

Original Article

The cost of managing complex surgical site infections following primary hip and knee arthroplasty: A population-based cohort study in Alberta, Canada

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Abstract

Objective: Nearly 800,000 primary hip and knee arthroplasty procedures are performed annually in North America. Approximately 1% of these are complicated by a complex surgical site infection (SSI), leading to very high healthcare costs. However, population-based studies to properly estimate the economic burden are lacking. We aimed to address this knowledge gap.

Design: Economic burden study.

Methods: Using administrative health and clinical databases, we created a cohort of all patients in Alberta, Canada, who received a primary hip or knee arthroplasty between April 1, 2012, and March 31, 2015. All patients who developed a complex SSI postoperatively were identified through a provincial infection prevention and control database. A combination of corporate microcosting data and gross costing methods were used to determine total mean 12- and 24-month costs, enabling comparison of costs between the infected and noninfected patients.

Results: Mean 12-month total costs were significantly greater in patients who developed a complex SSI compared to those who did not (CAD\$95,321 [US\$68,150] vs CAD\$19,893 [US\$14,223]; $P < .001$). The magnitude of the cost difference persisted even after controlling for underlying patient factors. The most commonly identified causative pathogen (38%) was *Staphylococcus aureus* (95% MSSA).

Conclusions: Complex SSIs following hip and knee arthroplasty lead to high healthcare costs, which are expected to rise as the yearly number of surgeries increases. Using our costing estimates, the cost-effectiveness of different strategies to prevent SSIs should be investigated.

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In Canada, more than 100,000 knee and hip replacements are performed annually,¹ including ~10,000 in the province of Alberta.² In the United States, ~700,000 hip and knee replacements are performed annually, and this number is expected to quadruple by the year 2030.³ These procedures can significantly reduce pain and improve mobility and quality of life; however, 1%–2% of patients undergoing joint replacements in North America develop infection after surgery.^{4,5} The Centers for Disease Control and Prevention (CDC) divides surgical site infections (SSIs) into superficial incisional, deep incisional, and organ-space infections, with the latter 2 considered complex.⁶ While superficial SSI can usually be managed with oral antibiotics and possibly local debridement, guidelines recommend more

intensive management for complex infections.⁷ A complex SSI generally requires repeat surgery, which can include debridement and retention of the prosthesis, or a complete revision of the joint done in a 1-stage or 2-stage process. All of these surgeries also require treatment with prolonged courses of antibiotics, often delivered intravenously.⁷

Given the interventions required to manage complex SSIs, these infections have a major impact on patients and healthcare payers. In the United States, ~US\$9.8 billion (2012 dollars) is spent on major healthcare-associated infections annually, with SSIs contributing 33.7% of the total.⁸ The true cost of managing patients with complex joint infections is uncertain, though a study in Canada using gross costing methods estimated that the average cost for a hospital admission for an infected knee arthroplasty is more than CAD\$20,000 (~US\$15,280).⁴ In the United Kingdom, the cost for just 1 admission related to revision surgery for SSI is ~22,000 pounds (~US\$28,300).⁹ A study from the United States estimated that the cost of SSIs following hip and knee arthroplasty has increased by US\$246 million from 2001 to 2009,

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and is projected to exceed US\$1.62 billion by 2020.¹⁰ Even after appropriate management, as many as 60% of patients are not cured and require chronic treatment.^{11–14}

There are uncertainties around the cost of managing joint infections caused by specific bacterial pathogens. *Staphylococcus aureus*, including the virulent methicillin-resistant *S. aureus* (MRSA), is the most common cause of postreplacement infections.² Given that these infections are difficult to cure,¹⁵ it is plausible that managing patients with infections caused by *S. aureus* including MRSA would be more costly compared to other pathogens. Additionally, patients with certain comorbidities (eg, diabetes) are more likely to develop a postoperative SSI; thus, it is important to determine the cost of managing patients with different clinical characteristics.¹⁶

Healthcare systems worldwide have finite resources and when considering investments in strategies to prevent SSI, value for money must be considered. More precise estimates of the costs of managing patients with SSIs after hip and knee arthroplasties are needed. In this study, we used a population-based cohort of patients receiving primary hip and knee arthroplasty in the province of Alberta to estimate the cost of managing patients who develop a postoperative complex SSI compared with those who do not. We use microcosting data when available to achieve greater accuracy.

Methods

Overview

We conducted a population-based cohort study of all patients receiving an elective primary hip or knee replacement in Alberta, Canada, a province of ~4 million people, with a single healthcare system, over a 3-year period. Data for all patients was linked to an infection prevention and control (IPC) database which accurately identifies all patients who develop a joint infection within 90 days of arthroplasty and to health administrative data that capture patient comorbidities and healthcare costs.

Data sources

The Alberta Bone and Joint Health Institute (ABJHI) database was used to identify all patients in Alberta who received a primary hip or knee replacement between April 1, 2012, and March 31, 2015. This database captures information on patients undergoing orthopedic surgeries in Alberta. If more than 1 primary arthroplasty was performed on a patient in the study period, only the initial arthroplasty on the first replaced joint was considered when creating the baseline cohort.

To assess for joint infections, we used data from the Alberta Health Services (AHS) IPC group. Their surveillance population includes all adults ≥ 18 years of age admitted to any public Alberta hospital facility for arthroplasty in urban and nonurban sites. Data for all complex SSIs found within 90 days of arthroplasty from April 2012 to March 2015 were collected. Cases of SSI were detected using several mechanisms: electronic review of microbiology laboratory results, review of patient charts including observation of the incision, physician record and pharmacy data, reoperation records, readmissions, emergency visit records, and clinic visit records. Provincial surveillance is centralized using a web-based data entry platform. An IPC Data Quality Working Group began completing an additional review of provincial admission and disease administrative codes in April 2013 to

ensure that no cases of SSI following hip and knee arthroplasty were being missed across the province. We also used this database to capture the causative organism of the infections.

Data from the IPC database and ABJHI database was linked to Discharge Abstract Database (DAD) records to obtain additional information around admissions secondary to infected arthroplasties (eg, length of stay [LOS]) in addition to the surgical procedures themselves. Patient comorbidities, categorized according to the Elixhauser index, were collected using diagnosis codes. This index includes 30 different patient conditions and is a predictor of in-hospital mortality.¹⁷

Microcosting data, described below, were obtained from corporate data for the major urban zones (Calgary and Edmonton). Costs for zones outside the major urban centers were based on gross costing methods, obtained from Alberta Health Services Division of Analytics, Data Integration, Measurement, and Reporting.

Cohort

We created a cohort of adults aged 18 years or older who received elective primary hip or knee replacements in the province of Alberta between April 1, 2012, and March 31, 2015. Age, sex, First Nations status, outmigration, and death were collected from the Alberta Health registry for all patients in the cohort. This cohort was then divided into those who developed a complex SSI within 90 days of arthroplasty (the infected cohort) and the remaining noninfected cohort. Because we were interested in the costs of complex SSI, the small proportion of superficial SSI were included in the noninfected cohort.

Outcomes

The primary outcome was 12-month cumulative healthcare costs, including index admission, hospitalizations and emergency room, day surgery, and day medicine costs. As secondary outcomes, we also determined 24-month cumulative healthcare costs because we hypothesized that the impact of a complex SSI on costs might continue even after the infection had been treated (typically within the first year), and number of days in hospital over the first 12 months in the infected versus the noninfected group. Costs associated with admissions to hospital included costs incurred during the admission (surgical procedures and days in hospital). Hospital costs were measured using microcosting, the gold standard for obtaining costing estimates, where each component of resource use is estimated and a unit cost derived for each.¹⁸ The resource use was then tracked to specific patients. Because microcosting data were only available for inpatient hospitalizations within the large urban hospitals in Alberta, we used microcosting data for inpatient hospitalizations for all patients in Calgary and Edmonton. We used gross costing methods based on resource intensity weights provided by the DAD records for the emergency room visits, day medicine, and day surgery visits as well as the inpatient hospitalizations outside of Calgary and Edmonton.¹⁸ Gross costing methods were used for ~30% of hospitalizations across Alberta. While these methods are not as accurate as microcosting, they still provide a reasonable overview of patient costs.

Costs related to other physician claims and outpatient antibiotics were not available. We used the perspective of the healthcare payer, therefore, patient-borne costs were not considered. All costs were inflated to 2016 Canadian dollars using the consumer price index. Where US dollars are included, the January, 2016 exchange rate was utilized.

Statistical analyses

As our primary method, we assessed costs for all of the patients' hospitalization and emergency room, day surgery, and day medicine visits over the subsequent 12 and 24 months. In a complementary analysis, to better estimate the incremental cost of the infection itself, we only included the cost of hospitalizations and emergency room, day surgery, and day medicine visits for admissions with *International Classification of Disease, Tenth Revision* (ICD-10) codes that were likely to represent infection. These were determined by tracking the infected cohort of patients over time and identifying the 6 most commonly used ICD-10 codes related to infection: T8453 (infection and inflammation reaction due to hip prosthesis), T8454 (infection and inflammation reaction due to knee prosthesis), Z508 (rehabilitation care), T814 (infection following a procedure), T847 (infection and inflammatory reaction due to other internal orthopedic prosthetic devices, implants and grafts), and T8403 (mechanical complication of hip prosthesis).

Once the mean costs were determined for the infected and noninfected cohorts, they were compared to each other using Mann-Whitney U tests. To adjust for differences in patients developing infections (ie, age, gender, and comorbidities), the association between having a complex SSI and 1-year costs was determined using multiple variable linear regression, with the goal

of determining an attributable cost of complex joint infection. A linear regression model using ordinary least squares estimation was used based on its interpretability and ability to model the mean costs for each group. While ordinary least squares estimation assumes a normal distribution of the residual values, if the sample size is large enough, then this assumption being violated does not impact the magnitude of coefficients when compared with other regression methods.¹⁹ When compared to other linear models including log total costs with smearing retransformation, negative binomial (γ), and inverse Gaussian distributions, ordinary least squares performed well on measures of concordance, mean absolute error, root mean squared error, and probability plots. All statistical analyses were conducted using Stata version 14 software (StataCorp, College Station, TX).

The University of Calgary Health Research Ethics Board approved this study.

Results

Baseline characteristics

The baseline characteristics for the population are listed in Table 1. In total, 24,925 primary hip and knee arthroplasties were completed in Alberta between April 1, 2012, and March 31, 2015.

Table 1. Baseline Characteristics for the Infected and Noninfected Cohort

	Entire Cohort (N = 24,667)	Infected Cohort (N = 258)	Non-Infected Cohort (N = 24,409)	P Value ^a
Age, mean y (SD)	66.5 (10.4)	66.8 (11.7)	66.5 (10.4)	.562
Female, no. (%)	14,044 (57.0)	123 (47.7)	13,921 (57.0)	.003
Joint replaced, no. (%)				
Hip	9,765 (39.6)	145 (56.2)	9,620 (39.4)	< .001
Knee	14,902 (60.4)	113 (43.8)	14,789 (60.6)	< .001
First Nations, no. (%)	354 (1.4)	5 (1.9)	349 (1.4)	.495
Socioeconomic status, no. (%)				
Income support	705 (2.9)	12 (4.7)	693 (2.8)	.082
Social assistance	14,448 (58.6)	156 (60.5)	14,292 (58.6)	.535
Other	8,591 (34.8)	85 (32.9)	8,506 (34.8)	.524
Comorbidities, no. (%)				
Congestive heart failure	157 (0.6)	7 (2.7)	150 (0.6)	< .001
Diabetes	2,608 (10.6)	35 (13.6)	2,573 (10.5)	.116
Diabetes with chronic complications	891 (3.6)	8 (3.1)	883 (3.6)	.658
Metastatic cancer	20 (0.1)	1 (0.4)	19 (0.1)	.082
Hypertension	8,800 (35.7)	127 (49.2)	8,673 (35.5)	< .001
Renal Failure	236 (1.0)	4 (1.6)	232 (1.0)	< .001
Elixhauser index 0	11,627 (47.1)	86 (33.3)	11,541 (47.3)	< .001
Elixhauser index 1 or 2	7,992 (32.4)	93 (36.1)	7,899 (32.4)	.208
Elixhauser index 3	5,048 (20.5)	79 (30.6)	4,969 (20.4)	< .001

^aP value comparing the infected vs noninfected cohorts.

Of these, 258 developed a complex infection within 90 days of arthroplasty: 145 following a hip replacement and 113 following a knee replacement. Therefore, the percentage who developed a complex infection was 1.04%: 1.48% for hips and 0.76% for knees. The most commonly identified pathogen for a complex SSI was *S. aureus*. We identified 94 cases of methicillin-sensitive *S. aureus* (MSSA) and 5 cases of MRSA, which accounted for 38% of all complex SSIs. A causative pathogen was not identified for ~9% of the complex SSIs.

Death was significantly more common in the infected cohort compared to the noninfected cohort (12% vs 3.8%; $P < .0001$). There was no significant difference in outmigration between the infected and noninfected cohorts (0.9% overall). Additionally, the proportion of patients with >2 Elixhauser comorbidities was significantly higher in the infected cohort (30.6% vs 20.5%; $P < .001$).

12- and 24-month costs

The 12-month costs were significantly higher in the infected versus noninfected cohort for hospitalizations, emergency room, day surgery, and day medicine visits. The total mean costs included initial arthroplasty and costs for admission at the time of infection for those in the infected cohort (Table 2). This was true for overall costs as well as when the specific ICD-10 codes were used for tracking costs. The costs at 24 months were not substantially higher than the 12-month costs; overall the total mean cost at 24 months was \$106,361 (IQR, 53,718–137,997) (US\$ 76,043) for the infected cohort and \$25,143 (IQR, 13,680–25,538) (US\$ 17,976) for the noninfected cohort. When only the ICD-10 codes related to infection were used to track costs, the 24-month cost was \$74,294 (IQR, 37,209–89,252) (US\$ 53,117) for the infected cohort and \$13,565 (IQR, 10,269–13,162) (US\$ 9,698) for the noninfected cohort.

When the overall total mean costs at 12 months were divided into subgroups, costs were all significantly higher in the infected versus the noninfected group (Table 3). The difference in costs between *S. aureus* and all other pathogens for the infected cohort can be found in Table 3. Overall, the costs of *S. aureus* infections following knee and hip arthroplasties were \$99,765 (US\$ 71,327) and \$116,417 (US\$ 83,232), respectively.

Adjusted costs

After adjustment for age, sex, First Nations status, and patient comorbidities, the total mean costs at 12 months for the infected and noninfected cohorts were \$94,183 and \$13,204, respectively (US\$ 67,336 and US\$ 9,440). When considering only hospitalization and emergency room, day surgery, and day medicine visits for infection-related ICD-10 codes, the total mean costs at 12 months for the infected and noninfected cohorts were \$69,699 and \$13,203, respectively (US\$ 49,831 and US\$ 9,440). Infection, advancing age (≥ 65 years), hip replacement, congestive heart failure, diabetes with chronic complications, renal failure, and increasing number of Elixhauser comorbidities were associated with increased 1-year costs (Table 4).

Length of stay

The mean LOS at time of initial arthroplasty was 5.1 days for those who subsequently developed a complex SSI versus 3.8 days for those who did not. Overall, the mean LOS for all hospital visits after the initial arthroplasty, in the first year for patients who developed an infection was 38.9 days (36.9 and 40.5 days for knee

Table 2. Mean Overall and Infection Related Costs Including Interquartile Range (IQR) Over 12 Months for Patients With and Without Complex Surgical Site Infection

Variable	Infected Cohort, \$ (IQR) ^a	Noninfected Cohort, \$ (IQR)
Cost of initial arthroplasty	14,071 (10,400–14,202)	12,203 (10,269–12,562)
Cost of admission at time of infection	16,870 (0–22,331)	...
Overall 1-year mean costs		
Hospitalization costs	54,499 (18,113–73,653)	4,351 (0–0)
Emergency room, day surgery and day medicine costs	9,881 (4,635–12,758)	3,340 (1,453–4,089)
Total Mean cost ^b	95,321 (49,623–120,636)	19,893 (12,610–19,723)
Infection related 1-year mean costs		
Hospitalization costs	38,397 (13,060–48,876)	953 (0–0)
Emergency room, day surgery, and day medicine costs	1,106 (369–1,490)	38 (0–0)
Total mean cost ^b	70,144 (35,923–86,368)	13,195 (10,269–13,049)

^aMann-Whitney U P values $< .001$ for all comparisons in the table between overall 1-year mean costs and infection related 1-year mean costs.

^bThese total mean costs include initial arthroplasty cost, cost of admission at time of infection (for the infected cohort), hospitalization costs, and emergency room, day surgery, and day medicine costs.

and hip, respectively), compared to 3.4 days (3.2 and 3.7 days for knee and hip, respectively) for the noninfected group ($P < .001$). When considering only hospitalizations for infection related ICD-10 codes, the mean LOS for hospital visits outside of the initial arthroplasty at 1 year was 28 days (27.9 and 28.1 days for knee and hip, respectively) versus 1.0 days (0.8 and 1.1 days for knee and hip, respectively) for the infected and noninfected cohorts, respectively ($P < .001$). For those who did develop a complex SSI, the mean LOS for those with an *S. aureus* infection was 15.4 days compared to all other pathogens, for which the mean LOS was 12.2 days.

Discussion

We observed significantly higher 1-year healthcare costs for those who developed a complex SSI following primary hip or knee arthroplasty, considering either total healthcare costs (\$95,321 vs \$19,893; $P < .001$ (US\$ 68,150 vs US\$ 14,223)), or only the subset of costs related to infection-related hospitalizations and emergency room, day surgery, and day medicine visits (\$70,144 vs \$13,195; $P < .001$ (US\$ 52,043 vs US\$ 9,790)). After adjusting for age, sex, First Nations status, and medical comorbidities, higher 1-year costs were associated with a higher number of Elixhauser comorbidities as well as diabetes with chronic complications, metastatic cancer, and renal failure.

Our results are similar to 2 prior studies completed in the United States, one looking at the economic burden associated with SSI following knee arthroplasty,²⁰ and one examining the

Table 3. Mean Overall Total 1-Year Costs Including Interquartile Range (IQR) for Infected and Noninfected Cohorts Overall and by Subgroup

Variable	Overall Costs ^a		Infection Related Costs ^b	
	Infected Cohort, \$ (IQR)	Non-Infected Cohort, \$ (IQR)	Infected Cohort, \$ (IQR)	Noninfected Cohort, \$ (IQR)
All Patients	95,321 (49,623–120,636)	19,893 (12,610–19,723)	70,144 (35,923–86,368)	13,195 (10,269–13,049)
Age < 65 y	90,717 (42,827–122,029)	17,787 (12,467–17,877)	68,356 (35,487–85,586)	12,534 (10,269–12,575)
Age ≥ 65 y	98,797 (55,351–120,447)	21,630 (12,762–21,579)	72,020 (36,148–88,389)	13,740 (10,269–13,616)
Joint replacement				
Hip	98,047 (51,938–124,428)	20,584 (13,042–19,906)	72,060 (41,582–89,042)	14,132 (11,434–13,783)
Knee	91,822 (46,204–110,921)	19,444 (12,287–19,622)	68,369 (31,868–82,968)	12,586 (10,190–12,432)
Elixhauser comorbidities				
0	78,721 (40,752–100,151)	17,903 (12,392–17,910)	58,510 (31,868–76,321)	12,287 (10,269–12,381)
1 or 2	93,103 (49,507–121,518)	20,967 (12,743–20,564)	68,401 (35,560–81,718)	13,490 (10,269–13,420)
≥ 3	116,002 (61,980–141,308)	22,808 (13,116–23,148)	85,839 (49,000–89,656)	14,836 (10,597–14,845)
<i>Staphylococcus aureus</i>	108–175 (50,794–150,830)	...	83, 638 (41,492–103,670)	...
Other pathogens	87, 317 (49,570–109,139)	...	62, 228 (34,780–78,210)	...

^aMann-Whitney U P values < .001.^bMann-Whitney U P values < .001.

economic burden from SSI following hip arthroplasty.²¹ While these studies using a matched design were much smaller than our study, they also noted significant differences in cost and length of stay for infected and noninfected patients.^{20,21}

Using the average 1-year total healthcare costs, in Alberta we spend ~\$8.3 million annually on patients who develop complex SSI following primary hip and knee arthroplasties compared to the \$1.67 million we would spend had those patients not developed a complex SSI. If the mean annual costs and infection rate (1.04%) is extrapolated to all of Canada, where there are ~100,000 arthroplasties annually,¹ \$133.5 million would be spent on patients annually who acquire a complex SSI versus \$28 million for the same number of patients with no infection. If we apply the same complex infection rate of 1.04% and costs to the United States, where there are 700,000 hip and knee arthroplasties annually,³ the annual expenditure would be ~\$694 million (US\$ 496 million) to manage the SSIs, compared to \$145 million (US\$ 104 million) that would be spent had no infection developed.

Staphylococcus aureus can be very difficult to eradicate from infected joints,¹⁵ which is consistent with our observation that patients with *S. aureus* SSI had higher mean 1-year costs compared to all other pathogens, \$108,175 versus \$87,317 ($P = .077$) (US\$ 77,340 vs US\$ 62,427), though it did not reach significance. When only the infection finding codes were used, patients with *S. aureus* SSIs did have significantly higher mean 1-year costs compared to all other pathogens: \$83,638 versus \$62,228 ($P = .006$) (US\$ 59,797 vs US\$ 44,490). Because

S. aureus is the most commonly isolated causative organism for complex SSI following hip and knee arthroplasty, targeting preventative efforts toward reducing this organism may be worthwhile because colonization with *S. aureus* is a risk factor for SSI.²² Decolonization protocols studied previously in joint arthroplasty do demonstrate a reduction in SSIs,²³ and given the high cost of *S. aureus* SSI, the use of decolonization protocols may be cost-effective.

Our study has several strengths. We performed a population-based study in a province of >4 million people, identifying all primary hip and knee replacements and all subsequent complex SSIs that occurred within 3 months of arthroplasty. We used high-quality microcosting data, which is not commonly done, and our estimates are likely generalizable to the rest of Canada. While costs are not always directly comparable between countries, these findings can still be used as a guide. Our study does have limitations. We have likely underestimated the cost differences across infected and noninfected patients because we did not include elements such as physician claims. Additionally, we did not consider costs borne by the patients themselves. For patients who are employed, there are costs associated with lost productivity, and for all patients with infections, there are additional patient-borne costs for outpatient antibiotics, rehabilitation, and costs related to travel for medical care. Finally, superficial SSIs were absorbed into the noninfected cohort, so it is possible that cost differences would have been even greater between the infected and noninfected cohorts had superficial infections been considered separately.

Table 4. Ordinary Least Squares Regression Analysis Examining the Demographic and Clinical Factors Associated With Mean Total 1-Year Costs for Patients Undergoing Hip or Knee Arthroplasty

Variable	Coefficient	P Value
Infected (vs noninfected)	34,276	< .001
Age \geq 65 y (vs <65 y)	3,312	< .001
Female (vs male)	209	.694
Hip replacements (vs knee)	2,596	< .001
First Nation (vs non)	1,559	.176
Comorbidities		
Congestive heart failure	15,649	< .001
Diabetes	-1,598	.243
Diabetes with chronic complications	4,336	< .001
Metastatic cancer	8,623	.073
Hypertension	-3,422	< .001
Renal failure	14,199	< .001
Elixhauser index 1 or 2 (vs 0)	4,291	< .001
Elixhauser index \geq 3 (vs 0)	6,852	< .001

In conclusion, we estimated the incremental cost of managing patients with complex SSI following primary hip or knee arthroplasty, noting a difference in total mean 1-year costs of more than \$75,000 (US\$ 53,621). Future research should consider the cost-effectiveness of different methods to prevent complex SSI following arthroplasty. Infectious diseases physicians should be encouraged to work with orthopedic surgeons and hospital administrators to promote the implementation of cost-effective strategies to prevent SSI.

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