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BASIC RESEARCH

What is the Long-term Economic Societal Effect of Periprosthetic Infections After THA? A Markov Analysis

Thomas J. Parisi MD, Joseph F. Konopka MD, Hany S. Bedair MD

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Abstract

Background Current estimates for the direct costs of a single episode of care for periprosthetic joint infection (PJI) after THA are approximately USD 100,000. These estimates do not account for the costs of failed treatments and do not include indirect costs such as lost wages.

Questions/purposes The goal of this study was to estimate the long-term economic effect to society (direct and indirect costs) of a PJI after THA treated with contemporary standards of care in a hypothetical patient of working age (three scenarios, age 55, 60, and 65 years).

Methods We created a state-transition Markov model with health states defined by surgical treatment options including irrigation and débridement with modular exchange, single-stage revision, and two-stage revision. Reoperation rates attributable to septic and aseptic failure modes and indirect and direct costs were calculated estimates garnered via multiple systematic reviews of peer-reviewed orthopaedic and infectious disease journals and Medicare reimbursement data. We conducted an analysis over a hypothetical patient's lifetime from the societal perspective with costs discounted by 3% annually. We conducted sensitivity analysis to delineate the effects of uncertainty attributable to input variables.

Results The model found a base case cost of USD 390,806 per 65-year-old patient with an infected THA. One-way sensitivity analysis gives a range of USD 389,307 (65-year-old with a 3% reinfection rate) and USD 474,004 (55-year-old with a 12% reinfection rate). Indirect costs such as lost wages make up a considerable portion of the costs and increase considerably as age at the time of infection decreases.

Conclusions The results of this study show that the overall treatment of a periprosthetic infection after a THA is markedly more expensive to society than previously estimated when accounting for the considerable failure rates of current treatment options and including indirect costs. These overall costs, combined with a large projected increase in THAs and a steady state of septic failures, should be taken into account when considering the total cost of THA. Further research is needed to adequately compare the clinical and economic effectiveness of alternative treatment pathways.

Level of Evidence Level II, economic and decision analysis.

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T. J. Parisi, J. F. Konopka, H. S. Bedair (✉)
Department of Orthopaedics, Massachusetts General Hospital, 55 Fruit Street, Yawkey Building 3B, Boston, MA 02114, USA
e-mail: HBedair@partners.org; hbedair@gmail.com

Introduction

When a THA is unsuccessful, the costs to the patient and to society are great [16, 18, 22, 42, 53]. Revision THAs generally are much more complicated, involving longer operative times, greater bone and blood loss, longer hospitalization, and are performed on patients who generally are older and have more medical comorbidities [15, 16]. When a revision arthroplasty is performed for aseptic failure, it often can be completed with one additional surgical procedure and hospitalization. However, when a THA fails owing to a periprosthetic joint infection (PJI), even if revision surgery can be limited to a single surgical procedure such as an irrigation and débridement or a single-stage exchange, the revision surgery and subsequent treatments are associated with extremely high direct medical costs consisting of long-term antibiotic treatment, multiple physician appointments, extended inpatient stays, increased physical therapy, and rehabilitation hospital admissions [4, 17, 21, 23, 30, 37, 41, 49, 53–57, 60, 63, 72, 80, 84, 85, 92, 98]. Moreover, the indirect costs such as time lost from work and a negative effect on quality of life and emotional wellbeing are considerable [13]. Because more THAs are being performed on younger patients, particularly those of working age, these indirect costs for septic failures become magnified.

The current estimate for the direct episodic cost of a two-stage revision THA for periprosthetic infection is USD 100,000 [18, 58, 59]. This is approximately four times the cost of a primary THA, estimated to be approximately USD 21,470 [18]. To our knowledge, the longer-term economic implications of PJIs after THA have not been assessed. Previous studies have evaluated direct costs of a single episode of care (ie, the direct costs of a two-stage revision or of an irrigation and débridement), but have not been able to evaluate longer-term costs [16, 18, 34, 40, 41, 53, 59]. Some of these studies also do not consider that current treatments for a PJI after THA are not 100% effective; even the gold standard, two-stage revision, has only a 70% to 90% likelihood of achieving infection control [1, 5]. Indirect costs associated with multiple surgical procedures such as lost wages also have not been evaluated. Although one decision analysis found single-exchange arthroplasty favorable to a two-staged approach regarding mortality rates and patient outcomes, it did not address any costs associated with these treatments [98].

The goal of our study was to estimate the long-term economic effect to society (direct and indirect costs) of a PJI after THA treated with contemporary standards of care in a hypothetical patient of working age (three scenarios, age 55, 60, and 65 years).

Materials and Methods

TreeAge Pro 2009 (TreeAge Software, Williamstown, MA, USA) was used to create a Markov state-transition model of a hypothetical patient of working age with a PJI after a THA who was undergoing treatment with three possible surgical strategies including irrigation and débridement, single-stage exchange, or two-stage exchange (Fig. 1). The process models patients' discrete and mutually exclusive health states at different times along with any associated health costs and/or earnings. The algorithm accounts for a fixed percentage of patients undergoing one of these three initial treatments based on available studies of current practices (Table 1) [30, 57, 60, 63, 84]. Defined and unique rates for treatment failures (septic and aseptic) and age-specific mortality rates during the first year and then subsequent years are used to predict transitions between different health states (Table 1). Patients who are modeled as having a successful treatment enter a well state with a fixed annual rate of repeat septic failure beyond the first year. Patients for whom treatment failed owing to sepsis will undergo a second procedure (two-stage exchange). This model accommodates for any patient to have two revisions where fixed components are removed and the hip subsequently is reconstructed (ie, one irrigation and débridement followed by two two-stage exchanges, one

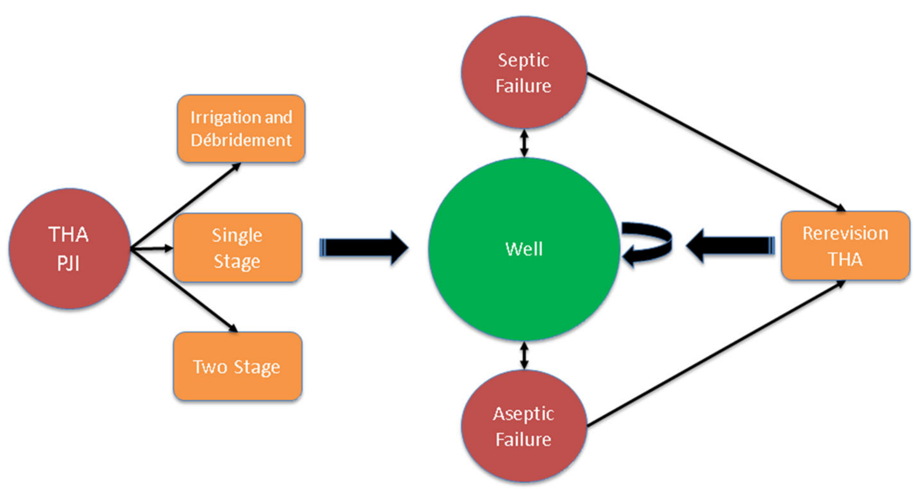

Fig. 1 The flow chart shows the different health states of the Markov state-transition decision model and the various pathways along which patients may transition with time. The curved arrows represent the patient remaining in the same health state for the next analytic cycle. The absorbing states of failed repeat two-stage exchange and death are not shown.

Table 1. Model input variables

Variable	Rate	
Rate of irrigation and débridement as an initial strategy	67%	
Rate of one-stage as an initial strategy	10%	
Rate of two-stage as an initial strategy	23%	
Failure rate for irrigation and débridement during the first year	30%	
Failure rate for irrigation and débridement after the first year	56.7%	
Failure rate for single-stage during the first year	9.8%	
Failure rate for single-stage after the first year	12.4%	
Failure rate for two-stage in the first year	4.27%	
Failure rate for two-stage after the first year	8.6%	
Rate of aseptic revision after infection (loosening, dislocation, fracture)	5.6%r	
Failure rate of aseptic revision THA	13.1%	
Rate and cost of medical complications after revision THA	Rate	Cost
Mortality	1.16%	
Deep vein thromboembolism	0.82%	$9287
Pulmonary embolism	0.48%	$10,411
Myocardial infarction	0.47%	$13,100
Pneumonia	0.93%	$6666
Urinary tract infection	1.56%	$896
Stroke	0.29%	$15,300
Transfusion	68.4%	$3071
Overall medical complication rate (not including transfusion or death)	4.55%	
Weighted average cost of complications	$2409	
Other costs		
Cost of aseptic revision THA	$35,997 (direct hospital costs)	
Treatment cost for the first year after infection	1st 90 Days	Remainder of 1st year (add $5386)
Inpatient rehabilitation (10.2%)	$80,491	$85,877
Skilled nursing facility (20.2%)	$48,955	$54,341
Home health care (25.2%)	$37,370	$42,756
Home with outpatient physical therapy (42.1%)	$31,558	$36,944
Weighted average for the first year postinpatient costs	$46,189	
Treatment cost after the first year	$187	
Cost of nonsurgical treatment for infection (long-term antibiotics)	Annual cost approximately $7500	

r = average of all studies listed in Tables 2–4.

single-stage and one two-stage, or two two-stage exchanges). Should a patient experience two failed fixed component exchanges, the model assumes that the patient will not undergo further surgery, but will enter a nonworking, suboptimal health state. Patients with failure owing to aseptic modes (ie, loosening or dislocation) are modeled to undergo revision surgery for aseptic failure with specific and unique revision rates and costs for aseptic revisions. The model also accounts for incidence and cost estimates associated with common perioperative medical complications such as pulmonary embolism, deep venous thrombosis, and myocardial infarction [2, 8, 14, 27, 44, 51, 62, 66, 69, 70, 77, 78, 88, 89].

Each health state is assigned a net cost for one analytic cycle (defined as 1 year), and transition probabilities determine the likelihood that a patient will either transition to the next health state or remain in the current one. The base case models patients at 65, 60, and 55 years old at the time of the initial revision procedure to estimate a typical patient of working age who might elect to have a THA. The simulation runs until all patients have died (based on US life expectancy data tables and systematic review) [3, 8, 27, 62, 65, 66, 69, 70, 77, 78, 88, 89]. We conducted one-way sensitivity analysis to determine how cost estimates would be affected by different rates of THA reinfection (during the first year of treatment and beyond the first year) based on the variability in published studies.

The health state transitions, probabilities and associated direct costs, and medical complication rates and costs were estimated via a systematic review of the literature

Table 2. Data from studies regarding irrigation and débridement of the hip

Study	Year	Sample size	Mean followup (months)	Rate of medical complications	Mortality rate related to surgery or infection	Annualized reinfection rate	Overall reinfection rate	Failure rates for other reasons	Overall infection eradication success rate
Azzam et al. [4]	2010	51	68	25%†	3%	11.6%	66%	NM	44%
Odum et al. [72]	2011	53	NM	NM	8%	69%*	69%	NM	31%
Byren et al. [23]	2009	52	27	NM	NM	11%	18%	NM	82%
Lora-Tamayo et al. [63]	2013	146	NM	NM	7%	38.5%*	45%	NM	55%
Cobo et al. [30]	2011	69	24	NM	3.6%	21.5%	43%	NM	57%
Buller et al. [21]	2012	62	34	NM	NM	40.6%*	48.2%	NM	52%
Koyonos et al. [54]	2011	60	54	NM	NM	14.5%	65%	NM	35%
El Helou et al. [37]	2010	40	24	NM	12.5%	32%	32%	NM	68%
Tornero et al. [92]	2012	39	46	NM	NM	6.3%	24%	NM	76%
Romano et al. [85]	2014	796	48	NM	NM	44.9%*	55%	NM	45%
Crockarell et al. [31]	1998	42	76	11.9%	7%	28%*	79%	4.7%	21%
Brandt et al. [19]	1997	30	48	NM	NM	54%*	69%	NM	31%
Meehan et al. [68]	2003	19	34	NM	NM	11%*	11%	NM	89%
Totals		1459	42.8			24.7%	56.7%	4.7%	43.3%

Weighted annual reinfection rate 30.1%; * rate stated explicitly in study; †packed red blood cell transfusion rate; NM = not mentioned.

Table 3. Data from studies of single-stage revision of the hip

Study	Year	Sample size	Mean followup (months)	Rate of medical complications	Mortality rate related to surgery or infection	Annualized reinfection rate	Overall reinfection rate	Failure rates for other reasons	Overall infection eradication success rate
Buchholz et al. [20]	1981	640	52	NM	2.7%	16%	23%	3.3%	76.8%
Wroblewski [99]	1986	102	38	NM	NM	3%	9%	NM	91%
Hope et al. [46]	1989	72	NM	NM	NM	NM	13%	3%	87%
Loty et al. [64]	1992	90	47	NM	1.1%	9%	10%	7.8%	79%
Elson [38]	1994	235	NM	NM	NM	NM	14%	NM	86%
Raut et al. [83]	1994	57	88	12.3%	7%	2%	14%	7%	86%
Raut et al. [82]	1996	15	120	NM	NM	1%	7%	6.7%	87%
Ure et al. [94]	1998	20	120	NM	0%	0%	0%	10%	100%
Callaghan et al. [24]	1999	24	120	NM	NM	1%	8.3%	4.2%	92%
Jackson & Schmalzried [49]	2000	1299	58	NM	0.8%	5%	17%	NM	83%
Vielpeau & Lortat-Jacob [96]	2002	127	36	NM	NM	12%	16%	NM	84%
Rudelli et al. [86]	2008	32	103	NM	NM	1%	6.2%	3.1%	94%
Wolf et al. [98]	2011	576	NM	NM	0.5%	12%*	28%	4.3%	72%
Beswick et al. [10]	2012	1225	24	NM	NM	5%	9%	NM	91%
Lange et al. [60]	2012	375	NM	NM	NM	NM	13%	NM	87%
Zeller et al. [100]	2014	157	41.6	NM	1.3%	3%	5%	5.7%	88%
Kunutsor et al. [56]	2015	2536	35	NM	NM	8%	8%	NM	92%
Totals		7582	67.8			5.1%	12.4%	5.5%	87.5%

Weighted annual reinfection rate 9.8%; * rate stated explicitly in study; NM = not mentioned.

performed in November and December 2016 via PubMed for: (1) outcomes and failure rates for septic THA treatments: irrigation and débridement (Table 2), single-stage revision (Table 3); and two-stage revision (Table 4); (2) direct medical costs for revision THA attributable to PJI; (3) failure rates and costs for aseptic revision THA; (4) perioperative complication rates and costs after septic and aseptic revision THA; and, (5) postdischarge costs after revision THA. The search terms "periprosthetic joint infection and total hip arthroplasty" OR "periprosthetic joint infection and total hip arthroplasty and cost" OR "revision total hip arthroplasty and aseptic" OR "revision total hip arthroplasty and complications" OR "revision total hip arthroplasty and complications and cost" OR "total joint arthroplasty and post discharge costs" yielded 1041 separate articles, 937 of which were excluded because they did not pertain to the specific diagnosis or treatments of interest, the study included less than 15 patients, the study had a mean followup less than 2 years, or was a duplication. Bibliographies of selected articles subsequently were hand-searched to ensure the inclusion of all pertinent studies [4, 5, 9–11, 19–21, 23, 24, 26, 30, 31, 33, 37–39, 45–47, 49, 52–56, 60, 63, 64, 67, 68, 72, 75, 82, 83, 86, 87, 90, 92, 94, 96, 98–100].

Direct cost input variables based on the above systematic reviews and Medicare reimbursement data were adjusted to 2016 US dollars using the medical component of the Consumer Price Index [6, 7, 12, 15, 17, 18, 25, 28, 29, 32, 35, 36, 41, 43, 48, 53, 61, 71, 73, 74, 79–81, 91, 95, 101]. Costs for surgery and nonsurgical complications for each procedure were accounted for, and nonsurgical costs related to outpatient treatments and followup care for the first year and beyond were considered (Table 5) [17, 18, 53, 59, 76, 80, 85]. Indirect costs in the form of lost wages were calculated using an assumption of 3 months out of work per surgical intervention for the average US worker until age 70 [93]. We estimated indirect costs by multiplying the US gross domestic product per capita by the proportion of the year spent recovering [93]. We ignored indirect costs after age 70 years because we

Table 5. Cost data

Procedure/source data	Converted to 2016 USD
Two-stage revision	
Hospital costs	
Parvizi et al. [76]	132,921.03
Klouche et al. [53]	85,568.24
Romano et al. [85]	99,079.44
Kurz et al. [59]	105,463.55
Bozic et al. [16]	135,554.94
Average	111,717.44
Outpatient charges	
Bozic et al. [16]	63,530.24
One-stage revision	
Klouche et al. [53]	49,243.89
Parvizi et al. [76]	67,781.07
Average	58,512.48
Irrigation and débridement	
Peel et al. [80]	55,593.41
Bozic et al [17]	47,599.44
Parvizi et al. [76]	73,506.26
Average	58,899.70

Table 4. Data from studies of two-stage revision of the hip

Study	Year	Sample size	Mean followup (months)	Rate of medical complications	Mortality rate related to surgery or infection	Annualized reinfection rate	Overall reinfection rate	Failure rates for other reasons	Overall infection eradication success rate
D'Angelo et al. [33]	2011	28	53	NM	NM	1%	4%	7.1%	96%
Babis et al. [5]	2015	31	30	NM	NM	0%	0%	0%	100%
Berend et al. [9]	2013	205	53	1%	4%	6%	24%	5%	76%
Biring et al. [11]	2009	99	144	NM	NM	1%	11%	9.1%	89%
Chen et al. [26]	2009	48	66	NM	NM	1%	4%	8.3	96%
Engesaeter et al. [39]	2011	283	24	NM	NM	4%	8%	13%	92%
Hofmann et al. [45]	2005	27	76	7.4%	0%	1%	6%	3.7%	94%
Hsieh et al. [47]	2004	42	55.2	NM	NM	2%	7%	NM	93%
Klouche et al. [52]	2012	46	24	NM	NM	2%	3%	NM	97%
Masri et al. [67]	2007	29	24	NM	6.9%	7%	14%	6.9%	86%
Oussedik et al. [75]	2010	39	60	NM	NM	1%	5%	NM	95%
Sanzen et al. [87]	1988	102	24	4.5%	1.8%	13%	25%	10.9%	75%
Lange et al. [60]	2012	929	NM	NM	NM	NM	10%	10%	90%
Shen et al. [90]	2014	33	60	NM	NM	0%	0%	0%	100%
Totals		1941	53.3	4.3%	3.2%	3.0	8.6%	6.7%	91.4%

Weighted annual reinfection rate 4.27%; NM = not mentioned.

Table 6. Results and sensitivity analysis of total costs of two-stage revision

Age at revision and rate of failure	Base failure rate	Theoretical year-one failure rate				
First-year failure rate	*4.27%*	*3%*	*6%*	*8%*	*10%*	*12%*
65 year-old	390,806	389,307	392,869	395,283	397,729	400,208
60 year-old	415,183	413,363	417,693	420,638	423,630	426,669
55 year-old	441,986	439,786	445,015	448,562	452,160	455,806
Annualized failure rate after first year	*8.6%*	*3%*	*6%*	*8%*	*10%*	*12%*
65 year-old	390,806	335,512	369,163	386,299	400,373	412,091
60 year-old	415,183	348,745	389,194	409,760	426,731	440,981
55 year-old	441,986	361,779	410,321	435,335	456,236	474,004

All costs listed in 2016 USD.

assumed that patients had retired. The annual costs for patient monitoring, including physician visit and radiographs, were obtained via systematic review and estimated using the Medicare Physician Fee Schedule [29]. The outcome of interest was the sum of direct medical costs and indirect costs in the form of lost wages. All costs were discounted by 3% annually [93]. Our analysis conformed to the guidelines reported by Weinstein et al. [97].

Results

Based on the input parameters of this model, the overall lifetime cost of treatment of a septic THA is USD 390,806 per patient aged 65 years with an infected THA. One-way sensitivity analysis (Table 6) showed that as infection rates increase, even by small increments in percentage, the overall cost increases accordingly. In patients at age 65 years, a 3% reinfection rate had a modeled cost of USD 389,307, whereas a 12% reinfection rate had a modeled cost of USD 412,091.

Indirect costs such as lost wages made up an increasingly considerable portion of the costs as the age of patients decreased. At the base infection rate of 4.27%, the modeled cost of a 65-year-old individual undergoing revision was USD 390,806. When decreasing the age by 5 years to 60 years (ie, 5 more years of income potential), this increases to USD 415,183, and when 55 years, this increases further to USD 441,986 (Table 6).

Discussion

Numerous studies have shown that the direct costs of treating a PJI after THA are shockingly high, with current cost estimates for two-stage revision arthroplasty exceeding USD 100,000, or approximately four times as much as a primary THA [18, 53, 59, 76, 85]. The current study shows that these previous estimates are relatively low because they do not account for the high failure rate of current treatments nor do they account for indirect costs. Even with a relatively low reinfection rate of 3% (lower than most published rates of failure for irrigation and débridement, single-stage, or two-stage revision), the overall costs are modeled to approach just less than USD 400,000, approximately four times previous estimates for a two-stage revision, and greater than seven times the published costs of an irrigation and débridement or a single-stage exchange [53, 76, 80]. When factoring in costs such as lost productivity, the costs become even higher. Modeled costs of a 55-year-old hypothetical patient who requires two-stage revision arthroplasty increase to almost half a million USD.

Our study has several limitations. The model was kept relatively simple with only 11 distinct, mutually exclusive health states. The idea that a patient would transition neatly from a state of infection to well after revision, reinfection, or death is an oversimplification that does not take into account the many other health states, such as noninfected but painful revision, or failure for other reasons such as aseptic loosening or periprosthetic fracture. Additionally, the analytic cycle timing was arbitrarily set for 1 year which is per convention, but may be an oversimplification with many reinfections occurring sooner than 1 year. Another arbitrary cutoff was the assumption that all patients would be retired by the age of 70 years. While average retirement ages have varied over the years, the most recent normal retirement age set by Social Security was 67 years. Finally, while the three most common treatments of septic THA were included in the model and every attempt was made to incorporate the typical treatment patterns and expected reinfection rates based on published studies, the model does not distinguish between an acute infection or chronic infection, nor does it take into account important variables such as type of organism, timing of symptoms, surgical approach, or other possible treatments such as resection arthroplasty, amputation, or long-term antibiotic suppression. Although it would be ideal to model each possible failure scenario with its prevalence and associated costs, the sheer complexity of the nearly infinite permutations makes it difficult to achieve this successfully. However, although our inability to model every possible health state, including every possible medical complication, may be a weakness of the study, we attempted to capture the most-common clinical scenarios with the sensitivity analysis serving to limit uncertainty attributable to these limitations.

Another major limitation of this study is that it does not directly compare the cost of different treatments available. While the majority of US studies quotes a two-stage revision as the gold standard for treatment, there is an increasing number of studies supporting single-stage revision owing to decreased morbidity and cost, and increased function and outcome in terms of quality-adjusted-life-years [50, 52, 53, 94, 98]. Although a true cost comparison would be helpful to payers and perhaps clinicians, we thought it was not possible to do a commensurate analysis given the relatively little amount of cost data available regarding single-stage exchange arthroplasty [53, 76]. We were able to find only two studies that adequately provided direct costs of a single-stage exchange, and those sources actually found single-stage exchange costs to be less than those for irrigation and débridement [53, 76]. Additionally, while single-stage exchange is increasingly used, we found that it is used only approximately 10% of the time as the initial treatment strategy for PJI [30, 56, 60, 63, 84]. Moreover, the use of single-stage exchange often is predicated on the susceptibility of the infection organism, a factor that we chose not to incorporate in this model. A direct cost comparison of single- and two-stage exchange would not be accurately represented by this model [50, 57, 60].

Because the precise estimation of the true cost in healthcare is difficult, the cost estimates in many models such as this one are limited. Direct costs of hospitalization and medical complications were estimated from published studies and garnered from Medicare data, and indirect costs were based solely on lost productivity from work [18, 28, 29, 53, 59, 66, 76, 80, 85, 93]. Other posthospitalization costs such as outpatient physical therapy were not accounted for, nor was lost productivity of loved ones taking care of patients who had undergone treatment.

This model illustrates the substantial costs of revision THA for septic failure and the economic implications of these costs on the individual and society. The majority of previously published cost estimates accounted for only direct hospital charges [18, 53, 59, 76, 80, 85], and few included posthospitalization costs and indirect costs such as lost productivity. Although it is known that revision THA for PJI is extremely expensive, this model estimates that even in the base case scenario, with relatively low treatment failure rates, the cost is at least three times as much as previously estimated. Fisman et al. [41], and Wolf et al. [98] found that less-invasive (and still less-effective) irrigation and débridement and single-stage exchange were more cost-effective in terms of overall quality of life years compared with two-stage revision, however further studies are needed to clarify overall clinical and economic outcomes of single- versus two-stage exchange. A multicenter, randomized clinical trial is necessary to compare the two treatments, and clarification of hospital costs (not charges) and outpatient costs is needed to more precisely estimate true costs of this increasingly profound problem. Our study puts into perspective how profound an economic problem PJI after THA continues to be, and highlights the need for policymakers and researchers to combine forces to do the necessary research to accurately determine which treatments are most effective clinically and economically.

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