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Review

Economic analysis of healthcare-associated infection prevention and control interventions in medical and surgical units: systematic review using a discounting approach

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S U M M A R Y

Nosocomial or healthcare-associated infections (HCAIs) are associated with a financial burden that affects both patients and healthcare institutions worldwide. The clinical best care practices (CBPs) of hand hygiene, hygiene and sanitation, screening, and basic and additional precautions aim to reduce this burden. The COVID-19 pandemic has confirmed these four CBPs are critically important prevention practices that limit the spread of HCAIs. This paper conducted a systematic review of economic evaluations related to these four CBPs using a discounting approach. We searched for articles published between 2000 and 2019. We included economic evaluations of infection prevention and control of *Clostridioides difficile*-associated diarrhoea, meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and carbapenem-resistant Gram-negative bacilli. Results were analysed with cost-minimization, cost-effectiveness, cost-utility, cost-benefit and cost-consequence analyses. Articles were assessed for quality. A total of 11,898 articles were screened and seven were included. Most studies (4/7) were of overall moderate quality. All studies demonstrated cost effectiveness of CBPs. The average yearly net cost savings from the CBPs ranged from $252,847 (2019 Canadian dollars) to $1,691,823, depending on the rate of discount (3% and 8%). The average incremental benefit cost ratio of CBPs varied from 2.48 to 7.66. In order to make efficient use of resources and maximize health benefits, ongoing research in the economic evaluation of

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infection control should be carried out to support evidence-based healthcare policy decisions.

Introduction

Nosocomial infections (NIs) or healthcare-associated infections (HCAIs) have been defined as "localized or systemic conditions resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s)" [1]. In addition, the condition should develop 48 h after admission to a healthcare setting, and there must be no previous evidence of the infection. HCAIs are a serious public health problem experienced around the world. They are associated with extra treatment costs, complications, reduction of quality of life, and mortality [2–4]. In 2013, The Public Health Agency of Canada reported that each year more than 200,000 patients contract an HCAI, which result in over 8000 deaths [5]. The same agency estimated that one in every 41 hospitalizations results in an HCAI, incurring costs of approximately $CAD 281 million (Canadian dollars), a sum representing 41% of the total cost of adverse events [6]. Since 2004, in Canada, there have been mandatory monitoring programmes for the prevention and control of four pathogens: *Clostridioides difficile*-associated diarrhoea (CDAD), meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) and carbapenem-resistant Gram-negative bacilli (CR-GNB) [7–10]. These programmes are generally based on four clinical best practices (CBPs) related to HCAI prevention and control interventions: hand hygiene, hygiene and sanitation, admission screening, and basic and additional precautions [11]. The COVID-19 pandemic has confirmed that these four CBPs are critically important prevention practices to limit the spread of HCAIs in hospitals and to protect patients and healthcare providers [12].

There are some literature reviews related to the economic impacts of HCAI prevention and control interventions. Most of them generally focus on the economic burden of HCAIs [13–15]. The systematic review conducted by Arefian and colleagues provided an economic analysis of the prevention and control of HCAIs in hospitals around the world [2]. It dealt with the prevention and control of falls, urinary tract infections, surgical site infections, blood infections, and pneumonia in medical, surgical, paediatric and intensive care units. However, this systematic review did not focus directly on the prevention and control of the four multi-drug-resistant organisms (MDROs) mentioned above (CDAD, MRSA, VRE and CR-GNB). Furthermore, among the interventions analysed, additional precautions (e.g., isolation of patients) and hygiene and sanitation were not considered. Other systematic and audit reviews of the literature have focused on the effectiveness of the prevention and control of a single HCAI [16–18]. Stone *et al.* undertook a systematic review of economic analyses of HCAIs [19]. However, their review was limited to research papers published between January 2001 and June 2004, and focused on interventions aimed at controlling surgical site infection, bloodstream infection, ventilator-associated pneumonia, and urinary tract infections. Prior to this, in 2002, Stone and colleagues performed an information audit of HCAI prevention and control programmes [20]. This audit highlighted their efficiency by considering different economic analyses: cost–minimization analysis (CMA); cost–effectiveness analysis (CEA); cost–utility analysis (CUA); and cost–benefit analysis (CBA) [21–25]. Unfortunately, this audit review was not a systematic review, and did not assess the quality or risk of bias of the included articles. It also did not assess the effectiveness of the four CBPs (hand hygiene, hygiene and sanitation of surfaces and equipment, admission screening, and additional precautions) simultaneously. Finally, few systematic reviews have used discounting approaches to report their findings, for example see MacDougall [18], which would facilitate comparisons between studies, the year of investigation, currencies and economic evaluation methods.

Faced with these gaps in the literature, a systematic review was needed to consolidate the evidence on economic evaluation of the four CBPs related to HCAI prevention and control interventions using a discounting approach. This review allowed our team to measure the return on investment or net cost savings of the CBPs for the prevention and control of the four most monitored HCAIs in medical and surgical units in Canadian hospitals. Furthermore, this review analysed the effectiveness of the interventions through five economic analysis approaches: CMA, CEA, CUA, CBA, and cost-consequences analysis (CCA). This systematic review answers the following question: what is the cost-effectiveness of the four CBPs related to HCAI prevention and control interventions in medical and surgical units in $CAD 2019 sing a discounting approach?

Methods

Theoretical framework

This study is based on the infection control intervention framework developed by Resar *et al.* [11] at the Institute for Healthcare Improvement in the United States, which defines a set of CBPs, or 'bundles', each of which consists of three to five evidence-based practices. These practices ensure that all healthcare professionals can provide safe care to their patients. This intervention framework supported the implementation, in Canadian healthcare institutions, of infection prevention and control strategies as well as the creation of Canadian [10] safe care campaigns. According to the Public Health Agency of Canada, best practices focusing on HCAI prevention and control would reduce the risk of contracting some HCAIs to nearly zero [26]. The four actions that will be considered in this study across all bundles are: (1) hand hygiene; (2) hygiene and sanitation of surfaces and equipment; (3) at admission, screening of patients with, or who are at-risk of, infection in accordance with the healthcare facility's protocols; and (4) the application of basic and additional precautions. This HCAI theoretical framework highlighting the four

Table I
Inclusion and exclusion criteria based on population, interventions comparators and designs and outcomes framework

Population	
Geographic area	OECD Countries
Establishment	Hospitals, acute care or short-term care facilities
Care unit	Medical and surgical
Patients	Hospitalized more than 48 h and less than 30 days Excluded: children (less than 18 years old)
Infections studied	CDAD and MDROs (MRSA, VRE, CP-GNB)
Interventions	
Clinical best practices*	Hand hygiene; hygiene and sanitation; screening; additional precautions
Type of design and comparators	Randomized clinical trial, quasi-experimental study, longitudinal study, case–control study, cohort study (prospective or retrospective)
Outcomes: types of economic evaluation	Cost assessment, cost minimization, cost-effectiveness, cost-utility, cost-benefit, cost-consequence

CDAD, *Clostridioides difficile*-associated diarrhoea; CP-GNB, carbapenem-resistant Gram-negative bacilli; MDRO, multi-drug-resistant organism; MRSA, meticillin-resistant *Staphylococcus aureus;* OECD, The Organisation for Economic Co-operation and Development; VRE, vancomycin-resistant enterococci.
* See details in Supplementary File S1.

CBPs associated with reduction of rates of infection is presented in Supplementary File S1.

Hand hygiene

Hand hygiene refers to the washing and disinfection of hands, wrists, and forearms using water, soap, hydro-alcoholic solutions, or alcoholic antiseptic solutions. This action begins with wetting the hands and continues until they are completely dry. The World Health Organization (WHO) estimates that hand hygiene could help reduce HCAIs by 30–70% [27].

Hygiene and sanitation of surfaces and equipment

In 2005, the Aucoin report, entitled *D'abord, ne pas nuire* (*First, do no harm*), stressed the importance of cleanliness and sanitation as a basic measure for infection prevention and control [28]. Neglecting the regular preventive cleaning and disinfection of surfaces and equipment results in a reservoir for the proliferation of micro-organisms. Hygiene and sanitation must be carried out with appropriate frequency (one or more times per day) depending on the prevalence of infection at the site [29,30].

Screening, upon admission, of patients who are carriers or who are at-risk

Screening is the systematic testing of persons for a previously undetected HCAI or who may be a potential carrier. Screening techniques differ depending on the type of organisms of concern which have the potential to cause an HCAI in the patient or in others. In general, it consists of making a clinical diagnosis and performing laboratory analyses. Any patient who is currently in triage or has been previously hospitalized is considered at risk if he or she presents with signs and symptoms related to an infection. Those patients who present without any signs or symptoms are considered colonized or potential carriers. Analyses of faeces and blood, nasal smears, laboratory tests, and blood cultures are used to detect pathogens, according to predefined surveillance protocols [31–33]. A bacterial strain is considered resistant if it meets certain clinical diagnostic criteria in conjunction with minimum inhibitory concentration tests used to determine the most appropriate antibiotics [31,34].

Basic and additional precautions

In addition to the three above-mentioned basic practices, additional precautions must be taken when an HCAI is reported. While these depend on the infection detected, they include, but are not limited to, the use of personal protective equipment, isolation measures and the application of contact precautions with patients who are carriers or infected [26]. In the event that a major outbreak is declared, CBPs must be intensively applied, and additional meetings and resources are added over the course of its duration [35].

Economic analysis and research questions

Before embarking on an economic analysis, it is important to clarify that the interpretation of economic studies must consider three elements: the analytical perspective, the time horizon, and the factors influencing cost, all the while considering the patient's prior condition [36]. The analytical perspective – patient, hospital, or societal – determines the choice of costs to include in the calculations. For example, from a hospital perspective, medical costs would not include patient-related costs after discharge, or costs related to lost productivity due to hospitalization. The time horizon sets the time frame within which medical costs are measured. Other factors influencing the costs of care are the stage and severity of disease, comorbidities, risk factors, admitting diagnosis, and length of stay [25,36].

We included several approaches in our economic analysis of intervention efficiency: CMA; CEA; CUA; CBA; and CCA [21–25]. The first three are based on comparing interventions. A CMA compares the costs of two similar processes or interventions to determine which one is the least expensive; it assumes identical outcomes and compares only intervention costs. A CEA measures both the costs (in monetary units) and health benefits (years of life gained) of an intervention in relation to another intervention, or in relation to the status quo. A CEA provides the differential cost-effectiveness ratio represented as the incremental cost divided by number of life-years gained. A CUA calculates the differential cost–utility ratio. Here costs are measured in monetary units; however, gains are adjusted to more accurately represent the value of the years of life that the intervention provides. A CUA is reported as the additional cost required for health-related quality of life (quality-adjusted life-year: QALY) improvements. In a CBA, costs and benefits are measured in monetary units. The difference between economic benefits and costs in terms of net gains or losses is estimated. In this approach, an examined intervention is compared against the status quo to determine its return on investment or profitability. Finally, a CCA is based on a tabular presentation of costs and consequences, leaving benefits (outcomes) in their natural units. Once the cost valuation has been completed, a list is drawn up of all possible intervention outcomes and the choice can be made to value certain potential outcomes.

Conducting an economic analysis of HCAI prevention and control therefore involves examining issues of quality management, prevention, and care safety. Thus, as Finkler stated, the cost of quality management takes into account both the cost of investing in preventive measures and the cost of disease or problems experienced [37,38]. The author suggests a certain level of quality can be achieved by investing in prevention. As such, there is a threshold, called the optimum, beyond which prevention could increase quality. Therefore, according to Finkler's model, the economic analysis of an HCAI prevention and control programme using CBPs requires that the following questions be asked: (i) What are the costs of HCAIs? (ii) What is the cost of investing in prevention through CBPs in HCAI prevention and control? (iii) What is the optimal break-even point to measure return on investment or cost savings when comparing prevention intervention costs against potential benefits?

Eligibility criteria

The inclusion and exclusion criteria were based on the Population, Interventions, Comparators and designs, Outcomes (PICO) framework, summarized in Table I.

Type of population (P)

This review included studies related to the prevention and control of the most commonly monitored pathogens in Quebec hospitals since 2004: CDAD and the three MDROs: MRSA, VRE and CR-GNB. We considered only the care of adult patients in acute-care wards (medicine and surgery) as these wards handle the highest numbers of hospitalized patients. Finally, countries belonging to the Organization for Economic Co-operation and Development (OECD) were targeted because, in general, they hold comparable health systems [39]. Paediatric as well as long-term care settings were excluded.

Type of interventions (I)

The interventions targeted by this review were based on the study's theoretical framework (Supplementary File S1). The four major types of intervention (hand hygiene, hygiene and sanitation, screening, and additional precautions) related to CBPs in HCAI prevention and control programmes were analysed. Studies that investigated any practice other than the four CBPs were excluded.

Types of comparators or designs

With regard to Comparators and Designs, this review included: randomized clinical trials (RCTs), quasi-experimental, case–control, cohort, retrospective, prospective, longitudinal, and cross-sectional studies. Any review or study that was purely clinical, or a technological assessment, or based solely on mathematical and statistical modelling was excluded. We also excluded pharmacoeconomic studies (i.e. those that compared the value of therapeutic or preventative drug interventions).

Type of outcomes (O)

Outcomes included all quantitative studies using CMA, CEA, CUA, CBA and CCA, as well as those combining any of these types of analyses. We considered healthcare facilities for the analytical frame and one year as the time horizon. Only studies that assessed the cost-effectiveness analysis of the four CBPs were included. Measurements of cost-effectiveness were reported as: net cost savings (savings - costs); incremental cost-effectiveness ratio (ICER = effectiveness/costs); incremental cost per QALY; incremental cost per disability-adjusted life year (DALY); and incremental benefit-cost ratio (IBCR = savings/costs).

Data sources and research strategy

This systematic review was registered with the Research Registry (unique identifying number 5355) [40] and conducted in accordance with the recommendations of PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-analysis) [41]. All specifications for elements related to the construction of the flow diagram were explicitly presented. Articles were selected from the scientific literature and only those written in English or French and published between 2000 and 2019 were included. The following six electronic bibliographical databases were considered, using iterative exploratory searches: MEDLINE via Ovid, CINAHL, Embase, Cochrane, Web of Science, and JSTOR. Grey literature, namely Cordis and OpenGrey, in the same period, were also added. Two nursing HCAI prevention and control programme officers (S.B. and N.P.) and co-authors (E.T., I.B., D.S., K.K., M.J., A.B., C.S.) contributed to the definition of the keywords. The databases were queried using descriptors or thesauri with the logical operators "AND" and "OR". We developed the search strategy in collaboration with an experienced librarian (C.S/) at the Saint-Jérôme campus of the Université du Québec en Outaouais and the research strategies to be tested were defined during the working meetings of the co-investigators. All query terms can be found in Supplementary File S2. In order to improve reliability, before the full screening of all of the articles, the authors (S.B., N.P., E.T., I.B., D.S., K.K., M.J., A.B., C.S.) screened the same 10% of the titles and abstracts.

Selection process

A research librarian (C.S.) implemented the research strategy for article selection and assisted with the preparation of Endnote bibliographic database. Duplicates were identified and removed. Citations were exported into Rayyan system [42] by two reviewers working independently. Two independent reviewers (E.T., I.B.) screened all of the titles and abstracts of the articles. Duplicates were again identified and removed. An algorithm with predefined eligibility criteria was used to select articles (Figure 1).

An article was retained if both independent reviewers considered it eligible after the first screening. If one of the reviewers rejected an article, a third reviewer (other co-authors) analysed the article title and abstract and made a final decision. An article was rejected if at least two of the three reviewers consider it ineligible. After screening, all the records with a conflict were reviewed (by E.T. and I.B.), and an agreement on rejection or acceptance was made. The full text of the selected articles was reviewed for this purpose. Finally, two PCI programme specialists (S.B. and N.P.) assessed the content to ascertain whether the final selected studies were technically sound and fell into HCAI prevention and control programs as defined by our four pathogens and CBPs.

Data extraction

For data extraction, an Excel spreadsheet built by the research team and based on Consolidated Health Economic

Evaluation Reporting Standards (CHEERS) [43] was used to extract the following information: authors, year of publication, title and abstract, objective of the study, country, type of clinical unit, design, type of economic evaluation, sample size, population size, currency and adjustment year, time horizon, outcomes related to incremental cost and funding sources. The extraction was made by one reviewer (I.B.) and the principal investigator (E.T.) validated all data.

Assessment of quality

The quality of included articles was assessed using three tools commonly used in economic evaluations. We used these tools because each assesses the economic evaluation components that may differ within, and between, articles. By using them simultaneously, we ensured the robustness of our assessment of quality analysis. We first used the audit guidelines for economic evaluation studies recommended by the Scottish Intercollegiate Guidelines (SIGN) [44]. Second, the Economic Evaluation criteria developed by Drummond *et al.* assessed the quality of the articles [25]. These criteria are commonly used in health economic evaluations and were used in previous research we conducted [23]. Third, the Cochrane criteria [45] for economic evaluation were used to ensure compliance with the standards of the *Cochrane Handbook for Systematic Reviews of Interventions*.

As with the extraction of articles, two reviewers (E.T. and I.B.) independently assessed the quality of the articles. If a consensus was not reached, a third reviewer (S.D.) arbitrated. Studies were classified as 'high quality' if the average score across quality assessment tools was at least 80%; 'moderate quality' if the average score was between 60% and 79.9%; and 'low quality' if below 60%.

Data analysis and aggregation of results

For each type of intervention, net cost savings, cost-effectiveness ratios, cost–utility ratios, and cost–benefit ratios were tabulated. The year of calculation and the currency used were also indicated. Based on the exchange rate, all currencies were converted to $CAD of the same benchmark year. Using the discount rates of 3%, 5% and 8% recommended by Montmarquette and Scott in 2007 [46] the values were converted to $CAD for 2019. The net cost savings and incremental ratios (cost-effectiveness, cost-utility, and cost-benefit) were estimated for each discount rate. Sensitivity analyses were carried out on the median values, indicating the maximum and minimum values of the outcomes. This approach was used in a study conducted by Tchouaket *et al.* [47].

Results

Results of searches and screening

The searches of MEDLINE, CINAHL, Embase, Cochrane, Web of Science, JSTOR, Cordis and OpenGrey databases produced 11,898 records, of which 3885 were duplicates. Screening titles and abstracts of 8013 lead to the exclusion of 7979 records based on the eligibility criteria. We had to settle 834

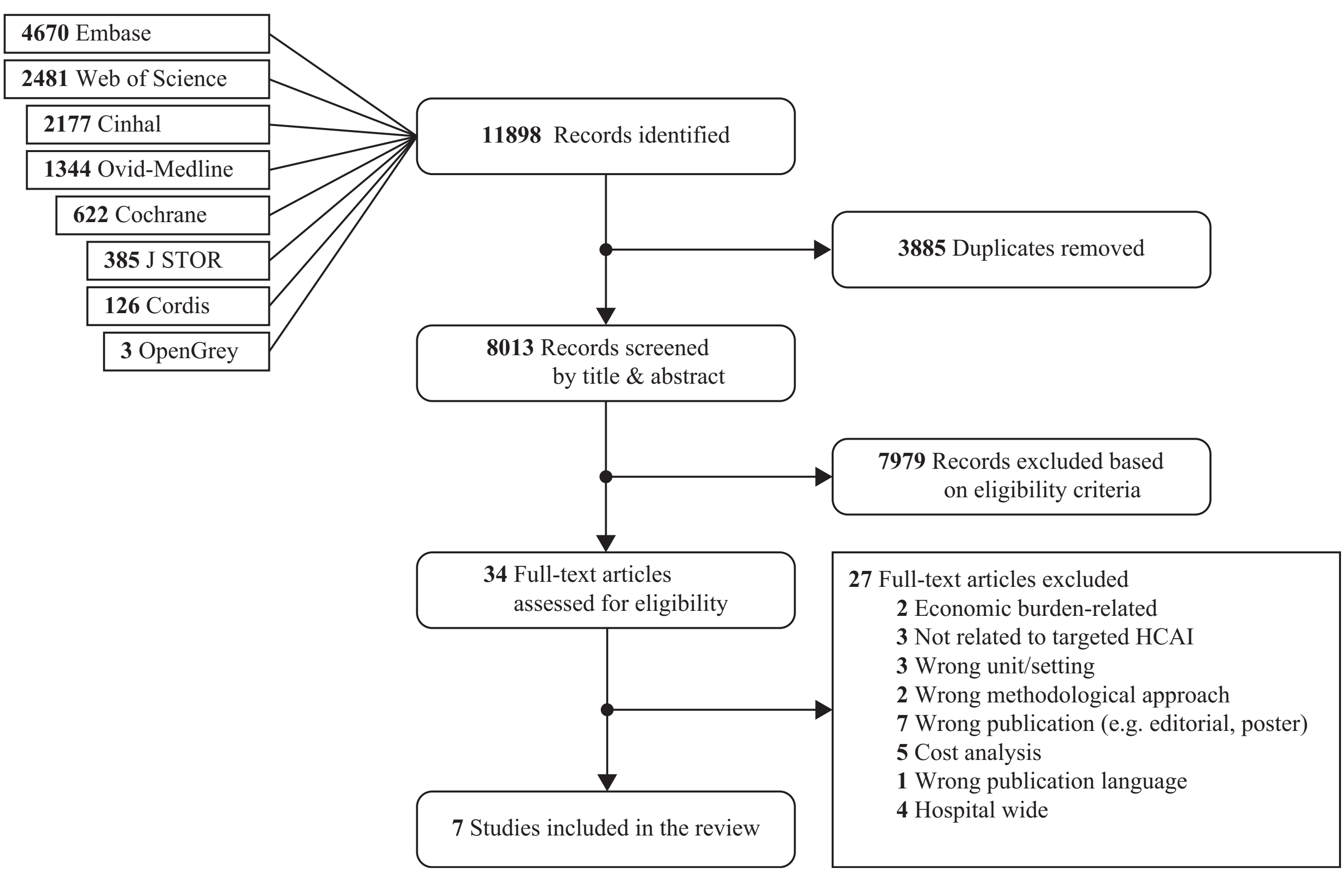

Figure 1. Flow diagram of studies selected for inclusion in systematic review. HCAI, healthcare-associated infection.

Table II
Characteristics of all studies included

Authors	Year of publication	Country	CBPs	HCAIs targeted	Study design	Population	Setting	Period of data collection
Chun *et al*. 2016	2016	Republic of South Korea	Hand hygiene	MRSA	Retrospective, one university hospital	372 episodes of MRSA and 470 episodes of MRSA were detected. MRSA was classified into community onset MRSA ($N = 225$) and hospital onset MRSA ($N = 245$).	Seoul National University Bundang Hospital	2008–2014
Chowers et al., 2015	2015	Israel	Prevention and control program (screening with nasal swab + additional contact isolation precautions + basic precautions with gloves and gowns + eradication treatment + nasal mupirocin and chlorhexidine body wash)	MRSA	Matched case–control historical cohort prospective study, one academic hospital	73 patients were admitted with the infection and 53 developed bacteraemia during hospitalization. In the latter group, i.e. cases with hospital-acquired MRSA bacteraemia, 101 patients were matched to as controls	Meir Medical Center is an academic hospital with 742 beds and approximately 60,000 admissions per year; single hospital in Israel	2005–2011
Bessesen et al., 2013	2013*	USA	Two additional contact precautions (contact precautions as defined by CDC + contact precaution use of gloves only)	MRSA	Prospective, comparative of 2 tertiary care hospitals	Hospital A, $N = 159$ Hospital B, $N = 145$ colonized patients	2 Department of Veterans Affairs tertiary care medical centres. Hospital A has 137 acute care beds; hospital B has 121 acute care beds	2006
Hassan et al., 2007	2007	UK	Screening using polymerase chain reaction	MRSA	Retrospective, one general hospital	686 consecutive patients admitted to two adult orthopaedic wards were screened for MRSA on admission over a period of 3 months in 2005 in a district general hospital. 10 infected	Rotherham General Hospital NHS Trust	3-month period during 2005
Montecalvo et al., 2001	2001	Netherlands	Prevention and control programme (screening + basic precautions with gloves and gowns + patient education by nurses + antimicrobial control using nurse monitoring)	VRE	Retrospective historical data, one hospital	520 admissions to the study unit	Adult oncology unit of a 650-bed hospital	—
van Rijen et al., 2009	2009	USA	Search and destroy (screening + additional precaution isolation + basic precautions with gowns, gloves, masks) + cleaning and sanitation + contact tracing + treatment of carriers + closure of wards + outbreak situation)	MRSA	Prospective, one teaching hospital	During the study period, on average, 38,943 patients were admitted annually to this hospital, with 282,585 patient days per year (mean numbers for the period 2001 through 2006)	Amphia hospital, a teaching hospital with 1370 beds	2001–2006
Wassenberg et al., 2011	2011	Netherlands	Different MRSA screening regimes using rapid diagnostic testing (using 'nares only' chromogenic agar, IDI, GeneXpert, and screening of all body sites) + additional precaution isolation	MRSA	Prospective, multicentre hospitals (five university hospitals, nine teaching hospitals)	Among 1764 patients at MRSA risk	Study was performed in 14 Dutch hospitals (five university hospitals, nine teaching hospitals)	December 2005 to June 2008

CBP, clinical best care practice; HCAI, healthcare-associated infection; MRSA, meticillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant enterococci.

disagreements (10.6% of screened records). Ultimately 34 records met the eligibility criteria for full-text assessment. We read and then excluded 27 manuscripts based on the following reasons: (i) the purpose of the study related to economic burden of HCAIs; (ii) studies had the wrong methodological approach or only reported costs of CBPs with no analysis of effectiveness; (iii) studies were editorials or poster publications; (iv) studies were conducted either hospital wide, or not in the target units (medical and surgical unit); (v) studies did not target at least one HCAI or CBP; and finally (vi) one study was not in English or French. Seven studies were included in our review (Figure 1).

Study characteristics

Table II summarizes the characteristics of all included studies.

All of the manuscripts were published in English from 2001 to 2016. Two studies (28.6%) were conducted in the USA [48,49], two (28.6%) in the Netherlands [50,51] and the remaining three in the Republic of South Korea [52], Israel [53] and the UK [54].

Clinical best practices included

One study (14.3%) referred exclusively to the effectiveness of a hand hygiene campaign [52]. One (14.3%) focused only on the effectiveness of a screening procedure using a polymerase chain reaction (PCR) assay [54], and one (14.3%) compared two additional contact precautions [48]. Four studies (57.1%) combined at least two CBPs: three (42.8%) referred to the effectiveness of screening with basic and additional isolation contact precautions [50,51,53], while one (14.3%) focused on the effectiveness of screening, cleaning and sanitation, and basic and additional contact isolation precautions [49].

Nosocomial infections targeted

All of the included papers focused on a single HCAI. Six (85.7%) targeted MRSA [48,49,51–54] and one (14.3%) VRE [50]. None of the included studies focused on CDAD or CR-GNB infections.

Study design used and population

Three (42.8%) studies used a non-experimental retrospective designs [50,52,54] using historical data. Chun *et al.* [52] collected data from January 2008 to December 2014, and included 245 episodes of hospital-onset MRSA. Hassan *et al.* [54] screened 686 patients, of which 10 had an MRSA infection, over a period of three months in 2005. Montecalvo *et al.* [50] assessed screening and basic and additional contact isolation precautions for VRE in 520 admissions over a period of one year.

Three (42.8%) focused on non-experimental prospective designs [48,49,51]. Bessesen *et al.* [48] compared, in 2006, the MRSA colonization bundle for contact precautions (contact precautions of the Centers for Diseases Control and Prevention (CDC) and contact precautions defined as the use of gloves only) for 159 and 145 colonized patients, respectively. From 2001 to 2006, van Rijen *et al.* [49] assessed yearly costs of MRSA screening, cleaning and sanitation, basic and additional contact isolation precautions of 38,943 admitted patients representing 282,585 patient days per year. Wassenberg *et al.* [51] measured screening from December 2005 to June 2008 in 1764 patients at risk for MRSA; 59 were MRSA infected. Only one study (14.3%) used a matched case–control historical prospective design from 2005 to 2011 [53]. In this study, 53 patients with MRSA were matched with 101 control patients without MRSA. Finally, none of the seven included studies used an experimental or quasi-experimental design.

Settings

Three studies (42.8%) were conducted in a single university or teaching hospital [50,52,53], one study (14.3%) in a teaching hospital [49] and one study (14.3%) in a general hospital [54]. Moreover, one study (14.3%) made the comparison of two tertiary-care hospitals [48], and one study (14.3%) conducted comparisons of 14 hospitals (five university hospitals, nine teaching hospitals) [51].

Economic evaluation characteristics

An overview of the reviewed studies using the CHEERS checklist is provided in Table III.

Economic evaluation design

Table IV summarizes the economic evaluation characteristics of all included studies. We found five studies (71.4%) reporting a cost benefit/cost savings analysis [49,50,52–54], one study (14.3%) presented a cost minimization analysis [48], and one study (14.3%) conduced a cost efficacy analysis [51]. None of the seven included studies used cost utility analysis or cost consequence analysis approaches.

Data included in the economic evaluations

Six studies (85.7%) used a hospital perspective and only one (14.3%) used a broader perspective (patient and caregiver) [52]. The time horizon was explicitly stated in three studies (42.8%) [49,51,53]. No study reported discounting of costs and effects, and only three studies (42.8%) performed sensitivity analyses for the calculation of costs and effects [49,52,53].

Cost-effectiveness of clinical best practices

Chun *et al.* [52] showed that the annual cost of hand hygiene for an MRSA prevention campaign was $US 167,495. The annual savings, due to a 33% reduction in MRSA incidence, was $US 851,565. Therefore, the incremental benefit–cost ratio (IBCR) using a 95% confidence interval (CI) with Bayesian model was 5.08 (0.94–8.76).

Chowers *et al.* [53] found that the annual cost of a prevention and control programme (screening with nasal swabs, additional contact isolation precautions, basic precautions with gloves and gowns, eradication treatment, nasal mupirocin and chlorhexidine body wash) was $US 208,100 per year. When the annual cost of prevention was compared with the annual cost of the reduction of MRSA bacteraemia cases per year (70% as assumed by the authors), the annual net cost savings of this programme was calculated to be $US 199,600.

Bessesen *et al.* [48] showed no difference in the reduction of the incidence of MRSA surgical site infections between MRSA contact precautions as defined by the CDC or when using only gloves (1.58 vs 1.56 MRSA transmissions per 1000 patient-days, respectively). The annual cost of MRSA contact precautions as defined by the CDC was $US 183,609 whereas costs from only the use of gloves was $US 25,812.

Hassan *et al.* [54] found that the annual cost savings of MRSA screening using PCR was £301,000 in the first year of

Table III

Summary of articles using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

Authors	Chun *et al.*	Chowers *et al.*	Bessesen *et al.*	Hassan *et al.*	Montecalvo *et al.*	van rijen *et al.*	Wassenberg *et al.*
Year of publication	2016	2015	2013	2007	2001	2009	2011
Country	Republic of South Korea	Israel	USA	UK	USA	The Netherlands	The Netherlands
Title	Impact of a hand hygiene campaign in a tertiary hospital in South Korea on the rate of hospital-onset methicillin-resistant Staphylococcus aureus bacteraemia and economic evaluation of the campaign	Cost analysis of an Intervention to prevent methicillin-Resistant Staphylococcus aureus (MRSA) transmission	Comparison of control strategies for methicillin-resistant Staphylococcus aureus	Financial implications of plans to combat methicillin resistant Staphylococcus aureus (MRSA) in an orthopaedic department	Costs and savings associated with infection control measures that reduced transmission of vancomycin-resistant enterococci in an endemic setting	Costs and benefits of the MRSA search and destroy policy in a Dutch hospital	Rapid diagnostic testing (RDT) of methicillin-resistant Staphylococcus aureus carriage at different anatomical sites: costs and benefits of less extensive screening regimens
Background and objectives	To assess the effect of a campaign to improve hand hygiene compliance on the incidence of hospital-onset MRSA bacteraemia (MRSAB) and to analyse its economic benefit	Our objective was to assess the cost implications of a vertical MRSA prevention program that led to a reduction in MRSA bacteraemia	We compared results of slightly different MRSA control bundles at 2 geographically similar Department of Veteran Affairs (VA) hospitals with comparable workload, case mix, staffing, and parallel surveillance methods for MRSA colonization to determine whether the use of cover gowns is an essential component of the MRSA control bundle	The aim of this study was to calculate retrospectively the cost of MRSA infections in the elective and trauma orthopaedic population in Rotherham District General Hospital in a 3-month period during 2005	To determine the costs and savings of a 15-component infection control program that reduced transmission of vancomycin-resistant enterococci (VRE) in an endemic setting	The objective of this study was to determine the costs and benefits of the MRSA Search and Destroy policy in a Dutch hospital during 2001 through 2006	To determine costs and effects of different MRSA screening regimes using RDT, by varying the number of body sites tested and whether or not conventional back-up cultures were included
Target population and subgroups	372 episodes of MRSA and 470 episodes of MRSA were detected. MRSA was classified into community onset MRSA (n = 225) and hospital onset MRSA (n = 245)	Seventy-three patients were admitted with the infection and 53 developed bacteraemia during hospitalization. In the latter group, i.e. cases with hospital-acquired MRSA bacteraemia, 101 patients were matched as controls	Hospital A, $N = 159$ Hospital B, $N = 145$ The patient population was 95% male, and the mean age was 64 years at hospital A. At hospital B, the population was 95% male, and the mean age was 65 years	686 consecutive patients, admitted to two adult orthopaedic wards were screened for MRSA on admission over a period of 3 months in 2005 in our district general hospital. Ten (10) were infected	Cost based on 520 admissions to the study unit.	During the study period, on average, 38 943 patients were admitted annually to this hospital, with 282 585 patient days per year (mean numbers for the period 2001 through 2006)	Among 1764 patients at risk, MRSA prevalence was 3.3% ($N = 59$)
Setting and location	Seoul National University Bundang Hospital	Meir Medical Center is an academic hospital with 742 beds and approximately 60,000 admissions per year; single hospital in Israel	Two Department of Veterans Affairs tertiary care medical centres. Hospital A has 137 acute care beds; hospital B has 121 acute care beds	Rotherham General Hospital NHS Trust	Adult oncology unit of a 650-bed hospital	Amphia hospital, a teaching hospital with 1370 beds	Study was performed in 14 Dutch hospitals (five university hospitals, nine teaching hospitals) between December 2005 and June 2008
Study perspective	Patient and caregivers	Hospital	Hospital	Hospital	Hospital	Hospital	Hospital
Intervention	Hand hygiene campaign	Intervention to prevent MRSA transmission (screening with nasal swab, contact isolation, gloves, gowns, eradication treatment and nasal mupirocin and chlorhexidine body wash)	Control strategies for MRSA	Screening elective cases of MRSA		MRSA screening and confirmation	Different MRSA screening regimes using rapid diagnostic testing (RDT)
Comparators	Pre- (January 2008 to September 2010) and post- (October 2010 to December 2014) campaign	Matched case–control cohort prospective study	Two bundles of measures for contact precautions: contact precautions of CDC and contact precautions use of only gloves				The isolation with 'nares only' screening using chromogenic agar, IDI and GeneXpert, respectively, compared with when all body sites had been screened
Design	We collected retrospective data from the microbiologic laboratory database on patients who had MRSAB	A single-centre, matched, historical cohort study and cost analysis	Prospective study	To calculate retrospectively the cost of MRSA infections	Historical control data	The data of all patients and healthcare workers that were found to be carrying MRSA during the years 2001 through 2006 were prospectively recorded in a database	A prospective multicentre study

(*continued on next page*)

Table III (*continued*)

Authors	Chun *et al.*	Chowers *et al.*	Bessesen *et al.*	Hassan *et al.*	Montecalvo *et al.*	van rijen *et al.*	Wassenberg *et al.*
Time horizon	Annual? (2008–2014)	Annual (2005–2011)	?	? (3-month period during 2005)	? Annual	Annual (2001–2006)	Daily (December 2005 to June 2008)
Discount rate							
Health outcomes	During the pre-intervention period, monthly performance rates varied substantially but reached a plateau of 90% by 2013. On average, 1000 events were monitored monthly. After the start of the hand hygiene campaign, the procurement of hand sanitizers increased from 8.55 L (January 2008) and reached a maximum of 25.82 L (March 2013) per 1000 patient days. During the intervention period, it averaged 15 L per intervention, we would have expected an average value of 6 L. The median value of hand sanitizer procurement was 5.56 L (interquartile range (IQR), 3.03) during the preintervention period and 14.50 L (IQR, 4.44) during the intervention period. According to the Bayesian model, the incidence of hospital-onset MRSAB decreased by 33% compared with the preintervention period (95% CI, −57% to −7.8%). The median value of the MRSAB incidence rate during the preintervention period was 11.59 (IQR, 8.70), and during the intervention period it was 18.64 (IQR, 12.21). Episodes of HO-MRSAB (observed $N = 130$; Predicted, $N = 195$ (95% CI) (145–242)) Total reduction, $N = 65$ (%) (95% CI) (33) (12–112)	Reduction of 70% of number of MSRA bacteraemia case yearly (assumption, not estimated)	Significant reduction of MRSA (1.58 per 1000 patients days hospital A and 1.56 hospital B)		Reduction of 6 patients out of 9 per year	Application of the Search and Destroy policy resulted in a transmission rate of 0.30 and was estimated to prevent 36 cases of MRSA bacteraemia per year, resulting in annual savings of €427 356 for the hospital and ten lives per year (95% confidence interval [CI] 8 −14).	Isolation day avoided
Measurement of effectiveness	Cost–benefit analysis: Benefit–cost ratio (i.e. benefit/cost) =5.08 (95% CI) (0.94–8.76)	Cost-savings analysis of prevention: $199,600 annually	Cost-minimization analysis	Not clearly defined	Costs and savings analysis. Cost based on 520 admissions to the study unit	Estimation of costs and estimation of benefits for the hospital	Cost-effectiveness analysis assuming isolation measures would have been based on RDT results of different hypothetical screening regimes
Estimating resources and costs	Savings because of HO-MRSAB prevention = $851,565 Maintenance costs of the hand hygiene campaign: total hand sanitizer costs =	Prevention costs: microbiology tests, single-use equipment, infection control personnel time: $208 100 per year. Cost/patient mean (SD):	Hospital A cover gown consumption averaged $16,965 per month, whereas average monthly cover gown usage at hospital B was $2385. Average gown cost	Cohort nursing; non-selective screening of all admissions to the orthopaedic wards; use of a polymerase chain reaction (PCR) assay as a diagnostic	The cost of enhanced infection control strategies for 1 year was $116,515. VRE BSI was associated with an increased length of stay of 13.7 days. The savings	MRSA Search and Destroy policy in a Dutch hospital during 2001 through 2006. Variable costs included costs for isolation, contact tracing, treatment of	Costs per isolation day avoided were calculated for regimes with single or less extensive multiple site RDT regimes without

$21 294 Campaign costs = $8182 Personnel costs = $138,019 Total costs =$167,495	(bloodstream infection (BSI) on admission *N* = 73) M = 14,300 (SD=12,488) $US; (Hospital-acquired BSI *N* = 53) M = 14,900 (SD=14,137) $US; (Control *N* = 101) M = 5600 (SD = 10,476) $US; *P* (hospital acquired vs control) = <0.001 Cost/patient surviving >72 h after BSI mean (SD): (BSI on admission *N* = 73) M = 16,600 (SD = 12; 136) $US; (Hospital-acquired BSI *N* = 53) M = 18,500 (SD = 13,615) $US; (Control *N* = 101) M = 5600 (SD =10,476) $US; *P* (hospital acquired vs control) <0.001	per package of 10 was $9.02 giving an estimated annual cost of $183,609 at hospital A and $25,812 at hospital B	tool; ring-fencing of beds; and separate wound dressing rooms for each ward. The total cost was projected to be £301,000. The cost of the PCR rapid MRSA detection device plus staffing for a year with culture media for the trauma cases will cost £149,000. The cost of screening elective cases is estimated at £12,000. The total cost for the first year would be £301,000; in subsequent years the cost would be £261,000 as the PCR assay will already have been purchased. This should be compared with the annual cost of MRSA infections (£384,000).	associated with fewer VRE BSIs ($123,081), fewer patients with VRE colonization ($2755), and reductions in antimicrobial use ($179,997) totaled $305,833. Estimated ranges of costs and savings for enhanced infection control strategies were $97,939 −148,883 for costs and $271,531−421,461 for savings. Year cost to the hospital for VRE enhanced infection control strategies (based on 520 admissions to the study unit) Patient−nurse cohorts = nurse assistant (*N* = 3): cost per item = $22,734/year; total cost = $68,202 Patient−nurse cohorts: cost per Item = $16.28/h; total cost = $704 Gowns: cost per Item = $52.50/100; total cost = $15,276 Gloves: cost per Item = $3.85/100; total cost = $3864 Surveillance cultures: personnel (microbiologist): cost per item = $18.00/h; total cost = $14,040 Surveillance cultures: personnel (nurse): cost per Item = $25.00/h; total cost = $6500 Surveillance cultures: supplies (perianal, new VRE+ (*N* = 41)): cost per item = $14.97; total cost = $614 Surveillance cultures: supplies (perianal, repeat VRE+ (*N* = 368)): cost per item = $3.30; total cost = $1214 Surveillance cultures: supplies (perianal, VRE (*N* = 1231)): cost per item = $1.41; total cost = $1736 Surveillance cultures: supplies (environmental, VRE+ (*N* =58)): cost per item = $3.30; total cost = $191 Surveillance cultures: supplies (environmental, VRE (*N* =271)): cost per	carriers and closure of wards. Fixed costs were the costs for the building of isolation rooms and the salary of one full-time infection control practitioner. To determine the benefits of the Search and Destroy policy, the transmission rate during the study period was calculated. Furthermore, the number of cases of (MRSA) bacteraemia prevented was estimated, as well as its associated prevented costs and patient lives. The costs of the MRSA policy were estimated to be €215,559 a year, which equals €5.54 per admission. The daily isolation costs for MRSA-suspected and -positive hospitalized patients were €95.59 and €436.62, respectively. Application of the Search and Destroy policy resulted in a transmission rate of 0.30 and was estimated to prevent 36 cases of MRSA bacteraemia per year, resulting in annual savings of €427,356 for the hospital and 10 lives per year (95% CI 8−14)	conventional back-up cultures and when PCR would have been performed with pooling of swabs. In all scenarios the negative predictive value was above 98.4%. With back-up cultures of all sites as a reference, the costs per isolation day avoided were €15.19, €30.83 and €45.37 with 'nares only' screening using chromogenic agar, IDI and GeneXpert, respectively, as compared with €19.95, €95.77 and €125.43 per isolation day avoided when all body sites had been screened

(*continued on next page*)

Table III (*continued*)

Authors	Chun *et al.*	Chowers *et al.*	Bessesen *et al.*	Hassan *et al.*	Montecalvo *et al.*	van rijen *et al.*	Wassenberg *et al.*
					item = $1.41; total cost = $382 Patient education (nursing time): cost per item = $25.00/h; Total cost = $2167 Antimicrobial control (nurse monitor): cost per item = $25.00/h; total cost = $1625 Total cost = $116,515 One-year actual costs and savings, and the range of estimates for costs and savings of enhanced infection control strategies (1995 $) Cost components: Nurse assistant = $68,202 ($49,725–93,600) Microbiologist = $14,040 ($14,040–19,188) Gowns = $15,276 ($15,276–21,994) Gloves = $3864 ($3765–4116) Surveillance cultures supplies = $4137 ($4137) Admitting personnel time = $704 ($704) Nurse for surveillance cultures patient education and antimicrobial control = $10,292 ($10,292) Total cost = $116,515 ($97,939–148,883) Savings components: Fewer patients with VRE BSI = $123,081 ($118,587–143,247) Gown and gloves = $2755 ($2742–3760) Reduction in antimicrobial use = $130,600 ($93,393–216,104) Administration of antimicrobials = $49,397 ($49,397) Total savings = $313,525 ($271,531–421,461)		
Currency	US dollars	US dollars	US dollars	Pound (£)	US dollars	Euro (€)	Euro (€)
Price date	2015	From 2005 through 2011?	?	2005	1995 Dollars	? 2001–2006 total costs (€)	? 2005 and June 2008
Choice of model	Bayesian Model						

Assumptions		Reduction of 70% of number of MSRA bacteraemia cases yearly (assumptions by author)					
Analytic methods							
Study parameters							
Incremental costs and outcomes	Savings due to HO-MRSAB prevention = $851,565 Maintenance costs of the hand hygiene campaign Total hand sanitizer costs = $21,294 Campaign costs =$8182 Personnel costs =$138,019 Total costs =$167,495						
Characterizing uncertainty							
Characterizing heterogeneity							
Sensitivity analysis	Bayesian Model and Confidence Interval	Decrease in MRSA bacteraemia cases of 54% and 15% in the percentage of time dedicated to the programme by the ICP team, the total cost of prevention increased from $202 300 to $214 000					
Study findings	"Procurement of hand sanitizers increased 134% after the intervention (95% CI 120–149%), compared with the pre intervention period (January 2008 –September 2010). In the same manner, hand hygiene compliance improved from 33.2% in September 2010 to 92.2% after the intervention. The incidence of HO MRSAB per 100,000 patient days decreased 33% (95% CI, −57% to −7.8%) after the intervention. Because there was a calculated reduction of 65 HO MRSAB cases during the intervention period, the benefit outweighed the cost (total benefit [$851 565]/ total cost [$167,495] = 5.08)"	"A vertical MRSA prevention program targeted at high-risk patients, which was highly effective in preventing bacteraemia, is cost saving. These results suggest that allocating resources to targeted prevention efforts might be beneficial even in a single institution in a high-incidence country."	"Significant reductions in MRSA HAIs were associated with implementation of the MRSA control bundle. The bundle that included full contact precautions for colonized patients was no more effective in prevention of MRSA transmissions than a similar bundle that omitted the use of cover gowns."	"The key in the fight against MRSA in the hospital setting is multifactorial and requires a combination of measures. Our solution is: cohort nursing; non-selective screening of all admissions to the orthopaedic wards; use of a PCR as a diagnostic tool; ring-fencing of beds; and separate wound-dressing rooms for each ward. The total cost is projected to be £301,000."	"The net saving due to enhanced infection control strategies for 1 year was $189,318. Estimates suggest that these strategies would be cost-beneficial for hospital units where the number of patients with VRE BSI is at least six to nine patients per year or if the savings from fewer VRE BSI patients in combination with decreased antimicrobial use equalled $100,000–150,000 per year."	"The costs of the MRSA policy were estimated to be €215,559 a year, which equals €5.54 per admission. The daily isolation costs for MRSA suspected and positive hospitalized patients were €95.59 and €436.62, respectively. Application of the Search and Destroy policy resulted in a transmission rate of 0.30 and was estimated to prevent 36 cases of MRSA bacteraemia per year, resulting in annual savings of €427,356 for the hospital and 10 lives per year (95% CI 8–14)."	"With back-up cultures of all sites as a reference, the costs per isolation day avoided were €15.19, €30.83 and €45.37 with 'nares only' screening using chromogenic agar, IDI and GeneXpert, respectively, as compared with €19.95, €95.77 and €125.43 per isolation day avoided when all body sites had been screened. Without back-up cultures costs per isolation day avoided using chromogenic agar screening added to multiple site conventional cultures is the most cost-effective MRSA screening strategy."
Journal title	American Journal of Infection control	PLOS One	American Journal of Infection control	Annals of the Royal College of Surgeons of England	Infection Control and Hospital Epidemiology	European Journal of Clinical Microbiology & Infectious Diseases	Clinical Microbiology and Infection

(?) = not defined clearly.
IPC: Nosocomial infections Prevention and Control.

Table IV
Economic evaluation characteristics of all studies included

									Costs (A)			Savings (B)			Net cost savings (B-A)			Incremental benefit cost ratio (IBCR) (B/A)		
Authors	CBPs	Economic evaluation method	Analysis perspective	Time horizon	Discounting	Sensitivity analysis	Price date	Currency	Min	Mean	Max	Min	Mean	Max	Min	Mean	Max	Min	Mean	Max
Chun et al., 2016	Hand hygiene	CBA (CB ratio)	Patient and caregivers	2008–2014	No	Yes	2005	$US		167 495			851 565					0.94	5.08	8.76
Chowers et al., 2015	Prevention and control program (screening with nasal swab + additional contact isolation precautions + basic precautions with gloves and gowns + eradication treatment + nasal mupirocin and chlorhexidine body wash)	CBA (CSA per year)	Hospital	2005–2011	No	Yes	2011	$US		208 100						199 600				
Bessesen et al., 2013	Two additional contact precautions (contact precautions as defined by CDC + contact precaution use of gloves only)	CMA (CSA per year)	Hospital	2006	No	No	2006	$US	25 812		183 609									
Hassan et al., 2007	Screening using PCR	CA (CSA per year)	Hospital	3-month period during 2005	No	No	2005	£	261 000		301 000									
Montecalvo et al., 2001	Prevention and control program (screening + basic precautions with gloves and gowns + patient education by nurses + antimicrobial control using nurse monitoring)	CBA (CSA per year)	Hospital	(–)	No	No	1995	$US	97 939		148 883	271 531		412 461		189 318				
van Rijen et al., 2009	Search and destroy (screening + additional precaution isolation + basic precautions with gowns, gloves, masks) + cleaning and sanitation + contact tracing + treatment of carriers + closure of wards + outbreak situation)	CBA (CSA per year)	Hospital	2001–2006	No	Yes	2006	€		215 559			427 356							
Wassenberg et al., 2011	Different MRSA screening regimes using rapid diagnostic testing (using 'nares only' chromogenic agar, IDI,	CEA (per isolation day avoided)	Hospital	December 2005–June 2008	No	No	2008	€							15.19	30.83	45.37			

	GeneXpert) + additional precaution isolation										
Wassenberg *et al.*, 2011	Different MRSA screening regimes using rapid diagnostic testing (using Chromogenic agar, IDI, GeneXpert when all body sites had been screened) + additional precaution isolation	CEA (per isolation day avoided)	Hospital	December 2005–June 2008	No	No	2008	€	19.95	95.77	125.43

CB, Cost Benefit Analyis; CBA, cost–benefit analysis; CBP, clinical best care practices; CDC, Centers for Disease Control; CEA, cost–effectiveness analysis; CSA, Cost Savings Analysis; MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction.

implementation and £261,000 in the second year; the annual average cost of MRSA infections was £384,000.

In the Montecalvo *et al.* study [50], the annual cost of a VRE prevention and control programme including screening, basic precautions with gloves and gowns, patient education by nurses, and antimicrobial control using nurse monitoring was between $US 97,939 and $US 148,883. The annual savings of this programme due to the reduction of six patients, from a total of nine per year with VRE, varied between $US 271,531 and $US 412,461. The average net cost savings associated with enhanced infection control strategies was $US 189,318 for one year.

In the van Rijen *et al.* study [49], the annual cost of the MRSA intervention search and destroy policy based on screening, additional isolation precautions, basic precautions with gowns, gloves and masks, cleaning and sanitation, contact tracing, treatment of carriers, closure of wards, and outbreak situation was estimated at € 251,559 a year, which equals € 5.54 per admission. This policy brought about savings of € 427,356 for the hospital due to a 30% of reduction in MRSA incidence and 10 lives saved per year.

Finally, Wassenberg *et al.* [51] showed that, because of MRSA screening using Chromogenic agar, IDI and GeneXpert in 'nare only', the cost per isolation day avoided was € 15.19, € 30.83 and € 45.37, respectively. The cost per isolation day avoided when all body sites were screened was € 19.9, € 95.77 and € 125.43, respectively.

Quality assessment

An overview of the quality assessment using SIGN, Drummond and Cochrane grids are provided in Table V. Tables VI–VIII summarize the quality for all studies as assessed by the SIGN, Drummond and Cochrane grids, respectively.

Only three studies (42.8%) met at least 80% of the criteria in the SIGN guidelines. These were the studies by Chun *et al.* [52], Chowers *et al.* [53] and Bessesen *et al.* [48]. The same three met at least 80% of the criteria in the Drummond grid. With regard to the Cochrane grid, none of seven studies reached 80% of the criteria. Two of them, Chun *et al.* [52] and Chowers *et al.* [53], met more than 70% of criteria. Overall, only two studies (28.6%) met a minimum average 80% of criteria for the three assessment guidelines and were considered 'high quality': Chun *et al.* [52] and Chowers *et al.* [53]. Four studies (57.1%) were considered 'moderate quality': Bessesen *et al.* [48], van Rijen *et al.* [49], Montecalvo *et al.* [50] and Wassenberg *et al.* [51]. Finally, one study (14.3%) Hassan *et al.* [54] was considered 'low quality'.

Synthesis of review results

Net cost savings of included studies in $CAD 2019

Table IX presents the net cost-savings and incremental cost–benefit ratios for every dollar invested in each CBP as it related to its target in an HCAI prevention and control programme. Values are estimated and presented in $CAD 2019, using discount rates of 3%, 5% and 8%.

The annual net cost savings of hand hygiene for MRSA prevention would be between $CAD 1,288,068 and $CAD 2,501,211 based on the discount rates of 3% and 8%, respectively.

Table V
An overview of the quality assessment of studies using SIGN, Drummond and Cochrane criteria

Authors	Overall			Quality
	High	Moderate	Low	
Chun et al., 2016	81.5%	6.8%	11.6%	High
Chowers et al., 2015	80.3%	8.1%	11.6%	High
Bessesen et al., 2013	76.7%	3.5%	19.7%	Moderate
Hassan et al., 2007	45.4%	26.7%	27.9%	Low
Montecalvo et al., 2001	63.5%	11.6%	24.8%	Moderate
van Rijen et al., 2009	70.4%	12.9%	16.7%	Moderate
Wassenberg et al., 2011	67.0%	11.5%	21.5%	Moderate

The annual net cost savings of a prevention and control programme (screening with nasal swabs, additional contact isolation precautions, basic precautions with gloves and gowns, eradication treatment, nasal mupirocin and chlorhexidine body wash) would be between $CAD 252,847 and $CAD 369,445 based on the discount rates.

The annual net cost savings of MRSA contact precautions as defined by the CDC would be between $CAD 304,688 and $CAD 564,262. Comparatively, the annual net cost savings of MRSA contact precautions, using only gloves, would be between $CAD 42,833 and $CAD 79,324. Furthermore, the annual net cost savings of MRSA screening using PCR would be between $CAD 871,251 and $CAD 1,691,823.

For the VRE prevention and control programme using screening, basic precautions with gloves and gowns, patient education by nurses, and antimicrobial control using nurse monitoring, the annual net cost savings would be between $CAD 527,237 and $CAD 1,644,684, based on discount rates of 3% and 8%, respectively.

The annual net cost savings of the search and destroy MRSA intervention, based on screening, additional precautions isolation, basic precautions with gowns, gloves and masks, cleaning and sanitation, contact tracing, treatment of carriers, closure of wards, and outbreak status would between $CAD 891,173 and $CAD 1,650,391, based on discount rates of 3% and 8%, respectively.

When screening for MRSA, the cost for each isolation day avoided using Chromogenic agar, IDI and GeneXpert in 'nare only' would be between $CAD 71.3 and $CAD 120.1. The cost for each isolation day avoided using Chromogenic agar, IDI and GeneXpert in all body sites would between $CAD 290.0 and $CAD 372.9. These are based on the discount rates of 3% and 8%, respectively.

Incremental cost–benefit ratios of included studies in $CAD 2019

For every dollar invested in the hand hygiene campaign, we would save between $CAD 9.3 and $CAD 18.1 based on the discount rates of 3% and 8%, respectively.

For every dollar invested in the prevention and control programme based on screening with nasal swabs, additional contact isolation precautions, basic precautions with gloves and gowns, eradication treatment, nasal mupirocin and chlorhexidine body wash, we would save between $CAD 2.5 and $CAD 3.6.

Table VI
Quality Assessment of studies using SIGN guidelines

SIGN criteria	Chun et al., 2016	Chowers et al., 2015	Bessesen et al., 2013	Hassan et al., 2007	Montecalvo et al., 2001	van rijen et al., 2009	Wassenberg et al., 2011
1. Is the paper an economic study (i.e. assessing the cost effectiveness of something), or is it just a study of costs? REJECT IF THE LATTER IS TRUE.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Is the paper relevant to the key question? Analyse using PICO. IF NO REJECT (give reason below). IF YES complete the checklist.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Section 1: internal validity							
1.1. The study addresses an appropriate and clearly focused question	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.2. The economic importance of the question is clear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.3. The choice of study design is justified	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.4. All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately	Yes	Yes	Yes	Yes	Yes	Yes	Yes
1.5. The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately	Yes	Moderate	Yes	Moderate	Yes	Moderate	Moderate
1.6 If discounting of future costs and outcomes is necessary, it has been performed correctly	No	No	No	No	No	No	No
1.7. Assumptions are made explicit and a sensitivity analysis performed	Yes	Yes	No	No	No	Moderate	No
1.8. The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes	Yes	Yes	Yes	No	Moderate	Yes	Moderate
1.9. The results provide information of relevance to policy makers	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Section 2: overall assessment							
High	10 (90.9%)	9 (81.8%)	9 (81.8%)	7 (63.6%)	8 (72.7%)	8 (72.7%)	6 (54.5%)
Moderate	0 (0%)	1 (9.1%)	0 (0%)	1 (9.1%)	1 (9.1%)	2 (18.2%)	3 (27.3%)
Low	1 (9.1%)	1 (9.1%)	2 (18.2%)	3 (27.3%)	2 (18.2%)	1 (9.1%)	2 (18.2%)

PICO, Patient or Population Intervention Comparison Outcome.

Table VII

Quality of studies as defined by Drummond criteria

Drummond criteria	Chun et al., 2016	Chowers et al., 2015	Bessesen et al., 2013	Hassan et al., 2007	Montecalvo et al., 2001	van Rijen et al., 2009	Wassenberg et al., 2011
1. Clarity of the question being asked	High	High	High	High	High	High	High
2. Comprehensive description of the competing alternatives	Moderate	High	High	Low	Low	Low	High
3. How the programme's effectiveness was assessed	High	High	High	Moderate	Moderate	High	Moderate
4. Identification of costs and consequences of each alternative being compared	High	High	High	Moderate	High	High	Moderate
5. Accurate measurement of costs and consequences using appropriate physical units	High	High	High	Moderate	High	High	Moderate
6. Credibility of the assessment of costs and consequences	High	High	High	Moderate	Moderate	High	Moderate
7. Costs adjusted based on timing: discounting	Low	Low	Low	Low	Low	Low	Low
8. Differential analysis of costs and consequences of competing alternatives	Moderate	Moderate	High	Moderate	Moderate	High	Moderate
9. Allowance made for uncertainty in estimates of costs and consequences: sensibility analysis	High	High	Low	Low	Low	Moderate	Low
10. Clarity of the presentation and discussion of the results: comparison of results against those of other studies and in other jurisdictions	High	High	High	High	Moderate	High	High
Overall assessment							
High	7 (70.0%)	8 (80.0%)	8 (80.0%)	2 (20.0%)	3 (30.0%)	7 (70.0%)	3 (30.0%)
Moderate	2 (20.0%)	1 (10.0%)	0 (0.0%)	5 (50.0%)	4 (40.0%)	1 (10.0%)	5 (50.0%)
Low	1 (10.0%)	1 (10.0%)	2 (20.0%)	3 (30.0%)	3 (30.0%)	2 (20.0%)	2 (20.0%)

Table VIII

Quality assessment of articles using Cochrane criteria

Cochrane criteria	Chun et al., 2016	Chowers et al., 2015	Bessesen et al., 2013	Hassan et al., 2007	Montecalvo et al., 2001	van Rijen et al., 2009	Wassenberg et al., 2011
1. Is the study population clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Are competing alternatives clearly described?	No	Yes	Yes	No	No	No	Yes
3. Is a well-defined research question posed in answerable form?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Is the economic study design appropriate to the stated objective?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Is the chosen time horizon appropriate to include relevant costs and consequences?	Moderate	Yes	No	No	No	Yes	Yes
6. Is the actual perspective chosen appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Are all important and relevant costs for each alternative identified?	Yes	Yes	Yes	Moderate	Yes	Yes	Yes
8. Are all costs measured appropriately in physical units?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Are costs valued appropriately?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Are all important and relevant outcomes for each alternative identified?	Moderate	Moderate	Yes	Moderate	Moderate	Moderate	Yes
11. Are all outcomes measured appropriately?	Yes	No	Yes	Moderate	Yes	Yes	Yes
12. Are outcomes valued appropriately?	Yes	No	Yes	Yes	Yes	Yes	No
13. Is an incremental analysis of costs and outcomes of alternatives performed?	Yes	Yes	Moderate	Moderate	Moderate	Moderate	No
14. Are all future costs and outcomes discounted appropriately?	No	No	No	No	No	No	No
15. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	Yes	Yes	No	No	No	No	No
16. Do the conclusions follow from the data reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
17. Does the study discuss the generalizability of the results to other settings and patient/client groups?	No	Yes	Moderate	Yes	Moderate	Yes	Moderate
18. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
19. Are ethical and distributional issues discussed appropriately?	Yes	Yes	No	No	No	No	No
Overall assessment							
High	14 (73.7%)	15 (78.9%)	13 (68.4%)	10 (52.6%)	11 (57.9%)	13 (68.4%)	13 (68.4%)
Moderate	2 (10.5%)	1 (5.3%)	2 (10.5%)	4 (21.1%)	3 (15.8%)	2 (10.5%)	1 (5.3%)
Low	3 (15.8%)	3 (15.8%)	4 (21.1%)	5 (26.3%)	5 (26.3%)	4 (21.1%)	5 (26.3%)

Table IX
Net cost-savings and incremental cost—benefit ratios for every dollar invested in each clinical best care practice (CBP) as it related to its target in a healthcare-associated infection (HCAI) prevention and control programme

Authors			Chun et al., 2016	Chowers et al., 2015	Bessesen et al., 2013	Hassan et al., 2007	Montecalvo et al., 2001	van Rijen et al., 2009	Wassenberg et al., 2011	Wassenberg et al., 2011
CBPs			Hand hygiene	Prevention and control programme (screening with nasal swab + additional contact isolation precautions + basic precautions with gloves and gowns + eradication treatment + nasal mupirocin and chlorhexidine body wash)	Two additional contact precautions (contact precautions as defined by CDC + contact precaution only use of gloves)	Screening using PCR	Prevention and control program (screening + basic precautions with gloves and gowns + patient education by nurses + antimicrobial control using nurse monitoring)	Search and destroy (screening + additional precaution isolation + basic precautions with gowns, gloves, masks) + cleaning and sanitation + contact tracing + treatment of carriers + closure of wards + outbreak situation)	Different MRSA screening regimes using rapid diagnostic testing (using 'nares only' chromogenic agar, IDI, GeneXpert) + additional precaution isolation	Different MRSA screening regimes using rapid diagnostic testing (chromogenic agar, IDI, GeneXpert, all body sites tested) + additional precaution isolation
Price date			2005	2011	2006	2005	1995	2006	2008	2008
Currency			$US	$US	$US	£	$US	€	€	€
Exchange rate			1.21	1.00	1.13	1.50	1.37	1.42	1.67	1.67
Discount rate 0%	Net cost savings (2019 $CAD)	Min			29,167		168,027		25.37	33.32
		Mean	851,565	199,600		576,000	259,365	606,845	51.49	159.94
		Max			207,478		430,895		75.77	209.47
	IBCR (2019 $CAD)	Min	1.14			1.91	2.49			
		Mean	6.15	1.96			3.29	2.82		
		Max	10.60			2.21	5.77			
Discount rate 3%	Net cost savings (2019 $CAD)	Min			42,833		341,565		35.11/isolation day saved	46.12
		Mean	1,288,068	252,847		871,251	527,236	891,173	71.27	221.39
		Max			304,688		875,921		104.88	289.95
	IBCR (2019 $CAD)	Min	1.72			2.89	5.07			
		Mean	9.30	2.48			6.68	4.13		
		Max	16.03			3.34	11.72			
Discount rate 5%	Net cost savings (2019 $CAD)	Min			54,999		541,906		43.39	56.98
		Mean	1,686,040	294,900		1,140,440	836,480	1,144,297	88.06	273.54
		Max			391,231		1,389,679		129.59	358.26
	IBCR (2019 $CAD)	Min	2.25			3.79	8.04			
		Mean	12.17	2.89			10.60	5.31		
		Max	20.99			4.37	18.60			
Discount rate 8%	Net cost savings (2019 $CAD)	Min			79,324		1,065,494		59.15	77.68
		Mean	2,501,211	369,445		1,691,823	1,644,684	1,650,391	120.05	372.91
		Max			564,262		2,732,383		176.66	488.40
	IBCR (2019 $CAD)	Min	3.34			5.62	15.81			
		Mean	18.05	3.63			20.85	7.66		
		Max	31.13			6.48	36.57			

CDC, Centers for Disease Control; IBCR, incremental benefit cost ratio; MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction.

For every dollar invested in the VRE prevention and control programme using screening, basic precautions with gloves and gowns, patient education by nurses, and antimicrobial control using nurse monitoring, we would save between $CAD 6.7 and $CAD 20.9 based on the discount rates of 3% and 8%, respectively.

Finally, for every dollar invested in the MRSA search and destroy intervention using screening, additional precautions isolation, basic precautions with gowns, gloves, masks, cleaning and sanitation, contact tracing, treatment of carriers, closure of wards and outbreak situation, we had savings between $CAD 4.1 and $CAD 7.7 based on the discount rates of 3% and 8%, respectively.

Discussion

Summary of evidence

The objective of this study was to conduct a systematic review of the literature to consolidate the evidence, using a discounting approach, of the economic evaluation of any of the four CBPs (hand hygiene, hygiene and sanitation of surfaces and equipment, admission screening, and additional precautions) related to HCAI prevention and control interventions. This review allowed our team to measure the net cost savings or incremental cost–benefit ratio of these practices for the prevention and control of the four most monitored pathogens (CDAD, MRSA, VRE, and CR-GNB), in medical and surgical units in Canadian hospitals.

To the best of our knowledge, this is the first systematic review that focuses on economic evaluations using a discounting approach of these four CBPs simultaneously as they relate to the four pathogens investigated, within the context of HCAI prevention and control interventions in medical and surgical units.

Our systematic review searched scientific and grey literature with a large number (eight) of databases. It identified seven studies that evaluated the net cost savings or incremental cost–benefit ratios associated with at least one of the CBPs related to two (MSRA and VRE) prevention and control interventions. Hand hygiene, contact isolation precautions, screening, and combinations of hand hygiene, cleaning and sanitation, contact isolation precautions, basic precautions with gloves, gowns, marks and screening were cost-effective.

To summarize, first, a hand hygiene MRSA prevention campaign could save more than $CAD 1.2 million annually, and up to $CAD 2.5 million depending on the proportion of the reduction of MRSA. Also, for every dollar invested in the hand hygiene campaign, we would save more than $CAD 9.3, and that translates into more than $CAD 18 based on the discount rates in medical and surgical hospital units.

Second, MRSA screening using PCR would provide an annual net cost saving of more than $CAD 870,000, and could reach $CAD 1.7 million. For every dollar invested in the MRSA screening using PCR, two studies show we could save more than $CAD 2.9 and possibly more than $CAD 6.5 in medical and surgical hospital units. Moreover, the MRSA screening intervention could permit healthcare facilities/systems to save more than $CAD 290 per isolation day and could surpass $CAD 372 per isolation day depending on the type of test and the sampling site (e.g., 'nare only' testing vs whole-body screening).

Third, MRSA contact precautions could provide minimum savings of $CAD 42,000. This could reach more than $CAD 564,000 if the MRSA contact precautions intervention is that of using only gloves.

Fourth, an MRSA prevention and control programme using a combination of screening with a nasal swab, additional contact isolation precautions, basic precautions with gloves and gowns, eradication treatment, nasal mupirocin and chlorhexidine body wash would provide an annual net cost savings more than $CAD 252,000, and could reach $CAD 369,000. Also, for every dollar invested in this programme, we could save more than $CAD 2.5.

Fifth, an MRSA search and destroy intervention based on the combination of screening, additional isolation precautions, basic precautions with gowns, gloves and masks, and cleaning and sanitation could allow for annual savings of more than $CAD 891,000. This amount could surpass $CAD1.6 million depending on the reduction in MRSA. For every dollar invested in this MRSA search and destroy program, the savings exceed $CAD4.1.

Finally, VRE prevention and control programmes using a combination of screening, basic precautions with gloves and gowns, patient education by nurses, and antimicrobial control using nurse monitoring, could help to save more than $CAD 527,000 annually and potentially more than $CAD 1.6 million, depending on the reduction of VRE. Also, for every dollar invested in this VRE prevention and control programme, we could realize savings surpassing $CAD 6.7.

Our systematic review revealed a lack of studies that made use of cost utility and cost consequence analyses of CBPs. Furthermore, none of the included studies used experimental or quasi-experimental designs comparing healthcare facilities with or without the implementation of the CBPs. From this extensive review (2000–2019), we noted that, since 2016, no relevant empirical research has been conducted on the economic evaluation of the four CBPs to prevent and control the four targeted pathogens that cause problematic and costly HCAIs.

Rigorous quality assessment using three tools (SIGN, Drummond and Cochrane) highlighted some limitations of the included studies. First, not all studies reported discounting of costs and effects. Only one study used an analysis from a perspective other than that of a hospital, such as the patient perspective [52]. Second, as also found by MacDougall *et al.* [18] none of the included studies estimated the societal costs of the four CBPs including: the infection prevention and control actions of the family, loved ones, caregivers and visitors. Third, in terms of the estimation, only three of the included studies clearly reported the date or the year of valuation of costs [50,52,54]. This is a fundamental parameter in economic evaluation [55,56] because it helps to know the year of the value of costs and savings in order to discount to the actual year for the comparisons in different jurisdictions. Similarly, only three of seven studies clearly reported the sensitivity analysis regarding the estimate of costs and effects of the interventions [49,52,53]. Due to the variation in the effect of the reduction in HCAIs and also the variation in the salary of professional staff according to their experience, it would be useful to present a sensitivity analysis for the real valuation of costs and savings.

Limitations

Our study has some limitations. First, in focusing only on English and French published studies, our research strategy may have missed publications in other languages. Second, we conducted our review of studies that exclusively took place in medical and surgical hospital units. Considering other types of care units (e.g., intensive care or emergency departments) could change the estimation of net cost savings/incremental benefit–cost ratios of the CBPs. Finally, estimating costs of infection in a fixed period of time does not consider the costs of future infection (or prevention of disease) as evidence suggests an initial infection predisposes patients to future infections [57,58].

Implications of findings

This systematic review evaluated the cost-effectiveness of implementing CBPs related to HCAI prevention and control. Studies related to MSRA and VRE found these practices provide an important cost-saving/cost-benefit. These financial benefits could be used by public authorities to strengthen the quality of the four CBPs in medical and surgical units of hospitals [47,59]. Savings could be used to strengthen medical human resources (physicians, nurses, nursing assistants, patient attendants, and hygiene and sanitation workers), material resources (gloves, gowns, masks), equipment and products (hydro-alcoholic solutions, hydrogen peroxide), as well as information resources (web/mobile applications for case detection) dedicated to infection prevention and control programmes.

Care providers should take better precautions before, during and after every care intervention by practicing good hand hygiene, thorough hygiene and sanitation, taking precautionary measures and respecting any required additional precautions. Health administrators must reinforce prevention and control procedures in their organization as these processes ultimately lead to cost savings. They could systematically assess the cost-effectiveness of CBPs to better administer HCAI prevention and control, and encourage the effective application of infection control guidelines [47,60].

Research results should be shared with patients and their families so that they can be made aware of the financial and human repercussions and benefits associated with infection prevention. They could thus better collaborate in infection prevention actions to ensure their own or their loved one's health and safety during hospitalization.

Finally, as seen with the COVID-19 pandemic, hand hygiene, cleaning and sanitation, screening, and basic precautions with gloves, gowns, masks, and additional isolation precautions are critically important prevention strategies to limit the spread of disease and protect patients and healthcare providers. Our study highlights its importance from an economic perspective. These results would be useful for comparison between OECD countries in terms of CBPs related to HCAI prevention and control. Future research should improve the quantity and quality of economic evaluations of CBPs related to HCAI prevention and control to provide relevant and timely information to healthcare policy makers. This investment in the assessment of cost-effectiveness would empower healthcare policy makers to make the most efficient use of valuable, shared and limited health resources in order to achieve the best health outcomes.

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Author contributions

E.T., S.B., C.S., N.P., I.B., K.K., D.S. and A.B. made substantial contributions to study conception and design for this research protocol. All authors were involved in drafting and making revisions to critical intellectual content in the manuscript. All authors gave final approval of the version to be published.

Conflict of interest statement
The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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