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Economic Evaluation of Quality Improvement Interventions for Bloodstream Infections Related to Central Catheters
A Systematic Review

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IMPORTANCE Although quality improvement (QI) interventions can reduce central–line-associated bloodstream infections (CLABSI) and catheter-related bloodstream infections (CRBSI), their economic value is uncertain.

OBJECTIVE To systematically review economic evaluations of QI interventions designed to prevent CLABSI and/or CRBSI in acute care hospitals.

EVIDENCE REVIEW A search of Ovid MEDLINE, Econlit, Centre for Reviews & Dissemination, New York Academy of Medicine's Grey Literature Report, Worldcat, prior systematic reviews (January 2004 to July 2016), and IDWeek conference abstracts (2013-2016), was conducted from 2013 to 2016. We included English-language studies of any design that evaluated organizational or structural changes to prevent CLABSI or CRBSI, and reported program and infection-related costs. Dual reviewers assessed study design, effectiveness, costs, and study quality. For each eligible study, we performed a cost-consequences analysis from the hospital perspective, estimating the incidence rate ratio (IRR) and incremental net savings. Unadjusted weighted regression analyses tested predictors of these measures, weighted by catheter-days per study per year.

FINDINGS Of 505 articles, 15 unique studies were eligible, together representing data from 113 hospitals. Thirteen studies compared Agency for Healthcare Research and Quality–recommended practices with usual care, including 7 testing insertion checklists. Eleven studies were based on uncontrolled before-after designs, 1 on a randomized controlled trial, 1 on a time-series analysis, and 2 on modeled estimates. Overall, the weighted mean IRR was 0.43 (95% CI, 0.35-0.51) and incremental net savings were $1.85 million (95% CI, $1.30 million to $2.40 million) per hospital over 3 years (2015 US dollars). Each $100 000-increase in program cost was associated with $315 000 greater savings (95% CI, $166 000-$464 000; $P < .001$). Infections and net costs declined when hospitals already used checklists or had baseline infection rates of 1.7 to 3.7 per 1000 catheter-days. Study quality was not associated with effectiveness or costs.

CONCLUSIONS AND RELEVANCE Interventions related to central venous catheters were, on average, associated with 57% fewer bloodstream infections and substantial savings to hospitals. Larger initial investments may be associated with greater savings. Although checklists are now widely used and infections have started to decline, additional improvements and savings can occur at hospitals that have not yet attained very low infection rates.

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Supplemental content

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About 60 400 primary bloodstream infections related to central venous catheters (CVCs) occur in US hospitals each year, costing $1.85 billion.[1-3] Accordingly, hospitals are implementing various infection-prevention practices, such as insertion checklists or bundles.[4] Yet little is known about the economic value of doing so, meaning associated changes in clinical outcomes and costs.[5,6] The program costs associated with implementing such interventions have seldom been evaluated systematically, and it is unclear whether hospitals tend to incur net savings or losses.

We sought to systematically review economic evaluations of quality improvement (QI) interventions for the prevention of bloodstream infection related to the use of CVCs in the hospital setting, considering both program costs and changes in infection-related costs. To identify such studies, we searched peer-reviewed and non-peer-reviewed literature. We then examined the nature of interventions that have been evaluated, their clinical effectiveness, the associated costs, and the quality of the economic evaluations.

Key Points

Question Are quality improvement interventions designed to prevent bloodstream infections related to central catheters associated with lower infection rates as well as net savings to hospitals?

Findings In this systematic review based on data from 113 hospitals, on average, bloodstream infections declined by more than half and hospitals achieved net savings of $1.85 million over 3 years. Larger investments in the interventions were associated with greater net savings, and infections and costs declined even when checklists were already in use, and when baseline infection rates were as low as 1.7 to 3.7 per 1000 catheter-days.

Meaning Interventions that prevent bloodstream infections can be of high value to hospitals even after infections have started to decline.

Methods

This review is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines,[7] and a protocol is registered on Prospero (CRD42015014950).[8] An 8-member technical expert panel provided input at key stages.

Catheter-related bloodstream infection (CRBSI) is a diagnosis based on specific laboratory testing that identifies a catheter as the source of a bloodstream infection. In contrast, central line-associated bloodstream infection (CLABSI) is a less specific surveillance definition that reflects a bloodstream infection in the presence of a recent central line without another source of infection.[9,10] We included both.

Data Sources and Searches

A reference librarian developed search terms for CLABSI and CRBSI, and expanded on terms related to economic evaluation that have demonstrated sensitivity[11] (eAppendix 1 in the Supplement). Databases of peer-reviewed literature included Ovid MEDLINE, Econlit, and the Centre for Reviews and Dissemination Economic Evaluations. To identify gray literature, we searched New York Academy of Medicine's Grey Literature Report and Worldcat. We searched IDWeek conference presentations for unpublished analyses (2013 to 2016).[12] We searched for English-language publications (January 2004 to July 2016), and hand-searched citations from previous systematic reviews.[4,5,13-17] We excluded earlier studies because infection rates and clinical practices have changed over time.

Study Selection

Eligible studies represented original investigations, addressed QI interventions designed to prevent CLABSI and/or CRBSI in acute care hospitals, reported or estimated clinical effectiveness, measured or modeled costs of the QI intervention, compared alternatives (eg, QI intervention vs usual care), and reported both program and infection-related costs. We excluded studies from low-income to middle-income countries,[18] but included all ages, hospital settings, clinical study designs, cost evaluation approaches, analytical perspectives, and time horizons. A QI intervention was defined as "an effort to change/improve the clinical structure, process, or outcomes of care by means of an organizational or structural change."[19] Studies were ineligible if they tested novel materials or equipment but omitted costs associated with organizational efforts to support implementation.

Two trained reviewers independently examined titles, abstracts, and full-text publications to determine eligibility. Discrepancies were resolved by consensus, or, when necessary, through discussion with the research team.

Data Extraction and Quality Assessment

Pairs of investigators with training in quality of care and economic evaluation extracted data; discrepancies were resolved by consensus, or, when necessary, through discussion with the research team.

QI Intervention, Context, and Clinical Evaluation

For each study, reviewers extracted the nature of the QI intervention, setting, clinical study design and reporting, funding source, and findings. We identified practices strongly recommended in a recent Agency for Healthcare Research and Quality (AHRQ) evidence review, including components of insertion checklists.[4,20] Contextual variables included academic status (major, minor, nonteaching) and location (urban, suburban or small city, rural). Clinical study designs included randomized controlled trial, nonrandomized controlled trial, controlled before-after analysis, uncontrolled before-after analysis (UCBA), interrupted time series and repeated measures studies, and modeling exercises.[21] Reviewers extracted selected items from the Minimum Quality Criteria Set, a tool for critically appraising the reporting of QI interventions.[22] Funding sources included government, nonprofit, commercial, and none. Finally, reviewers extracted infection rates in intervention and comparison groups.

Economic Evaluation

Reviewers extracted the evaluation approach (cost analyses such as cost-consequences or business-case analyses vs cost-effectiveness and related analyses); perspective (hospital, health system, payer, society); time horizon; discount rate; year and currency of cost data; and incremental program, infection-related, and net costs.

To identify relevant costs in each article, we used the Quality-Cost Framework.[23] Together, structure and process-related costs comprise an intervention's program costs. Structure-related costs are fixed costs associated with start-up and maintenance, such as training providers, monitoring adherence, and making capital purchases (eg, ultrasound machines). Process-related costs are variable recurring costs associated with the care of individual patients, such as provider time spent on catheter-related care. Outcome-related costs are health care expenditures related to infections.

Study Quality

Reviewers assessed whether economic evaluations met basic standards using a modified version of the Quality of Health Economics Studies Checklist (mQHES).[24,25] Questions address whether the study objective is clear, the perspective is stated, cost and effectiveness estimates are from the best sources, and effects of uncertainty and variability are described. We divided each question into subparts for easier scoring and added 2 questions related to competing alternatives and overall credibility. To calculate total mQHES scores (scale, 0-115), we determined the percentage of "yes" responses to subparts of each question, weighted each question's raw score per QHES scoring guidelines[24] (using estimated weights for new questions), and summed weighted values.

Data Standardization

To facilitate comparisons, we performed a cost-consequences analysis from the hospital perspective for each study, where clinical and economic outcomes included the incidence rate ratio (IRR) and incremental net cost per hospital. If authors did not report an IRR, we calculated it by dividing the infection rate in the intervention group by the rate in the comparison group.

For each study, we standardized program and infection-related costs by converting to 2015 US dollars and discounting recurring costs over a 3-year time-horizon (discount rate, 3%).[26] Infection-related costs were based on numbers of infections averted multiplied by the cost per infection. We based the cost per infection on a recent meta-analysis ($51 770 in 2015 US dollars),[3] except for 2 studies in which authors reported site-specific estimates. Finally, to yield the incremental net cost, we summed standardized program and incremental infection-related costs (eAppendix 3 in the Supplement).

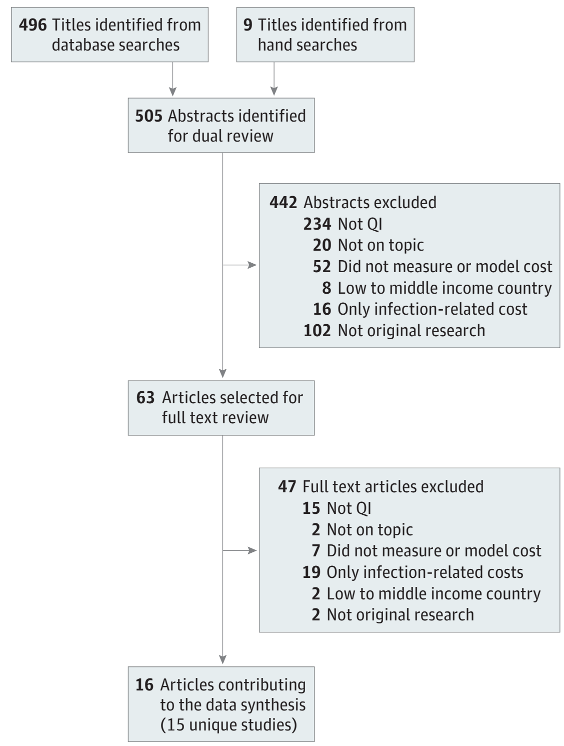
Analysis

To identify factors potentially associated with greater effectiveness (lower IRR) and savings (lower incremental net cost) among the studies, we conducted 7 sets of unadjusted weighted regression analyses. We separately examined 5 factors potentially associated with effectiveness (study size in CVC-days per study-year, measure of infection, baseline infection rate, whether interventions included use of checklists, and program cost) and 7 factors potentially associated with incremental net costs (same factors plus mQHES score and effectiveness). In each analysis (other than study size), we weighted each study by the number of CVC-days per study-year.

Quality improvement interventions were heterogeneous and generally included multiple components, limiting our ability to perform subgroup analyses. However, we were able to classify studies using 3 clinically relevant categories: (1) interventions involving checklists vs usual care (reference group); (2) other practices vs usual care; and (3) other practices vs usual care with checklists already in use.

In a series of sensitivity analyses, we sequentially dropped each of the 8 largest studies, and we dropped the 2 pediatric studies to determine whether results changed. There were too few studies for multivariate regression analyses, and not enough data on variance for inverse variance weighted meta-regression analyses.

Figure 1. PRISMA Flow Diagram



Results

Study Selection

We identified 505 records, selecting 63 for full-text review; 16 articles met all eligibility criteria, reflecting 15 unique studies.[27-42] Eleven articles focused on CLABSI,[27-29,32,33,36,37,39-42] and 5 on CRBSI.[30,31,34,35,38] Two articles drew from a study on CLABSI and ventilator-associated pneumonia. We focused on a cost analysis from the hospital perspective,[40] rather than a cost-effectiveness analysis from the societal perspective.[41] Another study addressed CLABSI, catheter-associated urinary tract infection, and ventilator-associated pneumonia.[28] Searches of gray literature did not identify eligible articles. Fifteen excluded studies tested materials or equipment but omitted costs associated with implementation.[15,43-56] See **Figure 1** for PRISMA diagram.

Study Characteristics and Quality Assessment

QI Interventions

One or more AHRQ-recommended practices were tested in 12 of the 15 unique studies (**Table 1**).[4,27-29,31-36,38-42] These included insertion checklists with 5 specific components (6 studies, plus 1 study with 4 components),[28,29,32,36,38-41] physician education (11 studies),[27-29,31,32,34-36,38-41] ultrasound-guided placement (3 studies),[29,33,38] all-inclusive catheter kits (5 studies),[27,28,35,38,39]

Table 1. Use of Practices Designed to Prevent CLABSI or CRBSI in Studies With Economic Evaluations

Practice	Allen et al,[27] 2014	Anderson et al,[28] 2011	Bond et al,[29] 2011	Burden et al,[30] 2012	Cohen et al,[31] 2010	Cooper et al,[32] 2014	Deutsch et al,[33] 2013	Fraher et al,[34] 2009	Frankel et al,[35] 2005	Herzer et al,[36] 2014	Kagan et al,[37] 2014	Kamboj et al,[42] 2015	Kim et al,[38] 2011	Miller et al,[39,62] 2010	Waters et al, 2011[40]/Dick et al,[41] 2015
Practices Strongly Recommended by AHRQ															
CVC checklists[a]	I, C	I	I	I, C	NU	I	NU	I, C	NU	I	I, C	I, C	I	I	I
Hand hygiene prior to catheter insertion[a,b]	I, C	I	I	I, C	NU	I	NU	I, C	NU	I	I, C	NU	I	I	I
Maximal sterile barrier precautions[a,b,c]	I, C	I	I	I, C	NU	I	NU	I, C	I, C	I	I, C	NU	I	I	I
Chlorhexidine skin antisepsis[a,b,c]	I, C	I	I	I, C	NU	I	NU	I, C	NU	I	I, C	NU	I	I	I
Avoidance of femoral and jugular sites[a,b]	I, C	I	I	I, C	NU	I	NU	I, C	I, C	I	I, C	NU	I	NU[d]	I
Remove nonessential catheters[a,b]	I, C	I	I	I, C	NU	I	NU	I, C	NU	I	I, C	NU	I	I	I
Antimicrobial catheters[a,c]	NU	I	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU
Chlorhexidine/silver sulfadiazine	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	I, C	NU	NU	NU	NU
Minocycline/rifampin	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU
All inclusive catheter carts or kits[a]	I	I	NU	I, C	NU	NU	NU	NU	I	NU	NU	NU	NU	I	NU
Disinfect hubs and needleless connectors[a]	NU	I	NU	NU	NU	NU	NU	NU	NU	NU	NU	I, C	NU	NU	NU
Ultrasound guided placement[a,b]	NU	NU	I	NU	NU	NU	I	NU	NU	NU	NU	NU	I	NU	NU
Cover catheter with sterile dressing[a,b]	I	I	NU	NU	NU	NU	NU	I, C	I	NU	NU	NU	I	I	NU
Chlorhexidine sponge[a] or antimicrobial dressing[c]	NU	I	NU	NU	NU	NU	NU	NU	NU	NU	NU	I, C	NU	I	NU
Education[a,b]	I	I	I	I, C	I	I	NU	I	I	I	NU	NU	I	I	I
Specialized catheter insertion teams[a]	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU
Other Practices															
Simulation-based training	I	NU	I	I	I	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU
Facility-wide surveillance and feedback[c]	I	I	I	NU	NU	NU	NU	NU	I	NU	NU	NU	I	I	NU
Reminders to consider removal	NU	NU	I	I, C	NU	NU	NU	NU	NU	NU	NU	NU	NU	I	NU
"Time out," empowering nurses to stop placement	I	NU	I	I, C	NU	NU	NU	NU	NU	NU	NU	NU	I	I	NU
Substitute midline catheter for central line in selected patients	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU	NU	NU	NU	NU
Reduce frequency of routine catheter changes[e]	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU
Reduce frequency of routine dressing, tubing, and cap changes	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	I	NU
Removal of lines placed in Emergency Department	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU
TPN surveillance by clinical nurse manager	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU	NU	NU	NU
Six sigma techniques	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU	NU	NU
Attending supervision of residents	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU	NU	NU
Specific documentation system	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU	NU	NU	NU
Disinfectant caps for catheters	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	NU	I	NU	NU	NU

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; C, practice used in control/usual care scenario; CDC, Centers for Disease Control and Prevention; CLABSI, central line-associated bloodstream infection; CVC, central venous catheter; I, practice used in intervention scenario; NU, practice not used; TPN, total parenteral nutrition.

[a] Strongly recommended in AHRQ Report, Making Healthcare Safer II.[4]

[b] Recommended by CDC guidelines.[9]

[c] Used in at least 25% of hospitals per national survey.[63]

[d] Not used because, per authors, femoral site is preferred in pediatric patients.[39,62]

[e] CDC guidelines recommend against routine replacement of central venous catheters.[9]

sterile dressings (5 studies),[27,28,35,38,39] chlorhexidine gluconate sponge or antimicrobial dressing (2 studies),[28,39] antimicrobial catheters (2 studies, one of which did not specify the antimicrobial agent).[28,35]

Other practices tested included: simulation-based training (4 studies),[27,29-31,35] facility-wide audit and feedback (5 studies),[27-29,35,38,39] "time out" or empowering nurses to stop placement (4 studies),[27,29,38,39] reminders to remove lines (2 studies),[29,39] and disinfectant caps for catheter hubs.[42] Seven studies had 1 or more unique practices.[33-35,37-39,42] No eligible studies considered daily bathing with chlorhexidine gluconate or intervention sustainability.

Investigators compared interventions involving checklists vs usual care in 7 studies,[28,29,32,36,38-41] other practices vs usual care in 3 studies[31,33,35] (although in 1, the usual care scenario included 2 common components of checklists),[35] and other practices vs usual care with checklists already in use in 5 studies.[27,30,34,37,42]

The 15 studies excluded because they omitted implementation costs examined maximum sterile barriers[47]; antibiotic-impregnated CVCs[45,46,49,51,52]; antimicrobial dressings,[15,44,48,53] 1-piece vs 2-piece chlorhexidine-gluconate-impregnated dressings,[43] chlorhexidine gluconate vs providone-iodine solutions for insertion site care,[49] standardized maintenance kits vs ad hoc supplies,[54] and disinfection caps for CVC hubs vs scrubbing the hubs.[55,56]

Context

Thirteen of the 15 unique studies (**Table 2**) were based in the US,[27-31,33,35-42] 1 in the United Kingdom,[32] and 1 in Ireland.[34] Most studies were set at a single hospital, although 1 study included 24 hospitals,[28] 1 study included 37 hospitals,[32] 1 study included 29 pediatric intensive care units (ICUs),[39] 2 studies included data from 6 hospitals each,[36,40,41] and 1 study was based at 2 affiliated hospitals.[29] In total, data were from 113 hospitals. Ten studies were based at only major academic institutions,[27,30,31,33-38,42] 2 studies were based at only community hospitals,[28,32] 2 studies were based at both,[29,40,41] and 1 study did not state academic status.[39]

All studies included or were limited to intensive care settings. The median estimated number of CVC-days per hospital per year was 3843 (interquartile range [IQR], 2917).[27-42] One study based at an oncology hospital had 40 711 CVC-days per year.[42] Two studies were limited to pediatric populations.[37,39] The median baseline rate of CLABSI and/or CRBSI was 4.0 (IQR, 4.3) per 1000 catheter-days among the 15 unique studies[27-40]; this equated to a median of about 18.3 infections per study hospital per year (IQR, 17.3).

Clinical Evaluation

The 15 unique studies compared the QI interventions with usual care scenarios (Table 2). Ten studies used UCBA designs[27,28,30,31,34,35,37,38,40-42] and 1 used a time-series analysis.[39] Four of the unique studies reported modeling exercises, including 1 based on a randomized controlled trial and 1 based on a UCBA design.[29,32,33,36,41]

In total, 13 studies, including 2 of the modeling analyses, used empirical data on changes in infection rates.[27,28,30-32,34-42] One modeling study of insertion checklists assumed a 50% decline in infections,[29] which is similar to prior literature.[64] Another modeling study estimated a decline in infections based on changes in CVC-days.[33] Excluding the study that assumed a 50% decline, the median IRR was 0.42 (IQR, 0.47),[27,28,30-41] which equated to a median of about 2.8 fewer infections per 1000 CVC-days (IQR, 2.6) and 9.8 (IQR, 12.2) fewer infections per study hospital per year.

Items from the minimum quality data set are given in eAppendix 2 in the Supplement.

Cost Evaluation

As noted, a cost-effectiveness analysis taking the societal perspective[41] and a cost analysis taking the hospital perspective were based on the same study.[40] Two other studies were cost-effectiveness analyses[32,36]; 1 considered the hospital perspective,[27,30,31,34,36,37] and 1 the health system perspective.[32] The remaining 12 studies were cost analyses; 11 used the hospital perspective[27-31,33-35,37,38,40,42] and 1 used the health system perspective.[39]

Among the 15 studies, the resources invested in infection prevention and the associated program costs varied. Six studies estimated start-up costs (standardized median, $108 000; IQR, $92 500),[29,31,33,36,38,40] such as the purchase of ultrasound machines,[29,31,38] vascular simulators, such as mannequins,[27,29-31,35] and vascular access carts.[31,38,40] All 15 studies estimated annually recurring costs (standardized median, $29 600 per year; IQR, $37 900),[27-40,42] such as catheters and supplies[27,30,31,33,35,37-40] and labor costs associated with time that physicians and nurses spent in training,[27-31,35,38,40] catheter-related care,[30,32,33,35,37,38,40,42] documentation,[27,29,38] data collection and analysis,[27-31,35,38-40] and leadership and oversight.[28,35,40] Program costs were negative in 2 studies: 1 substituted placement of peripheral midline catheters by resident physicians for placement of central lines by interventional radiologists,[33] and the other reduced the frequency of routine catheter changes.[37]

Study Quality

Cost evaluation methods were of moderate to high quality (**Table 3**), with median mQHES scores of 100.5 (IQR, 8.3) among the 16 articles.

Data Standardization

Among the 15 unique studies, the median total program cost per hospital over 3 years was $271 000 (IQR, $417 000), and the median incremental infection-related cost was −$2.27 million (IQR, $2.16 million),[27-42] relative to usual care. Based on differences between program and incremental infection-related costs, the median net savings was $1.85 million (IQR, $1.77 million)[27-42] (**Figure 2**). These estimates are unweighted. Program costs could be more than 6.8-fold higher than we observed before net savings would be eliminated.

Among the 7 studies testing checklists, the median net savings was $1.12 million (IQR, $1.31 million).[28,29,32,36,38-41] In the study that assumed a 50% decline in infections, there was a net loss of $90 000 owing to a low baseline rate of CLABSI (1.0 per 1000 CVC-days) and relatively high program cost ($400 000).[29] Six studies with lower baseline infection rates (1.7 to 3.7 CLABSI per 1000 CVC-days) were associated with declines in infections as well as net savings.[28,29,32,33,37,42]

Analysis

In unadjusted regression analyses weighted by CVC-days per study per year, the mean IRR among the 15 studies was 0.43 (95% CI, 0.35-0.51) (Table 3), reflecting a 57% decline in infections. Compared with

Table 2. Summary of Data Extracted From Economic Evaluations for QI Interventions Designed to Prevent CLABSI and CRBSI

	QI Intervention and Clinical Evaluation						Cost Evaluation						
Source	Intervention Components	Setting	Population	Design and Comparator	Baseline Rate of Infection	Effectiveness	Approach and Perspective	Start-up Program Costs in Year 1	Recurring Program Costs in Year 1 and Beyond	Infection-Related Costs	Incremental Net Cost	Year of Costs	mQHES Score
Use of CVC Checklists													
Anderson et al,[28] 2011	Checklists, audit and feedback for CLABSI, CAUTI, VAP, MRSA	US, 24 hospitals, community	Population NR	UCBA, usual care	3.7 CLABSI per 1000 CVC-days	IRR, 0.53	Cost analysis, hospital	NR	\$20 000 to \$40 000 per hospital per year	−\$82 722 to −\$159 902 per hospital per year (literature)	−\$7.94 million to −\$15.4 million over 24 hospitals over 5 years	2010	102
Bond et al,[29] 2011	Checklists, simulation-based training, "time out," audit and feedback	US, 800-bed hospital system with 1 academic and 1 community hospital	Patients with CVCs placed outside of operating room, including children	Model based on assumption, usual care	1 CLABSI per 1000 CVC-days	Authors assumed 50% decline	Cost analysis, hospital	\$106 750 for 2-hospital system	\$63 610 for 2-hospital system per year	−\$16 350 per infection averted (literature)	First year: \$223 per catheter; Later years: \$44 per catheter	2009	101
Cooper et al,[32] 2014	Checklists	UK, 37 ICUs, community	Patients in ICUs, age NR	Model based on UCBA, usual care	1.31 CLABSI per 100 ICU patients (3.7 per 1000 CVC-days)	IRR, 0.40	CEA, health system	NR	£1548 per 100 ICU patients	−£3940 per infection averted (literature)	−£1557 per 100 ICU patients; −£573 per QALY	2011	106
Herzer et al,[36] 2014	Checklists	US, 6 hospitals, academic	Adults in ICUs	Model based on RCT, usual care	CLABSI in 5.2% of 423 ICU patients with catheters per year (literature)	IRR, 0.19 (95% CI, 0.06-0.57)	CEA, hospital	\$83 725 per hospital	\$192 291 per hospital per year	−\$18 793 per infection averted (literature)	−\$249 000 per 1000 ICU patients with catheters	2013	113
Kim et al,[38] 2011	Checklists, audit and feedback, "time out"	US, 1 hospital, academic	Patients in ICUs, age NR	UCBA, usual care	9.0 CRBSI per 1000 CVC-days	IRR, 0.70 (95% CI, 0.59-0.77)	Cost analysis, hospital	\$100	\$0	−\$32 254 per infection averted (literature and site data)	−\$32 254 per infection averted	2009	85
Miller et al,[39] 2011	Checklists, catheter kits and care, "time out"	US, 29 hospitals	Children in pediatric ICUs	Time series, usual care	5.2 CLABSI per 1000 CVC-days	IRR, 0.44 (95% CI, 0.37-0.53)	Cost analysis, health system	NR	\$75 000 per hospital per year	−\$45 000 per infection averted (literature)	−\$31 million for 29 hospitals over 3 years	2009	99
Waters et al,[40] 2011	Checklists for CLABSI and VAP	US, 6 hospitals, academic and community	Patients in ICUs, age NR	UCBA, usual care	7.7 CLABSI per 1000 CVC-days	IRR, 0.14	Cost analysis, hospital	\$64 420 per hospital (2004)	\$146 973 per hospital per year (2008)	−\$36 500 per infection averted (literature)	−\$1.1 million per hospital per year	2004-2008	105
Dick et al,[41] 2015	Checklists for CLABSI and VAP	US, 6 hospitals, academic and community	Elderly patients in ICUs	Model based on UCBA, usual care	5.0 CLABSI per 1000 CVC-days	IRR, 0.24 based on prior literature	CEA, society	Excluded	\$145 000 per hospital per year	Inpatient plus outpatient costs (literature)	\$26 996 per QALY	2013	111

(continued)

Table 2. Summary of Data Extracted From Economic Evaluations for QI Interventions Designed to Prevent CLABSI and CRBSI (continued)

	QI Intervention and Clinical Evaluation						Cost Evaluation						
Source	Intervention Components	Setting	Population	Design and Comparator	Baseline Rate of Infection	Effectiveness	Approach and Perspective	Start-up Program Costs in Year 1	Recurring Program Costs in Year 1 and Beyond	Infection-Related Costs	Incremental Net Cost	Year of Costs	mQHES Score
Use of Other Practices Strongly Recommended by AHRQ													
Allen et al,[27] 2014	Simulation-based training, all-inclusive kits	US, 1 hospital, academic	Patients in medical and surgical ICUs	UCBA, usual care	2.0 CLABSI per 1000 CVC-days	IRR, 0.37	Cost analysis, hospital	NR	$13 043 per hospital per year	−$71 165 per infection averted (site data)	−$1.67 million per hospital over 3 years	2009	93
Frankel et al,[35] 2005	Six Sigma, antimicrobial catheters, kits, others	US 1 hospital, academic	Patients in a surgical ICU	UCBA, usual care	11.0 CRBSI per 1000 CVC-days	IRR, 0.15	Cost analysis, hospital	NR	$5000 per hospital per year	−$3000 per infection averted	−$66 000 per hospital per year	2002	94
Use of Other Practices													
Burden et al,[30] 2012[O]	Simulation-based training	US, 1 hospital, academic	Patients in ICUs, age NR	UCBA, usual care	6.5 CRBSI per 1000 CVC-days	IRR, 0.38	Cost analysis, hospital	NR	$64 487 per hospital per year	−$23 472 per infection averted (literature)	−$539 902 per hospital over 2 years	2008	103
Cohen et al,[31] 2010	Simulation-based training	US, 1 hospital, academic	Medical and surgical patients in an ICU	UCBA, usual care	4.2 CRBSI per 100 ICU patients with catheters	IRR, 0.10	Cost analysis, hospital	$111 916 per hospital	$89 455 per hospital per year	−$82 730 per infection averted (site data)	−$704 034 per hospital per year	2008	111
Deutsch et al,[33] 2013	Substitute midline for central line	US, 1 hospital, academic	Adults in a surgical ICU	Model based on catheter days avoided, usual care	1.7 CLABSI per 1000 CVC-days (literature)	−283 CVC-days per ICU per 6 months (IRR, 0.72)	Cost analysis, hospital	$30 000	−$1413 per CVC, 60 CVCs per hospital per year	−$29 156 per infection averted (literature)	NR	2011	87
Fraher et al,[34] 2009	TPN surveillance nurse	Ireland, 1 hospital, academic	Patients in ICUs and wards, age NR	UCBA, usual care	20.5 CRBSI per 1000 CVC-days	IRR, 0.71	Cost analysis, hospital	NR	€56 700 per hospital per year	−€13 775 per infection averted	−€78 300 per hospital per year	2007	99
Kagan et al,[37] 2014	Reduced frequency of routine catheter changes	US, 1 children's hospital, academic	Children with burns, unit type NR	UCBA, usual care	3.1 CLABSI per 1000 CVC-days	IRR, 0.90 (NS)	Cost analysis, hospital	NR	$100 per CVC change, 280 fewer changes per year	$0 owing to lack of effectiveness	−$28 000 per hospital per year	2009	98
Kamboj et al,[42] 2014	Change from scrubbing CVC hubs to using disinfection caps	US, 1 cancer hospital, academic	Oncology patients	UCBA, usual care	2.46 CLABSI per 1000 CVC-days	IRR, 0.711 (95% CI, 0.56-0.87)	Cost analysis, hospital	NR	$202 707 per hospital per year	−$3 471 696 per hospital per year	−$3 268 990 per hospital per year	2012	100

Abbreviations: CAUTI, catheter-associated urinary tract infection; CEA, includes cost-effectiveness, cost-benefit, and related analyses; CLABSI, central line-associated bloodstream infection; CRBSI, catheter-related bloodstream infection; CVC, central venous catheter; ICU, intensive care unit; IRR, incidence rate ratio; MRSA, methicillin-resistant staph aureus; mQHES, modified Quality of Health Economics Studies Checklist; NR, not reported; QALY, quality-adjusted life-year; QI, quality improvement; RCT, randomized controlled trial; TPN, total parenteral nutrition; UCBA, uncontrolled before-after analysis; US, United States; UK, United Kingdom; VAP, ventilator-associated pneumonia.

Table 3. Results of Weighted Regression: Associations Between Setting, Study, and Intervention Characteristics and Predicted Incidence Rate Ratio (IRR) or Incremental Net Cost per Hospital Over 3 Years

Characteristics and Subgroups Being Compared	No.[a]	Incidence Rate Ratio (95% CI)	*P* Value for Characteristic	Incremental Net Cost in Millions (95% CI), $	*P* Value
Results including all 15 studies	15	0.43 (0.35 to 0.51)		−1.85 (−2.40 to −1.30)	
Study size					
≥40 000 CVC days per study per year	4	0.52 (0.27 to 0.77)	.61	−1.78 (−3.03 to −0.53)	.95
<40 000 CVC days per study per year	11	0.44 (0.29 to 0.59)		−1.74 (−2.49 to −0.98)	
Measure of Infection					
CLABSI	10	0.43 (0.36 to 0.50)	.73	−1.84 (−2.36 to −1.31)	.82
CRBSI	5	0.35 (0 to 0.82)[b]		−2.24 (−5.60 to 41.11)	
Baseline rate of infection[c]					
Weighted mean rate, 4.49 per 1000 CVC days	15	0.43 (0.36 to 0.49)	.08	−1.85 (−2.35 to −1.35)	.31
10% higher, 4.94 per 1000 CVC days	15	0.41 (0.34 to 0.48)		−1.92 (−2.44 to −1.40)	
Program cost per hospital over 3 years					
Weighted mean cost, $290 000	15	0.43 (0.36 to 0.50)	.48	−1.85 (−2.19 to −1.51)	<.001
$100 000 higher, $390 000		0.42 (0.34 to 0.50)		−2.16 (−2.54 to −1.79)	
Types of infection-prevention practices evaluated					
Checklists vs usual care	7	0.40 (0.34 to 0.47)	[Reference]	−1.66 (−2.16 to −1.16)	[Reference]
Other practices vs usual care	3	0.20 (0 to 0.75)[c]	.48	−2.76 (−7.07 to 1.55)	.63
Other practices vs usual care with checklists	5	0.65 (0.47 to 0.83)	.03	−3.17 (−4.55 to −1.79)	.07
Effectiveness					
Weighted mean IRR, 0.43	15	NA		−1.85 (−2.37 to −1.33)	.89
10% higher, 0.47				−1.84 (−2.38 to −1.29)	
Study quality					
Weighted mean mQHES score, 103	15	NA		−1.84 (−2.35 to −1.35)	.33
10% higher, 113				−1.29 (−2.46 to −0.12)	

Abbreviations: CLABSI, central-line-associated blood-stream infection; CRBSI, catheter-related bloodstream infection; CVC-days, central-venous catheter-days; IRR, incidence rate ratio; NA, not applicable.

[a] Number of studies in group.

[b] IRRs cannot be less than 0; therefore, we truncated any values below zero.

[c] For characteristics that involve continuous variables (baseline rate of infection, program cost, effectiveness, and study quality), we report results for 2 values, the mean for the variable and, generally, a value 10% higher. *P* values reflect the significance of the characteristic overall, not the specific values selected.

studies that tested use of checklists, infections declined less in studies that tested other practices when checklists were already in use (IRR, 0.40 vs 0.65; *P* = .03).

The mean incremental net savings was $1.85 million (95% CI, $1.30 million to $2.40 million) over 3 years. Larger investments in infection prevention (program costs) were associated with greater net savings (*P* = .001): each additional $100 000 invested was associated with $315 000 (95% CI, $166,000-$464,000) higher savings.

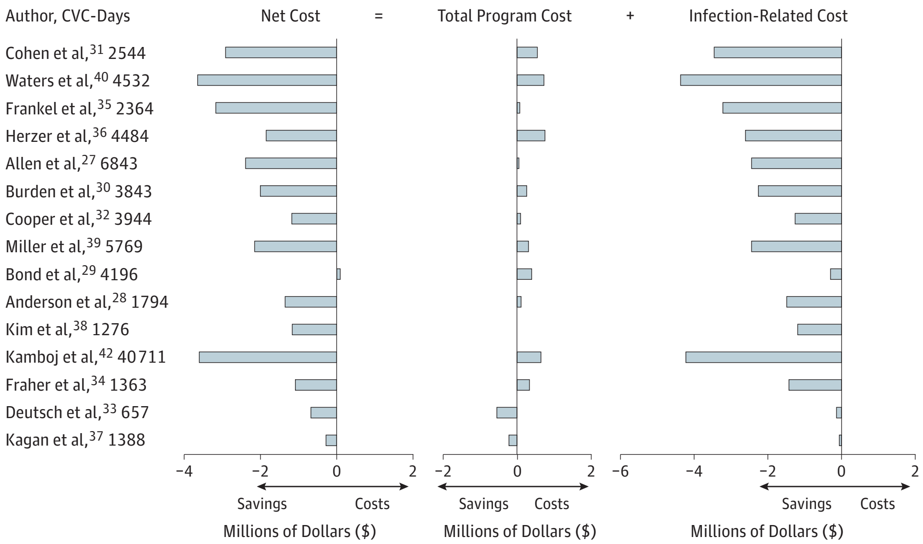
These results were robust to sequential elimination of the largest studies and the 2 pediatric studies, with 1 notable exception. The oncology study had a relatively high IRR (0.711) and incremental net savings (−$3.85 million) as well as ten times more CVC days than other hospitals. Excluding this study, the type of infection-prevention practice tested was no longer associated with effectiveness. However, investments in infection prevention were associated with greater effectiveness (*P* = .002): each additional $100 000 invested was associated with 4% greater effectiveness (IRR, 0.40 vs 0.36), or approximately 2.4 fewer infections per hospital. In addition, a higher baseline infection rate and greater effectiveness were both associated with larger net savings (eAppendix 4 in the Supplement).

Discussion

Based on our analysis, QI interventions that are effective at reducing bloodstream infections related to CVCs are generally a good value for hospitals because they are associated with improved clinical outcomes and lower costs. We identified 15 eligible, unique economic evaluations that together included data from 113 hospitals.[27-42] Most interventions involved practices strongly recommended by AHRQ.[4,27-29,31-36,38-41] On average, these interventions were associated with a 57% decline in infections (IRR, 0.43; 95% CI, 0.35-0.51) and net savings of $1.85 million (95% CI, $1.30 million to $2.40 million) per hospital over 3 years.[27-41] Each additional $100 000 invested was associated with $315 000 greater net savings in unadjusted analyses. Larger investments were also associated with greater effectiveness when the study from an oncology hospital was excluded.[42]

In assessing value, both clinical effectiveness and cost are important.[6] The effectiveness of the interventions we studied was similar to prior studies.[4,65] One meta-analysis reported pooled odds ratios for CLABSI of 0.34 (95% CI, 0.27-0.41) for interventions with

Figure 2. Net Costs Associated With Prevention of CLABSI and/or CRBSI Interventions From the Hospital Perspective Over 3 Years (2015 US Dollars)



checklists vs usual care, and 0.45 (95% CI, 0.36-0.55) for interventions without checklists.[65] Another meta-analysis that compared checklists with usual care reported a pooled IRR for CLABSI of 0.44 (95% CI, 0.39-0.50) among 79 primary studies.[64] (Herein, we refer to CLABSI or CRBSI when the literature cited does).

To determine the total cost of an intervention, both program and infection-related costs should be considered. Yet prior literature has emphasized infection-related costs.[3,16] To our knowledge, until now there has been no synthesis of program costs—meaning the value of the resources that hospitals invest in infection prevention, such as equipment, supplies, and time spent by physicians and nurses on planning, training, clinical care, and surveillance. Our results suggest that effective interventions tend to be a good value for hospitals, despite the program costs involved.

Hospitals have come under increasing pressure to invest in preventing health care associated infections (HAIs) over the past decade, and federal and state policymakers have partnered together and with stakeholder groups to eliminate HAIs.[66-69] The Centers for Medicare and Medicaid Services (CMS) have established multiple incentives to reduce HAIs including CLABSI, including public reporting, nonpayment for hospital-associated complications, value-based purchasing, and, starting in 2015, sizeable payment penalties.[70-73] Accordingly, the use of prevention practices has risen substantially since 2005, and infection rates have declined.[74,75] A 2013 national survey found that 98% to 99% of hospitals used 2 common insertion checklist components (maximum barrier precautions and chlorhexidine site antisepsis), 90% monitored rates hospital-wide, 78% used antimicrobial dressings, 34% used antimicrobial catheters.[63] According to AHRQ, from 2010 to 2013, rates of CLABSI fell by 49%, averting 8800 infections as well as $150 million in infection-related costs.[68] Rates of CLABSI in medical and surgical ICUs reached 0.8 to 1.4 per 1000 CVC-days as of 2013.[74] Net savings from these changes may have been somewhat smaller than AHRQ's estimates, which did not account for program costs.

Now that checklists are used widely and infection rates have declined, what are the prospects for additional reductions in infections and net savings? Hospitals that have already attained very low infection rates would likely see smaller clinical benefits and savings than in the studies we have reviewed. Nonetheless, we found that QI interventions can be associated with declines in CLABSI and/or CRBSI and net savings when checklists are already in use,[27,30,34,37,42] and when hospitals have CLABSI rates as low as 1.7 to 3.7 per 1000 CVC-days.[27,28,32,33,37,42]

Despite the possibility of net savings, investing in the prevention of HAIs like CLABSI and CRBSI may be burdensome for hospitals with limited financial resources. Prevention of HAIs is labor intensive, wages and benefits account for two-thirds of all spending by hospitals, and a quarter of hospitals have had negative operating margins in recent years.[76] We found that, for CLABSI- and CRBSI-prevention interventions, median program costs were about $270 000 per hospital over 3 years—but reached $500 000 to $750 000 in some studies. Higher program costs were generally associated with greater net savings and possibly larger declines in infection rates. This suggests that both patients and hospitals might benefit when hospitals invest more in effective prevention programs. However, we were unable to control for hospital characteristics. Hospitals with ample financial resources, for example, may both invest more heavily in HAI prevention and have better trained providers who implement interventions more effectively. Even if some hospitals can achieve greater net savings from larger, costlier HAI prevention programs, success is not assured and many hospitals may lack the cash flow or other resources to make sizeable up-front investments.[77] Future research should more thoroughly examine the relationships among hospital financial performance, economic investments in QI, and effects on quality of care.

Limitations

This analysis had several limitations. Only a few studies have examined the cost of QI interventions related to CLABSI and/or

CRBSI, and most of these used weak uncontrolled before-after designs. We could only include interventions for which economic evaluations have been performed. Studies used 2 different measures of infection; CLABSI is a more sensitive measure, but eligible studies using CRBSI reported relatively high rates of infection (4.0-28.3 CVC-days per 1000 patient-days).[30,31,34,35,38] We were unable to identify specific practices that are associated with higher value owing to the complexity of the interventions, or to assess the role of contextual factors. Nonetheless, these findings reflect more than 100 sites, and the changes in CLABSI rates we observed are consistent with other sources. We were unable to formally test for publication bias, but found no evidence that lower quality studies with greater net savings were published preferentially. Authors may have omitted some program costs; however, a several-fold underestimate would be needed to eliminate the net savings. We attributed all inpatient infection-related costs to the hospital perspective, when private payers may reimburse some of these costs. We did not account for Medicare policies that preclude payment and impose penalties for hospital-acquired infections, which may underestimate benefits to hospitals.

Conclusions

Interventions designed to prevent CLABSI were, on average, associated with a 57% decline in infections as well as $1.85 million net savings to hospitals within 1 to 3 years, making them of high value to hospitals. Interventions that involve larger initial investments of resources may be associated with greater net savings. Although checklists are now widely used and infection rates have declined, additional improvements and cost savings can occur at hospitals that have not yet attained very low infection rates.

ARTICLE INFORMATION

Correction: This article was corrected online on December 5, 2016. The title was changed to clarify what types of studies were included in the analysis.

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Concept and design: Nuckols, Shekelle.
Acquisition, analysis, or interpretation of data: Nuckols, Keeler, Morton, Doyle, Booth, Shanman, Grein, Shekelle.
Drafting of the manuscript: Nuckols, Morton, Shanman.
Critical revision of the manuscript for important intellectual content: Nuckols, Keeler, Morton, Doyle, Booth, Grein, Shekelle.
Statistical analysis: Nuckols, Keeler, Morton, Doyle, Booth.
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