total hip arthroplasty. J Arthroplasty. 2013;28:490–493. doi:10.1016/j.arth.2012.07.015.
[96] Dixon JM, Carver RL. Daily chlorohexidine gluconate bathing with impregnated cloths results in statistically significant reduction in central line-associated bloodstream infections. Am J Infect Control. 2010;38:817–821. doi:10.1016/j.ajic.2010.06.005.
[97] Kuo SJ, Huang PH, Chang CC, Kuo FC, Wu CT, Hsu HC, et al. Hepatitis B virus infection is a risk factor for periprosthetic joint infection among males after total knee arthroplasty. Medicine. 2016;95:e3806. doi:10.1097/MD.0000000000003806.
[98] Orozco F, Post ZD, Baxi O, Miller A, Ong A. Fibrosis in hepatitis C patients predicts complications after elective total joint arthroplasty. J Arthroplasty. 2014;29:7–10. doi:https://doi.org/10.1016/j.arth.2013.03.023.
[99] Kildow BJ, Politzer CS, DiLallo M, Bolognesi MP, Seyler TM. Short and long-term postoperative complications following total joint arthroplasty in patients with human immunodeficiency virus, hepatitis B, or hepatitis C. J Arthroplasty. 2017. doi:10.1016/J.ARTH.2017.10.061.
[100] Deleuran T, Vilstrup H, Overgaard S, Jepsen P. Cirrhosis patients have increased risk of complications after hip or knee arthroplasty A Danish population-based cohort study. Acta Orthop. 2015;86:108–113. doi:10.3109/17453674.2014.961397.
[101] Seol YJ et al. Outcome analysis of hip or knee arthroplasty in patients with cirrhotic liver disease. J Orthop. 2017;14:171–175. doi:http://dx.doi.org/10.1016/j.jor.2016.12.011.
[102] Pour AE, Matar WY, Jafari SM, Purtill JJ, Austin MS, Parvizi J. Total joint arthroplasty in patients with hepatitis C. J Bone Joint Surg Am. 2011;93:1448–1454. doi:10.2106/JBJS.J.00219.
[103] Hsieh PH, Chen LH, Lee MS, Chen CH, Yang WE, Shih CH. Hip arthroplasty in patients with cirrhosis of the liver. J Bone Joint Surg Br. 2003;85:818–821.
[104] Cohen SM, Te HS, Levitsky J. Operative risk of total hip and knee arthroplasty in cirrhotic patients. J Arthroplasty. 2005;20:460–466. doi:10.1016/j.arth.2004.05.004.
[105] Chalmers BP, Ledford CK, Statz JM, Perry KI, Mabry TM, Hanssen AD, et al. Survivorship after primary total hip arthroplasty in solid-organ transplant patients. J Arthroplasty. 2016;31:2525–2529. doi:10.1016/j.arth.2016.04.012.
[106] Ledford CK, Chalmers BP, Statz JM, Perry KI, Mabry TM, Hanssen AD, et al. Primary total knee arthroplasty after solid organ transplant: survivorship and complications. J Arthroplasty. 2017;32:101–105. doi:10.1016/j.arth.2016.07.018.
[107] Simpson PMS, Brew CJ, Whitehouse SL, Crawford RW, Donnelly BJ. Complications of perioperative warfarin therapy in total knee arthroplasty. J Arthroplasty. 2014;29:320–324. doi:10.1016/j.arth.2012.11.003.
[108] McDougall CJ, Gray HS, Simpson PM, Whitehouse SL, Crawford RW, Donnelly WJ. Complications related to therapeutic anticoagulation in total hip arthroplasty. J Arthroplasty. 2013;28:187–192. doi:10.1016/j.arth.2012.06.001.
[109] Cordero-Ampuero JJ, De Dios M. What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? Clin Orthop Relat Res. 2010;468:3268–3277. doi:10.1007/s11999-010-1411-8.
[110] Rotevatn TA, Bøggild H, Olesen CR, Torp-Pedersen C, Mortensen RN, Jensen PF, et al. Alcohol consumption and the risk of postoperative mortality and morbidity after primary hip or knee arthroplasty - a registerbased cohort study. PLoS ONE. 2017;12. doi:10.1371/journal.pone.0173083.
[111] Tonnesen H, Rosenberg J, Nielsen HJ, Rasmussen V, Hauge C, Pedersen IK, et al. Effect of preoperative abstinence on poor postoperative outcome in alcohol misusers: randomised controlled trial. BMJ. 1999;318:1311–1316. doi:10.1136/BMJ.318.7194.1311.
[112] Springer BD. Modifying risk factors for total joint arthroplasty: strategies that work nicotine. J Arthroplasty. 2016;31:1628–1630. doi:10.1016/j.arth.2016.01.071.
[113] Kapadia BH, Issa K, Pivec R, Bonutti PM, Mont MA. Tobacco use may be associated with increased revision and complication rates following total hip arthroplasty. J Arthroplasty. 2014;29:777–780. doi:10.1016/j.arth.2013.08.023.
[114] Duchman KR, Gao Y, Pugely AJ, Martin CT, Noiseux NO, Callaghan JJ. The effect of smoking on short-term complications following total hip and knee arthroplasty. J Bone Joint Surg. 2015;97:1049–1058. doi:10.2106/JBJS.N.01016.
[115] Maradit Kremers H, Kremers WK, Berry DJ, Lewallen DG. Social and behavioral factors in total knee and hip arthroplasty. J Arthroplasty. 2015;30:1852–1854. doi:10.1016/j.arth.2015.04.032.
[116] Singh JA, Schleck C, Harmsen WS, Jacob AK, Warner DO, Lewallen DG. Current tobacco use is associated with higher rates of implant revision and deep infection after total hip or knee arthroplasty: a prospective cohort study. BMC Med. 2015;13:283. doi:10.1186/s12916-015-0523-0.
[117] Sahota S, Lovecchio F, Harold RE, Beal MD, Manning DW. The effect of smoking on thirty-day postoperative complications after total joint arthroplasty: a propensity score-matched analysis. J Arthroplasty. 2017;33:30–35. doi:10.1016/j.arth.2017.07.037.
[118] Gonzalez AI, Luime JJ, Uçkay I, Hannouche D, Hoffmeyer P, Lübbeke A. Is there an association between smoking status and prosthetic joint infection following primary total joint arthroplasty? J Arthroplasty. 2018;33(7):2218. doi:https://doi.org/10.1016/j.arth.2018.02.069.
[119] Mills E, Eyawo O, Lockhart I, Kelly S, Wu P, Ebbert JO. Smoking cessation reduces postoperative complications: a systematic review and meta-analysis. Am J Med. 2011;124:144–154.e8. doi:10.1016/j.amjmed.2010.09.013.
[120] Azodi OS, Bellocco R, Eriksson K, Adami J. The impact of tobacco use and body mass index on the length of stay in hospital and the risk of post-operative complications among patients undergoing total hip replacement. J Bone Joint Surg Br. 2006;88:1316–1320. doi:10.1302/0301-620X.88B10.
[121] Munoz-Fernandez S, Macia MA, Pantoja L, Cardenal A, Pena JM, Martin Mola E, et al. Osteoarticular infection in intravenous drug abusers: influence of HIV infection and differences with non drug abusers. Ann Rheum Dis. 1993;52:570–574. doi:10.1136/ard.52.8.570.
[122] Ang-Fonte GZ, Rozboril MB, Thompson GR. Changes in nongonococcal septic arthritis: Drug abuse and methicillin-resistantstaphylococcus aureus. Arthr Rheum. 1985;28:210–213. doi:10.1002/art.1780280217.
[123] Lehman CR, Ries MD, Paiement GD, Davidson AB. Infection after total joint arthroplasty in patients with human immunodeficiency virus or intravenous drug use. J Arthroplasty. 2001;16:330–335. doi:10.1054/arth.2001.21454.
[124] Padegimas EM, Maltenfort M, Ramsey ML, Williams GR, Parvizi J, Namdari S. Periprosthetic shoulder infection in the United States: incidence and economic burden. J Should Elbow Surg. 2015;24:741–746. doi:10.1016/J.JSE.2014.11.044.

[125] Su YJ, Lin SY, Huang HT, Chang JK, Chen CH. Intravenous drug abuse is a risk factor in the failure of two-stage treatment for infected total hip arthroplasty. Kaohsiung J Med Sci. 2017;33:623–629. doi:https://doi.org/10.1016/j.kjms.2017.08.005.
[126] Pitta M, Esposito CI, Li Z, Lee Y, Wright TM, Padgett DE. Failure after modern total knee arthroplasty: a prospective study of 18,065 knees. J Arthroplasty. 2018;33:407–414. doi:https://doi.org/10.1016/j.arth.2017.09.041.
[127] Bauer DE, Hingsammer A, Ernstbrunner L, Aichmair A, Rosskopf AB, Eckers F, et al. Total knee arthroplasty in patients with a history of illicit intravenous drug abuse. Int Orthop. 2018;42:101–107. doi:10.1007/s00264-017-3655-3.
[128] Wieser K, Zingg PO, Betz M, Neubauer G, Dora C. Total hip replacement in patients with history of illicit injecting drug use. Arch Orthop Trauma Surg. 2012;132:1037–1044. doi:10.1007/s00402-012-1509-4.
[129] Namba RS, Inacio MCS, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. J Bone Joint Surg Br. 2012;94:1330–1338. doi:10.1302/0301-620X.94B10.29184.
[130] Singh JA, Chen J, Inacio MCS, Namba RS, Paxton EW. An underlying diagnosis of osteonecrosis of bone is associated with worse outcomes than osteoarthritis after total hip arthroplasty. BMC Muscul Dis. 2017;18:8. doi:10.1186/s12891-016-1385-0.
[131] Ridgeway S, Wilson J, Charlet A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. J Bone Joint Surg Br. 2005;87:844–850. doi:10.1302/0301-620X.87B6.15121.
[132] Geubbels ELPE, Grobbee DE, Vandenbroucke-Grauls CMJE, Wille JC, Boer AS de. Improved risk adjustment for comparison of surgical site infection rates. Infect Control Hosp Epidemiol. 2006;27:1330–1339. doi:10.1086/509841.
[133] Ibrahim SA, Stone RA, Han X, Cohen P, Fine MJ, Henderson WG, et al. Racial/ethnic differences in surgical outcomes in veterans following knee or hip arthroplasty. Arthr Rheum. 2005;52:3143–3151. doi:10.1002/art.21304.
[134] Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res. 2008;466:1710–1715. doi:10.1007/s11999-008-0209-4.
[135] Bohl DD, Sershon RA, Fillingham YA, Della Valle CJ. Incidence, risk factors, and sources of sepsis following total joint arthroplasty. J Arthroplasty. 2016;31:2875–2879.e2. doi:10.1016/j.arth.2016.05.031.
[136] SooHoo NF, Farng E, Lieberman JR, Chambers L, Zingmond DS. Factors that predict short-term complication rates after total hip arthroplasty. Clin Orthop Relat Res. 2010;468:2363–2371. doi:10.1007/s11999-010-1354-0.
[137] Mahomed NN, Barrett JA, Katz JN, Phillips CB, Losina E, Lew RA, et al. Rates and outcomes of primary and revision total hip replacement in the United States Medicare population. J Bone Joint Surg Am. 2003;85-A:27–32. doi:10.1001/jama.1996.03530350040032.
[138] Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. Clin Orthop Relat Res. 2010;468:52–56. doi:10.1007/s11999-009-1013-5.
[139] Dowsey MM, Choong PFM. Obese diabetic patients are at substantial risk for deep infection after primary TKA. Clin Orthop Relat Res. 2009;467:1577–1581. doi:10.1007/s11999-008-0551-6.
[140] Dowsey MM, Choong PFM. Obesity is a major risk factor for prosthetic infection after primary hip arthroplasty. Clin Orthop Relat Res. 2008;466:153–158. doi:10.1007/s11999-007-0016-3.
[141] Choong PFM, Dowsey MM, Carr D, Daffy J, Stanley P. Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampinbased regimen. Acta Orthop. 2007;78:755–765. doi:10.1080/17453670710014527.
[142] Babkin Y, Raveh D, Lifschitz M, Itzchaki M, Wiener-Well Y, Kopuit P, et al. Incidence and risk factors for surgical infection after total knee replacement. Scand J Infect Dis. 2007;39:890–895. doi:10.1080/00365540701387056.
[143] Bozic KJ, Ward DT, Lau EC, Chan V, Wetters NG, Naziri Q, et al. Risk factors for periprosthetic joint infection following primary total hip arthroplasty: a case control study. J Arthroplasty. 2014;29:154–156. doi:10.1016/j.arth.2013.04.015.
[144] Poultsides LA, Triantafyllopoulos GK, Sakellariou VI, Memtsoudis SG, Sculco TP. Infection risk assessment in patients undergoing primary total knee arthroplasty. Int Orthop. 2018;42:87–94. doi:10.1007/s00264-017-3675-z.
[145] Berbari EF, Osmon DR, Carr A, Hanssen AD, Baddour LM, Greene D, et al. Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study. Clin Infect Dis. 2010;50:8–16. doi:10.1086/648676.
[146] Aslam S, Reitman C, Darouiche RO. Risk factors for subsequent diagnosis of prosthetic joint infection. Infect Control Hosp Epidemiol. 2010;31:298–301. doi:10.1086/650756.
[147] Ravi B, Jenkinson R, Austin PC, Croxford R, Wasserstein D, Escott B, et al. Relation between surgeon volume and risk of complications after total hip arthroplasty: propensity score matched cohort study. BMJ. 2014;348:g3284. doi:10.1136/bmj.g3284.
[148] Greenky Ba M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? Clin Orthop Relat Res. 2012;470:2695. doi:10.1007/s11999-012-2435-z.
[149] SooHoo NF, Lieberman JR, Ko CY, Zingmond DS. Factors predicting complication rates following total knee replacement. J Bone Joint Surg Am. 2006;88:480–485. doi:10.2106/JBJS.E.00629.
[150] Wilson MG, Kelley K, Thornhill TS. Infection as a complication of total knee-replacement arthroplasty. Risk factors and treatment in sixty-seven cases. J Bone Joint Surg Am. 1990;72:878–883.
[151] Chesney D, Sales J, Elton R, Brenkel IJ. Infection after knee arthroplasty a prospective study of 1509 cases. J Arthroplasty. 2008;23:355–359. doi:10.1016/j.arth.2007.05.052.
[152] Kessler B, Sendi P, Graber P, Knupp M, Zwicky L, Hintermann B, et al. Risk factors for periprosthetic ankle joint infection: a case-control study. J Bone Joint Surg Am. 2012;94:1871–1876. doi:10.2106/JBJS.K.00593.
[153] Buller LT, Rosas S, Sabeh KG, Roche MW, McLawhorn AS, Barsoum WK. Hypothyroidism increases 90-day complications and costs following primary total knee arthroplasty. J Arthroplasty. 2017. doi:10.1016/j.arth.2017.10.053.
[154] Newman ET, Watters TS, Lewis JS, Jennings JM, Wellman SS, Attarian DE, et al. Impact of perioperative allogeneic and autologous blood transfusion on acute wound infection following total knee and total hip arthroplasty. J Bone Joint Surg. 2014;96:279–284. doi:10.2106/JBJS.L.01041.
[155] Carroll K, Dowsey M, Choong P, Peel T. Risk factors for superficial wound complications in hip and knee arthroplasty. Clin Microbiol Infect. 2014;20:130–135. doi:10.1111/1469-0691.12209.
[156] Innerhofer P, Klingler A, Klimmer C, Fries D, Nussbaumer W. Risk for postoperative infection after transfusion of white blood cell–filtered allogeneic or autologous blood components in orthopedic patients undergoing primary arthroplasty. Transfusion. 2005;4545:103–110.
[157] Asensio A, Ramos A, Munez E, Vilanova JL, Torrijos P, Garcia FJ. Preoperative low molecular weight heparin as venous thromboembolism prophylaxis in patients at risk for prosthetic infection after knee arthroplasty. Infect Control Hosp Epidemiol. 2005;26:903–909. doi:10.1086/505451.
[158] Huang RC, Parvizi J, Hozack WJ, Chen AF, Austin MS. Aspirin is as effective as and safer than warfarin for patients at higher risk of venous thromboembolism undergoing total joint arthroplasty. J Arthroplasty. 2016. doi:10.1016/j.arth.2016.02.074.
[159] Roberts KC. AAOS clinical practice guideline and systematic review methodology. J Am Acad Orthop Surg. 2015;21:571.
[160] Boraiah S, Joo L, Inneh IA, Rathod P, Meftah M, Band P, et al. Management of modifiable risk factors prior to primary hip and knee arthroplasty: a readmission risk assessment tool. J Bone Joint Surg. 2015;97:1921–1928. doi:10.2106/JBJS.N.01196.

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QUESTION 2: Is the diagnosis of post-traumatic arthritis associated with increased risks of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs) after joint arthroplasty?

RECOMMENDATION: Yes. Total joint arthroplasty (TJA) for patients with post-traumatic arthritis of the hip or knee carries higher risks of developing SSIs/PJIs. The incidence is markedly higher in patients with previous surgeries and retained implants.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 97%, Disagree: 1%, Abstain: 2% (Unanimous, Strongest Consensus)

RATIONALE

Symptomatic arthritis of the hip, knee and ankle has been reported to be secondary to traumatic causes 12% of the time [1]. There have been few high-quality studies assessing the impacts of the preoperative diagnoses on the risks for SSIs and PJIs. However, numerous