Infection Control Studies

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Implementation of Disposable Blood Pressure Cuffs as a Novel Approach to Reduce Fomite Transmission of Healthcare-Associated (HCA) Clostridium difficile Infection (CDI) in a Community Hospital or Twice Implemented is Once Credible

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Issue: CDI has garnered increased attention over the past several years. Current recommendations include contact precautions and hypochlorite disinfection of surfaces and equipment. Fomites have been implicated in HCA CDI. Little research is available for blood pressure (BP) cuffs.

Project: Equipment purchases over the years resulted in a variety of reusable woven, nonwoven and disposable BP cuffs in inpatient and outpatient locations and inconsistent disinfection of cuffs. The Environmental Services Department was adept at hypochlorite disinfection of units due to other diarrheal outbreaks the prior year. The Nursing staff was adept at instituting contact precautions for all patients admitted with diarrhea. It was decided that the next logical step was a more rigorous application of ''dedicated equipment'' for contact precautions. At an institutional level, standardized and adaptive BP equipment was ordered and disposable BP cuffs were implemented in December 2004. Due to budget constraints, the institution ceased ordering the disposable cuffs in January 2006. The Infection Control Team discovered this when rates of CDI rose and we observed re-use of disposable cuffs and woven cuffs put back into service. Disposable cuffs were re-implemented in July 2006 and are now for single patient use only. This created a natural history experiment with two before and after periods for the intervention. CDI rates from January 2004 through June 2007 were analyzed. A Poisson model was used to evaluate the binary variable ''intervention'' with least squares mean estimates. The mathematical model is: cases/patient days (by month) 5 intervention.

Results: Predicted cases per month (X1000) 5 1.63 without the disposable cuffs (p,.0001) and 0.76 with disposable cuffs (p,.0001). Patients are 53% less likely to have CDI with disposable BP cuffs (p5.001).

Lessons Learned: Fomites contribute to CDI. Disposable blood pressure cuffs and ''dedicated equipment'' yield a statistically significant reduction in HCA CDI. Collect and discard replaced equipment to prevent it from being put back into service, circumventing the original patient safety intent and cost benefit. This analysis reinforced the importance of formalizing results to validate both intervention and process. Medical and executive staff and front line managers gain comfort with the paradigm for improvement and cost-benefit analyses that cross unit specific line item budgets.

Blood Pressure Cuff Selection: A Simple Step Toward Reducing the Spread of MRSA

Summary

The transmission of hospital-acquired methicillin-resistant Staphylococcus aureus (MRSA) infections and other infections that cannot be treated with common antibiotics is a well-known yet growing problem. The cost associated with treating these infections is staggering.

Current measures commonly used in most healthcare facilities to prevent the spread of MRSA and other infections are largely inadequate. Studies have shown that contamination of blood pressure cuffs and other patient care equipment is widespread. Additional measures such as using single-patient use cuffs or reusable cuffs with lifelong antimicrobial coatings can be part of an effective MRSA control strategy.

Background

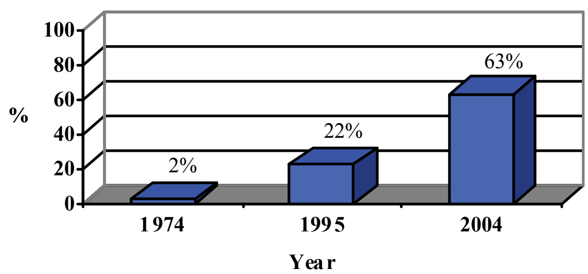
Hospital Acquired Infections

Nearly two million patients in the U.S. alone get a hospital acquired infection (HAI) each and every year, and about 90,000 of those patients die as a result of their infection.[1] In fact, HAIs kill more than five times as many Americans as AIDS.[2] Further, the annual cost to treat hospital infections in the U.S. is $30.5 billion, at an average cost of $15,272 per patient.[3]

MRSA and Multidrug-Resistant Organisms

The battle against MRSA is not new. For decades, MRSA has been the most common multidrug-resistant organism (MDRO) in much of the world, and its prevalence is on the rise. MDROs are estimated to cause more than 70% of HAIs[4], and the increase in MRSA as a percentage of all staph infections since the 1970s is alarming:

MRSA as Percentage of Total Staph Infections



Source: Centers for Disease Control and Prevention (CDC)[5]

It is estimated that there are over 94,000 MRSA infections resulting in over 18,000 deaths in the U.S. each year.[6] While reports of MRSA cases found in community settings make the headlines, healthcare settings account for the largest number of MRSA infections (85%), and thus the greatest threat.[7] Patients infected with MRSA and other MDROs have increased lengths of stay, require additional tests and procedures, and experience higher mortality rates.

Economic Considerations

A study of published hospital-associated infections reports and interventions conducted by infection control professionals from 1990-2000 found the mean cost attributable to a MRSA infection to be $35,367. In 2006, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) estimated the annual cost to treat MRSA in hospitalized patients in the U.S. to be between $3.2 billion and $4.2 billion. These costs were associated with prolonged hospital stays - as much as 10 days longer than for patients with methicillin-sensitive *Staphylococcus aureus* infections - and the cost of critical care stays associated with these complications.[8]

The estimated annual cost to treat MRSA in hospitalized patients in the U.S. is between $3.2 billion and $4.2 billion.

Further, there is the risk of legal action by the patient or the patient's family. For example, since 2004, there have been 13 lawsuits filed against Martin Memorial Hospital in Florida by or on behalf of patients who claim they acquired MRSA while in the hospital for surgery.[9]

Hospital reimbursements may also be at risk. Medicare is adopting policies to encourage hospitals to reduce the likelihood of hospital-acquired conditions (HACs), including certain infections, and will no longer pay for the increased costs of care resulting from one of the included conditions. Although the Centers for Medicare & Medicaid Services (CMS) has not explicitly included MRSA in their list of HACs for which reimbursements would be limited, it can be a trigger for some of the conditions that are included in the ruling. For example, if MRSA were the cause of a vascular catheter-associated infection, the HAC payment limitation would apply.[10] It is conceivable that in the future rulings related to MRSA may emerge.[11]

Additionally, many states and private payors are considering or implementing their own policies regarding reimbursement of care associated with hospital acquired infections.

MRSA Transmission

Healthcare Settings

MRSA occurs most frequently in patients undergoing invasive medical procedures or who have weakened immune systems and are being treated in a hospital or other healthcare facility. The most serious MRSA infections take place in healthcare settings.[12]

An individual can be a MRSA carrier without realizing it. The bacteria only cause an infection when they get inside the body, usually via a catheter, ventilator, or an incision or open wound. When a carrier is admitted to the hospital or visits a doctor's office, the organisms are transmitted to bedrails, wheelchairs, stethoscopes, and many other surfaces such as blood pressure cuffs, where MRSA can live for weeks.[13] [14] In fact, MRSA can survive more than 38 weeks on environmental surfaces such as door knobs, faucets, keyboards, telephones, and sterile goods packaging. [15]

A 1997 study showed that 73% of the hospital rooms containing patients infected with MRSA and 69% of the rooms containing patients colonized with MRSA had some environmental contamination: 96 (27%) of 350 surfaces in the rooms of 38 patients colonized or infected with MRSA tested positive for MRSA.[16] These contaminated surfaces and equipment can then, in turn, be the source of hand contamination thus resulting in further transmission.

Blood Pressure Cuff Contamination

A study published in 1996 revealed that 57 (81%) of the 70 blood pressure cuffs included in the study and presumed to be "clean" were tested positive for bacterial colonization. More specifically, 100% of the cuffs from the OR, PACU, Burn Special Intensive Care Unit (BSICU), and ER had bacterial colonization. In the SICU, 90% were colonized, and 80% of the cuffs in the MICU were colonized.[17]

100% of the cuffs from the OR, PACU, BSICU, and ER had bacterial colonization.

A 2003 study examining 203 blood pressure cuffs used in various hospital departments showed that 27 (77%) of 35 cuffs on nurses trolleys, 26 (63%) of 41 individually-located cuffs, 30 (52%) of 57 cuffs located on walls, and 9 (17%) of 52 stored cuffs were contaminated. The ICU had the highest overall rate of contamination, 20 (83%) of 24.[18] Forty-five percent of the contaminated cuffs carried MRSA. [19]

Blood pressure cuffs are often falsely perceived as innocuous and not requiring vigorous sanitization between patients. Additionally, locating documentation on official cuff cleaning protocols within the hospital can be problematic, and commonly-held perceptions of proper procedures are, by and large, grossly underestimated.[20]

Guidelines and Recommendations

The Situation Today

Good hand hygiene has long been considered a major element in preventing the spread of MRSA and other infections. However, despite the CDC's long-standing recommendation for hand washing following patient contact, most studies assessing healthcare workers' hand hygiene have shown low compliance rates, averaging approximately 40% and ranging as low as 10%.[21]

Moreover, the CDC has been criticized as underestimating the prevalence of MRSA as well as establishing guidelines that are not stringent enough.[22] In 2007 the Consumers Union urged hospitals to be more aggressive in their efforts to stop the spread of MRSA.[23] According to Lisa McGiffert, Director of Consumers Union's Stop Hospital Infections Campaign, "MRSA is lurking in every U.S. hospital and poses a serious and sometimes deadly health risk to patients who are unwittingly exposed to these superbugs. Unfortunately, most hospitals are not doing enough to keep these antibiotic-resistant germs in check. It's time for hospitals to aggressively step up their efforts to protect patients from these preventable infections."

"MRSA is lurking in every U.S. hospital"

- Lisa McGiffert, Director of Consumers Union's Stop Hospital Infections Campaign

McGiffert goes on to say, "We know how to control MRSA, but most U.S. hospitals are not consistently following these successful infection control practices. Hospitals need to make a commitment and invest the resources necessary to protect patients from MRSA. In the long run, that will save money and lives."

What Should Healthcare Professionals Do?

In January 2009, the U.S. Department of Health and Human Services unveiled their plan for a national strategy to reduce healthcare-associated infections. Their *Action Plan to Prevent Healthcare-Associated Infections* establishes national goals to prevent and possibly eliminate healthcare-associated infections. The proposed 5-year target relevant to MRSA is a 50% reduction in incidence rate of all healthcare-associated invasive MRSA infections.[24]

The CDC's Standard Precaution relative to handling of patient care equipment and instruments/devices is as follows: [25]

"Handle used patient-care equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of microorganisms to other patients and environments. Ensure that reusable equipment is not used for the care of another patient until it has been appropriately cleaned and reprocessed and that single-use items are properly discarded. Clean and disinfect surfaces that are likely to be contaminated with pathogens, including those that are in close proximity to the patient (e.g., bed rails, over bed tables) and frequently-touched surfaces in the patient care environment (e.g., door knobs, surfaces in and surrounding toilets in patients' rooms) on a more frequent schedule compared to that for other surfaces (e.g., horizontal surfaces in waiting rooms)."

The CDC's list of Contact Precautions includes the following recommendation relative to patient care equipment and instruments/devices:[26]

"In acute care hospitals and long-term care and other residential settings, use disposable noncritical patient-care equipment (e.g., blood pressure cuffs) or implement patient-dedicated use of such equipment. If common use of equipment for multiple patients is unavoidable, clean and disinfect such equipment before use on another patient. In home care settings limit the amount of non-disposable patient-care equipment brought into the home of patients on Contact Precautions. Whenever possible, leave patient-care equipment in the home until discharge from home care services. If noncritical patient-care equipment (e.g., stethoscope) cannot remain in the home, clean and disinfect items before taking them from the home using a low- to intermediate-level disinfectant. Alternatively, place contaminated reusable items in a plastic bag for transport."

Specific to equipment, the Society for Healthcare Epidemiology of America (SHEA) makes the following recommendation: [27]

"Dedicate the use of noncritical patient-care equipment to a single patient (or cohort of patients infected or colonized with the pathogen requiring precautions) to avoid sharing between patients. If use of common equipment or items is unavoidable, then adequately clean and disinfect them before use for another patient."

Further, the Joint Commission addresses prevention of healthcare associated infections due to MRSA and other MDROs in their 2009 National Patient Safety Goal NPSG.07.03.01[28] as well as Standard IC.02.02.01[29] which requires implementation of infection prevention and control activities when handling medical equipment, devices, and supplies.

Blood Pressure Cuff Options

As discussed, proper handling of equipment is an essential part of a MRSA control program. Blood pressure cuffs, being a ubiquitous item throughout most every location in which healthcare services are provided, are a key element in such programs. Appropriate selection and use of blood pressure cuffs is crucial.

Single-Patient Use Cuffs: Manufacturers such as CAS Medical Systems[30] and others offer a variety of single-patient use cuffs. By

dedicating a cuff to a single patient, the risk of infection and cross-contamination is reduced. Single-patient use, or disposable, cuffs are durable enough for multiple inflations. CAS offers a variety of Adult and Neonatal cuffs in their SoftCheck® line of disposable cuffs.

Reusable Cuffs: Reusable cuffs can be an economical alternative to single-patient use cuffs. When selecting a reusable cuff, a consideration to aid in the control of MRSA is to use cuffs treated with an antimicrobial agent. A few manufacturers, including CAS Medical Systems, offer antimicrobial cuffs.

CAS UltraCheck® blood pressure cuffs utilize the antimicrobial agent Micropel 5. Micropel 5 provides long term preservation from fungal and bacteria attack and helps prevent surface growth, permanent staining, and premature product failure. Materials incorporating Micropel 5 resist fungal and bacterial deterioration after long-term exposure to heat and severe weathering conditions. [31]

The antimicrobial properties of the CAS UltraCheck reusable blood pressure cuff are maintained for the full lifetime of the cuff.

The Micropel agent is added to the polyurethane resin of the CAS UltraCheck cuff prior to the formation of the film used for the laminated coating on the outside of the nylon fabric. This process of adding the antimicrobial agent directly to the polyurethane resin within the cuff itself allows it to maintain its antimicrobial properties through multiple cleanings.

This design has been in use for over seven years with no reported incidents of microbial growth or biocompatibility.[32] Micropel 5 guards against MRSA as well as dozens of other microorganisms.[33]

Hospitals Have Been Successful Using MRSA-Reduction Strategies

MRSA has been successfully controlled for decades at many hospitals throughout the world that have instituted rigorous infection control practices incorporating a combination of strategies. In Denmark, for example, the prevalence of methicillin resistance among *S. aureus* blood isolates reached a peak of 33% in the 1960s then declined steadily after introduction of a MRSA control transmission policy. The rate there has been maintained at less than 1% for 25 years.[34]

Some U.S. hospitals are following suit. A pilot program started in 2001 at the VA Pittsburgh Healthcare System (VAPHS) in Pennsylvania resulted in a 70% reduction in infections in the hospital's surgical unit[35] and an 82% reduction in the rate of MRSA infections after two years following expansion of the program to include the SICU. This program incorporated a combination of active surveillance, hand hygiene, and contact precautions into the standard nursing processes. The VAPHS largely attributes its success to empowering the staff and creating a staff-owned and operated MRSA prevention program.[36]

The University of Pittsburgh Medical Center reduced MRSA in its intensive care units by 90%; this program consisting of screening tests, gowns and other measures cost just $35,000 per year but saved over $800,000 a year in infection costs.[37] Other hospitals using similar approaches with notable results include the University of Virginia Health System, Evanston Northwestern Healthcare in Illinois, and the Brigham and Women's Hospital in Boston.[38] [39]

Conclusion

As a step toward controlling the transmission of MRSA and other HAIs, single patient use (disposable) blood pressure cuffs and proper handling of reusable cuffs is imperative. To augment standard cleaning and disinfection practices, reusable cuffs with antimicrobial properties provide an added level of protection. CAS Medical Systems' reusable cuffs are manufactured with an antimicrobial agent that provides protection against MRSA for the full lifetime of the cuff.

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ANTIMICROBIAL RESISTANCE & INFECTION CONTROL

RESEARCH **Open Access**

Prolongation of length of stay and *Clostridium difficile* infection: a review of the methods used to examine length of stay due to healthcare associated infections

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Abstract

Background: It is believed that *Clostridium difficile* infection (CDI) contributes to a prolongation of length of stay (LOS). Recent literature suggests that models previously used to determine LOS due to infection have overestimated LOS, compared to newer statistical models. The purpose of this review is to understand the impact that CDI has on LOS and in doing so, describe the methodological approaches used.

Aim: First, to investigate and describe the reported prolongation of LOS in hospitalised patients with CDI. Second, to describe the methodologies used for determining excess LOS.

Methods: An integrative review method was used. Papers were reviewed and analysed individually and themes were combined using integrative methods.

Results: Findings from all studies suggested that CDI contributes to a longer LOS in hospital. In studies that compared persons with and without CDI, the difference in the LOS between the two groups ranged from 2.8 days to 16.1 days. Potential limitations with data analysis were identified, given that no study fully addressed the issue of a time-dependent bias when examining the LOS. Recent literature suggests that a multi-state model should be used to manage the issue of time-dependent bias.

Conclusion: Studies examining LOS attributed to CDI varied considerably in design and data collected. Future studies examining LOS related to CDI and other healthcare associated infections should consider capturing the timing of infection in order to be able to employ a multi-state model for data analysis.

Keywords: *Clostridium difficile* infection, *Clostridium difficile* associated diarrhoea, Cost, Healthcare associated infection, Length of stay, Time dependent bias

Background

Clostridium difficile infection (CDI) is the leading cause of infectious diarrhoea in hospitalised patients [1]. According to the Centers for Disease Control and Prevention (CDC), the annual incidence of CDI in the USA exceeds 250 000 hospitalised cases, with a mortality of 1–2.5% [2]. The disease's symptoms can range from colonisation to life-threatening colitis. The incidence of morbidity related to CDI is increasing due to an epidemic of a hypervirulent strain of *C.difficile* (BI/NAP1) that has been reported in the USA and other countries. In addition to significant morbidity and mortality, CDI increases healthcare costs due to patients' extended hospitalisations and re-hospitalisations [3]. A recent systematic review investigating the economic costs to healthcare associated with CDI concluded that despite a lack of common methods employed by the studies, it is clear that the economic consequences of CDI are considerable [4].

One important step towards understanding the burden that CDI has on the health service is to examine the economic cost of CDI in hospitalised patients. One of the

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major costs associated with any healthcare associated infection (HAI) is excess hospitalisation, or prolongation of length of stay (LOS). A challenge for researchers is to design a study that accurately accounts for prolonged lengths of stay. Recent literature suggests that models that have been previously used to determine the additional LOS in hospital due to infection overestimated the additional LOS, compared to newer statistical models [5-10]. It is therefore vital that studies are designed in such a way as to evaluate and analyse this effectively. Determining the additional LOS due to an HAI, including CDI, is challenging due to the need to manage time-dependent bias—that is, the longer a person stays in hospital, the greater the risk of acquiring an infection. Time dependent bias is a term used to describe problem occurring when variables in the model change value after the start of patient observation. Such variables are called "time dependent," because their value can change over time [11]. One study demonstrating this bias examined readmission hospital and whether persons with a discharge summary were followed up by a physician after discharge. When the time dependent variable was analysed as a fixed variable, there were significantly lower readmissions in patients who saw physicians with the summary. This was shown to be a biased association as patients with early hospital readmission did not have a chance to see a physician and these patients were placed in a 'non discharge summary' group [12]. There are numerous other publications which also demonstrate this issue [7-9,13,14]

Therefore, managing issues such as time-dependent bias and sampling bias are important. The purpose of this review is to understand the impact that CDI has on LOS in hospitalised patients and, in doing so, to describe the methodological approaches used.

Methods

Design

An integrative review design was used in the same manner as described by Whittemore and Knafl [15]. To allow for a synthesis of results, an integrative design was selected based on the summation of different methodological approaches used in the empirical and theoretical literature. As a result, the design provides a more comprehensive understanding of particular issues [15].

Search strategy

The literature was accessed through searches on electronic databases *Medline* and *Pubmed* and was limited to the 1st January 2000 to 30 April 2011. Other limits included only searching literature that was published in English and studies involving humans. Key terms used were "*Clostridium difficile* and economic", "*Clostridium difficile* and length of stay", "*Clostridium difficile* and cost" and "*Clostridium difficile* and burden". These searches were combined, with duplicate studies being removed. Following this step, a review of these articles was conducted. Only case-controlled, cohort or review studies were included. Furthermore, articles were only included if they examined the LOS of hospitalised patients with CDI. Finally, letters to the editor and interventional studies, for example the effect of immunoglobulin treatment on LOS, were excluded.

Search outcome

The initial search yielded 330 articles. After the removal of studies that were not case-controlled, cohort or review studies, 26 studies remained. A further ten articles were excluded because they were either letters to the editor or were interventional studies. Figure 1 summarises the search strategy and outcomes.

Results

The majority of the 16 studies identified through the search strategy were retrospective in design. Two reviews and two prospective studies were identified. Table 1 summarises the characteristics and results from the 16 studies identified for this review.

The search strategy used to identify articles for this review did not identify the same articles in the latest review published by Ghantoji, Sail et al. [4]. Two articles included in the review by Ghantoji, Sail et al. [4] were not include in our review. Conversely, our study identified and included eight studies not used by Ghantoji, Sail et al. [4]. The primary reason for both these discrepancies is that our review examined the prolongation of LOS, whereas the focus by Ghantoji, Sail et al. [4] was economic cost . Similarly our review did not include two articles identified by the review conducted by Dubberke & Wertheimer (2009), but did identify a further 11 articles not used by Dubberke & Wertheimer (2009). The reasons for this are the same as those just previously described in addition to the inclusion of recent publications. Nine articles were common to both reviews. The review by Ghantoji, Sail et al. [4] identified four articles not identified by Dubberke & Wertheimer (2009). Conversely, Dubberke & Wertheimer (2009) identified five articles not used by Ghantoji, Sail et al. [4].

The manner in which participants were identified for the studies differed, with several studies using International Classification of Disease (ICD) codes to identify cases [16-21]. The use of ICD codes to identify participants does have the potential to reduce sensitivity and specificity when identifying cases of CDI as coding data is likely to underestimate cases. In addition, coding practices can vary between hospitals, and therefore multi-centred studies have a greater potential for variation in sample selection. Furthermore, the timing of an episode of CDI cannot be determined by such an approach.

Excluding the reviews, only three of the remaining fourteen studies were undertaken in countries other than

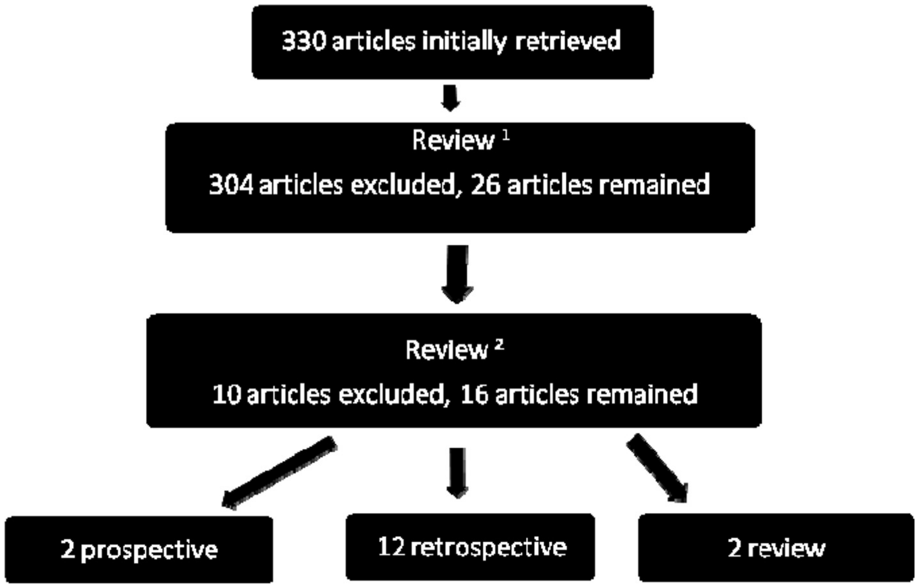

Figure 1 Summary of search strategy. [1]Articles were excluded if they were not case controlled, cohort or review studies or if they did not examine length of stay in hospitalised patients. [2]Letters to the editor and interventional studies were excluded.

the United States. The systematic review examining the economic costs of CDI undertaken by Ghantoji, Sail et al. [4] identified only four of thirteen articles from the United States. In the review undertaken by Dubberke and Wertheimer [22], one Australian study undertaken was identified as having been published as a letter to the editor [23].

The data collected in the various studies differed considerably. The majority of studies collected basic demographic data, such as age and gender. Some studies collected data about co morbidities and used a severity index such as the Charlson co morbidity index [18,24,25]. Data collected about variables such as antibiotic exposure or other drug therapies were limited [25-27].

Findings from all studies suggested that CDI contributes to a longer LOS in hospital. It was not possible to pool data because studies varied considerably in design, sampling and data analysis techniques. In studies that used a comparison between persons with CDI and those without, the difference in the LOS between the two groups ranged from 2.8 days to 16.1 days [24,28]. These data suggest that CDI does play a role in increasing the LOS in hospital.

In a retrospective cohort of over 18 000 non-surgical patients hospitalised for more than 48 h, Dubberke et al. [24] took a nested subset using a matched-pairs analysis and found that the increase in LOS that could be attributed to CDI was 2.8 days. Controls were matched to cases by a propensity score developed for data analysis. Using logistic regression, patient-specific probabilities of developing CDI were developed. The median LOS was determined for cases and controls, with the various median pair-wise lengths of stay being compared by using the Wilcoxon signed-ranked test. Attributable LOS was determined by calculating the median pair-wise difference between CDI cases and the controls [24]. As this study did not include surgical patients, it is possible that patients with severe CDI, those requiring colectomies, were excluded, leading to a potential bias. The use of a propensity score to match controls was used in an attempt to reduce any potential bias between controls and cases when determining CDI-attributable LOS.

A study undertaken by Lumpkins et al. [28] suggested a considerably longer LOS then that reported by Dubberke et al. [24]. In a prospective cohort study comprising of critically ill patients admitted to an intensive care unit, those with and without CDI were compared. A logistic regression model was used for data analysis. The mean hospital LOS was 15.9 days greater in patients who developed CDI compared to those who did not (34.9 days versus 19.0 days, $p = 0.003$). When cases were compared regarding antibiotic exposure, those with minimal exposure were found to have a shorter LOS in hospital, but data regarding all antibiotic exposure prior to admission, such as outpatients, were not obtained in this study [28]. Such a finding would suggest that collecting data on antibiotic exposure is needed in future studies that employ a similar methodology.

The methods of data analysis varied, as shown in Table 1. In the majority of studies, a regression model was developed to determine the impact that CDI had on LOS [16,18,20,21,24,26-30]. The studies did not collect data concerning the time of onset of CDI; therefore, it is not possible to exclude the possibility of reverse causality, in

Table 1 Summary of included articles

Author	Study type	Country	Statistical analysis	Results
Ananthakrishnan, McGinley, & Binion 2008	Retrospective case control	US	Multivariate regression	Three times the length of stay (CDI + IBD) vs. controls (IBD) IBD = irritable bowel disease
Bajaj et al. 2010	Retrospective case control	US	Multivariate regression	12.7-day case vs. 6.7-day control
Dubberke, Butler et al. 2008	Retrospective cohort	US	Multivariate regression, matched-pairs analysis	9.6-day cases vs. 5.8-day controls
Dubberke & Wertheimer 2009	Review	Not applicable	Not applicable	Not applicable
Ghantoji et al. 2010	Review	Not applicable	Not applicable	Not applicable
Kenneally et al. 2007	Retrospective cohort	US	Multiple logistic regression	27.3 (CDI) vs. 22.8 (non CDI)
Lawrence et al. 2007	Retrospective cohort	US	Multiple logistic regression	CDI stay twice as much non-CDI in ICU
Lumpkins et al. 2008	Prospective cohort	US	Multiple logistic regression	34.9 day LOS with CDI vs. 19 LOS without CDI
Miller et al. 2002	Retrospective cohort	Canada	Not discussed	9% of 269 patients with CDI deemed to have extension of LOS due to CDI
Nguyen, Kaplan, Harris, & Brant 2008	Retrospective cohort	US	Multiple linear regression	65% increase in LOS in patients with CDI & Crohn's disease 46% increase in LOS in patients with CDI & ulcerative colitis
O'Brien, Lahue, Caro, & Davidson 2007	Retrospective cohort	US	Descriptive	6.4-day LOS in patients with primary CDI diagnosis
Pepin, Valiquette, & Cossette 2005	Retrospective case control	Canada	Not discussed	10.7-day additional LOS in patient with CDI
Song et al. 2008	Retrospective match cohort	US	Logistic regression Wilcoxon Linear regression	1-day LOS increase (with CDI)
4-day LOS increase (CDI) when compared to matched diagnosis related group DRG				
Vonberg et al. 2008	Prospective match cohort	Germany	Wilcoxon Kolmogorov-Smirnov test	27-day LOS cases vs. 20-day LOS controls
Zerey et al. 2007	Retrospective cohort	US	Multiple logistic regression	16-day-longer LOS (with CDI)
Zilberberg et al. 2009	Retrospective cohort	US	Propensity score Multivariate analysis	6.1-day longer LOS (with CDI)

which longer lengths of hospitalisation may have increased the risk of CDI. The issues associated with controlling for a potential time-dependent bias caused by the LOS in hospital raises some significant concerns, which will now be discussed.

Discussion

As demonstrated in a published systematic review examining the economic costs of CDI, the focus of many studies was to view costs through the eyes of an accountant [4]. An accountant's model for determining the cost of HAIs is to count fixed and variables costs. Variable costs may include items such as dressings, personal protective equipment and laboratory test materials. Fixed costs include salary, electricity and heating. As fixed costs are often jointly shared—for example, one doctor does not treat one patient—the accountant's model determines a measure of usage for these fixed costs (cost per unit) and allocates this to patients or to the health provider accordingly. Comparisons between the average cost per infected patient and average cost per non-infected patient are often used to attribute the cost of HAIs. However, this may be misleading [31]. According to Graves, using such a model is not suitable for economic appraisal or for informing decisions about HAIs. An implication of the economic model is that by reducing or eradicating a specific infection, a fixed figure could be saved. An accountant's model ignores the cost of increased investments towards reducing infections and fails to consider which costs actually change with infections, as many fixed costs remain [31].

An economist model uses a cost-analysis approach to determine if there are any savings. For example, the consumables may be reduced by decreasing the instances of HAIs. The capacity gained by a reduction in HAIs is valuable and should thus be redeployed for other use. The redeployment of resources could be used for tasks such as elective surgery and, in turn, could cause other variable costs to increase [31].

An economist's approach in evaluating the cost of HAIs is supported by the argument that the majority of the costs associated with hospital care are fixed [32,33]. Therefore, in describing how costs change in relation to HAIs, it is important to demonstrate the number of bed days caused by HAIs [31]—and therefore the number of beds that are made available by preventing these infections—before deciding who will utilise these extra beds. Accurately determining the prolongation of LOS due to CDI will assist in developing an economic model for its prevention and control.

All of the studies identified in this literature review suggested that CDI contributes to a longer LOS in hospital. However, the method used to determine LOS should account for the fact that an HAI, such as CDI, can occur at any point during hospitalisation and that LOS is affected by other variables, such as co morbidity and primary diagnosis [5]. Matched cohort studies suffer from two types of bias. First, insufficient matching will not control all the bias. Second, strict matching criteria will result in censoring. The variable nature of when the infection might have started also poses an issue in matched studies: infections can occur at any time. However, data analysis in matched studies often compared infected and uninfected patients by their total hospital stay. If the timing of infections is not taken into account, then costs associated with pre- and post-infection are included and can dramatically amplify the time-dependent bias [5]. Statistical models can be used to address this issue at the data-analysis stage rather than at the design stage. A model can be built to describe the relationship between LOS and the predictors of that outcome [5,34]. Previously, models that ignored the time of infection often used a linear model that assumed a gamma distribution, where waiting times between events are relevant, in this case LOS and an independent variable of infected ("yes" or "no") [14]. One recent study examining CDI did attempt to use the principles of managing time-dependent bias in their study [35].

Methods have recently been developed to address these issues when estimating LOS associated with healthcare-associated infections. These methods include a multi-state model in which the infection is the intermediate event between admission and discharge and in which patients are given one of three states: non-infected, infected and discharged [6,14,36]. Therefore, for future research examining the prolongation of LOS for people with an HAI including CDI, collecting data at the commencement and completion of infection will enable the use of a multi-state model in data analysis.

Conclusion

Studies examining lengths of stay attributed to CDI varied considerably in their design and the data they collected. Several studies used administrative codes, such as ICD codes, to identify cases of CDI. The use of administrative data for this purpose did lead to some limitations, including the potential for ascertainment bias and a lack of sensitivity and specificity. A limited number of studies captured data regarding co morbidities. Co morbidities would clearly influence the LOS in hospital, and therefore this information should be collected when possible. Researchers, should consider whether data concerning antibiotic exposure needs to be included in future studies.

Despite these differences, there was a clear indication that CDI played some role in prolonging hospitalised patients' lengths of stay. As LOS in a hospital is a major contributor to healthcare cost, it is a logical assumption that CDI contributes an economic cost to the health system, a view shared by Ghantoji, Sail et al. [4]. Only a very limited number of studies identified in this literature review or in the two published reviews by Ghantoji, Sail et al. [4] and Dubberke and Wertheimer [22] did so outside of the United States or Canada. The provision of health services and the epidemiology of CDI varies between countries, and thus it is vital that future studies are undertaken in a variety of countries. In particular, studies outside of the United States and Canada are needed.

Potential issues in data analysis were identified, given that no study fully addressed the issue of a time-dependent bias when examining the LOS caused by CDI. Recent literature suggests that a multi-state model should be used to manage the issue of time-dependent bias. In order for a multi-state model to be used, the timing of CDI infection must be captured. However, no study identified in the literature search, including the two published reviews examining the economic cost of CDI, used or identified a multi-state model design. In fact, no study identified the onset and cessation of CDI infection and used this data to inform data analysis. Future studies examining LOS and CDI should consider capturing the timing of CDI infection in order to be able to employ a multi-state model for data analysis. Such an approach can also be extended in order to study HAIs other than CDI.

Competing interests
The authors declare they have no competing interests.

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Author contributions
BM and AG were responsible for the study concept and design. BM performed data collection. BM and AG were responsible for data analysis and the draft of the manuscript. All authors have read and approved the manuscript.

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A C. DIFFERENT APPROACH
TO FIGHTING HOSPITAL-ACQUIRED INFECTIONS

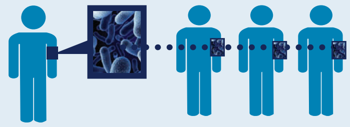
While most types of hospital-acquired infections are declining,
Clostridium difficile (C. diff)—
remains at historically high levels.[1]

C. diff by the numbers[1]

$1 billion annual U.S. treatment costs

14,000 deaths

BP Cuffs harbor C. diff spores

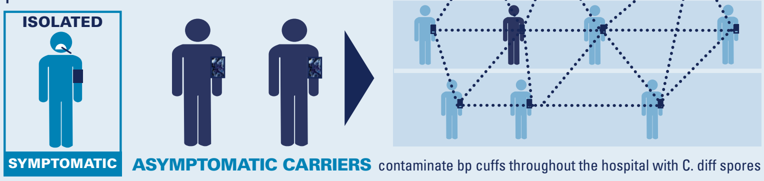


Studies show using the same blood pressure cuff on multiple patients contributes to the spread of C. diff.[2]

Isolating symptomatic C. diff patients is not enough

ONLY 1 OUT OF 3

patients with C. diff will be isolated[3]



Disinfecting your cuffs between patients? Think again

Germicidal wipes have not been proven effective against C. diff on soft, porous surfaces (like bp cuffs).

Disinfectant Wipe	Effective against C. diff Spores	Effective on Porous Surface
Quat[1]	✗	✗
Chlorine Bleach[2]	✔	✗
Hydrogen Peroxide	✗	✗
Hydrogen Peroxide/ Peracetic Acid	✔	✗

[1]Alcohol / Quaternary Ammonium [2]Sodium Hypochorite (Chlorine)

HELP YOUR HOSPITAL reduce C. diff rates

ONE HOSPITAL REDUCED C.DIFF RATES BY 53% AFTER SWITCHING TO A SINGLE-PATIENT-USE CUFF MODEL[2]

SINGLE-PATIENT-USE:
ASSIGN A NEW CUFF TO EACH PATIENT UPON ADMISSION

For more information, visit www.welchallyn.com/cuffs

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[1]Source: http://www.cdc.gov/vitalsigns/hai/
[2]Implementation of Disposable Blood Pressure Cuffs as a Novel Approach to Reduce Fomite Transmission of Healthcare-Associated (HCA) Clostridium difficile Infection (CDI) in a Community Hospital or Twice Implemented is Once Credible, American Journal of Infection Control, June 2009.]
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