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Economic Burden of Periprosthetic Joint Infection in the United States

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Abstract: This study characterizes the patient and clinical factors influencing the economic burden of periprosthetic joint infection (PJI) in the United States. The 2001-2009 Nationwide Inpatient Sample was used to identify total hip and knee arthroplasties using *International Classification of Diseases, Ninth Revision*, procedure codes. The relative incidence of PJI ranged between 2.0% and 2.4% of total hip arthroplasties and total knee arthroplasties and increased over time. The mean cost to treat hip PJIs was $5965 greater than the mean cost for knee PJIs. The annual cost of infected revisions to US hospitals increased from $320 million to $566 million during the study period and was projected to exceed $1.62 billion by 2020. As the demand for joint arthroplasty is expected to increase substantially over the coming decade, so too will the economic burden of prosthetic infections. **Keywords:** periprosthetic joint infection, total knee arthroplasty, total hip arthroplasty.

Periprosthetic joint infection (PJI) is the most challenging complication associated with total joint arthroplasty in the 21st century [1,2] and, from the perspective of patients, surgeons, hospitals, and the health care system, perhaps the most grievous [3-5]. The problems posed by PJI are multifaceted. Periprosthetic joint infection can be difficult to diagnose [6-8]. It can present at any time after index arthroplasty [9,10] and requires surgical intervention, often multiple, to treat [5,11]. It places a greater burden on hospital and surgeon resource utilization relative to other types of revision surgery [4,12]. The true economic burden of PJI on the US health care is currently unknown as there are very few published studies relevant to this issue [3,4,12-14].

Our research group has previously examined the incidence of PJI in the United States using the Nationwide Inpatient Sample (NIS), which is a nationally representative inpatient database maintained by the Agency for Healthcare Quality and Research [13]. The previous analysis was limited to historical US data between 1993 and 2004; neglected the first stage of a 2-stage revision for infection; and included only the hospital charges, rather than the estimated costs associated with infected revisions [13]. We also used the historical data available at the time to develop projections for the impact of PJI in the United States [14]. These analyses and projections all predicted increased incidence of PJI between 2005 and 2020.

With the availability of further NIS data, from years 2005 to 2009, we thought it an opportune time to update our previous assessment of the PJI and forecast its economic impact on the hospital health care system in the United States. This study addressed the following 3 research questions: (1) Did the trends of incidence, length of stay, and inpatient costs for PJI observed between 2001 and 2004 extend throughout 2005 to 2009? (2) Which patient and clinical factors influence the hospitalization cost of PJI? (3) What is the projected incidence and economic cost of PJI to the US inpatient health care system for the coming decade?

Methods and Materials

We used the NIS to identify primary and revision arthroplasty performed in the United States between January 1, 2001, and December 31, 2009. The NIS is an annual, statistically valid survey of approximately 1000 hospitals, containing 7 to 8 million records representing approximately 20% of all hospital discharges in the United States. The NIS is specifically designed by the Healthcare Cost and Utilization Project (HCUP) to assist

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with the development of health care policy. We also used the statistical trend files provided by HCUP to properly adjust for the slight year-to-year variances in the sampling methods used by the survey, as described previously [15].

Surgical procedures performed, disease diagnoses, and complications are incorporated into the NIS using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). We used *ICD-9-CM* procedure codes for primary or revision total hip arthroplasty (THA) (81.51 and 81.53, 00.70-00.73) as well as primary or revision total knee arthroplasty (TKA) (00.80-00.84, 81.54-81.55). We included arthrotomy for removal of a hip or knee prosthesis (80.05 or 80.06, respectively) in the analysis to capture the first stage of 2-stage infection treatment procedures. Hip and knee arthroplasties with PJI were identified by the 996.96 *ICD-9* diagnosis code.

The incidence of THA and TKA and those that involve infection was extracted and identified from the NIS database for 2001 to 2009. An estimate of the national total and the associated confidence interval (CI) was obtained using the sample weight and the survey stratification and clustering factors from the NIS data. Projected future numbers of THA and TKA through 2020 was obtained using a Poisson model, coupled with projected population from the US Census Bureau.

The Poisson regression model estimated rate of surgery as a function of the patient's age, sex, race, and geographic location (census region) as well as adjusting for the type of surgery (THA/TKA; primary/revision) and whether infection was diagnosed. This rate is allowed to vary linearly with calendar year. Interaction among the demographic factors and interaction between demographic and surgical factors and calendar year were also part of the Poisson model, allowing for differential trends among demographic and surgery subgroups in the data. Thus, future number of infected and noninfected THA or TKA (and the corresponding upper and lower bounds) is estimated by "scoring" the rates estimated by the model against the future population size provided by the Census Bureau. The total number of infected cases beyond 2009 is estimated by summing the estimated number of such cases for each demographic and surgery subgroups. Assuming independence among different subgroups, an approximate CI of the total is obtained by summation of the estimated variance from each component estimates provided by the model as the variance of the total.

The total hospital charge for each discharge was part of each record from the NIS survey. The HCUP has developed a set of companion files (2001 and onward) called the "cost-to-charge ratio" that allow the total hospital charges to be converted to an estimated cost to that institution. For a particular hospitalization in which a THA or TKA was performed, the exact cost to that hospital is unknown. The hospital cost is estimated using the overall cost conversion ratio for that hospital. One should note that this is only the institutional cost associated with the hospitalization. The costs associated with a surgeon's service, the service of other physicians (eg, infection specialist, anesthesiologist), or subsequent expenses in physical therapy were not included in these data.

Both the charge and the estimated cost for the hospitalization were adjusted by the Consumer Price Index for Medical Care, which is published monthly by the Bureau of Labor Statistics (Series CUSR0000SAM). All dollar amounts in this report were adjusted to January 2010. Each year, approximately 15% to 20% of hospitals, due to state regulation or other reasons, did not provide cost data to allow for determination of the cost-to-charge ratio. The HCUP did provide a "group" average conversion factor in many cases where hospital-specific conversion factors were not available. For a few remaining hospitals for which neither hospital-specific nor group-level conversion factor was available, an estimated conversion value was calculated based on the conversion factors from other hospitals in the same NIS sampling stratum.

We developed a statistical model for projections of the future national cost due to infected hip and knee arthroplasty surgeries up to 2020. The total cost for treating infected and noninfected hip and knee arthroplasty cases was entered into a companion model that was used for modeling frequency of arthroplasty surgeries. Cost was again expressed as a function of demographic and surgical factors and stratified by the corresponding patient subpopulation. The projected cost beyond 2009 was calculated by the trajectory in cost from the previous 10 years, allowing for differential trends in cost for different demographic and surgery groups. The total future cost associated with infection was obtained by summation of this cost for different infected subgroups in the year 2010 to 2020.

Results

There were 159 360 procedures for infected hip (54 292) and knee (105 068) replacements in US hospitals between 2001 and 2009 (Fig. 1). The annual number of infected hip arthroplasty cases increased from 4545 (2001) to 7162 (2009) (Table 1; available online at www.arthroplastyjournal.org). The PJI incidence rate, as a percentage of the total number of hip arthroplasties performed, increased from 1.99% (CI, 1.78%-2.21%) in 2001 to 2.18% (CI, 1.97%-2.39%). Adjusting for other patient demographic factors (age, sex, race, census region), there was a significant year-to-year increase in the risk of hip infection over the study period (odds ratio, 1.053; $P < .001$). Among knee arthroplasties, the estimated annual number of infected cases increased from 7113 (2001) to 14 802 (2009) (Table 1; available

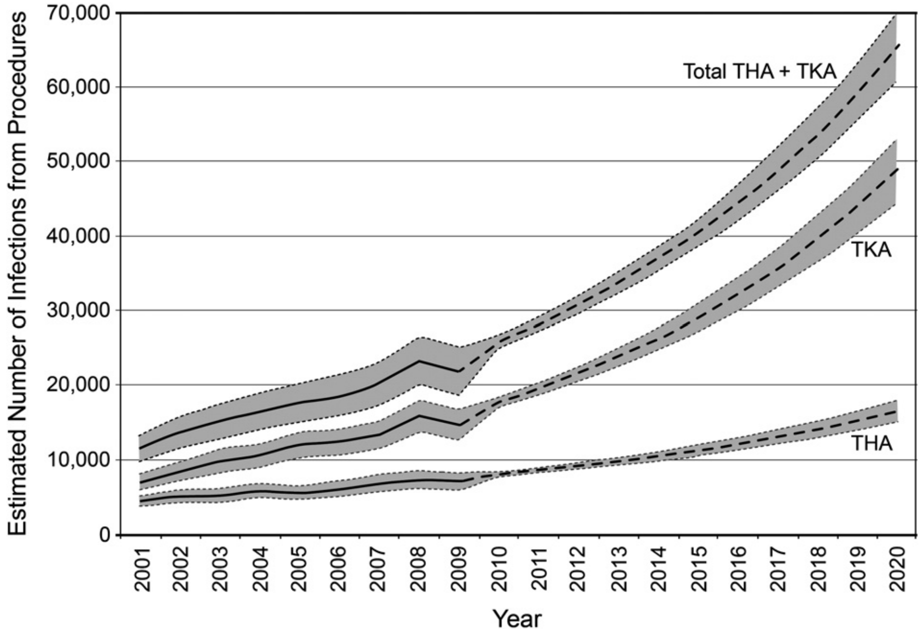

Fig. 1. Historical and projected number of infected THA, TKA, and total (THA + TKA) procedures in the United States (2001-2020). The dashed lines represent the projected values per surgery type, and the dotted lines represent the 95% CIs of the historical estimates (2001-2009) and the statistical projections (2010-2020).

online at www.arthroplastyjournal.org), and the corresponding incidence rates were 2.05% (CI, 1.86%-2.23%) in 2001 and 2.18% in 2009 (CI, 1.99%-2.37%), respectively. Compared with hip, a more gradual but still significant increase in the risk of infection was found over time among knee arthroplasty cases (odds ratio, 1.016; $P = .003$).

Despite the increase in PJI incidence, the length of stay required for hip patients decreased from an average of 11.5 (CI, 10.3-12.7) days in 2001 to 9.5 (CI, 8.8-10.2) days in 2009 (Table 1; available online at www.arthroplastyjournal.org). For knee patients with PJI, the length of stay also saw a similar decrease from 9.3 (CI, 8.2-10.4) days in 2001 to 7.2 (CI, 6.9-7.5) days in 2009 (Table 1; available online at www.arthroplastyjournal.org). The estimated hospital costs for treating PJI cases, however, remained relatively stable over the study period, despite an obvious increase in the total amount of charges. For hip patients, the average cost was $31 300 (CI, $28 300-$34 300) in 2001 and a similar value of $30 300 (CI, $27 600- $33 000) in 2009 (Table 1; available online at www.arthroplastyjournal.org). The corresponding average total charges for infected hip revision were $72 700 in 2001 and $93 600 in 2009. The treatment costs for PJI knee patients were generally lower than the PJI in the hip. The average cost for hospitalization of knee patients with PJI was $25 300 (CI, $22 500-$28 100) in 2001 and $24 200 (CI, $22 800-$25 600) in 2009 (Table 1; available online at www.arthroplastyjournal.org). The corresponding average charges were $58 700 in 2001 and $74 900 in 2009.

The average difference between hip and knee in terms of the cost to treat PJI cases was $5965 ($P < .001$), and this cost difference was relatively stable between 2001 and 2009 ($P = .37$), after adjusting for other patient factors. Another factor that had a significant effect on the cost of treating PJI arthroplasty cases was the geographic census region in which the patient lived ($P < .001$). In terms of geographic difference, patients living in the South or the Midwest had a lower cost ($4000-$5000) than those in the West or the Northeast. Minority patients of any race were associated with significantly higher costs than white patients ($P = .013$). For example, Asian patients were associated with, on average, approximately $4700 more in costs than white patients, and African American patients were associated with, on average, an additional $1700 than white patients.

Interestingly, neither age ($P = .70$) nor sex ($P = .26$) was found to be a significant factor for the hospitalization cost of PJI on their own, but the combination (ie, age-sex interaction) was found to be significant ($P = .005$). At a given age level, female patients incurred a higher PJI treatment cost than male patients. However, this difference diminished with increasing patient age. For example, for patients between the ages 45 and 54 years, female patients incurred an additional cost of about $3800. For patients between the ages 75 and 79 years, this difference was reduced to $1800.

At the beginning of this decade (2010), an estimated 8136 (CI, 7832-8441) PJI cases associated with hips and 17 781 cases (CI, 17 098-18 464) associated with knees were expected. By the end of the decade (2020), the number of PJI cases is projected to be 16 584 (CI, 15 081-

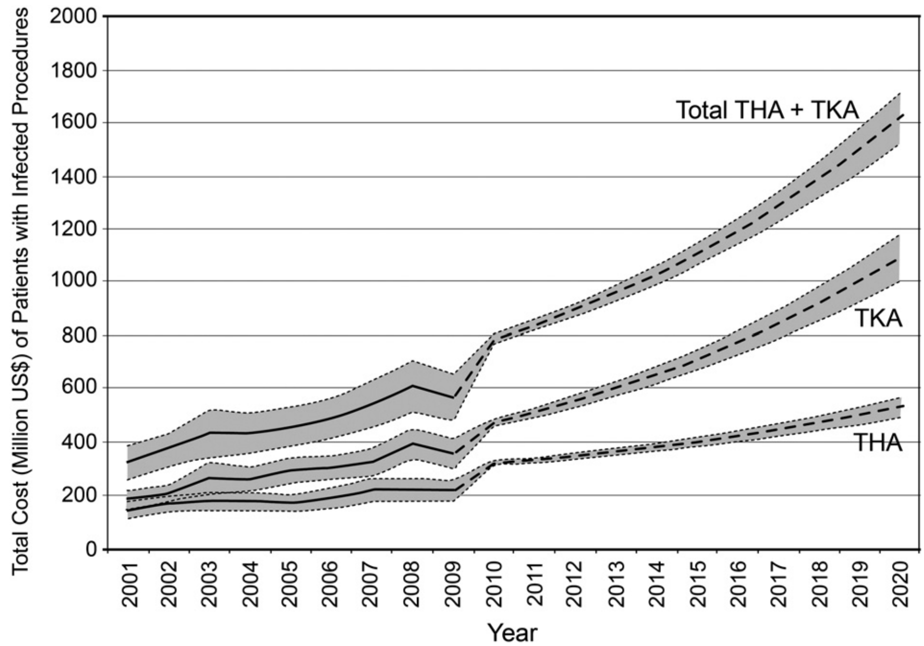

Fig. 2. Historical and projected total inpatient cost of infected THA, TKA, and total (THA + TKA) procedures in the United States (2001-2020). The total cost (in millions of USD) is adjusted to 2011 using the Consumer Price Index. The dashed lines represent the projected values per surgery type, and the dotted lines represent the 95% CIs of the historical estimates (2001-2009) and the statistical projections (2010-2020).

18 087) associated with hips and 48 971 (CI, 44 647-53 295) associated with knees (Table 2; available online at www.arthroplastyjournal.org; Fig. 2). Nationwide, a total of 60 000 to 70 000 PJI cases associated with hip or knee arthroplasty would require treatment in 2020. The estimated total hospital cost incurred for treating PJI cases was $320 million in 2001 and $566 million in 2009. Based on the hospital cost estimated from the present data, the future PJI cases are expected to incur a cost to US hospitals around $785 million (CI, $769-802 million) in 2010 and $1.62 billion (CI, $1.53-1.72 billion) in 2020 (Fig. 2). This cost would reach 1 billion by 2014 (Fig. 2).

Discussion

Periprosthetic joint infection continues to pose a great challenge to the medical community [1,2]. The current options available to treat PJI are imperfect [3-5]. Patients with PJI are often subjected to multiple surgical procedures with variable success [5,11]. The current "criterion standard" to treat chronic PJI of the hip and knee involves 2-stage exchange arthroplasty that carries between 65% and 90% success rate [5,11]. Thus, there remains a group of patients who despite enduring multiple surgeries continue to be afflicted by PJI, requiring salvage procedures such as fusion, resection arthroplasty, or amputation. For the next decade, an increasing population in the United States and the continued adoption and acceptance of total joint arthroplasty as a treatment modality for degenerative joint conditions are expected to provide upward momentum on the total number of arthroplasties performed and, correspondingly, the expected total number of PJI cases that would require treatment in the future.

The NIS data set and this study have certain limitations. Like any study using national administrative claims databases, our results are limited by inadequate clinical data collection related to PJI. Although the accuracy of coding in PJI in administrative claims data has recently been validated [16], the claims data are limited to *ICD-9-CM* procedure and diagnosis codes and, thus, does not capture clinical observations relevant to PJI, such as the organism responsible for the infection. The estimated hospital costs in this study did not include the cost of the surgical service provided by the orthopedic surgeons or services from other physicians (eg, infection specialists and anesthesiologists). It also did not include costs from subsequent care, physical therapy, rehabilitation, home care, or pharmaceutical treatments. Thus, insofar as the cost estimates are concerned, the economic burden of infection offered in the present study is almost surely understated. A key strength of the study is the use of a large and nationally representative data set of hospital discharges in the United States. It must be emphasized, however, that our 2001-2009 data represent an estimate of the historical national experience of PJI and, as such, must be interpreted within the context of the 95% CIs, which we also report in this study to aid the reader in judging the statistical uncertainty associated with the national data.

Our research group has been involved in performing several projection analyses related to the burden of various musculoskeletal conditions and impact of anticipated future changes to the surgeon workforce on orthopedic health care in the United States [14,15,17-19]. The estimates for infected surgeries and their associated costs must be understood within the context of a mathematical projection, rather than as an absolute "prediction." These mathematical projections rely on the historical trends, which, in the present study, were observed between 2001 and 2009, being applicable throughout the projection period of 2010 to 2020. Future changes in national health care policy, Medicare benefits, coverage, and eligibility rules as well as the sudden introduction of new disruptive technologies to treat PJI are just a few of the factors that cannot be easily factored into the statistical model but could substantially alter the current practice of total joint arthroplasty and treatment for those who will become infected. As new national health care data become available, it is important to revisit earlier projections to test their validity and evaluate the future implications of trends in joint care on the national health care system [15]. Notwithstanding all of these limitations, the latest national data and the projections presented in the current study will be useful for developing desperately needed policies related to the reduction of PJI.

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Table 1. Inpatient Procedures, Cost, and Length of Stay Including 95% CIs for Infected THA and TKA in the United States (2001-2009)

Year	No. of Infected THA Procedures in the United States (95% CI)	Mean Cost Per Case of Infected THA (Thousands 2011 US$) (95% CI)	Mean LOS Per Infected THA (d) (95% CI)	No. of Infected TKA Procedures in the United States (95% CI)	Mean Cost Per Case of Infected TKA (Thousands 2011 US$) (95% CI)	Mean LOS Per Infected TKA (d) (95% CI)
2001	4545 (3759-5331)	31.3 (28.3-34.3)	11.5 (10.3-12.7)	7113 (6041-8184)	25.3 (22.5-28.1)	9.3 (8.2-10.4)
2002	5219 (4349-6089)	31.7 (28.9-34.5)	12.1 (11.2-13.1]	8532 (7250-9815)	24.3 (22.5-26.0)	9.0 (8.4-9.7)
2003	5271 (4391-6152)	33.1 (29.6-36.5)	12.5 (11.4-13.5)	9936 (8380-11 491)	26.5 (22.9-30.0)	9.0 (8.0-10.0)
2004	5933 (4967-6899)	29.6 (27.2-32.0)	10.5 (9.7-11.3)	10 677 (9105-12 248)	24.3 (22.5-26.1)	8.4 (7.8-8.9)
2005	5634 (4728-6540)	30.0 (27.3-32.6)	10.8 (10.0-11.6)	12 113 (10 345-13 880)	24.2 (22.5-25.9)	7.9 (7.5-8.3)
2006	6217 (5170-7264)	30.2 (27.7-32.8)	11.1 (10.2-12.1)	12 488 (10 756-14 219)	24.4 (23.3-25.4)	8.1 (7.8-8.5)
2007	6931 (5812-8049)	31.4 (28.7-34.2)	10.5 (9.7-11.4)	13 424 (11 556-15 293)	24.4 (22.9-25.9)	7.8 (7.4-8.2)
2008	7380 (6200-8559)	30.0 (27.7-32.2)	9.5 (8.9-10.0)	15 983 (13 845-18 120)	25.0 (23.6-26.3)	7.4 (7.1-7.7)
2009	7162 (6008-8315)	30.3 (27.6-33.0)	9.5 (8.8-10.2)	14 802 (12 687-16 918)	24.2 (22.8-25.6)	7.2 (6.9-7.5)

Source: NIS. Abbreviation: LOS, length of stay.

Table 2. Projected Inpatient Procedures and Cost including 95% CIs for Infected THA and TKA in the United States, 2010-2020

Year	Projected No. of Infected THA Procedures in the United States (95% CI)	Projected Mean Cost Per Case of Infected THA (2011 US$) (95% CI)	Projected Total Inpatient Costs for Infected THA (Million 2011 US$) (95% CI)	Projected No. of Infected TKA Procedures in the United States (95% CI)	Projected Mean Cost Per Case of Infected TKA (2011 US$) (95% CI)	Projected Total Inpatient Costs for Infected TKA (Million 2011 US$) (95% CI)
2010	8136 (7832-8441)	32 746 (30 561-34 931)	316.6 (308.4-324.7)	17 781 (17 098-18 464)	27 142 (25 262-29 021)	469.3 (455.1-483.5)
2011	8659 (8298-9019)	32 444 (30 317-34 570)	329.1 (319.6-338.6)	19 543 (18 706-20 379)	26 893 (25 100-28 687)	506.8 (489.4-524.1)
2012	9248 (8820-9676)	32 142 (30 081-34 202)	343.5 (332.4-354.6)	21 569 (20 545-22 593)	26 645 (24 951-28 339)	549.7 (528.5-570.8)
2013	9896 (9390-10 403)	31 840 (29 855-33 824)	359.7 (346.7-372.7)	23 820 (22 573-25 067)	26 397 (24 817-27 977)	597.3 (571.5-623.1)
2014	10 593 (9996-11 191)	31 537 (29 639-33 436)	377.2 (362.0-392.3)	26 313 (24 801-27 824)	26 148 (24 701-27 596)	649.4 (618.2-680.6)
2015	11 357 (10 657-12 057)	31 235 (29 434-33 037)	396.4 (378.7-414.0)	29 120 (27 295-30 946)	25 900 (24 611-27 190)	707.3 (669.7-745.0)
2016	12 190 (11 371-13 008)	30 933 (29 243-32 624)	417.3 (396.8-437.7)	32 234 (30 043-34 424)	25 652 (24 555-26 749)	770.6 (725.5-815.8)
2017	13 146 (12 187-14 106)	30 631 (29 068-32 194)	441.9 (418.0-465.7)	35 711 (33 101-38 320)	25 404 (24 558-26 249)	841.4 (787.5-895.3)
2018	14 180 (13 063-15 297)	30 329 (28 915-31 744)	468.2 (440.6-495.9)	39 592 (36 498-42 686)	25 155 (24 712-25 599)	918.2 (854.2-982.1)
2019	15 312 (14 016-16 608)	30 027 (28 790-31 265)	496.5 (464.6-528.5)	43 971 (40 311-47 631)	24 907	1002.0 (926.5-1077.5)
2020	16 584 (15 081-18 087)	29 725 (28 708-30 742)	527.9 (491.0-564.8)	48 971 (44 647-53 295)	24 659	1094.3 (1005.5-1183.1)