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Systematic Review and Meta-Analysis

Direct Hospital Costs per Case of Periprosthetic Hip and Knee Joint Infections in Europe — A Systematic Review

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ABSTRACT

Background: The rise of periprosthetic joint infections (PJIs) due to aging populations is steadily increasing the number of arthroplasties and treatment costs. This study analyzed the direct health care costs of PJI for total hip arthroplasty and total knee arthroplasty (TKA) in Europe.
Methods: The databases PubMed, Scopus, Embase, Cochrane, and Google Scholar were systematically screened for direct costs of PJI in Europe. Publications that defined the joint site and the procedure performed were further analyzed. Mean direct health care costs were calculated for debridement, antibiotics, and implant retention (DAIR), one-stage, and 2-stage revisions for hip and knee PJI, respectively. Costs were adjusted for inflation rates and reported in US-Dollar (USD).
Results: Of 1,374 eligible publications, 12 manuscripts were included in the final analysis after an abstract and full-text review. Mean direct costs of $32,933 were identified for all types of revision procedures for knee PJI. The mean direct treatment cost including DAIR for TKA after PJI was $19,476. For 2-stage revisions of TKA, the mean total cost was $37,980. For all types of hip PJI procedures, mean direct hospital costs were $28,904. For hip DAIR, one-stage and 2-stage treatment average costs of $7,120, $44,594, and $42,166 were identified, respectively.
Conclusions: Periprosthetic joint infections are associated with substantial direct health care costs. As detailed reports on the cost of PJI are scarce and of limited quality, more detailed financial data on the cost of PJI treatment are urgently required.

Periprosthetic joint infection (PJI) is a serious complication that can occur after total joint arthroplasty. A PJI is defined as an infection involving the prosthetic joint implant and surrounding tissues. In Europe, the incidence of PJI ranges from 0.6 to 1.3% [1]. The prevalence of PJI is increasing due to the aging population and the increasing number of joint arthroplasties being performed [2,3]. In Germany, the number of primary implantations is expected to increase by 45% for total knee arthroplasty (TKA) and by 23% for total hip arthroplasty (THA) by 2040 [3]. Treatment of PJI is complex and costly, often requiring multiple operations, long-term antibiotic treatment, and extended hospital stays. Patients having PJI face severe consequences with markedly reduced quality of life, including impairment of joint and limb function combined with psychological distress [4]. For PJI treatment by 2-stage revisions, a loss of 6.4 quality-adjusted life years has been calculated [5]. In addition, PJI may lead to significant morbidity and mortality, with an up to 3.7 times increased risk of death in the first 2 years after diagnosis [6,7]. Thus, PJI can have a major impact on both the individual patient and the health care system, resulting in a substantial socioeconomic burden [8]. Recently, the combined annual hospital costs associated with PJI of the knee and the hip were projected to be $1.85 billion in the United States by 2030 [9].

Cost analysis, especially stratified by treatment modality, is an essential tool to guide future management strategies and to provide objective views on treatment costs and reimbursement. Yet, such data are scarce in Europe, and comprehensive reviews addressing

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Table 1
Summary of Included Cohort Studies.

Author	Year	Country	Case Number	Joint	Procedure	Follow-Up
Oduwole [11]	2010	Ireland	20	Knee	Two-stage revision	Not reported
Romano [12]	2010	Italy	40	Hip	Two-stage revision	Minimum 2 y, mean 4 y
Garrido-Gomez [13]	2013	Spain	38	Knee	DAIR	Minimum 2 y
			41	Knee	Two-stage revision	
Assmann [14]	2014	Germany	30	Hip	Two-stage revision	Not reported
Lieb [15]	2015	Germany	17	Knee	Two-stage revision	Not reported
			15	Hip	Two-stage revision	
Kasch [16]	2016	Germany	30	Hip	Two-stage revision	Not reported
Kasch [17]	2017	Germany	35	Knee	Two-stage revision	Not reported
Fischbacher [18]	2018	Switzerland	8	Knee	Two-stage revision	Not reported
			13	Hip	Two-stage revision	
Sousa [19]	2018	Portugal	8	Hip	DAIR	Not reported
			7	Hip	Two-stage revision	
			8	Knee	DAIR	
			8	Knee	Two-stage revision	
Musil [20]	2019	Czech Republic	6	Knee	DAIR	Not reported
			17	Knee	Two-stage revision	
Serrier [21]	2021	France	61	Knee	Two-stage revision	2 y
			55	Hip	Two-stage revision	
Blom [22]	2022	United Kingdom/Sweden	60	Hip	Single-stage revision	18 mo
			68	Hip	Two-stage revision	18 mo

DAIR, debridement, antibiotics, implant retention.

this topic are lacking. Therefore, the aim of this study was to identify and critically appraise the available European economic evidence on the direct health care costs of PJI, with special reference to the different surgical strategies used to treat PJI of the hip and knee.

Methods

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and in accordance with recent publications on health care costs [10].

Search Strategy

The databases PubMed, Scopus, Embase, Cochrane, and Google Scholar were searched using the combination of each European country and the search term *cost* AND (infection OR PJI) AND (prosthesis OR knee OR hip OR "TKA" OR "THA" OR arthroplast*)*. The considered time period was January 1, 1980, to October 31, 2022. To identify relevant articles, titles and abstracts were first screened by 2 of the authors. In addition, reference lists of identified articles were screened. Articles were considered eligible if they met the following criteria: (1) articles were written in English or German; (2) studies were conducted in a European country (geographically); and (3) studies reported on direct health care costs to the treating hospital in association with PJI treatment. Further inclusion criteria were (4) the report of direct health costs; (5) separate data on infected joint; and (6) information on the performed surgical procedure with focus on debridement, antibiotics, and implant retention (DAIR), single-stage or 2-stage revisions. Publications with no clear information on localization of the affected prosthesis, surgical treatment, or lacking data on direct health care costs for the hospital or virtual cost model calculations were excluded (Table 1).

Data Extractions and Syntheses

The Consensus on Health Economic Criteria checklist (CHEC-list) was used for quality assessment. The selected studies were assessed by 2 researchers, and individual assessments were compared to reach consensus on each component (Table 2). In the

Table 2
Quality Assessment of Cohort Studies (Adopted From Blom et al, 2022 [22]).

Author, Year	Inclusion of Consecutive Patients	Representativeness	Completeness of Cost Information	Reported Cost Items	Concerns
Oduwole, 2010 [11]	95% of patients	Single hospital	Reasonable	Surgery, implant, antibiotic treatment, hospital stay, staff	No follow-up costs
Romano, 2010 [12]	Consecutive	Single hospital	Reasonable	Surgery, implant, antibiotic treatment, hospital stay, staff, follow-up, and rehabilitation	
Garrido-Gomez, 2013 [13]	Consecutive	Single hospital	Reasonable	Surgery, implant, antibiotic treatment, hospital stay, staff, follow-up, and rehabilitation	
Assmann, 2014 [14]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Lieb, 2015 [15]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Kasch, 2016 [16]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Kasch, 2017 [17]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Fischbacher, 2018 [18]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Sousa, 2018 [19]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Musil, 2019 [20]	Consecutive	Single hospital	Partial	Surgery, implant, antibiotic treatment, hospital stay, staff	No costs for follow-up
Serrier, 2021 [21]	Consecutive	Single hospital	Reasonable	Surgery, implant, antibiotic treatment, hospital stay, staff, follow-up, Rehabilitation	
Blom, 2022 [22]	Consecutive	Multicenter	Reasonable	Surgery, implant, antibiotic treatment, hospital stay, staff, follow-up	

case of disagreement, a third person was involved. All identified publications were classified according to the procedure performed and the joint involved. Procedures were divided into DAIR, single-stage, and 2-stage revision. The quality of publications was assessed according to Blom et al in terms of representativeness, treatment of consecutive patients, and completeness of cost information [23]. All reports with costs indicated in local currencies were converted to US dollars according to the exchange rates of the World Bank at the time of publication and adjusted for inflation using the method described by Turner et al [24]. The reported costs were adjusted for local inflation according to the World Bank's Gross Domestic Product (GDP) deflator by country for the year of publication and for 2022 and converted to US dollars according to the exchange rates at the time of publication [24].

Initially, 1,374 publications were screened. Application of the inclusion criteria revealed in 26 reports eligible for full-text search. Of these, only twelve full texts met the inclusion criteria. There were 4 publications excluded due to the lack of clearly stating the site of the PJI, and ten reports were excluded due to the lack of information on whether the patient was treated with DAIR, one-stage revision, or 2-stage revision (Figure 1).

Overall, 3 references on direct hospital costs of the DAIR procedure were identified and 8 on 2-stage procedures for PJI after TKA. For hip PJI, this systematic review yielded one study reporting the cost of the DAIR procedure and one study reporting the cost of single-stage revision, while 8 studies reported the cost of 2-stage revision for PJI after THA.

The majority of the included studies were conducted in Germany (n = 5). The other analyses were performed in Ireland, Italy, Spain, Switzerland, Portugal, Czech Republic, United Kingdom, Sweden, and France (n = 1 each) (Table 1).

Results

Mean direct costs of $32,933 were identified for revision procedures for knee PJI. Direct costs for knee PJI treated with a DAIR procedure were on average $19,476 (minimum [min]: $5,163; maximum [max]: $27,881). For 2-stage revisions in knee PJI, average direct costs of $37,980 were found (min: $15,213; max: $87,185) (Table 3).

For hip PJI, mean direct hospital costs were $28,904. For DAIR, only one study could be included that reported direct costs of $7,120. Only one publication reported on single-stage revisions with direct costs of $44,594. Average costs of $42,166 (min: $ 14,071; max: $ 89,873) were found for 2-stage revision procedures (Table 3).

Discussion

The current work with inclusion of twelve full-text articles identified average direct costs for knee PJI procedures of USD 32,933 with USD 19,476 and USD 37,980 for DAIR and 2-stage revisions, respectively. For all types of hip PJI procedures, mean direct hospital costs were USD 28,904. For DAIR, one-stage and 2-stage

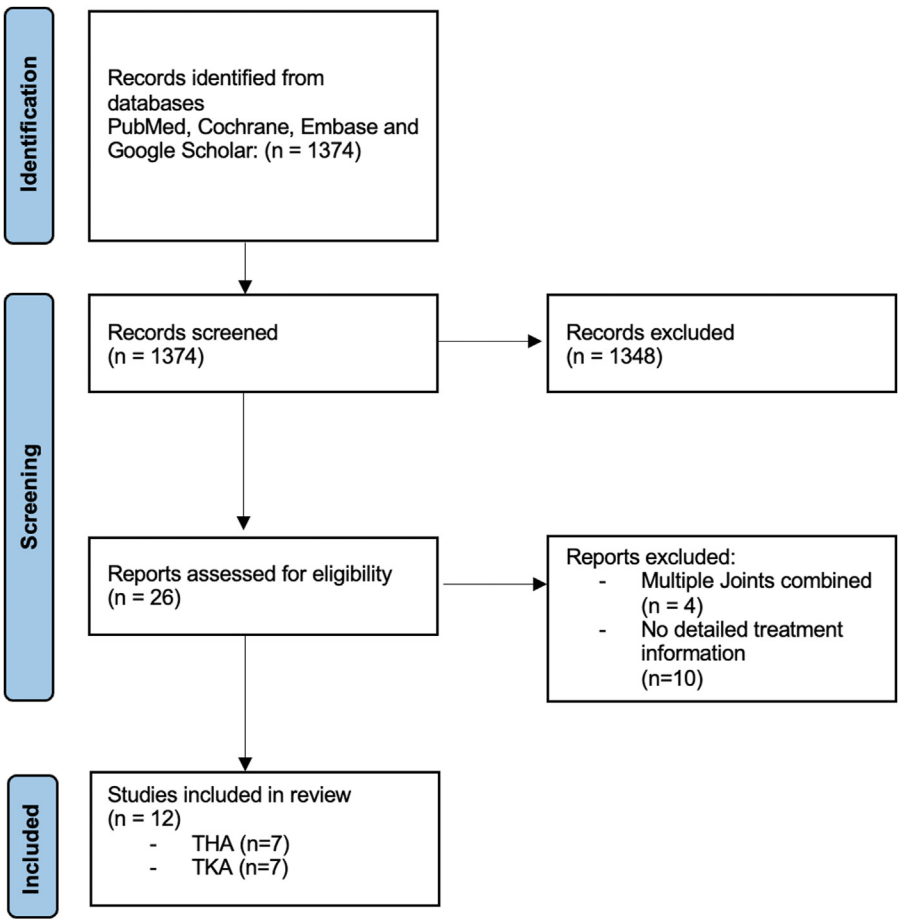

Fig. 1. PRISMA flow diagram presenting the process of identification, screening, eligibility, and final inclusion of relevant articles (* some studies reporting costs for THA and TKA). PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Table 3
Reported Costs of Debridement, Antibiotics, and Implant Retention (DAIR), One-Stage Revisions, and Two-Stage Revisions in Knee and Hip PJI.

Localization	Author	Country	Debridement, Antibiotics, and Implant Retention (DAIR)		One-Stage Revision		Two-Stage Revision	
			Number of Cases	Costs in USD	Number of Cases	Costs in USD	Number of Cases	Costs in USD
TKA-PJI	Oduwole, 2010 [11]	Ireland					20	37,512
	Garrido-Gomez, 2013 [13]	Spain	38	27,881			41	87,185
	Lieb, 2015 [15]	Germany					17	24,636
	Kasch, 2017 [17]	Germany					35	15,213
	Fischbacher, 2018 [18]	Switzerland					8	71,118
	Sousa, 2018 [19]	Portugal	8	5,163			8	17,765
	Musil, 2019 [20]	Czech Republic	6	25,384			17	25,384
	Serrier, 2021 [21]	France					61	25,025
	Mean costs in USD			19,476				37,980
	Standard derivation (SD)			10,172				24,877
THA-PJI	Romano, 2010 [12]	Italy					40	89,873
	Assmann, 2014 [14]	Germany					30	23,445
	Lieb, 2015 [15]	Germany					15	26,313
	Kasch, 2016 [16]	Germany					30	14,071
	Fischbacher, 2018 [18]	Switzerland					13	85,016
	Sousa, 2018 [19]	Portugal	8	7,120			7	14,702
	Serrier, 2021 [21]	France					55	26,941
	Blom, 2022 [22]	United Kingdom/Sweden			60	44,594	68	56,963
	Mean costs in USD			7,120		44,594		42,166
	Standard derivation (SD)			-		-		28,957

PJI, periprosthetic joint infection; THA, total hip arthroplasty; TKA, total knee arthroplasty; USD, US-Dollar.

treatment, average costs of USD 7,120, USD 44,594, and USD 42,166 were identified, respectively. Both for knee and hip PJI treatment, a 3- to 6-fold increased financial burden was observed when comparing 2-stage revisions with DAIR procedures. Interestingly, each revision surgery was more expensive in patients who have PJI after THA than in patients who have PJI after TKA.

Analysis of the direct health care costs of PJI in Europe showed a high average financial burden of over $35,000 per patient treated. Outside of Europe, a similar pattern of in-hospital treatment costs for PJI has been reported. Already in 2012, Kurtz et al demonstrated direct health care costs ranging from $24,200 to $31,300 for PJI treatment in the United States [8]. The mean cost of a 2-stage revision ($37,980) for PJI after TKA was approximately 2 times higher than that of a DAIR procedure ($19,476) [11,13,17–21]. In the United States, the average financial burden for all types of revisions for PJI after TKA was $25,300 [8]. A more detailed analysis of treatment costs showed a sum of $38,776 for DAIR procedures in the context of TKA-PJI revisions and $56,900 for 2-stage revisions [25]. A publication in 2012 by Haenle et al reported an economic burden of €25,194 for a collective in Germany [26]. In the United Kingdom, costs of up to €34,775 were reported for all types of revisions in TKA-PJIs in 2015 [27]. However, both publications did not differentiate between procedures and were therefore not included in the current study.

In our systemic review, the mean direct health care cost of PJI in THA was approximately $6,000 higher than that of PJI-TKA revisions. The financial burden of 2-stage hip revisions after PJI was at least $42,000[12,14–16,18,19,21,28]; for DAIR procedures, only one reference was available with a reported cost of $7,120 [19]. For single-stage revisions, there was only one publication in Europe, which stated costs of $44,594 [22]. In 2021, in the United States, Yao et al reported direct hospital costs of $39,597 for DAIR procedures and $58,369 for 2-stage revisions of hip arthroplasties [25]. For all types of THA-PJI procedures in the United States, a cost of $31,300 was reported [8]. These higher health care costs in the United States than in Europe can be explained by the high standard deviation reported in our review due to the different health care systems and cost variations in European countries. Furthermore, the United States has the highest per capita health expenditure of all Organization for Economic Co-operation and Development (OECD) nations, which is twice that of the United Kingdom. In 2021, the United States spent 17.8% of its GDP on health care, which is almost twice the average of all OECD countries [29].

Other publications that reported combined costs for revisions of PJI but did not distinguish between procedures and affected joints were not included in this analysis. However, Haenle et al found a financial burden of €29,331 for all types of revisions for PJI in hip arthroplasties in Germany [30]. Garfield et al and Vanhegen et al reported similar costs of €48,242 and €25,419 for THA-PJI in the United Kingdom [28,31]. In 2016, in Spain, Gonzáles-Vélez et al reported direct health care costs of €25,225 for THA-PJI [32], and direct costs of €21,569 were reported for THA-PJI in the Netherlands [33].

When assessing health care expenditures, it is important to distinguish between direct costs covered by hospitals for the treatment of PJI and the reimbursement of treatment costs by health insurance companies. The discrepancy between actual costs and reimbursement has been highlighted before. Sousa et al reported a financial loss for the treatment of PJI ranging from $1,685 to $11,109 depending on the joint treated and the procedure performed. The DAIR procedure for TKA resulted in a loss of $1,685, but the amount not covered by the health insurance for a 2-stage revision surgery after TKA was $11,109. The same lack of reimbursement was found after THA with a loss of $3,642 for DAIR and a loss of $8,046 for 2-stage revision [19]. Data from Switzerland by Fischbacher et al [18] showed a similar significant financial loss for the treating hospital, but with even higher amounts of up to $47,000. The relatively high treatment costs for Switzerland compared to all European countries are attributable to the second highest health spending per capita within all OECD countries (12.1% of the GDP per capita in 2015) and the high price levels in Switzerland [34]. Furthermore, differences between direct costs and reimbursement for PJI cases of up to €12,658 were reported in different studies (minimum: €1,695; maximum: €44,715) [26,27,30,31,35,36].

Hierl et al (2021) demonstrated in a case simulation for 2-stage hip PJI treatment a reimbursement of €23,965 and €27,551 for a fast-track procedure performing both revisions within one hospital stay and for a slow-track procedure when patients were dismissed within the implant-free interval and reoperated during a second

hospital stay, respectively [37]. It is obvious that direct treatment costs or other health-economic parameters including the findings of the current study should not dictate surgical treatment. Revision strategies for PJI should be guided by the underlying key parameters of the case that has to be treated and not by financial findings.

The DAIR procedures are the treatment of choice for acute PJIs, whereas chronic PJIs mostly require implant exchange. A 2-stage revision is reported to be the gold standard in the treatment of PJI recommended by several guidelines but also one-stage revisions have been reported with good outcome in patients who have chronic infections, and good soft tissue coverage together with non-difficult-to-treat microorganisms [38,39]. Especially in cases of compromised soft tissue and presence of difficult-to-treat microorganisms, a 2-stage revision is the preferred treatment of choice [38]. Analyses of the socioeconomic costs of single-stage and 2-stage revisions have reported significant cost reductions for single-stage revisions. A recent study by Blom et al identified cost savings of up to £11,000 in the United Kingdom for single-stage compared to 2-stage hip PJI treatment [22]. Okafor et al described in their cost-utility analysis the superiority of a single-stage revision in patients with the correct indication [40]. Clinical results have also reported similar eradication rates in single-stage and 2-stage revisions. In addition to the socioeconomic benefit, the results also demonstrate the clinical equivalence with less invasive surgical techniques due to the need of only one operation [38,41,42]. Nevertheless, attention must be paid to correct patient selection and other specific factors, such as microorganisms, soft tissue, and bone status for the final treatment recommendation [43].

This systematic literature review has several potential limitations. Due to the research question of the review, only publications on the treatment of PJI in Europe were included in the analysis, thus minimizing the number of references. Another limitation was the predominance of publications from high-income countries, such as Germany and Switzerland. The cost of PJI treatment in these countries is higher than in countries with a lower GDP resulting in relatively high standard deviations, particularly due to the relatively high treatment costs in Switzerland. In addition, the heterogeneity in terms of health care systems and data availability as well as the presence of little or no literature on the health economics of PJI make a more detailed analysis of the topic difficult. In addition to data availability, there are significant differences in implantation rates and life expectancy, making it almost impossible to project total European costs. These drawbacks are the reasons why reliable projections of PJI and PJI-related health care costs are not yet available for Europe. The financial figures are given in USD, although the focus of the review was European countries. However, in order to make the data comparable particularly with data from the United States, the current analysis was performed in USD and not in EUR.

Overall, the number of high-quality publications on hospital costs of PJI in Europe is low and further detailed analysis is necessary on the socioeconomic burden of PJI in Europe. Furthermore, a lack of data on DAIR and single-stage revisions was detected, which should also be of interest in the future.

Conclusions

The current systematic review addresses the published literature on direct health care costs for hospitals for the treatment of hip and knee PJI in Europe. The number of detailed reports on PJI costs is limited and only 12 studies could be included. An average financial burden of $32,933 and $28,904 were identified for all types of revision procedures for knee and hip PJI, respectively, with a high difference between DAIR and exchange procedures. However, indication of therapy should only be based on patient characteristics and both surgical and antimicrobial therapy options and not on financial aspects. Due to highly limited literature, there is a strong need for further, more detailed financial data on the costs of PJI treatment for Europe and all other health care systems worldwide.

CRediT authorship contribution statement

Dominik Szymski: Conceptualization, Formal analysis, Validation, Visualization, Writing – original draft, Writing – review & editing. **Nike Walter:** Conceptualization, Formal analysis, Methodology, Resources, Software, Writing – review & editing. **Katja Hierl:** Formal analysis, Investigation, Software, Supervision, Writing – review & editing. **Markus Rupp:** Conceptualization, Data curation, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Volker Alt:** Project administration, Resources, Software, Supervision, Visualization, Writing – review & editing.

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