Exploring the real costs of healthcare-associated infections: an international review

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ABSTRACT

Purpose: Healthcare-associated infections acquired a high degree of dissemination, being considered a serious public health problem and assumed as one of the most common adverse events associated with healthcare. They have a significant impact on health systems by increasing hospital expenses, and compromising the healthcare quality and effectiveness. Surgical site infections (SSI) are considered one of the most serious complications that can occur after an orthopaedic surgery. The aim of this study is to contribute to the development of a framework to analyse the costs of infections related to hip and knee arthroplasties.

Methods: A literature review was conducted on databases, and articles published between January 2005 and April 2016 were searched.

Findings: A total of 14 articles met the inclusion criteria. Costs were grouped in hospitalization and treatment dimensions. For hospitalization, the indicators were the length of stay (LOS) and/or monetary costs; For treatment, the indicators were number of surgeries and LOS, or monetary costs. We observed that LOS is the most commonly used to estimate SSI direct costs. Patients who developed hip or knee arthroplasty infections remained in hospital 2.5–3 times longer and incurred hospital costs almost three times higher, when compared with an uninfected patient.

KEYWORDS
Hip and knee arthroplasties; healthcare-associated infections (HAI); surgical site infections (SSI); length of stay; costs

Introduction

Nosocomial infections, currently named by healthcare-associated infections (HAI), are according to the European Centre of Disease Prevention and Control (ECDC) and the National Nosocomial Infection Surveillance (NNIS), those arising from adverse reactions to the presence of an infectious agent or its toxins, but they were not expressed neither undergoing an incubation period, at the time of patient's admission to the hospital [1,2].

Currently, these have acquired a high degree of dissemination, being considered a serious public health problem. HAIs are assumed as one of the most common adverse events associated with healthcare and is estimated that about one in ten hospitalized patients will acquire an infection after admission. Its high transcendence is due to its high morbidity and mortality, having become one of the major causes of death in hospitalized patients [3–5]. Also, these have a very significant impact on health systems by increasing hospital expenses and may compromise the healthcare quality and effectiveness. These extra costs are justified by the increase of the length of stay (LOS) in about 4–8 days for each infected patient, and the additional diagnostics and therapeutic interventions. As a result, patients who developed HAI remained in hospital 2.5 times longer than uninfected patients and incurred hospital costs almost three times higher [3,6,7].

Although it is a very current topic, since the beginning of the 1990s several international projects have been developed in order to improve knowledge about HAI and at the same time, developed surveillance strategies to promote and guide efforts towards the prevention and control of this kind of infection [8,9]. In this matter is noteworthy the work done by WHO, CDC, OECD, and the Council of Europe in the development of these projects [9], emerged in 1994 in Europe the first international programme of HAI active surveillance, the Hospitals in Europe Link for Infection Control through Surveillance (HELICS), that has been expanding and suffering continuous improvement since then [10]. Since the creation of HELICS, other programmes have been developed, such as 'First Patient Safety Challenge: Clean Care is Safer Care' [11] and 'Second Patient Safety Challenge: Safe Surgery saves lives' [12] by the WHO, 'Prohibit' [13], and 'BURDEN' [14] by the European Union and the HAI-net [15] by ECDC.

However, the impact of these programmes has not been as expected. A group of researchers, through a review article, identified a number of barriers to the success of these programmes, clustered in three dimensions: structure, processes, and results [16]. With regard to structures, they referred to the lack of quality of hospital infrastructure; lack of human resources, especially nurses dedicated full-time to HAI prevention and control programmes; hospital environmental contamination and the organization's own culture. With regard to processes, they indicated failures in clinical processes and management processes, such as poor infection control practices, wards management, healthcare teams' management, hospital and cleaning services management and the inappropriate use of resources. With regard to results, all identified barriers are related with the lack of effective surveillance systems and the unreliability of epidemiological data [16].

There are four major groups of HAI: ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections, surgical site infections (SSI), and bloodstream infections (CLABSI). In this systematic literature review, our attention turned to the SSI, focusing on the orthopaedics area, selecting only those associated with hip or knee arthroplasties.

This work is organized in four major chapters: the first is a brief introduction to hip and knee arthroplasty infections; in the second is presented the methodology used, including database search, data collection, and analysis; the third chapter is dedicated to results presentation; and in the final chapter are presented the study's conclusions.

Hip and knee arthroplasty infections

As the average life expectancy is increasing in industrialized countries, the number of patients who need orthopaedic implant surgery also increases, accentuating the risk of developing a greater number of infections [17].

SSI are considered one of the most serious complications that can occur after arthroplasty [18] and between 1.5 and 2.5% of all knee and hip arthroplasties tend to become infected [19]. In agreement with previous reports, these values can range between 2 and 6% [20].

The LOS is one of the factors that suffers the biggest changes when the patient gets an infection, and it is the indicator most commonly used to estimate the direct costs of SSI [21].

Despite the increase of the hospitalization costs, SSI also represent a major clinical problem leading to painful and persistent symptoms in infected patients, need for new surgical interventions, extra antibiotic treatments, and casual removal or replacement of the prosthesis and, in more severe cases to save the patient, a local amputation is performed [22–24].

The presence of microorganisms on the prosthesis surface is one of the preconditions for the infection occurrence. The most often bacteria related with orthopaedic implant infections are *Staphylococcus aureus* and *Staphylococcus epidermidis*, particularly the first agent that is responsible for most of these infections, which are especially difficult to treat when caused by *Methicillin-resistant Staphylococcus aureus* (MRSA) [20,25].

There is evidence that, for example, if the screening and the decolonization of *Staphylococcus aureus* in hip or knee replacement surgeries was carried out, about seven times the costs of the prevention programme implementation could be avoided [26]. According to Slover et al. [27] the cost of SSI associated with these procedures is so great that the cost of a screening programme would be recovered by only a small decrease in infection rate. Reducing the infections will decrease hospitalization time and increase the availability of beds for more days. With this, patients would enter and leave the hospital at a faster rate, reducing the average cost per patient treated [26].

It is also crucial to develop methods for the early detection of arthroplasty's infection, based on symptoms such as fever, pain, and tumefaction. If early detection was achieved, the infection could be treated by debridement and implant retention. In this way, costs would be significantly reduced, shortening the recovery period, and avoiding the costly two-stage revisions [18]. Hereupon, every effort is justified in order to prevent infection such as strict epidemiological surveillance and prevention programmes to avoid factors that may contribute to the onset of infection and, above all, best clinical practices of all staff involved in surgery [28].

In view of the increased costs related with these infections, the aim of this study is to perform a systematic review about the infection costs of hip and knee arthroplasties in several countries around the world, in order to better understand their economic impact.

Methodology

The systematic literature review was done according to the PRISMA guidelines [29].

Database search

Research was carried out in April 2016 using B-ON, PubMed, and Science Direct databases in order to find articles related with hip or knee arthroplasty infection costs, published between January 2005 and April 2016. To carry out this research, a combination of terms (Table 1) and an inclusion criterion (publication period) were applied. In each database, searches were performed separately for hip and knee arthroplasties. After carrying out both searches within each one of these databases, the articles that are repeated were excluded.

As a result of this research method, 37 articles were identified from PubMed, 38 from B-ON, and 29 from Science Direct.

Table 1. MeSH and terms related.

Cross infection
HAI
Hospital infection
SSI
Hip arthroplasty
Knee arthroplasty
Hip replacement
Knee replacement
Cost

Table 2. Inclusion and exclusion criteria.

Inclusion criteria	*Exclusion criteria*
• Publication year: January 2005 to April 2016; • Language: English, Portuguese, and Spanish; • Contain abstract; • Only apply to hospitals with Orthopaedic services/department; • Be published and available in a journal in public domain; • Discuss about costs for hip or knee arthroplasty; • Discuss about costs for infections treatment applied to hip or knee arthroplasty; • Discuss about cost-effectiveness of strategies claiming to reduce the risk of hip or knee arthroplasty infections.	• Articles not related with hip or knee arthroplasty infections; • Articles with description of methods, models, and theories without empirical data; • Other healthcare entities that are not hospitals.

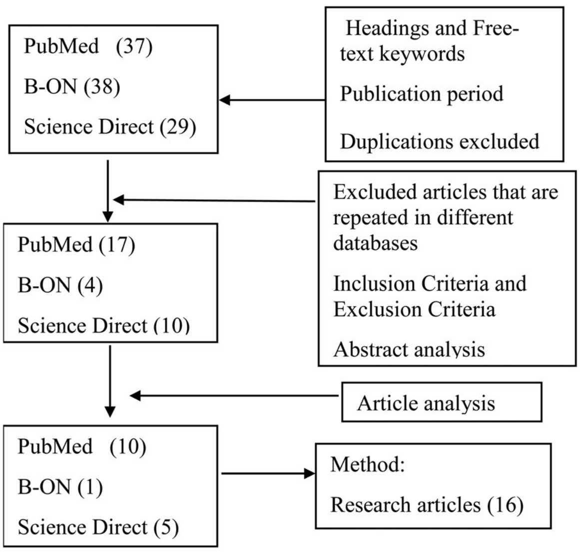

Figure 1. Search strategy.

To the articles obtained from this initial research method, more inclusion and exclusion criteria were applied (Table 2). In order to keep only one copy of each article, we exclude the repetition of the same article in different databases. A final number of 31 articles were obtained: PubMed [17], B-ON [4], and Science Direct [10].

After verification and further evaluation of the 31 articles, only 16 fulfilled every criteria of inclusion: PubMed [10], B-ON [1], and Science Direct [5], as shown in Figure 1.

Data collection and analysis

After the analysis of each article, the following data were extracted in an excel file: article name, publication year, country, setting (hospitals, teaching hospitals, tertiary care centre), study methodology, keywords, summary, and topics (key points).

Results

Through the literature review performed, we identified a number of key issues responsible for the increased hospitalization costs, as well as the costs of some treatments and prevention methods for hip or knee arthroplasty infections, which can reduce costs and patient suffering.

Costs for hospitalization and infection treatment

In Table 3 are presented the results of different studies in several countries, divided into two major dimensions: hospitalization and treatment. With regard to hospitalization, the charges will be presented in LOS and/or monetary costs. With regard to treatment, the charges will be presented in number of surgeries and LOS, or monetary costs.

Infection prevention and control

In Table 4 are presented the results of a study conducted in Australia. The researchers evaluated the cost-effectiveness of implemented strategies claiming to reduce the risk of deep SSI in hip arthroplasties.

Discussion

Through the literature review performed, we identified the main costs caused by HAI in hip and knee arthroplasties and the costs of some treatments and prevention methods for these situations. In agreement with the current state of the art, this review identified LOS as the indicator most commonly used to estimate the direct costs of SSIs, and according to some authors, this happens because, in addition to the direct relationship between the LOS and the risk of HAI, the extension of hospitalization days is an easily understood measure either by physicians or by hospital managers, which translates in the consumption of health resources to treat a complication [21,35,43]. According to Plowman [6], patients who developed HAI remained in hospital 2.5 times longer and incurred hospital costs almost three times higher, when compared with an uninfected patient who underwent the same surgical procedure. According to the articles reviewed, and with regard to LOS and HAI's treatment costs, the results were very similar to those found in the literature related with HAI issues.

Table 3. Costs for hospitalization and infection treatment.

Dim	Authors	Study description	Costs: Arthroplasty without HAI	Costs: Arthroplasty with HAI
Hospitalization	Jodra et al. [21]	Study conducted in Madrid, between January 2000 and June 2004. Additional cost for infection treatment based on excess LOS attributable to hip arthroplasty infections was estimated.	*Hip:* Average LOS: 17 days The mean cost per day for a patient admitted to the orthopaedic unit: 437.44 €.	*Hip:* Average LOS: 53 days Additional cost per patient who develops SSI : 14,216.80 €
	Irribaren et al. [28]	Comparative case–control study carried out in Chile, between January 2000 and December 2004 about excessive direct costs attributed to hip arthroplasty infections.	*Hip:* Average LOS: 13 days Average cost: $2354	*Hip:* Average LOS: 54 days Average cost: $6174,8 (additional cost : $3820,1)
	Coello et al. [30]	Study conducted in England, based on surveillance data of SSI from 140 English hospitals, included in NINSS (National Nosocomial Infection Surveillance Service), between October 1997 and June 2001.	*Hip:* Average LOS: 11.1 days *Knee:* Average LOS: 10.3 days	*Hip:* Average LOS: 22.6 days Additional cost: $3342 *Knee:* Average LOS: 21.2 days Additional cost : $3168
	Alp et al. [31]	Study conducted in Turkey, between April 2011 and April 2013, to evaluate the incidence and economic burden of prosthetic joint infections.	*Hip and Knee*: Average LOS: 7 days Average cost: $5937	*Hip and Knee*: Average LOS: 49 days Average cost: $16999
	Poultsides et al. [32]	Study conducted in USA to analyse the hospitalization data from the National Inpatient Sample (NIS) for hip and knee arthroplasties between 1998 and 2007.	*Hip*: Average LOS: 4.2 days Average cost: $14,286 *Knee:* Average LOS: 4 days Average cost: $1,334	*Hip*: Average LOS: 13.4 days Average cost: $31432 *Knee:* Average LOS: 9.7 days Average cost: $24 458
	Kurtz et al. [33]	Study conducted in USA, based on NIS to identify the primary and revision arthroplasty performed between January 2001 and December 2009 and to predict the economic impact of periprosthetic joint infection on the US health system.	–	*Hip:* Average of cost and LOS: *2001*: $31 300; 11.5 days *2009*: $30 300; 9.5 days *Knee:* Average of cost and LOS: *2001*: $25 300; 9.3 days *2009*: $24 200; 7.2 days
	Kapadia et al. [34]	Study with a group control conducted in USA, between January 2007 and December 2011. The impact of periprosthetic joint infections on the LOS, readmissions and associated costs measured.	*Knee:* Average LOS: 3 days Days in hospital (mean): 3.4 days Readmissions (mean): 0.14 Average cost: $28 249.57	*Knee:* Average LOS: 5.3 days Days in hospital (mean): 23.7 days Readmissions (mean): 3.43 Average cost: $116 382. 65
	Dal-Paz et al. [35]	Study conducted between 2006 and 2007 in Brazil to estimate the direct costs of the 34 patients' treatment who acquired knee arthroplasty infections, by analyzing medical records.	–	*Knee:* Average LOS: 29,7 days Additional Average |Cost: $2,701.29
	Garrido-Gómez et al. [18]	Retrospective study conducted between January 2005 and January 2010 in Spain, with 79 patients who were diagnosed and treated for knee arthroplasty infection.	–	*Knee:* Average Cost: 40 542 €.
	Klouche et al. [36]	Retrospective study conducted in France between January and December 2006, to determine the cost of revision of infected hip arthroplasty and to compare these costs to those of primary and revision of non-infected hip arthroplasty.	*Hip:* Average cost of primary arthroplasty: 9028€ Average cost of aseptic revision : 12 409 €	*Hip:* Average Cost of septic revision: 32 546€
	Peel et al. [37]	Study conducted at St. Vincent's Hospital Melbourne, between January 2011 and June 2012, to evaluate the direct hospital costs in the first 30-day follow-up of patients undergoing total hip and knee arthroplasties (data were extrapolated for Australian population).	–	*Hip and Knee:* SSI raise the arthroplasty's cost around 76% in the hip, and around 54% in the knee. The estimated average cost in the first 30 days following surgery to Australian population: $97.2 million AU
	González-Vélez et al. [38]	A matched case–control study conducted at Ramon y Cajal University Hospital in Spain between 1 January 2005 and 31 December 2011. The researchers estimated the excess direct costs of hip arthroplasty	*Hip*: Average LOS: 21 days Average Cost : 10 828 €	*Hip*: Average LOS: 58 days Average Cost :25 288 €
	Gow et al. [39]	Retrospective case–control study conducted at Auckland City Hospital (New Zealand) to determine the excess costs attributable to hip and knee arthroplasty infections.	–	*Hip and Knee*: Excess Average LOS: 42 days Excess Average Cost: $40,121

(*Continued*)

Table 3. Continued.

Dim	Authors	Study description	Costs: Arthroplasty without HAI	Costs: Arthroplasty with HAI
Treatment	Merollini et al. [40]	Study conducted in Australia, with patients undergoing primary hip arthroplasty and treatment for infection between January 2006 and December 2009. Different treatments costs were identified from 114 patients with deep hip arthroplasty infection.	–	*Hip:* *Debridement, antibiotics and implant retention:* Average cost per patient: $19 688 AU *1-stage revision:* Average cost per patient: $26 722 AU *2-stage revision:* Average cost per patient: $44 744 AU *excision of arthroplasty:* Average cost per patient: $23 805 AU
	Moojen et al. [41]	Retrospective study of a prospective database conducted in two large teaching hospitals in Holland, between 2001 and 2008. Data from 68 patients treated to a deep postoperative infection of a total hip arthroplasty were obtained. One of the hospitals used a single surgical debridement to treat the infection, the other used a system with multiple surgical debridement.	–	*Hip:* *Single surgical debridement:* Average number of surgeries: 1 Average length of antibiotic treatment: 13 weeks; Average LOS: 29 days. *Multiple surgical debridement:* Average number of surgeries: 3 Average length of antibiotic treatment: 23 weeks; Average LOS: 59 days

It can also be concluded that comparing the LOS and treatment costs between hip arthroplasty infection and knee arthroplasty infection, the first were, in general, higher. Also, and being more specific, patients who developed deep incisional and organ/space SSI, in case of hip or knee arthroplasties, remained in hospital two times longer than those with superficial SSI [21,30].

In addition to the LOS average cost, some articles reviewed were even more specific, discriminating the antimicrobial costs, readmission's number, laboratory tests and even the influence of age, gender, and race in HAI's treatment costs. According to Iribarren et al. [28], in cases of arthroplasty infection, only the antimicrobial's additional costs was about $2421 per patient treated. According to Dal-Paz et al. [35], the additional costs in antibiotic therapy and laboratory tests to treat infections of a knee replacement, were approximately $600 per patient.

Besides the extension of the LOS, the readmission's number also undergo a considerable change. Kapadia et al. [34], in his study about knee arthroplasty infections, concluded that the readmission's rate increased about four times in infected patients.

Besides the costs previously referenced, another USA-based study went further and concluded that there are other factors related to the patient and with its geographical location, even within the same country, which will affect the HAI's treatment costs [33]: Patients from different geographic locations generate different costs, e.g. patients living in the South or the Midwest had a lower cost ($4000–$5000) than those in the West or the Northeast. The patient's race also has an influence on costs, e.g. Asian and African-American patients generated, on average, an additional expense of $4700 and $1700, respectively, when compared with caucasian patients. Another important issues are age and gender, e.g. at a given age level, female patients incurred a higher HAI's treatment cost than male patients, with particular emphasis in the ranges between the ages 45 and 54 years and the ages 75 and 79 years.

Treatment

Regarding HAI's treatment method, as mentioned previously, the state of art reveals that if early detection was achieved, the infection could be treated by debridement and implant retention [18]. According to Merollini et al. [40] study, four HAIs treatment methods were applied. They concluded that the treatment with debridement, antibiotics, and implant retention, had an average cost around $19,688 AU and a two-stage revision had an average cost of $ 44,744 AU, which is more than double than the first one. The importance of primary prevention should not be ignored, because the occurrence of SSI might be reduced by introducing more cost-effective infection prevention measures.

According to Moojen et al. [41], we should aim treatment strategies that are both efficient and cost-effective. They concluded that the strategy of a single debridement appears to be at least as successful for retention of the primary implant and control of infection as a strategy with multiple surgical debridements, without compromising the clinical effectiveness. However, considering equal clinical results, the first one will reduce the costs of multiple surgeries (2 less surgeries), hospitalizations (2 times lower), and revision implants. The single debridement will also reduce the morbidity and psychological discomfort of the patient.

Table 4. Cost of strategies to prevent infection.

Authors	Study description	Strategies	Costs	QALY*	Savings per QALY*
Merollini et al. [42]	At this study, the researchers simulated long-term health and cost outcomes of a hypothetical cohort of 30,000 patients undergoing total hip arthroplasty. Baseline use of AP was compared with no AP, antibiotic-impregnated cement (AP + ABC), and laminar air operating rooms (AP + LOR).	AP vs. no AP	No AP would increase costs by about $1.5 million AU	No AP would lose 163 QALYs.	–
		AP vs. (AP + ABC)	(AP + ABC) would save about $126 000 AU	(AP + ABC) would generate an extra 32 QALYs	The use of (AP + ABC) would prevent 46 deep infections and would save $3,909 AU per QALY gained
		AP vs. (AP + LOR)	(AP + LOR) would increase costs by about $4.6 million AU	(AP + LOR) would lose 127 QALYs.	–

*QALY – quality-adjusted life years.

Prevention

Regarding infection prevention and control methods, several studies show resources or costs that may be saved through effective prevention programmes. However, authors do not provide information about the cost of infection prevention efforts or number and quality-of-life years gained through those investments [26].

If costs are reduced by the implemented changes, there is no need to show the health benefits in terms of years of life gained or quality-adjusted life years gained. However, in cases where the cost savings do not compensate the increase of total costs, the health outcomes need to be demonstrated [26].

According to Merollini, Crawford et al. [42], scarce resources should be used efficiently and for this, it is important to establish a cost-effective approach to preventing SSI in the total hip arthroplasty. The prevention of these infections can not only be centred in costs reduction but also in patient's suffering reduction. The additional use of antibiotic-impregnated (AP+ ABC), compared with only antibiotic prophylaxis (AP), would prevent 46 deep SSI and save $3,909 for each QALY gained, leading to cost savings. Using antibiotic cement in addition to antibiotic prophylaxis (AP + ABC) would generate an extra 32 QALYs while saving over AUD $123,000. Not using AP would increase costs by approximately $1.5 million with a 163 QALYs lost. Using laminar air operating rooms (AP+ LOR) would increase costs by approximately $4.6 million, and 127 QALYs are lost. If all hospitals adopted the antibiotic-impregnated cement strategy (AP+ ABC), besides improving health outcomes among hospitalized patients and save lives, they could save many resources that could be used in other areas in need.

Conclusion

Quantifying the exact economic impact of HAI is an ongoing international challenge and the use of the direct hospitalization costs has been suggested as the best method to estimate the direct HAI's costs. These represent the real costs to the hospital for the items and services used by each patient and have a direct impact on hospital budget.

This study has some limitations, mainly related with the difficulties to obtain articles related with HAI cost analysis from databases, and limited access to cost information (e.g. no cost discrimination).

In the majority of the articles reviewed in this study, the cost analyses of HAI, more specifically about hip and knee arthroplasties infections, focus primarily on direct hospitalization costs. The LOS was the most commonly used indicator to estimate the direct costs of these SSIs in the reviewed articles. By using this indicator, evidence suggests that patients who developed HAI remained in hospital 2.5–3 times longer and incurred hospital costs almost three times higher, when compared with an uninfected patient who underwent the same surgical procedures. However, this indicator is restricted to the direct medical costs, and does not include information with regard to the real cost to patients and society in lost earnings (indirect costs).

The measurement of indirect cost is indeed a fundamental healthcare management challenge as there is high degree of difficult to account for exact cost and, generally, these are assumed to be much higher than direct costs. Thus, evidence gathered in this article allows us to argue that the cost analysis of HAI performed in international studies has been continuously underestimating real economic impacts of HAI in hip and knee arthroplasties. This key idea can no longer be ignored by healthcare managers and decision makers and further research must be done to explore better these issues.

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