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Projecting Hip and Knee Arthroplasty Procedures and Surgical Site Infections Using a Markov Chain Monte Carlo Decision Tree for the Years 2020 through 2030

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A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Introduction: Surgical site infections (SSIs) occur in 0.69% of total hip and knee arthroplasty (THA/TKA) patients (Berrios-Torres et al., 2014). As the U.S. population ages, the number of arthroplasty procedures is expected to increase as arthroplasty is more common among individuals age 65 and older. If the infection rate remains stable, we expect to see an increase in the infection burden. This analysis projects the burden of SSIs in the years 2020 through 2030 to provide evidence for or against a significant increase in the infection burden.

Methods: Historical procedure rates were estimated using the National Inpatient Sample (NIS) dataset by averaging the years 2012 through 2014. Infection rates obtained from the National Healthcare Safety Network (NHSN) were averaged across the years 2006 through 2009. All rates were stratified by age and gender. We used a Markov Chain Monte Carlo (MCMC) decision tree to model the U.S. population in the years 2020 through 2030 and track the procedures and infections in each year. We then used the Cox-Stuart test for trend to test for significant increases in procedures and infections.

Results: The model projected a significant increase in infections from 2020 to 2030 for both hip and knee arthroplasty (Cox-Stuart test, $p = 0.04$ for THA infections; $p = 0.004$ for TKA infections). The average projected SSIs following THA increased from 3,850 in 2020 to 4,360 infections 2030 while the average projected SSIs following TKA increased from 4,710 in 2020 to 5,060 infections in 2030. The age 65 to 84 cohort contributed the largest number of projected procedures and infections and females contributed more procedures and infections than males.

Discussion: Given a projected increase in infection burden, we expect that attributable patient hospital costs and mortality will increase as well. We should consider interventions to reduce the potential impact on the U.S. healthcare system. Our results indicate that females age 65 to 84 are a high-risk group that would be available to target for interventions. Next steps in this research include adding the infection risk of additional patient characteristics and assessing the effect of interventions on overall SSI burden.

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Chapter 1. Introduction

Background

The goal of this project is to demonstrate the burden of surgical site infections (SSI) in total hip and knee arthroplasty (THA/TKA) between the years 2020 through 2030. Arthroplasty has been shown to improve the quality of life for patients who elect to have the procedure (Lovald et al., 2013, 2014). The demand for these procedures is increasing and is expected to continue to do so, based on the aging United States (U.S.) population (S. M. Kurtz, Ong, Lau, & Bozic, 2014; S. M. Kurtz et al., 2007; Pollock, Somerville, Firth, & Lanting, 2016). As of 2009, for every 1,000 THA and TKA procedures, roughly 6.9 patients developed a deep incisional or organ/space surgical site infection (SSI) (Berrios-Torres et al., 2014). These infections increase the negative outcomes for a patient, including higher comorbidity burden, higher perioperative mortality rate, increased length of stay, increased cost of in-hospital care and the patient is more likely to need additional surgical procedures to address the infection (Poultsides et al., 2013). Despite a less than one percent infection rate, due to the large number of procedures conducted, this may yield a large burden of disease.

Problem Statement and Purpose Statement

Previous studies have reported SSI rates to demonstrate the impact of these infections. However, as the number of arthroplasty procedures increases, the number of SSIs, and thus patients affected by SSI, will increase even if the infection rate remains stable. Therefore, infection rates cannot reliably demonstrate the increase in medical issues and economic burden caused by an increased burden of arthroplasty. This analysis will project the arthroplasty infection burden to provide evidence either for or against an increased burden of SSIs between 2020 and 2030.

Significance Statement

SSIs are part of the larger public health problem of healthcare associated infections (HAIs). HAIs impact 5% of patients, cause an estimated 100,000 deaths and cost $33 billion in excess medical expenses in U.S. hospitals annually (Frieden, 2010). However, HAIs are preventable and the

Centers for Disease Control and Prevention (CDC) has established four pillars of HAI elimination: “1) adherence to evidence-based practices, 2) alignment of incentives, 3) innovation through basic, translational, and epidemiological research, and 4) data to target prevention efforts and measure progress” (Cardo et al., 2010). Several federal initiatives have supported HAI prevention, including the creation of an Action Plan to Prevent Healthcare-Associated Infections from the U.S. Department of Health and Human Services, federal funding to support HAI program infrastructure and public HAI reporting at state health departments through the American Recovery and Reinvestment Act of 2009, and the Patient Protection and Affordable Care Act of 2010 (*Eliminating Healthcare Associated Infections: State policy options*, 2011). The Centers for Medicare and Medicaid Services (CMS) has “pay for reporting” programs and “pay for performance” programs that require hospitals to report on quality measures, including HAIs, and achieve national performance benchmarks in order to receive full Medicare reimbursement ("Quality Reporting and Pay-for-Performance," 2014). In addition to federal support, states are encouraged to develop their own HAI programs and legislation. As of 2016, 34 states and the District of Columbia mandated HAI reporting to the CDC ("Facilities in these states are required by law to report HAI data to NHSN," 2016). The CDC recommends that states developing their own policy interventions “establish a set of priority infections for initial focus” (*Policies for Eliminating Healthcare-Associated Infections: Lessons learned from state stakeholder engagement*, 2012).

The Targeted Assessment for Prevention (TAP) Strategy was developed by the CDC to provide a framework for focused infection prevention. This strategy utilizes the cumulative attributable difference (CAD) metric to prioritize facilities with the highest excess burden of infections. Facilities with a CAD greater than zero experienced more infections than predicted and the CAD value indicates the number of infections that needed to be prevented in order to meet their target. Targeting locations with high CAD metrics for intervention will have the greatest impact on overall burden. Thus, it is important to provide a clear picture of the current and future burden of

SSIs so that policy makers prioritize accordingly. This project will add to the body of work on HAI occurrence to help assess the scope of the problem, provide targets for prevention strategies and achieve progress towards elimination. ("TAP Strategy 'How To' Guide for the Individual Facility User," 2016)

Definition of Terms

Community hospitals - "short-term, non-federal, general and other hospitals" excluding "hospital units of other institutions…long-term care, rehabilitation, psychiatric and alcoholism and chemical dependency hospitals" (*National Inpatient Sample*, 2016)

Complex Surgical Site Infection - a category of surgical site infections that combines deep incisional surgical site infections and organ/space surgical site infections (Berrios-Torres et al., 2014).

Deep Incisional Surgical Site Infection – "date of event for infection occurs within 30 or 90 days after the NHSN operative procedure (where day 1 = the procedure date) according to the list in Table 2 **AND** involves deep soft tissues of the incision (e.g., fascial and muscle layers) **AND** patient has at least ***one*** of the following:

- purulent drainage from the deep incision.
- a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician** or other designee and organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST) or culture or non-culture based microbiologic testing method is not performed **AND** patient has at least ***one*** of the following signs or symptoms: fever (>38°C); localized pain or tenderness. A culture or non-culture based test that has a negative finding does not meet this criterion.
- an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test"

(*The National Healthcare Safety Network Manual*, 2017)

Healthcare Associated Infections (HAI)- “infections that patients acquire when receiving healthcare treatment” (*Eliminating Healthcare Associated Infections: State policy options*, 2011)

Healthcare Cost and Utilization Project (HCUP) - the largest set of all-payer health care databases publicly available for community hospitals in the U.S. (*National Inpatient Sample*, 2016)

Markov Chain Monte Carlo (MCMC) model – a model that utilizes the Markov Chain process and the Monte Carlo method.

Markov Chain process – a stochastic process such that the conditional distribution of Y_m given $Y_1 \ldots Y_{m-1}$ depends on Y_{m-1} alone ("Building and Analyzing Markov Models," 2016; Geyer, 2011; Mazumdar, 2010)

Monte Carlo method - an approximation of an expectation by the sample mean of a function of simulated random variables (E. C. Anderson, 1999)

National Healthcare Safety Network (NHSN) – a U.S. surveillance system operated by the Centers for Disease Control and Prevention (CDC) that allows healthcare facilities to report healthcare associated infections and prevention activities (*Eliminating Healthcare Associated Infections: State policy options*, 2011)

National Inpatient Sample (NIS) - a database in HCUP that provided national estimates on hospital inpatient stays (*National Inpatient Sample*, 2016)

Organ/Space Surgical Site Infection – “date of event for infection occurs within 30 or 90 days after the NHSN operative procedure (where day 1 = the procedure date) according to the list in Table 2 **AND** infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure **AND** patient has at least ***one*** of the following:

- purulent drainage from a drain that is placed into the organ/space (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage)

- organisms are identified from an aseptically-obtained fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method, which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST).
- an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection.

AND meets at least ***one*** criterion for a specific organ/space infection site."

(*The National Healthcare Safety Network Manual*, 2017)

Static model - each trial in the model has an outcome probability independent from the results of any other trial (Brisson & Edmunds, 2006)

Stochastic model – a collection of random elements $Y_1 \ldots Y_m$ that is a function of time m (M. Scott, 2013).

Superficial Surgical Site Infection – "date of event for infection occurs within 30 days after any NHSN operative procedure (where day 1 = the procedure date) **AND** involves only skin and subcutaneous tissue of the incision **AND** patient has at least ***one*** of the following:

- purulent drainage from the superficial incision.
- organisms identified from an aseptically-obtained specimen
- from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method, which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST).
- superficial incision that is deliberately opened by a surgeon, attending physician or other designee and culture or non-culture based testing is not performed **AND** patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat.

- diagnosis of a superficial incisional SSI by the surgeon or attending physician or other designee."

(*The National Healthcare Safety Network Manual*, 2017)

Surgical Site Infection (SSIs) – a category of health care acquired infection containing superficial surgical site infections, deep incisional surgical site infections and organ/space surgical site infections (*The National Healthcare Safety Network Manual*, 2017).

Total Hip Arthroplasty (THA) - replaces the femoral head and cartilage with prosthetic implants ("Total Hip Replacement," 2015)

Total Knee Arthroplasty (TKA) - resurfaces the femur, tibia and (optional) patella (Foran, 2015)

Chapter 2. Review of the Literature

Arthroplasty is a surgical procedure used when other medical treatments no longer alleviate joint pain or disability. In arthroplasty, the joint can be repaired by resurfacing the bones or implanting an artificial joint ("Arthroplasty,"). A number of medical conditions can require arthroplasty, including fracture, rheumatoid arthritis or traumatic arthritis, but osteoarthritis is the most common reason for the procedure ("Arthroplasty,"). Osteoarthritis occurs when the cartilage cushioning the joint wears away and is most common in individuals over the age of 50 ("Total Hip Replacement," 2015). Total hip arthroplasty (THA) replaces the femoral head and cartilage with prosthetic implants. This procedure was first performed in 1960 ("Total Hip Replacement," 2015). An alternative procedure is partial hip arthroplasty (hip hemiarthroplasty) where only the femoral head is replaced ("Hip Fractures," 2009). Total knee arthroplasty (TKA) resurfaces the femur, tibia and (optional) patella and was first used in 1968 (Foran, 2015). Partial knee replacement (also unicompartmental knee replacement) is another procedure where only part of the knee is resurfaced, appropriate for patients where the disease is limited to one area (Foran, 2016). In both hip and knee procedures, it is possible that the initial (primary) surgery fails, and requires a revision surgery where one or more of the implants are replaced (Cross, 2015; Sheth, 2013). For the purposes of this study, we considered only primary total arthroplasty procedures. Patients with hip and knee arthroplasty procedures have been shown to have increased medical costs but also have the potential to increase the patient's quality of life. Hip osteoarthritis patients who underwent THA had a lower risk of mortality, heart failure and depression (Lovald et al., 2014). A reduced risk of diabetes was also shown one to three years after surgery (Lovald et al., 2014). However, arthroplasty patients incurred more medical costs than patients who did not receive arthroplasty (Lovald et al., 2013, 2014). A study following patients for 7 years after their initial osteoarthritis diagnosis found that THA patients paid $6,366 more (including THA surgery costs) for medical care over the seven years than non-THA patients (Lovald et al., 2014). Knee osteoarthritis patients treated with TKA had a lower probability of heart failure and mortality, although at a total increased medical cost of $19,843 (including surgery costs) for the seven years following the initial diagnosis (Lovald et al., 2013).

In order to obtain national estimates on the number of THA and TKA procedures, we utilized the Healthcare Cost and Utilization Project (HCUP) as an estimate of annual procedures performed. HCUP has access to the largest set of all-payer health care databases publicly available for community hospitals in the U.S.. Community hospitals were defined as "short-term, non-federal, general and other hospitals" excluding "hospital units of other institutions…long-term care, rehabilitation, psychiatric and alcoholism and chemical dependency hospitals"("Introduction to the HCUP National Inpatient Sample (NIS) 2014," 2016). The National Inpatient Sample (NIS) is a part of HCUP that provides national estimates on hospital inpatient stays. As of 2014, the data was a sample of more than 7 million discharges from over 4,000 hospitals participating in HCUP. This roughly 20% sample of national discharges was used to estimate more than 35 million hospitalizations nationally ("Introduction to the HCUP National Inpatient Sample (NIS) 2014," 2016). In the NIS, diagnoses and procedures for each hospitalization were identified through International Classification of Diseases, Ninth Revision (ICD-9) administrative codes. Administrative coding for primary vs. revision THA has been shown to be 96% accurate (sensitivity 99%, specificity 91%, PPV 91%). Primary vs. revision coding for TKA was 95% accurate (sensitivity 89%, specificity 98%, PPV 97%) (Daneshvar, Forster, & Dervin, 2012). For this project, inpatient discharges from the NIS were included based on ICD-9 procedure codes located under all-listed procedures (TKA 81.54; THA 81.51, 81.52). Outpatient or same-day discharge surgeries for THA/TKA have been rare (0.75%-6.2% of THA/TKA procedures) and so we only considered inpatient procedures for this study (Bovonratwet et al., 2017; Sher et al., 2016).

THA and TKA procedures have been more common in those over the age of 65, a growing population in the U.S.. The average age of the U.S. population is increasing, due in large part to the number of people born between 1946 and 1964, referred to as the "baby boom cohort".

Starting in 2011, this baby boom cohort turned 65 and the elderly were expected to rapidly increase in size through the year 2030 (Siegel, 1996). Between the years 2020 and 2030, the population between 65 and 84 was expected to grow from 50 to 65 million. During the same time frame, the population over 85 was projected to increase from 6.7 million to 9.1 million (*2014 National Population Projections*, 2014). This is relevant to arthroplasty projections as previous studies have shown the average age of hip and knee arthroplasty patients was between 60 and 65 (64.3 length of stay (LOS) > 1) (Sher et al., 2016). Studies have shown a significant association between patient age and THA/TKA procedure incidence with incidence gradually increasing to peak between the ages of 70-79 then decreasing in age groups 80 and over (Singh et al., 2010). Roughly, 4.2% of the U.S. population age 50 and older have had a total knee replacement (Weinstein et al., 2013).

Previous studies have hypothesized that the increase in population over 65 will increase the burden of THA and TKA procedures (Aynardi, Post, Ong, Orozco, & Sukin, 2014; S. Kurtz, Ong, Lau, Mowat, & Halpern, 2007; Pollock et al., 2016). From 2009 to 2010 alone, the number of primary THA and TKA increased by roughly six percent (S. M. Kurtz et al., 2014). These procedures were growing in popularity due to the aging population (Pollock et al., 2016). From 2005 to 2030, Kurtz et al. demonstrated the demand for primary TKA was expected to increase 673% (3.48 million procedures in 2030). Over the same time period, they showed the demand for primary THA was expected to increase 174% (roughly 574,000 procedures in 2030) (S. Kurtz et al., 2007).

Surgical procedures, including hip and knee arthroplasty, have many potential health risks. HAIs are a possible consequence of any surgery or hospitalization. SSIs are the most common HAI, accounting for roughly one third of all HAIs among hospitalized patients (Magill et al., 2012). A 2011 prevalence survey conducted by the CDC found that there were an estimated 157,500 SSIs associated with inpatient surgeries (Magill et al., 2014). Among primary THA and TKA patients, 0.69% contracted a complex SSI (680,489 arthroplasty procedures with complex SSIs across 880

NHSN hospitals) (Berrios-Torres et al., 2014). This rate generally increased as patient age increased, with the odds ratio for severe adverse events (including SSIs) in patients 70-79 estimated at 2.33 (95% CI 1.18-4.59) and patients 80 years and older estimated at 4.17 (95% CI 1.18- 8.58) for same day THA/TKA surgeries as compared to patients less than 50 years of age (Sher et al., 2016). The Medicare population produced complex SSI rates of 0.90% for THA procedures (30 SSIs in 3,316 procedures) and 1.11% for TKA procedures (79 SSIs in 7,102 procedures) (Yi, Baggs, Culler, Berrios-Torres, & Jernigan, 2015).

SSI patients following primary THA and TKA procedures have a higher comorbidity burden, higher perioperative mortality rate, a longer average length of hospital stay and double the average cost of in-hospital care (Poultsides et al., 2013). Revision surgeries are commonly used to treat SSIs, which increase the economic burden and create an additional risk of infection (S. M. Kurtz et al., 2007). Certain comorbidities increased the risk of SSI in Medicare patients receiving THA such as rheumotological disease, obesity, preoperative anemia and coagulopathy (Bozic, Lau, Kurtz, Ong, Rubash, et al., 2012). Similarly, comorbidities associated with increased risk of SSI after TKA were congestive heart failure, chronic pulmonary disease, preoperative anemia, diabetes, depression, renal disease, pulmonary circulation disorders, obesity, rheumatologic disease, psychoses, metastatic tumor, peripheral vascular disease and valvular disease (Bozic, Lau, Kurtz, Ong, & Berry, 2012).

The research was unclear on how long surveillance for SSIs should continue after an arthroplasty procedure. Different studies used different lookout windows to identify SSIs and an optimal definition has not been identified. Over half of SSIs were detected within 90 days of the procedure (57% for THA and 59% for TKA) (Yi et al., 2015). However, the National Healthcare Safety Network's (NHSN) definition for a look-out period is one year (with an implant procedure where prosthetic material is left inside the body) (*The National Healthcare Safety Network Manual*, 2017). In a study comparing a one-year follow-up to a 30-day follow up for complex SSIs, using a 30-day definition would have left out two-thirds of SSIs in TKA and almost one fourth of THAs (Lankiewicz et al., 2012). A 90-day definition would have included all SSIs in THA, but only 70% of SSIs in TKA (Lankiewicz et al., 2012). Based on previous research and literature, an optimal lookout window for SSIs is difficult to identify.

To avoid inconsistency in SSI definition and lookout window, this project utilized the NHSN definition of SSI and NHSN surveillance data. SSIs were a reportable event to NHSN within three categories, superficial incisional, deep incisional or organ/space. Superficial SSIs involved only skin and subcutaneous tissue of the incision and an infection that occurs within 30 days. Deep incisional SSIs were an infection of the deep soft tissues while organ/space SSIs involved an infection of any body part manipulated during the operation excluding skin, fascia, or muscle layers (*The National Healthcare Safety Network Manual*, 2017). Deep incisional and organ/space SSIs were combined in this study into a "complex" category of SSIs where infection can occur within 1 year of an implant procedure.

NHSN is the CDC's HAI tracking system. This system uses hospital surveillance and reporting to collect data. Over 17,000 medical facilities reported HAI data to NHSN, including acute care hospitals, long-term acute care hospitals, psychiatric hospitals, rehabilitation hospitals, outpatient dialysis centers, ambulatory surgery centers, and nursing homes (*National and State Healthcare Associated Infections Progress Report*, 2016). Information from NHSN was used to identify intervention targets and measure progress in HAI reduction. As of the 2014 NHSN Report, 1,928 acute care hospitals reported SSI procedures following hip arthroplasty and 1,907 acute hospitals reported SSI procedures following knee arthroplasty (*National and State Healthcare Associated Infections Progress Report*, 2016). NHSN-participating medical facilities collect SSI and operative procedure data in all selected procedure categories. They conduct active surveillance through review of medical records or surgery clinic patient records, ICU and ward visits, surgeon surveys by mail or phone or patient surveys by mail or phone. The NHSN definition of SSIs must be used in identification and all reported SSIs must be associated with a

NHSN operative procedure and the facility in which that procedure was performed (*The National Healthcare Safety Network Manual*, 2017).

Instead of active hospital surveillance, an alternative method of identifying SSIs is to use administrative codes. Administrative codes used in payer-based claims data allow for large sample studies that include not only operative hospitals but also all healthcare utilization (Calderwood et al., 2012). Studies assessing SSIs using administrative codes have indicated that sensitivity and positive predictive value (PPV) were highly variable between studies (10-100% sensitivity; 11-95% PPV) (Bolon et al., 2009; Rusk et al., 2016; van Mourik, van Duijn, Moons, Bonten, & Lee, 2015). Sensitivity was similar across hospitals within a study suggesting that sensitivity varies due to study design, rather than from differences in hospital coding practices (Calderwood et al., 2014). Administrative claims surveillance (administrative claim identification + chart review) increased the detection of complex SSIs in THA by a factor of five, but had no effect on detection in complex SSIs in TKA (Calderwood et al., 2012). However, even using a restricted list of administrative codes for complex SSIs (996.60, 996.62, 998.51, 998.59) confirmed SSIs were only 54% of flagged hip arthroplasty procedures and 26% of flagged knee arthroplasty procedures (Calderwood et al., 2012). For this study, we elected to use hospital surveillance data to avoid the variable sensitivity and potential over reporting found in administrative code data.

A few papers have looked at the impact of age demographics on projected procedure burden. Kurtz et al. (2007) used a Poisson regression model with historical procedure rates, adjusting for age, gender, race, ethnicity, and census region to project procedure rates and burden through the year 2030. The same researchers also updated this model to identify the impact of the economic downturn on projected procedure burden through the year 2021 (S. M. Kurtz et al., 2014). However, their initial study used procedures rates from 1990 to 2003, did not provide breakouts to identify trends in age cohorts, and did not consider the impact on adverse events, such as surgical site infections (SSIs). The updated study included procedure rates from 1993 to 2010, but only projected burden through the year 2021. Our study aims to validate the Kurtz study on increasing procedure burden using a different method while also including an analysis of infection burden, for which we could find no similar studies. We hope to address the lack of detailed analysis on age demographics and infection burden in the literature and provide evidence to support or reject the hypothesis that the burden of SSIs after THA and TKA will increase between the years 2020 through 2030.

Chapter 3. Methodology

To demonstrate the burden of SSIs in hip and knee arthroplasty from the years 2020 to 2030, this study employed the Markov chain Monte Carlo (MCMC) method to produce a static, stochastic model. Model inputs for the decision tree were derived from the published literature and analyses of unpublished data sources.

We used a static model to project infections for this study. A static model implied that each trial had a probability of infection independent from the results of any other trial (Brisson & Edmunds, 2006). The infection status of one patient undergoing THA or TKA could not change the probability of infection of any other patient in the sample, and the age-specific infection rates were stable over time. We chose a static model as the SSI rates were low (0.47%-1.18%, see Table 1). In addition to low rates, SSIs are caused by different disease-carrying agents (methicillin-resistant *S. aureus*, methicillin-susceptible *S. aureus*, *Escherichia coli*, and *Enterococcus* spp. are some of the most common), and adjusting for SSI clustering has minimal effect on infection rate estimates, indicating little common transmission (Baker et al., 2016). Thus, we considered a static model an appropriate selection.

For this project, we opted to use a stochastic process. A stochastic process implied that the collection of random elements $Y_1 \ldots . Y_m$ was a function of time ($m = 11\ years$) (M. Scott, 2013). Each trial $x_i \in Y_j$ was assigned a starting age, then completed a random walk through the decision tree based on probability tables to create the random element Y_{j+1}. This method allowed for first order and second order uncertainty. First order uncertainty is the variability of current and future states of one modeled trial x_i as it completes a random walk. Second order uncertainty is parameter uncertainty or a lack of precision in an aspect of the system that applies to the entire stochastic process $Y_1 \ldots . Y_m$ ("Monte Carlo Simulation, Distributions and Probabilistic Sensitivity Analysis," 2016). Both levels of uncertainty were appropriate due to the uncertainty inherent in the individual risk of procedure and infection and the imprecision of historical population, procedure and infection rates applied to future years.

Monte Carlo Method

The Monte Carlo method approximated an expectation by the sample mean of a function of simulated random variables. Given our random samples $X_1 \ldots X_n$, and a function g(x), the Monte Carlo estimator of $E[\ g(X)\ ]$ is

$$\tilde{g}_n(X) = \frac{1}{n}\sum_{i=1}^{n} g(X_i)$$

The variance of this estimator for a discrete random variable X can be computed by

$$Var\big(\tilde{g}_n(X)\big) = Var\left(\frac{1}{n}\sum_{i=1}^{n} g(X_i)\right) = \frac{Var(g(X))}{n} = \frac{1}{n}\sum_{x \in X}\big[g(x) - E\big(g(X)\big)\big]^2 f_X(x)$$

(E. C. Anderson, 1999)

Markov Chain Process

A Markov model was defined as a stochastic process such that the conditional distribution of Y_m given $Y_1 \ldots Y_{m-1}$ depends on Y_{m-1} alone. Random variables $Y_1 \ldots Y_m$ can take on any value in E, the state space of the Markov chain. Therefore, given A contained in E:

$$P\{Y_m \in A |\ Y_1 \ldots Y_{m-1}\} = P\{Y_n \in A |\ Y_{m-1}\}$$

Discrete-time Markov models define a time period of interest m divided into a finite set of equal intervals, or stages k. Initial probabilities determine the distribution of the cohort within the state space at the beginning of the process. The conditional probability

$$P\{Y_{k+1} = j |\ Y_k = i\} = P_{ij}\{Y\}$$

$$k = 1, 2 \ldots m-1$$

was defined as the transition probability that, given the chain is in state i after k-transitions, the chain would be in state j after k+1 transitions. The transition probability matrix was

$$\boldsymbol{P} = \{P_{ij}\}_{i,j\ \in E}$$

and defined possible changes in state during each stage of the Markov chain. A traditional Markov model transitioned each element at the end of each stage, despite the likelihood that the cohort would transition throughout the stage. ("Building and Analyzing Markov Models," 2016; Geyer, 2011; Mazumdar, 2010)

Markov Chain Monte Carlo (MCMC) Model Design

Our model used the MCMC method to allow our cohort to transition through various states between cycles. The steps of the model were as follows:

1. Assign each trial x a starting value to create our cohort Y_1.
2. Initialize each trial x at a state in $k = 0$.
3. For each stage k , set $\sum x = 0$
4. Apply the transition probability matrix $\boldsymbol{P}$ to our random variable Y_k such that trials may transition through different states and increase $\sum x$ by 1 for each applicable x.
5. We now have random element Y_{k+1} conditional only on Y_k. If $k + 1 = m$, terminate the chain, else increase the value of each trial and k by 1 and go to step 3.

We performed this process for each sample $X_1 \ldots X_n$. Our random variables $Y_1 \ldots Y_m$ followed the Markov Chain process such that each conditional distribution of Y_k depends on Y_{k-1} alone. We obtained mean and variance estimates by applying the Monte Carlo method to samples $X_1 ... X_n$.

Model Inputs

Population Cohort

To ensure that the population modeled in 2020 was accurate, we set the initial population cohort to match the U.S. Census Bureau's population projections for the year 2020. These population projections were based on U.S. Census estimates of the resident population on July 1, 2013 (which in turn were based on the 2010 Census). These projections were produced via the cohort-component method. The Census Bureau projected components of birth, death, and net migration separately for each birth cohort, stratified by age, sex, race, and Hispanic ethnicity. The cohort component method was expressed as

$$P_t = P_{t-1} + B_{t-1,t} - D_{t-1,t} + M_{t-1,t}$$

where:

$$P_t = population\ at\ time\ t$$

$$P_{t-1} = population\ at\ time\ t-1$$

$$B_{t-1,t} = births\ in\ the\ interval\ from\ time\ t-1\ to\ time\ t$$

$$D_{t-1,t} = deaths\ in\ the\ interval\ from\ time\ t-1\ to\ time\ t$$

$$M_{t-1,t} = net\ migration\ in\ the\ interval\ from\ time\ t-1\ to\ time\ t$$

(*2014 National Population Projections*, 2014).

This method provided us with population projections for the year 2020, accounting for birth, death and migration within each stratified cohort. For our MCMC model, the model assigned each individual an age from 0 to 100 to match the year 2020 population projections. This process resulted in each individual in our cohort being assigned an age, such that the total cohort matched the U.S. population distribution at year 2020.

Procedure Counts

Primary arthroplasty procedure counts were estimated for the years 2012 to 2014 from the NIS. The number of procedures was identified using discharges with ICD-9 procedure codes (THA 81.51, 81.52; TKA 81.54) located in any position on the discharge record. THA and TKA procedures were stratified by age and gender (18-44, 45-64, 65-84 and greater or equal to 85; male, female) and standardized by resident population estimates from the U.S. Census for the same age cohorts, then averaged to estimate the arithmetic mean across years 2012 to 2014. Our model assumed time stable procedure rates for each age and gender cohort.

Table 1. Total knee arthroplasty and total hip arthroplasty procedure and infection rates stratified by age cohort and gender

Age Cohort	TKA Procedure Rate	TKA Infection Rate	THA Procedure Rate	THA Infection Rate
Male				
18-44	0.01%	1.13%	0.02%	0.81%
45-64	0.26%	0.83%	0.19%	0.76%
65-85	0.76%	0.70%	0.46%	0.78%
85 and over	0.28%	0.72%	0.76%	0.99%
Female				
18-44	0.01%	0.86%	0.01%	1.18%
45-64	0.39%	0.60%	0.18%	0.76%
65-85	1.07%	0.47%	0.64%	0.76%
85 and over	0.26%	0.57%	1.02%	0.84%

Infection Rates

Primary SSI rates were estimated from NHSN data for hip and knee arthroplasty for the years 2006 through 2009 stratified by age and gender. Annual data reports provided the number of infections and the number of procedures for THA and TKA. We utilized infection counts standardized by NHSN procedure totals stratified by age and gender cohorts (18-44, 45-64, 65-84 and greater or equal to 85; male, female) averaged across the years 2006 to 2009. In recent years, infection rates following hip and knee arthroplasty have not shown a significant increase or decrease in the United States. For this analysis, we assumed time stable infection rates for each age and gender cohort.

Background Mortality Rate

Background mortality for the whole cohort was obtained from population and death projections from the U.S. Census Bureau for 2020 through 2030 stratified by year of age (until age 85 where the mortality rate applied to age 85 and over). Our model applied the mortality rate based on the current year and current age of the individual.

Applying Model Parameterization to MCMC

Using the model inputs specified we applied the MCMC method to our project. The state space E for our model contained the values “Active”, “Prior Procedure”, and “Mortality”. All trials in our cohort represented the U.S. population at the year 2020. The transition probability matrix was comprised of the procedure rates, infection rates, and mortality rates stratified by age or age cohort. We defined sums to count the population (pop.), procedures (proc.) and infections in each age cohort.

$$\sum\nolimits_{a1} = pop\ 18-44, \quad \sum\nolimits_{a2} = pop\ 45-64, \sum\nolimits_{a3} = pop\ 65-84, \sum\nolimits_{a4} = pop\ 85+$$

$$\sum\nolimits_{p1} = proc\ 18-44, \quad \sum\nolimits_{p2} = proc\ 45-64, \sum\nolimits_{p3} = proc\ 65-84, \sum\nolimits_{p4} = proc\ 85+$$

$$\sum\nolimits_{i1} = infections\ 18-44, \quad \sum\nolimits_{i2} = infections\ 45-64, \sum\nolimits_{i3} = infections\ 65-84, \sum\nolimits_{i4} = infections\ 85+$$

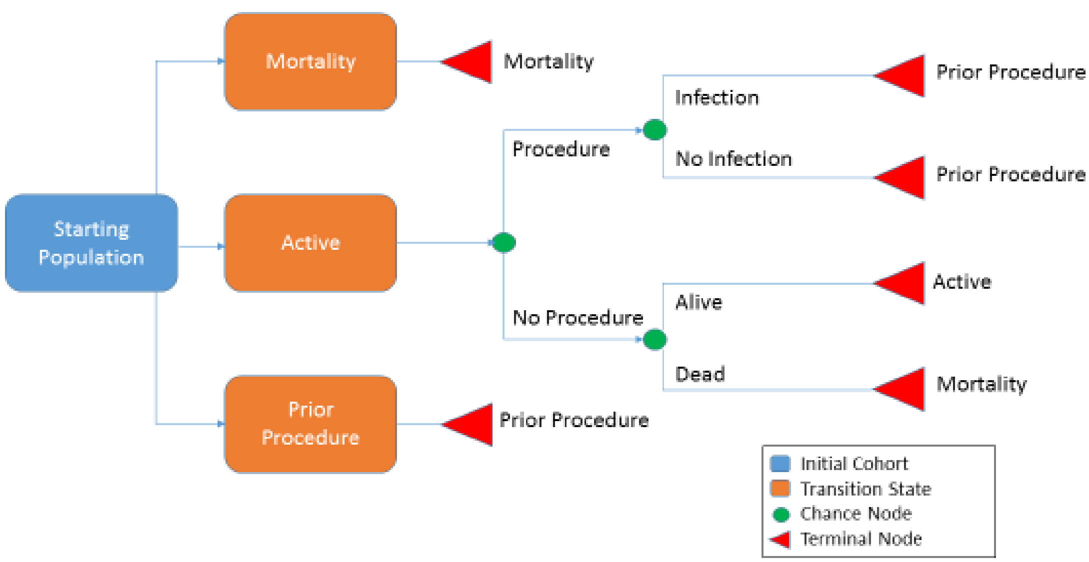
Sums $\sum_a$, $\sum_p$, $\sum_i$ tracked the population, procedures and infections in each age cohort respectively. Our time period of interest was m = 11 years and the stages k of the model were equivalent to one year, such that stage 0 (k =0) was the year 2020 and stage 10 ($k = 10$) was the year 2030. Separate models were created for males and females and hip and knee arthroplasty. The steps of the model were as follows:

1. Assign each trial x a starting age using the population distribution of the United States population at the year 2020 to create our cohort Y_1.
2. Initialize each trial x at the Active state in k = 0
3. For each trial in the Active state, set $\sum_a = \sum x \in age\ cohort\ in\ Y_k$, set $\sum_p = 0$ and $\sum_i = 0$
4. Apply the transition probability matrix $\boldsymbol{P}$ to our random variable Y_k such that trials may transition to states "Active", "Prior Procedure" or "Mortality" and increase $\sum_p$ and $\sum_i$ by 1 for each x in the appropriate age cohort whose random walk utilizes the branches "Procedures" and "Infections" respectively.
5. We now have random element Y_{k+1} conditional only on Y_k. If $k + 1 = m$, terminate the chain, else increase the age of each trial and k by 1 and go to step 3.

In Figure 1, the "Starting Population" block represents the initial cohort. The initial probability distribution assigned each individual to the "Active" transition state. Each chance node applied a probability table to account for the first order uncertainty in each individual's transition state.

Terminal nodes indicated the individual had reached the end of the year and determined in which transition state the individual would start the next year. Once an individual transitioned to the "Prior Procedure" or "Mortality" state, they were removed from further analysis because our analysis assumed that each individual might only have one procedure and one infection. Similarly, each individual may only die once. Birth rate was not utilized in the model as we are not interested in the procedures for ages 0 to 17 and we did not run the model for enough years for persons age 0 to age out of this age cohort. The model steps were completed for 100 samples ($X_1 \ldots X_{100}$) of each model and the expected value of $\sum_a$, $\sum_p$, $\sum_i$ for each stage and each age cohort was calculated using the Monte Carlo estimator. Similar methods can be found in additional resources (Chiu et al., 2011; Trikalinos & Lau, 2007)

Figure 1. Markov Chain Monte Carlo decision tree for hip or knee arthroplasty



NOTE: terminal nodes indicate the individual has reached the end of the year and will start the next year in the identified transition state
NOTE: decision tree terminated after 11 years

Statistical Analysis

Model Outputs

Our model output Monte Carlo estimators for active population projections, procedure burden and infection burden for each year 2020 through 2030. We developed separate models for hip and knee arthroplasty, thus separate estimators were obtained for each procedure type. Separate models were also created for each gender, but Monte Carlo estimators were summed to obtain total population burden for each procedure type. For every year modeled, we obtained the estimated average population eligible for a primary procedure across 100 samples stratified by age cohort. The model also produced the estimated average primary total procedure burden across 100 samples stratified by age cohort. Finally, Monte Carlo estimators were calculated for the average infection burden among primary total procedures across 100 samples stratified by age cohort. All output values were included in tables and analyzed for trend.

Credible Intervals

Using the model output, we calculated Bayesian credible intervals for each Monte Carlo estimator. Credible intervals are calculated using a parameter θ and the marginal posterior cumulative distribution function Π(θ|D) where D represents the model output. The credible interval is given by

$$\Pi\left(\theta^{\frac{\alpha}{2}}\middle|\mathrm{D}\right) = \frac{\alpha}{2}\ and\ \Pi\left(\theta^{1-\frac{\alpha}{2}}\middle|\mathrm{D}\right) = 1 - \frac{\alpha}{2}$$

For this project, we selected $\alpha = 0.05$. Thus for each Monte Carlo estimator, there is a 95% probability that the true value of the infection and procedure burden lies within the credible interval.

(Chen, 1999)

Test for Trend

Using the Cox-Stuart test for trend, we assumed independent observations from a continuously distributed population. The test is sensitive to monotonic trends in location. The statistical hypotheses for testing for trend are:

$H_0: A\ upward\ monotonic\ trend\ does\ not\ exist\ in\ the\ series$

$H_A: A\ upward\ monotonic\ trend\ exists\ in\ the\ series$

Given m = 11 years, set $c = \frac{m-1}{2}$. Let w_j equal the infection burden in the given year j where $j = 1, \ldots c$. We used an indicator variable t_j where t_j =1 if $w_j - w_{c+j} < 0$ or t_j =0 if $w_j - w_{c+j} > 0$. The test statistic was

$$S = \sum_{j=1}^{n} t_j \, , S \sim Bin(c, \frac{1}{2})$$

To test our hypothesis, we converted S to a z score through the formula

$$Z = \frac{\left(S + \frac{1}{2}\right) - \frac{c}{2}}{\sqrt{\frac{c}{4}}}, \alpha = 0.05$$

(Marascuilo & McSweeney, 1977; Rutkowska, 2015)

Limitations

Several limitations exist due to our chosen method of analysis and model inputs. Using the MCMC method incorporates randomness via computer simulation, but cannot completely capture the randomness of real-world phenomena. All mean and variance estimates are “Monte Carlo approximations”, but cannot be considered point estimates. Point estimates are calculated using real world data, and should not be confused with Monte Carlo approximations. (Geyer, 2011) Monte Carlo approximations incorporated first order uncertainty as a modeled trial experienced variability of current and future states as it completes a random walk ("Monte Carlo Simulation, Distributions and Probabilistic Sensitivity Analysis," 2016). This MCMC model also required inputs to produce the transition probabilities between states. As our time period of interest was 2020 to 2030, we did not have exact model inputs and had to extrapolate using historical data.

This introduced second order uncertainty (parameter uncertainty) into our model by applying a lack of precision to the stochastic process ("Monte Carlo Simulation, Distributions and Probabilistic Sensitivity Analysis," 2016).

Additionally, we limited our model by making assumptions on model inputs. We first assumed that the 2020 population projections provided by the U.S. Census were accurate and invariant. This was not realistic, as we cannot know the exact population in the year 2020, however it was considered reasonable based on a review of the U.S. Census methodology and previous projection estimates.

Procedure rates for hip and knee arthroplasty were assumed to be stable across years within each age stratification. Age stratification accounted for any increase in procedure rates due to an aging population; however, several sources indicated that the demand for arthroplasty might increase due to proven success rates (Pollock et al., 2016; Singh et al., 2010). As the increasing utilization was difficult to quantify, we accepted this as a limitation of our study and considered our obtained estimates to be lower bounds of the procedure and infection burden.

Infection rates were also assumed stable across years within each age stratification. HAI reporting within the U.S. has been inconsistent in recent years due to changes in mandatory reporting legislation and inconsistent definitions within the reporting system (*Eliminating Healthcare Associated Infections: State policy options*, 2011). Although NHSN data was available on SSIs from 2006 through 2014, we did not use it to validate the infection rate assumptions due to changes in the number of hospitals. We felt that using four years of data provided a large enough, yet most stable sample of infection rates. Additionally, studies have shown that obesity increased the risk of SSIs in arthroplasty patients (Bozic, Lau, Kurtz, Ong, & Berry, 2012; Bozic, Lau, Kurtz, Ong, Rubash, et al., 2012). Obesity has been increasing in the U.S. and in 2010, 37.4% of American adults were considered obese. If these trends continue 51.1% of U.S. adults are expected to be obese in the year 2030 (Wang, Beydoun, Liang, Caballero, & Kumanyika, 2008). As obesity and SSI are comorbid conditions, increasing obesity rates may impact infection rates. Thus, assuming a stable infection rate may oversimplify future trends in SSIs, however due to additional assumptions needed to identify time trends in infection rates, we opted to include stable rates in our model.

Another limitation of our method was that Bayesian methods of analysis, such as the MCMC model, have no statistical significance measure (i.e. p-values, confidence intervals) (Sutton & Abrams, 2001). Confidence intervals are not appropriate, so we utilized credible intervals to obtain an interval that contains the true parameter with a 95% probability. Credible intervals account for both the first and second order uncertainty in our model. These intervals do not require an assumption of normality, which would be inappropriate for our data given that infections are a rare event and unlikely to meet the requirements of the central limit theorem. However, due to the inherent variability in our model and the rare rate of infection, we expect our credible intervals to be conservative and wide (Sutton et al., 2002).

Software Packages

Population and mortality data were analyzed and Cox-Stuart test statistics and credible intervals were calculated using R version 3.3.1 ("R: A language and environment for statistical computing," 2016). Procedure counts input was analyzed using SAS 9.4 ("Base SAS 9.4 Utilities: Reference," 2013). All model creation and MCMC methods were conducted using TreeAge Pro Suite 2015 ("TreeAge Pro," 2015).

Chapter 4. Results

Total Hip Arthroplasty

Tables 2-4 provide the Monte Carlo estimators across 100 samples for THA among females, males, and the total population. In the "all ages" strata, females were projected to have on average more procedures and more infections during the 11 years. From 2020 to 2030, the model projected a mean of 6,049,700 procedures (3,561,570 female; 2,488,130 male) and 47,610 infections (27,630 female; 19,980 male). Over the 11 years, the model predicted a 15% increase in average procedures (510, 560 in 2020; 588,860 in 2030) and a 13% increase in average infections (3,850 in 2020; 4,360 in 2030). For females, the model predicted a 16% increase in average procedures (298,790 in 2020; 345,780 in 2030) and a 17% increase in average number of SSIs (2,210 in 2020; 2,590 in 2030) from 2020 to 2030. For males, the model predicted a 15% increase in average procedures (211,770 in 2020; 243,080 in 2030) and an 8% increase in average infections (1,640 in 2020; 1,770 in 2030) from 2020 to 2030. In both males and females, the age 65 to 84 group contributed the largest number of procedures and infections to the mean for all years. Similarly, the age 18 to 44 group contributed the fewest number of average procedures and infection for all years.

In the "all ages" category, all gender cohort procedure and infection means were projected to significantly increase from 2020 to 2030 using the Cox-Stuart test for trend ($p= 0.004$ for all procedures; $p=0.04$ for all infections). Average procedures were projected to significantly increase in the age 65 to 84 cohort and the age 85 and over cohort for both genders and the total (p-value = 0.004 for all cohorts). In the age 45 to 64 cohort, there was a significant increase in average infections projected for males and the total burden (male p-value = 0.04; total p-value = 0.04). In the age 65 to 84 cohort, the female and total infection means were projected to significantly increase (female p-value = 0.004; total p-value = 0.004). In the age 85 and over cohort, the male infection burden was the only mean projected to significantly increase (p-value = 0.04).

Table 2. Total hip arthroplasty Monte Carlo estimators for annual procedure and infection burden for males stratified by age with results of the Cox-Stuart test for trend

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population, in thousands	127,163	127,698	128,230	128,741	129,235	129,724	130,187	130,567	130,918	131,259	131,560		
Procedures	211,770	215,030	216,290	219,670	224,610	226,730	226,000	231,380	235,930	237,640	243,080	2.68	**0.004***
Infections	1,640	1,740	1,780	1,990	1,700	1,910	1,900	1,820	1,910	1,820	1,770	1.79	**0.037***
Age 18-44													
Population in thousands	60,954	61,063	61,125	61,155	61,146	61,013	60,914	60,724	60,530	60,368	60,110		
Procedures	9,950	9,990	9,940	9,980	10,210	9,330	9,990	9,490	9,250	9,590	10,020	-0.89	0.81
Infections	60	80	90	80	150	120	50	50	60	30	40	-1.79	0.96
Age 45-64													
Population in thousands	40,990	40,678	40,374	40,094	39,867	39,727	39,578	39,499	39,436	39,357	39,409		
Procedures	79,530	77,290	76,790	75,410	75,450	74,260	74,730	74,730	75,550	73,260	75,560	-0.89	0.81
Infections	610	560	510	610	490	640	640	740	570	510	570	1.79	**0.037***
Age 65-84													
Population in thousands	22,788	23,495	24,240	24,942	25,612	26,307	26,935	27,471	27,902	28,367	28,758		
Procedures	104,050	108,320	110,550	115,160	118,420	122,640	120,580	125,080	127,890	130,070	132,750	2.68	**0.004***
Infections	840	900	950	1,070	890	940	1,010	850	1,040	1,030	930	0.89	0.19
Age 85+													
Population in thousands	2,431	2,462	2,492	2,550	2,610	2,678	2,759	2,873	3,050	3,167	3,283		
Procedures	18,240	19,430	19,010	19,120	20,530	20,500	20,700	22,080	23,240	24,720	24,750	2.68	**0.004***
Infections	130	200	230	230	170	210	200	180	240	250	230	1.79	**0.037***

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total hip arthroplasty in the given year

Table 3. Total hip arthroplasty Monte Carlo estimators for annual procedure and infection burden for females stratified by age with results of the Cox-Stuart test for trend

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population in thousands	133,212	133,623	134,019	134,404	134,781	135,159	135,521	135,806	136,069	136,298	136,498		
Procedures	298,790	307,530	311,160	312,490	319,050	324,270	328,080	334,620	337,750	342,050	345,780	2.68	**0.004***
Infections	2,210	2,420	2,590	2,330	2,430	2,700	2,450	2,570	2,370	2,970	2,590	1.79	**0.037***
Age 18-44													
Population in thousands	59,119	59,165	59,154	59,119	59,051	58,875	58,728	58,498	58,269	58,073	57,801		
Procedures	6,790	7,210	7,270	7,060	6,900	7,310	7,290	6,630	6,650	6,760	7,070	0	0.5
Infections	90	130	110	110	70	150	100	80	80	100	80	0	0.5
Age 45-64													
Population in thousands	42,872	42,486	42,105	41,740	41,422	41,178	40,933	40,758	40,591	40,403	40,341		
Procedures	77,200	77,080	75,890	74,090	75,300	75,130	72,840	73,610	73,470	73,620	72,120	-1.79	0.96
Infections	530	590	660	490	470	590	520	510	470	600	420	-0.89	0.81
Age 65-84													
Population in thousands	26,926	27,687	28,478	29,226	29,949	30,684	31,350	31,906	32,346	32,817	33,202		
Procedures	170,750	179,040	183,680	187,770	191,910	196,410	203,030	206,900	207,970	211,780	214,630	2.68	**0.004***
Infections	1,140	1,210	1,410	1,410	1,500	1,510	1,530	1,560	1,430	1,820	1,650	2.68	**0.004***
Age 85+													
Population in thousands	4,295	4,285	4,282	4,319	4,359	4,422	4,511	4,644	4,862	5,005	5,154		
Procedures	44,050	44,200	44,320	43,570	44,940	45,420	44,920	47,480	49,660	49,890	51,960	2.68	**0.004***
Infections	450	490	410	320	390	450	300	420	390	450	440	0	0.5

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total hip arthroplasty in the given year

Table 4. Total hip arthroplasty Monte Carlo estimators for annual procedure and infection burden stratified by age with results of the Cox-Stuart test for trend

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population in thousands	260,375	261,321	262,249	263,145	264,015	264,884	265,708	266,373	266,987	267,558	268,058		
Procedures	510,560	522,560	527,450	532,160	543,660	551,000	554,080	566,000	573,680	579,690	588,860	2.68	**0.004***
Infections	3,850	4,160	4,370	4,320	4,130	4,610	4,350	4,390	4,280	4,790	4,360	1.79	**0.037***
Age 18-44													
Population in thousands	120,073	120,228	120,279	120,274	120,197	119,888	119,642	119,222	118,799	118,441	117,911		
Procedures	16,740	17,200	17,210	17,040	17,110	16,640	17,280	16,120	15,900	16,350	17,090	-0.89	0.81
Infections	150	210	200	190	220	270	150	130	140	130	120	-1.79	0.96
Age 45-64													
Population in thousands	83,862	83,164	82,479	81,833	81,288	80,905	80,511	80,257	80,028	79,760	79,751		
Procedures	156,730	154,370	152,680	149,500	150,750	149,390	147,570	148,340	149,020	146,880	147,680	-1.79	0.96
Infections	1,140	1,150	1,170	1,100	960	1,230	1,160	1,250	1,040	1,110	990	1.79	**0.037***
Age 65-84													
Population in thousands	49,714	51,182	52,717	54,168	55,561	56,991	58,285	59,377	60,248	61,184	61,959		
Procedures	274,800	287,360	294,230	302,930	310,330	319,050	323,610	331,980	335,860	341,850	347,380	2.68	**0.004***
Infections	1,980	2,110	2,360	2,480	2,390	2,450	2,540	2,410	2,470	2,850	2,580	2.68	**0.004***
Age 85+													
Population in thousands	6,726	6,747	6,774	6,869	6,969	7,100	7,270	7,518	7,912	8,172	8,437		
Procedures	62,290	63,630	63,330	62,690	65,470	65,920	65,620	69,560	72,900	74,610	76,710	2.68	**0.004***
Infections	580	690	640	550	560	660	500	600	630	700	670	0	0.5

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total hip arthroplasty in the given year

Total Knee Arthroplasty

Monte Carlo estimators for TKA across 100 samples are provided in Tables 5-7. In the "all ages" category, females contributed more procedures and more infections to the total mean than males. From 2020 to 2030, the model projected 8,857,080 average procedures (5,467,030 female; 3,390,050 male) and 53,500 average infections (28,140 female; 25,360 male). In the year 2020, the model reported an average of 763,280 total procedures and 4,710 total infections. Over the 11 years, the model predicted a 10% increase in mean number of procedures (837,740 procedures in 2030) and a 7% increase in mean number of infections (5,060 infections in 2030). For females, the model predicted an 8% increase in procedure mean (473,960 in 2020; 513,670 in 2030) and a 2% increase in infection mean (2,640 in 2020; 2,690 in 2030) from 2020 to 2030. For males, the model predicted a 12% increase in average procedures (289,320 in 2020; 324,070 in 2030) and a 14% increase in average infections (2,070 in 2020; 2,370 in 2030) from 2020 to 2030.

The procedure burden for the "all ages" category showed a significant increase in the male, female and total cohorts (p-value = 0.004 in all categories). The procedure burden in all categories for the age 65 to 84 cohort and the age 85 and over cohort projected a significant increase in burden (p-value = 0.004 in all categories). For the infection burden, the all ages category demonstrated a significant increase across all categories (male p-value = 0.004; female p-value = 0.04; total p-value 0.004). All categories in the age 45 to 64 cohort projected a significant increase in infection burden (male p-value = 0.04; female p-value = 0.004; total p-value = 0.04). Additionally, infection burden was projected to significantly increase in all categories in the age 65 to 84 cohort (male p-value = 0.004; female p-value = 0.04; total p-value = 0.004). No other cohorts projected a significant increase in burden.

Table 5. Total knee arthroplasty Monte Carlo estimators for annual procedure and infection burden for males stratified by age with results of the Cox-Stuart test for trend

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population in thousands	127,163	127,615	128,068	128,500	128,921	129,341	129,731	130,029	130,305	130,570	130,810		
Procedures	289,320	292,710	296,610	300,490	302,680	308,820	313,960	320,430	319,900	321,060	324,070	2.68	**0.004***
Infections	2,070	2,180	2,000	2,100	2,340	2,240	2,640	2,260	2,640	2,520	2,370	2.68	**0.004***
Age 18-44													
Population in thousands	60,954	61,073	61,143	61,181	61,181	61,055	60,964	60,781	60,595	60,439	60,186		
Procedures	390	450	460	430	400	410	450	400	350	430	410	0	0.50
Infections	0	0	10	0	0	10	10	0	10	10	0	0	0.50
Age 45-64													
Population in thousands	40,990	40,655	40,324	40,024	39,773	39,615	39,451	39,355	39,274	39,186	39,223		
Procedures	107,080	106,580	105,310	105,610	103,410	103,320	103,060	104,700	102,680	102,780	102,380	-1.79	0.96
Infections	900	780	860	800	860	930	1,030	780	890	810	760	1.79	**0.037***
Age 65-84													
Population in thousands	22,788	23,419	24,092	24,726	25,333	25,967	26,533	27,002	27,369	27,770	28,117		
Procedures	175,260	178,860	184,280	187,660	191,700	197,640	203,190	207,780	208,720	209,610	211,950	2.68	**0.004***
Infections	1,130	1,350	1,100	1,230	1,410	1,250	1,590	1,460	1,690	1,660	1,580	2.68	**0.004***
Age 85+													
Population in thousands	2,431	2,468	2,508	2,569	2,633	2,703	2,783	2,891	3,067	3,174	3,284		
Procedures	6,590	6,820	6,560	6,790	7,170	7,450	7,260	7,550	8,150	8,240	9,330	2.68	**0.004***
Infections	40	50	30	70	70	50	10	20	50	40	30	-0.89	0.81

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total knee arthroplasty in the given year

Table 6. Total knee arthroplasty Monte Carlo estimators for annual procedure and infection burden for females stratified by age with results of the Cox-Stuart test for trend

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population in thousands	133,212	133,445	133,672	133,876	134,081	134,289	134,480	134,584	134,680	134,756	134,799		
Procedures	473,960	478,830	483,430	486,550	493,630	498,740	505,530	508,330	507,220	517,140	513,670	2.68	**0.004***
Infections	2,640	2,500	2,370	2,400	2,670	2,690	2,300	2,560	2,650	2,670	2,690	1.79	**0.037***
Age 18-44													
Population in thousands	59,119	59,164	59,155	59,121	59,054	58,878	58,730	58,500	58,271	58,073	57,800		
Procedures	7,390	7,370	7,290	6,950	7,260	6,810	7,130	6,940	7,020	6,970	7,120	-0.89	0.81
Infections	50	60	50	100	70	70	40	60	70	40	30	-0.89	0.81
Age 45-64													
Population in thousands	42,872	42,398	41,939	41,503	41,117	40,816	40,516	40,284	40,071	39,844	39,745		
Procedures	166,720	164,870	163,300	162,000	161,060	158,560	160,160	158,540	154,580	156,250	155,240	-1.79	0.96
Infections	910	940	950	1,000	1,100	920	1,030	1,030	1,080	1,030	1,120	2.68	**0.004***
Age 65-84													
Population in thousands	26,926	27,568	28,241	28,870	29,478	30,091	30,645	31,090	31,416	31,777	32,052		
Procedures	289,030	295,240	301,160	306,640	314,080	321,320	325,890	331,260	332,960	341,060	338,430	2.68	**0.004***
Infections	1,580	1,430	1,280	1,260	1,440	1,600	1,130	1,450	1,390	1,500	1,460	1.79	**0.037***
Age 85+													
Population in thousands	4,295	4,315	4,336	4,382	4,432	4,505	4,589	4,710	4,923	5,062	5,202		
Procedures	10,820	11,350	11,680	10,960	11,230	12,050	12,350	11,590	12,660	12,860	12,880	2.68	**0.004***
Infections	100	70	90	40	60	100	100	20	110	100	80	0.89	0.19

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total knee arthroplasty in the given year

Table 7. Total knee arthroplasty Monte Carlo estimators for annual procedure and infection burden stratified by age with results of the Cox-Stuart test for trend

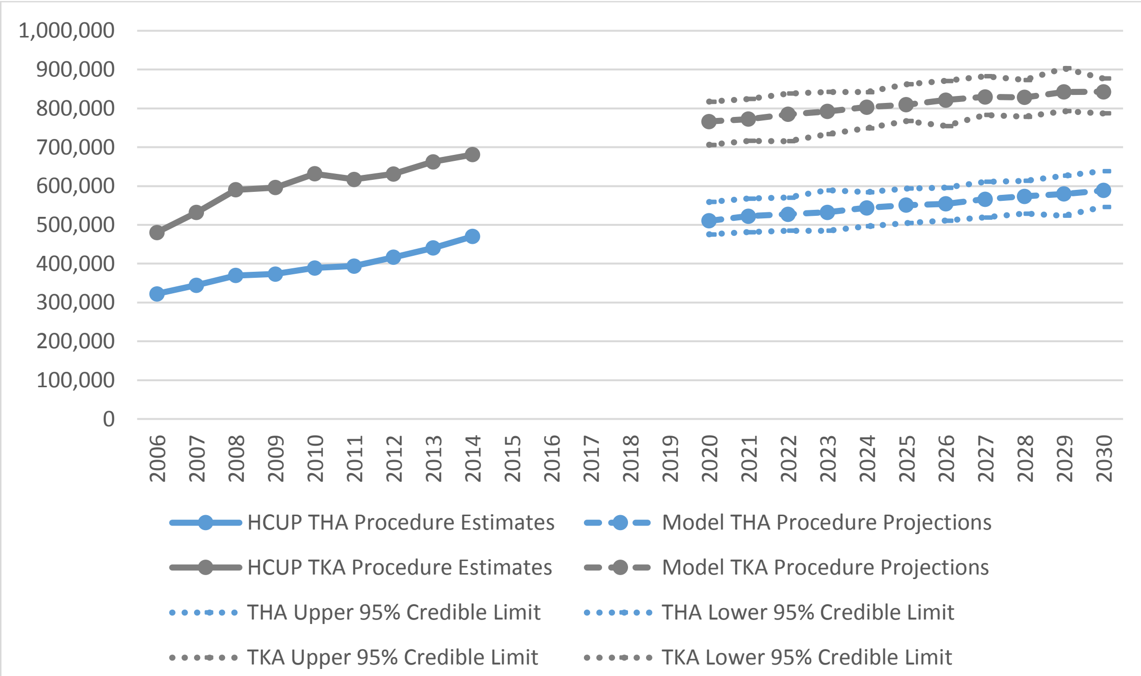
	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Z-Score	P-Value
All Ages													
Population in thousands	260,375	261,060	261,740	262,376	263,002	263,630	264,211	264,613	264,985	265,326	265,609		
Procedures	763,280	771,540	780,040	787,040	796,310	807,560	819,490	828,760	827,120	838,200	837,740	2.68	**0.004***
Infections	4,710	4,680	4,370	4,500	5,010	4,930	4,940	4,820	5,290	5,190	5,060	2.68	**0.004***
Age 18-44													
Population in thousands	120,073	120,237	120,299	120,302	120,236	119,932	119,694	119,281	118,866	118,513	117,986		
Procedures	7,780	7,820	7,750	7,380	7,660	7,220	7,580	7,340	7,370	7,400	7,530	-0.89	0.81
Infections	50	60	60	100	70	80	50	60	80	50	30	0	0.50
Age 45-64													
Population in thousands	83,862	83,053	82,263	81,527	80,890	80,431	79,967	79,639	79,345	79,031	78,968		
Procedures	273,800	271,450	268,610	267,610	264,470	261,880	263,220	263,240	257,260	259,030	257,620	-1.79	0.96
Infections	1,810	1,720	1,810	1,800	1,960	1,850	2,060	1,810	1,970	1,840	1,880	1.79	**0.037***
Age 65-84													
Population in thousands	49,714	50,987	52,333	53,596	54,811	56,058	57,178	58,091	58,785	59,547	60,169		
Procedures	464,290	474,100	485,440	494,300	505,780	518,960	529,080	539,040	541,680	550,670	550,380	2.68	**0.004***
Infections	2,710	2,780	2,380	2,490	2,850	2,850	2,720	2,910	3,080	3,160	3,040	2.68	**0.004***
Age 85+													
Population in thousands	6,726	6,783	6,844	6,951	7,065	7,208	7,371	7,601	7,990	8,236	8,486		
Procedures	17,410	18,170	18,240	17,750	18,400	19,500	19,610	19,140	20,810	21,100	22,210	2.68	**0.004***
Infections	140	120	120	110	130	150	110	40	160	140	110	0	0.50

*Indicates significance at the $\alpha = 0.05$ level
NOTE: Population represents the population eligible to receive a primary total knee arthroplasty in the given year

Comparing 2006 to 2014 estimates to model projections

In Figure 2, we plot the HCUP estimated procedures for THA and TKA in the years 2006 through 2014 with our model projections for the years 2020 to 2030. Hip arthroplasty procedures were projected to increase by roughly 40,000 from 2014 to 2020, while knee arthroplasty procedures were projected to increase by almost 90,000 during the same period. Both estimated and projected procedures show a roughly positive linear trend, although the increase is steeper in the HCUP estimates (46% increase in THA; 42% increase in TKA) than in the model projections (15% increase in THA; 10% increase in TKA). Credible intervals for THA and TKA indicate that there is a 95% probability that TKA has a greater procedure burden than THA. While greater in number, projected knee procedures displayed a similar increasing trend to projected hip procedures (THA p-value = 0.004; TKA p-value = 0.004). Estimated knee procedures showed a positive trend (42% increase), though with greater variation then the estimated hip procedures (46% increase).

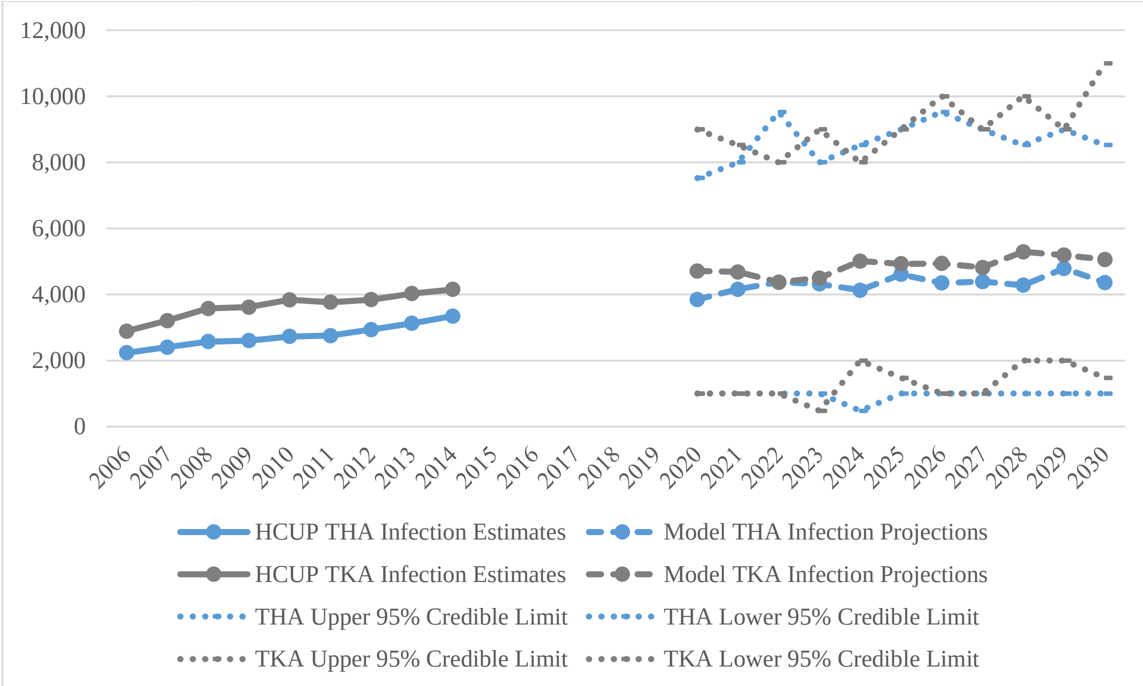
Figure 2. Graph of estimated and projected total hip and knee arthroplasty (THA/TKA) procedures from 2006-2030



NOTE: Healthcare Utilization Project (HCUP)

Figure 3. provides the estimated and projected infections for the years 2006 through 2014 and 2020 through 2030. Estimated infections were obtained using the HCUP estimated procedures for 2006 through 2014 multiplied by the age and gender stratified infection rates from NHSN (see Table 1 for rates). Model results were used to produce the projected infections for the years 2020 through 2030. The estimated infection burden from 2006 through 2014 was increasing for both THA and TKA (50% for THA; 44% for TKA). Infections following TKA produced a greater total burden than THA between 2006 and 2014. The results of our model produced greater variation across the years 2020 through 2030. There is a roughly positive trend in both the THA and TKA infections burden (13% increase in THA, p-value = 0.04; 7% increase in TKA, p-value = 0.004). The overall increase in infections from 2020 to 2030 is less than from 2006 to 2014, but the infection burden is greater from 2020 to 2030, then 2006 to 2014 for THA and TKA. On average, TKA projected a greater infection burden than THA, with the exception of the year 2022. However, credible intervals overlapped, so there is not a significant difference between the infection burden in THA and TKA.

Figure 3. Graph of estimated and projected surgical site infections as a result of total hip and knee arthroplasty (THA/TKA) from 2006-2030



NOTE: Healthcare Utilization Project (HCUP)
NOTE: Infections from 2006 through 2014 estimated using HCUP procedure estimates and National Healthcare Safety Network infection rates

Chapter 5. Discussion

Summary of Results

The results of our study provided evidence that the overall procedure and infection burden in the years 2020 through 2030 will increase despite stable rates. Hip and knee arthroplasty displayed increasing trends in procedure burden across both genders in the “all ages” category (p-value = 0.004 in all categories). The increase in total procedure burden was largely driven by increases in procedures in the age 65 to 84 and 85 and over cohorts for both hip and knee arthroplasty.

Infections following hip and knee arthroplasty maintained an increasing trend across both genders in the all ages category (p-value < 0.04 in all categories). The age 65 to 84 cohort contributed the largest number of infections in any age group for both males and females. From 2020 to 2030, the model projected an average THA infection burden of 4,328 SSIs for each year, compared to the average estimated annual infection burden of 2,746 SSIs per year from 2006 to 2014. For TKA, the model projected an annual infection burden of 4,864 SSIs from 2020 to 2030, while the average estimated annual infection burden from 2006 to 2014 was 3,658 SSIs.

Conclusions

Infection Burden

This project’s goal was to evaluate the future infection burden in the years 2020 through 2030 and relate the burden to potential medical cost increases and intervention benefits. Our study projected that the SSI burden for THA and TKA will increase, despite stable infection rates. Thus, not prioritizing SSIs because infection rates are low and stable will increase medical costs and burden on the healthcare system. In 2009, it was estimated that each SSI accounts for $12,000 to $35,000 in direct hospital expenditures (R. D. Scott, 2009). Applying these values to our projections, hospital costs could increase anywhere from $10.3 to $30.1 million on average between 2020 and 2030 due to SSIs following THA and TKA. In 2014, Medicare paid for 55% of TKA and 59% of THA claims nationally (*National Inpatient Sample*, 2016). Assuming similar rates in 2020 through 2030, Medicare would likely be responsible for $30.6 to $89.4 million for infections following THA and $32.1 to $93.6 million for infections following TKA.

Impact of Age

The aging population is an important factor in the increased burden of both arthroplasty procedures and SSIs. In both THA and TKA, the majority of procedures occur in the 65 and older age group. Our study demonstrated that the ages 65 to 84 cohort contributes the largest number of infections on average. As the age 65 and older cohort grows larger, given the higher procedure rates and increased risk of infection, it is reasonable to expect the infection burden to increase.

The age 65 and older population is also the population eligible for Medicare. We previously estimated a several million-dollar increase in Medicare costs given the increased infection burden and stable Medicare usage rates. However, if the majority of the infection burden increase is the result of increases in the population age 65 and older, Medicare costs may increase by an even larger amount.

Impact of Gender

In both THA and TKA, females projected more procedures and infections on average than males. Between 2020 and 2030, our model projected females between the ages of 65 and 84 to account for 34% of SSIs following THA and 29% of SSIs following TKA. This could be due to several factors. Women may be more likely to utilize healthcare, including a higher number of visits to a primary care physician, diagnostic services, and osteoarthritis healthcare visits preceding arthroplasty (Bawa, Weick, & Dirschl, 2016; Bertakis, Azari, Helms, Callahan, & Robbins, 2000). The increased healthcare utilization makes it more likely that women elect to receive a procedure, in turn making them more susceptible to SSIs. Additionally, women have a longer lifespan than men do. As hip and knee arthroplasty is more common among the population age 65 and older, women have an increased chance of receiving a procedure in their lifetime.

Impact of Surgery Type

Consistently, the U.S. population experiences more TKA procedures than THA procedures. Our model projects that from 2020 to 2030, a greater burden of SSIs can be attributed to TKA procedures than THA procedures. We did note that the credible intervals for the infection burden of TKA overlapped with the credible intervals for the THA infection burden so we cannot say that the difference was significant. However, with the greater procedure burden, it is possible that targeting TKA procedures for SSI prevention would have a greater impact on the overall infection burden.

Limitations

Static Model

Several limitations exist in the current study. We conducted our analysis with a static model, which did not account for possible transmission of infection between patients. We selected a static model as the infection rates were low, SSIs have different infection etiologies, and previous studies have shown clustering has little effect on overall infection rates (Baker et al., 2016). However, transmission is possible and future studies should consider dynamic models to assess the possible impact.

Stable Historical Rates

The model also used stable historical rates for both the procedure and infection rates. Stratifying by age provided adjustments based on the changing age demographics, however it did not account for rate changes due to outside factors. Several studies have mentioned that the procedure rate may be increasing due to the increasing popularity of the surgery (Pollock et al., 2016; Singh et al., 2010). Also, our procedure rates did not include outpatient or same-day discharge surgeries (0.75-6.2% of THA/TKA procedures) which are rare but may potentially increase in order to decrease surgical costs in the future (Bovonratwet et al., 2017; Sher et al., 2016). Thus, our model provided the lower bound of procedure burden estimates. Omitting outpatient or same-day discharge surgeries may also have an impact on infection burden estimates. The literature on infection rates in outpatient knee and hip surgeries is inconclusive.

Some studies have shown no significant difference between adverse events following outpatient vs. inpatient surgery, however outpatient surgical patients tend to have fewer risk factors to begin with (Aynardi et al., 2014; Sher et al., 2016). Additionally, the infection rate did not account for patient comorbidities, such as obesity. Obesity and SSIs have been shown to be positively correlated in arthroplasty patients (Bozic, Lau, Kurtz, Ong, & Berry, 2012; Bozic, Lau, Kurtz, Ong, Rubash, et al., 2012). The obesity rate is expected to increase in the United States, and the infection burden may be impacted given their association (Wang et al., 2008). If the obesity rate increases, we would expect the infection burden to increase given the correlation between obesity and infection.

Small Sample Size

Another limitation was the small sample size used in our model. For this project, we completed 100 samples of each model. This number was chosen as a large number of samples that could be run through the model in a reasonable amount of time. We were able to complete one model with 1,000 samples and compared it to the model output from 100 samples. Credible intervals and Monte Carlo mean estimates were found to be similar between the two outputs as shown in Table 8. Based on our processing resources and model run-time, we selected 100 samples for our study.

Credible Intervals

As shown in Figure 3, the results of this study produced wide credible intervals for the infection burden parameter. Although we identified a significant increasing trend in infection burden using the Cox-Stuart test for trend, we did not find that hip and knee SSI burdens were significantly different from each other or from 2006 to 2014 estimates using credible intervals. SSIs following hip and knee arthroplasty are a rare event among the total population (less than 1% of the less than 1% receiving each surgery). Given the inherent variability in the MCMC model, it is unsurprising that we obtained such wide credible intervals. Bayesian methods include all parameter uncertainty in the analysis and have no automatic measure of statistical significance (i.e. p-value) (Sutton & Abrams, 2001). Additionally it can be difficult to assume normality for rare events, as the data is sparse, so the central limit theorem does not apply. However, not specifying the distribution leads to more conservative estimates. As there is no statistical significance measure and we cannot assume normality (which is required for confidence intervals), we calculated credible intervals. Due to the above factors, credible intervals are more conservative for rare events, which lead to wider credible intervals (Sutton et al., 2002).

Table 8. Comparison of credible intervals (CR) and Monte Carlo mean estimates for 100 samples and 1,000 samples in male total hip arthroplasty

	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Results from 1,000 Samples											
Population in thousands	127,163	127,702	128,232	128,739	129,234	129,727	130,184	130,559	130,910	131,242	131,535
Population 95% CR	127,163 - 127,163	127,630 - 127,781	128,131 - 128,335	128,621 - 128,853	129,100 - 129,367	129,564 - 129,882	130,003 - 130,343	130,387 - 130,734	130,725 - 131,092	131,042 - 131,427	131,324 - 131,743
Procedure Estimate	209,505	213,423	239,689	216,061	219,172	222,837	225,779	229,009	231,986	236,400	238,788
Procedure 95% CR	182,000 - 237,000	188,000 - 242,000	208,000 - 270,000	187,000 - 245,000	190,000 - 247,000	195,000 - 251,000	197,000 - 257,000	201,975 - 259,000	202,000 - 262,025	208,000 - 265,000	208,000 - 269,000
Infection Estimate	1,616	1,647	1,911	1,724	1,701	1,793	1,830	1,913	1,883	1,879	1,896
Infections 95% CR	0 - 5,000	0 - 5,000	0 - 5,000	0 - 4,025	0 - 5,000	0 - 5,000	0 - 5,000	0 - 5,000	0 - 5,000	0 - 5,000	0 - 5,000
Results from 100 Samples											
Population in thousands	127,163	127,698	131,560	128,230	128,741	129,235	129,724	130,187	130,567	130,918	131,259
Population 95% CR	127,163 - 127,163	127,628 - 127,774	131,346 - 131,725	128,121 - 128,356	128,579 - 128,897	129,080 - 129,413	129,580 - 129,918	130,001 - 130,376	130,391 - 130,745	130,741 - 131,066	131,062 - 131,416
Procedure Estimate	211,770	215,030	243,080	216,290	219,670	224,610	226,730	226,000	231,380	235,930	237,640
Procedure 95% CR	179,950 - 241,000	184,325 - 243,525	211,325 - 277,150	191,375 - 243,525	183,475 - 252,575	197,950 - 253,050	192,950 - 253,525	194,000 - 257,050	205,425 - 252,525	211,475 - 264,000	207,475 - 268,050
Infection Estimate	1,640	1,740	1,780	1,990	1,700	1,910	1,900	1,820	1,910	1,820	1,770
Infections 95% CR	0 - 4,000	0 – 5,000	0 – 5,525	0 - 4,000	0 - 4,000	0 - 4,000	0 - 5,525	0 - 5,000	0 - 5,000	0 – 4,525	0 - 4,000

NOTE: Population represents the population eligible to receive a primary total hip arthroplasty in the given year

Immigration
In the creation of our model, we did not include immigration as a model input. To check the accuracy of our model and the impact of immigration on the population cohorts, Table 9 compares the model Monte Carlo population means to the U.S. Census projections in 2030. The age 18 to 44 cohort had the largest difference between the census and the model. As this cohort also has the lowest number of procedures and infections, we did not believe this would influence our model projections significantly. All other age cohorts in the model projected similar numbers to the census.

Table 9. Comparison of Monte Carlo population estimators to U.S. Census projections in 2030

	18-44 years	45-64 years	65-84 years	85 and over	Cumulative 18 and over
U.S. Census Projections	126,588	82,434	64,976	9,132	283,129
TKA Model Projections	117,986	81,618	65,272	8,677	273,553
THA Model Projections	118,078	81,256	65,081	9,103	273,519

Recommendations for Further Study

Future studies can improve upon the procedure and infection burden projections by validating our results using different methods and improving rate estimates by considering comorbidities and the impact of possible interventions.

Poisson Regression Validation
Another possible method of analysis is a Poisson regression model to estimate the expected count of procedures and infections. Kurtz et al. utilized this method (S. Kurtz et al., 2007; S. M. Kurtz et al., 2014) for their procedure projections. Updating their model to use current rates and including infection projections would provide a validation for the results that our model produced.

Comorbidity Rates
As we developed the model, several additional inputs or outputs were considered that were not included due to time restraints and missing information. SSIs following arthroplasty procedures are comorbid with several medical conditions. In THA, SSIs are comorbid with rheumotological

disease, obesity, preoperative anemia and coagulopathy (Bozic, Lau, Kurtz, Ong, Rubash, et al., 2012). In TKA, SSIs are comorbid with congestive heart failure, chronic pulmonary disease, preoperative anemia, diabetes, depression, renal disease, pulmonary circulation disorders, obesity, rheumatologic disease, psychoses, metastatic tumor, peripheral vascular disease and valvular disease (Bozic, Lau, Kurtz, Ong, & Berry, 2012). Accounting for expected trends in these medical conditions may provide more accurate burden projections for infections.

Mortality

Using these comorbid conditions in our analysis, we may be able to track mortality following SSIs as an additional output based on the severity of the infection and comorbid conditions. Operative patients have a 2 to 11 times higher mortality rate if they have an SSI (D. J. Anderson et al., 2014). Tracking the mortality burden associated with increased infections would provide important outcome information for the public health community.

Interventions

Additionally, it would be valuable to include the effect of interventions on the projected infection burden. Roughly 60% of SSIs are estimated to be preventable by following evidence-based guidelines (D. J. Anderson et al., 2014). At a high level, the CDC recommends interventions such as "providing incentives for HAI prevention, increasing survey and certification activities, implementing licensure and training requirements, increasing adherence of healthcare facilities and providers to infection control recommendations, implementing or expanding public reporting, (and) ensuring appropriate regulatory oversight" (*Eliminating Healthcare Associated Infections: State policy options*, 2011). Specific to SSIs, recommendations are available regarding patient characteristics (smoking, obesity, diabetes, etc.) and perioperative care (skin preparation, antimicrobial prophylaxis, operative time, etc.) with high levels of evidence that they have an effect on the probability of infection (D. J. Anderson et al., 2014). Using findings from previous studies, rate reductions based on specific interventions can be used to assess the intervention's overall impact on the infection burden.

Public Health Implications

SSIs are common and costly HAIs that increase patient stays, comorbidity risks and mortality (D. J. Anderson et al., 2014). It has been estimated that $3.5 to $10 billion in direct hospital costs can be attributed to SSIs annually (R. D. Scott, 2009). Per SSI patient, SSIs account for approximately $12,000 to $35,000 in direct hospital expenditures (R. D. Scott, 2009). Specific to SSIs following THA and TKA, infections cost Medicare an average increased reimbursement cost of $50,000 over non-infected THA/TKA procedures (Yi et al., 2015). This study demonstrates that the burden of infection in arthroplasty patients will increase through 2030, and we can expect that the patient hospital costs will increase as well. Additionally, we expect the majority of the increased infection burden to come from the population age 65 and older, increasing Medicare expenses. For these reasons, it is important to consider SSI interventions that can not only improve patient health but also reduce the economic burden on the U.S. healthcare system.

When developing HAI interventions, policy makers set health priorities for prevention. The CDC recommends that states identify priority infections when developing their policy interventions (*Policies for Eliminating Healthcare-Associated Infections: Lessons learned from state stakeholder engagement*, 2012). Adapting the TAP strategy to include SSIs and help identify facilities with an excess burden of hip and knee infections will become imperative if infection rates remain stable, yet the burden of infection increases ("TAP Strategy 'How To' Guide for the Individual Facility User," 2016). SSIs are a significant burden of HAI costs, and account for anywhere from 3 to 22 times the patient hospital costs of central line-associated bloodstream infections (CLABSIs), ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTIs) and clostridium difficile infections (CDIs) (R. D. Scott, 2009). Given this, and the increasing burden, SSIs should be a high priority for intervention.

Additionally, the results show that certain populations contribute a large number of infections to the overall total. Females between the ages of 65 and 84 accounted for 34% of SSIs following THA and 29% of SSIs following TKA in our model. Targeting these high-risk populations for interventions can increase the impact of interventions, while keeping costs reasonable.

Final Summary

The results of our study indicate that the number of THA and TKA procedures and SSIs will increase in the years 2020 to 2030, even if the infection rate remains stable. The aging population is a contributing factor to the projected increase. This increase will have an impact on hospital and healthcare system costs and public health policy priorities. Hospital and Medicare costs are likely to increase due to infections following arthroplasty and the growing population over the age of 65. Public health policies are set by evaluating the overall burden of disease and this study provides evidence that SSIs should be a high priority for intervention. Given that the majority of infections occur in females age 65 to 84, targeting these high-risk groups may provide the greatest impact on overall burden. SSIs should be targeted as a public health priority to reduce overall burden and medical costs and further studies should evaluate the effectiveness of different interventions.

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