Prevention of Central Line–Associated Bloodstream Infections Through Quality Improvement Interventions: A Systematic Review and Meta-analysis

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This systematic review and meta-analysis examines the impact of quality improvement interventions on central line–associated bloodstream infections in adult intensive care units. Studies were identified through Medline and manual searches (1995–June 2012). Random-effects meta-analysis obtained pooled odds ratios (ORs) and 95% confidence intervals (CIs). Meta-regression assessed the impact of bundle/checklist interventions and high baseline rates on intervention effect. Forty-one before–after studies identified an infection rate decrease (OR, 0.39 [95% CI, .33–.46]; P < .001). This effect was more pronounced for trials implementing a bundle or checklist approach (P = .03). Furthermore, meta-analysis of 6 interrupted time series studies revealed an infection rate reduction 3 months postintervention (OR, 0.30 [95% CI, .10–.88]; P = .03). There was no difference in infection rates between studies with low or high baseline rates (P = .18). These results suggest that quality improvement interventions contribute to the prevention of central line–associated bloodstream infections. Implementation of care bundles and checklists appears to yield stronger risk reductions.

Keywords. central line–associated bloodstream infection; catheter-related bloodstream infection; quality improvement intervention; meta-analysis.

Central venous catheters are indispensable devices in the intensive care unit (ICU), necessary for infusion of medication, fluid, or blood products; hemodialysis; blood withdrawal; or hemodynamic monitoring. However, these invasive devices predispose patients to preventable central line–associated bloodstream infections (CLABSIs), defined as bloodstream infections in patients with a central line 48 hours before infection onset, not related to another site (Table 1). CLABSIs are associated with increased morbidity, leading to increased length of hospitalization and resource use [3, 4], and might impact mortality and compromise patient prognosis [5–7].

Infection prevention measures during central line insertion or maintenance, such as hand hygiene, maximal sterile barriers during catheter insertion, chlorhexidine skin disinfection, optimal catheter site selection, and daily review of line necessity with prompt removal of unnecessary lines, are known to decrease CLABSI risk [8, 9]. The Institute for Healthcare Improvement (IHI) recommends use of aforementioned items, in a central line care bundle, to decrease CLABSI occurrence. Despite the availability of evidence-based interventions summarized in guidelines [10, 11], CLABSI remains a substantial threat for hospitalized patients, with pooled estimated mean occurrence rates of 4.4 CLABSIs per 100 devices inserted (95% confidence interval [CI], 4.1–4.9) and 2.7 CLABSIs per 1000 catheter-days (95% CI, 2.6–2.9) [12]. In recent years, it has become clear that the limiting factor to infection prevention resides in the
Abbreviations: CLABSI, central line for Central Line

Medline was systematically searched (1995–June 2012) through a combination of search terms: catheter-related infections/prevention and control; catheterization, central venous/adverse effects; catheters, indwelling/adverse effects; infection control/methods; infection control/standards; intensive care units; quality control; quality of healthcare; and bundle (Supplementary Appendix 1). Extra studies were identified via reference lists, manually and through Ovid and ScienceDirect databases.

Study Selection

Eligible studies used before–after, interrupted time series (ITS), controlled before–after, nonrandomized controlled trial, or randomized controlled trial study designs that complied with the Cochrane Effective Practice and Organisation of Care Group methodological criteria. ITS studies report at least 3 data points before and after a defined point in time in which the intervention is implemented. Participants consisted of adult ICU patients with central line catheters. Trials implemented quality improvement interventions aimed at increasing professional adherence to evidence-based infection prevention processes. The primary outcome measure was the number of CLABSIs per catheter-days pre- and postintervention. Only English-language papers were included. Medline search results were screened by title and abstract. Selected papers underwent a full-text assessment, and eligibility issues were resolved between authors.

Data Extraction

Extracted data included author and year of publication, settings and study populations, study designs and periods, quality improvement and preventive interventions implemented in the baseline and intervention periods, compliance measures, number of CLABSI and catheter-days, and applied CLABSI definitions. Study authors were not contacted for additional data. To obtain effect sizes for ITS studies, infection rate data were extracted from study figures using the program Plot Digitizer. Results reported as a mix from both included and excluded study participants were included. Quality improvement interventions were classified under general headers (Table 2), and only preventive interventions described by Centers for Disease Control and Prevention (CDC) guidelines [10] and applicable to the majority of ICU patients were noted.

Quality Assessment

The Downs and Black checklist ascertained study methodological risk of bias [17]. It consists of 27 questions that evaluate the reporting, external validity, internal validity, and power of non-randomized studies of healthcare interventions. Studies were scored based on these item criteria, adapted for CLABSI prevention research.

Statistical Analysis

A random-effects meta-analysis using the DerSimonian-Laird estimator obtained odds ratios (ORs) and 95% CIs for CLABSI rate reductions. The Higgins $\hat{I}^2$ test was predefined to quantify heterogeneity ($\hat{I}^2 \leq 25\%$ for low, $25\% < \hat{I}^2 < 50\%$ for moderate, and $\hat{I}^2 \geq 50\%$ for high), and funnel plots assessed publication bias. Subgroup analysis through meta-regression for before–after study designs compared studies with or without bundle/

### Table 1. Centers for Disease Control and Prevention Definitions for Central Line–Associated Bloodstream Infection Terminology

<table>
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<tr>
<th>Terminology</th>
<th>Definition</th>
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<tr>
<td>CLABSI</td>
<td>An LCBI where a central line was in place for &gt;2 calendar days and a central line was in place on the date of event or the day before.</td>
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<tr>
<td>LCBI</td>
<td>To be defined as LCBI, it must meet 1 of the following criteria: (1) Patient has a recognized pathogen cultured from 1 or more blood cultures, and organism cultured from blood is not related to an infection at another site; (2) Patient has at least 1 of the following signs or symptoms: fever (&gt;38°C), chills, or hypotension, and positive laboratory results are not related to an infection at another site and the same common commensal is cultured from 2 or more blood cultures drawn on separate occasions.</td>
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Central line days A daily count of the number of patients with a central line in the patient care location during a time period. A patient with multiple central lines for a day only counts as 1 central line day.

Patient-days A daily count of the number of patients in the patient care location during a time period.

Device utilization ratio Central line utilization ratio is calculated by dividing the number of central line days by the number of patient-days.

Adapted from the Centers for Disease Control and Prevention [1, 2].

Abbreviations: CLABSI, central line–associated bloodstream infection; LCBI, laboratory-confirmed bloodstream infection.
checklist interventions, baseline rates above or below 4.0 CLAB-SIs per 1000 catheter-days, and power scores above or below 0.75. Univariate analysis calculated changes in device utilization rates. Sensitivity analysis identified heterogeneous studies that influenced the meta-analysis.

Monthly ITS data were standardized for meta-analysis by dividing the outcome and standard error (SE) by the standard deviation (SD) of the preintervention trend. One study reported annual data points, which were used for the 12- and 24-month follow-up analyses [18]. SPSS version 22 calculated the intervention effect using segmented time series regression analysis, adjusting for time trend and autocorrelation. A negative change in level or slope indicated an infection rate reduction [19]. A P value <.05 was considered statistically significant.

RESULTS

The search algorithm identified 634 records (627 in PubMed and 7 in Ovid and ScienceDirect). Forty-three studies, published in English between January 1995 and June 2012 involving 584 ICUs, were included for meta-analysis (Figure 1). Two studies [20, 21] continued their quality improvement initiatives and republished old data with new results [9, 22]. The older study by Coopersmith et al [20] was included for ITS analysis, and the
article by Pronovost et al [21] was accessed to supplement information. One trial was not included for subgroup analysis because, although pre- and postintervention initiatives were qualitatively different, no new intervention types were implemented [23]. Another study included multiple data sets, of which the set with the longest follow-up period was chosen [24]. Eleven studies could not be included for ITS analysis because they implemented interventions in a stepwise manner [22, 23, 25–33].

The 43 studies involved primarily medical-surgical ICUs, implemented quality improvement interventions without simultaneously introducing novel prevention measures, and applied CDC methods and definitions for CLABSI diagnosis (Supplementary Appendix 2).

The 584 included ICUs consisted of 564 adult, 11 pediatric [24, 34, 35], and 9 neonatal units [24]. Four studies reported the number of adult ICUs studied, but did not specify the ICU type (n = 270) [35–38]. The remaining 294 adult ICUs involved medical-surgical (n = 135), medical (n = 51), and surgical (n = 61).

The meta-analysis consisted of 35 before–after [8, 22, 24, 26–28, 33–61], 7 ITS [18, 20, 40, 62, 63, 64, 65], and 1 controlled before–after study [66]. Five ITS studies were included in the meta-analysis of before–after study designs [18, 40, 63–65].

Duration of study periods ranged from 9 months [58] to 180 months [18], with a mean length of 26.75 months.

Up to 14 different types of interventions were reported. Studies introduced multiple quality improvement interventions in different combinations, usually implementing 1–5 interventions (n = 34). Four studies implemented initiatives through improvement systems such as plan-do-study-act, Six Sigma, and root cause analysis [36, 38, 42, 52].

Quality improvement interventions, details of their description, methods used to apply them, and compliance measure reporting varied. Educational interventions consisted of single, monthly, quarterly, or yearly sessions. Feedback reporting of infection or compliance rates occurred at monthly or quarterly intervals. Surveillance of compliance with preventive interventions was implemented daily, periodically, or at random intervals. Likewise, studies reported compliance with different items or only during the intervention period.

Twenty-eight studies reported before–after device utilization rates (n = 10) [8, 27, 28, 34, 38, 44, 45, 54, 56, 57], catheterization duration (n = 11) [22, 24, 27, 39, 43, 51, 53, 57, 58, 61, 63], or prevention measure compliance (n = 18) [22, 24, 27, 33, 35, 36, 45, 46, 49, 53, 55–60, 63, 66]. Some studies reduced [24, 51] or increased duration of catheterization [27, 58], yet most improved compliance (n = 10) [24, 27, 35, 36, 46, 49, 56, 60, 66]. Analysis of 7 studies revealed device utilization rate increases [38, 45, 57] and decreases (Supplementary Appendix 3) [8, 54, 56].

Half of trials implemented bundles or checklists (n = 20). Trials either introduced bundles without checklists (n = 2) [8, 45], only checklists because bundles were used during baseline (n = 9) [38, 44, 52, 53, 55, 57, 59, 62, 63], or both bundle and checklist interventions (n = 9) [27, 28, 33, 35, 37, 41, 43, 47, 54].

Differing amounts of preventive care items were grouped together to form a bundle or checklist. Two trials [52, 59] did not report which items their bundle comprised, and 1 trial used a checklist a sole item [53]. Other trials used all 5 (n = 7) [8, 27, 37, 38, 43, 54, 63], 4 (n = 5) [28, 33, 41, 47, 62], 3 (n = 3) [35, 44, 55], or 2 (n = 2) [45, 57] IHI items in their bundle or checklist. The items “optimal catheter site selection” and “daily review of line necessity” were included least (Figure 2).

Four studies targeted other healthcare-associated infections such as ventilator-associated pneumonia (VAP) [36], both VAP and catheter-associated urinary tract infections [28, 59], or VAP and surgical site infections [34]. Eight studies initiated new prevention measures alongside quality improvement interventions [26, 39, 40, 42, 43, 48, 52, 53].

The baseline CLABSI incidence varied; rates ranged from 2.1 [34] to 46.3 CLABSIs per 1000 catheter-days [46]. Trials reported baseline rates <5 [26, 27, 34–37, 43, 51–53, 57–59, 61, 62, 64] and >15 CLABSIs per 1000 catheter-days [18, 24, 41, 46, 49, 60].

Downs and Black quality assessment scores ranged from 15 [59] to 26 [22, 24, 49], with a mean of 21.2 (Supplementary

Figure 1. Study selection flow diagram. Abbreviations: CLABSI, central line–associated bloodstream infection; QI, quality improvement.

QUALITY IMPROVEMENT • CID 2014:59 (1 July) • 99
The results of the sensitivity analysis of before-after study designs revealed a change in level for the CLABSI rate at 3 months postintervention (OR, 0.30 [95% CI, .10–.88]; P = .028, Figure 3) in trials with care bundles or checklists (OR, 0.34 [95% CI, .27–.41]) than in those without them (OR, 0.45 [95% CI, .36–.55]). Further analysis revealed that studies with baseline rates >4.0 CLABSI per 1000 catheter-days (OR, 0.37 [95% CI, .33–.46]) did not demonstrate more pronounced risk reductions (P = .18) compared with studies below this baseline infection rate (OR, 0.49 [95% CI, .37–.66]). Low-power (OR, 0.33 [95% CI, .26–.42]) and high-power studies (OR, 0.44 [95% CI, .36–.54]) exhibited near-different rate reductions (P = .06).

Funnel plots displayed an asymmetrical pattern for before-after, but not ITS, study designs (Supplementary Appendix 6). The results of the sensitivity analysis of before-after study designs suggest that 2 studies contribute to residual heterogeneity; removing them from the meta-analysis would reduce variability between studies [49, 52]. However, because this did not affect the results, these studies were retained (Supplementary Appendix 7).

DISCUSSION

This meta-analysis of 43 studies, involving 584 ICUs, provides evidence that quality improvement interventions reduce CLABSI rates in adult ICUs. The effect size of 41 studies was significant yet highly heterogeneous. This infection rate decrease was more pronounced in studies using bundles or checklists, suggesting that their implementation alongside other initiatives leads to stronger rate reductions. The change in infection rate level
for 6 studies at 3 months postintervention also demonstrates the beneficial impact of quality improvement interventions, with low heterogeneity. However, only 1 of these studies showed significant rate decreases [62], and the overall intervention effect was not sustained over longer follow-up periods. These findings may reflect the presence of the Hawthorne effect and need for CLABSI awareness promotion through continuous, stepwise, multifaceted quality improvement interventions.

This study offers a broad look on the state of current research and applicable interventions, and applies a novel classification system to synthesize evidence for quality improvement initiatives. The meta-analysis is the first to include before-after studies.

studies and identify an additive preventive effect associated with bundle and checklist interventions. Two previous systematic reviews were unable to conclude which quality improvement interventions should be recommended for widespread implementation [16, 67]. Another recommended the use of educational programs and multidisciplinary teams [68]. A meta-analysis of ITS studies likewise demonstrated effect sizes with broad confidence intervals; however, they used different population criteria and studies, calculated rate reductions per quarter-year, reported mixed effects with small effect sizes, and did not investigate compliance measures. Additionally, the exclusion of before–after study designs discards much observational evidence, negatively impacting the external validity of the results [19]. Comparable points of criticism were the low quality of included studies due to high baseline infection rates, inadequate reporting of multiple CLABSI data points, compliance measurements, and intervention details.

Although interventions implemented in settings with higher baseline rates would appear more likely to be successful, no difference ($P = .18$) was found between studies with baseline infection rates above or below a suboptimal rate of 4.0 CLABSI per 1000 catheter-days. Furthermore, high-power studies demonstrated CLABSI rate decreases not significantly different from low-power studies ($P = .06$). Noteworthy is that the study with the lowest baseline rate (2.1 CLABSI per 1000 catheter-days) still achieved a significant rate reduction by providing feedback of biannual infection rates [34].

Strengths of this study include the comprehensive search strategy encompassing various quality improvement interventions, the methodological quality assessment of trials, and the random-effects model analysis with multiple studies and ITS study designs. It is, however, hampered by certain limitations: a lack of randomized or controlled study designs, inconsistent reporting of prevention measure compliance, and heterogeneity. Before–after studies run a higher risk of bias due to their liberal study design, as they hamper the ability to recognize phenomena that influence the CLABSI rate such as virulent epidemic outbreaks or spontaneous regression to the mean [16]. There is some evidence to suggest that the effects of quality improvement interventions are overestimated when based on before–after studies. Time series designs limit this risk of bias by detecting whether an intervention had an effect significantly greater than the underlying baseline trend [69]. However, because these designs require initiatives to begin at a well-defined point in time, 11 studies with multifaceted stepwise intervention implementation had to be excluded. This limitation could lead to an underestimation of the effect, as there is evidence for the effectiveness of gradual intervention introduction [70].

There are several issues related to the meta-analysis of before–after studies. All quality improvement interventions were considered to have an equal impact, yet this assumption may not be fair. Assuming interventions take months to implement, those introduced in a later study period could have less effect compared with earlier initiatives. Inclusion of studies from identical authors can lead to bias [24, 49, 56, 60, 61, 65, 66]. Two of these studies were performed in the same hospital, which could overestimate the intervention effect due to hospital experience in intervention implementation [60, 66]. The forest plot of before–after studies revealed a lack of smaller studies with less drastic infection rate decreases, suggesting publication bias; however, subgroup analysis of high-power studies revealed CLABSI decreases. Nevertheless, analysis of ITS studies aims to avert these barriers, and there was little evidence of publication bias among those studies.

Interventions to change risk exposure confound results. Although statistically equivalent, a catheter-day from days 1–2 contains less infection risk than days 14–15 due to microbial biofilm development and accumulating gaps in prevention measure adherence. Studies that reduce device utilization rates with increased average catheterization duration, reflecting a cohort of patients no longer managed with short-term central line usage, could underestimate intervention effects and vice versa [27].
This impact is unclear, as studies with significant changes in device utilization rates and duration of catheterization reported mixed effects. Analysis of catheterization duration was not feasible because CLABSIs definitions do not account for usage of multiple catheters per patient.

Clinical and methodological heterogeneity stemmed from the use of differing intervention strategies, study designs, population characteristics, and baseline standards of care. No distinction was made between interventions applied as part of a general program or introduced to solve a specific recurring problem. For example, one study formed a team of nurses to evaluate care processes related to an infection rate increase. By applying a comparable yet distinct multifaceted quality improvement strategy, they decreased their rate from 1.5 to 0 CLABSIs per 1000 catheter-days [23]. Differing standards of care hinder comparison through meta-analysis. The effect of implemented quality improvement interventions is dependent on the efficacy or amount of baseline prevention measures. Simultaneous introduction of daily chlorhexidine bathing alongside a quality improvement initiative may have influenced one ITS study’s intervention effect [40]. Last, this review did not aim to identify strategies that lead to optimal uptake of quality improvement initiatives.

In conclusion, the results of this meta-analysis provide evidence that quality improvement interventions reduce CLABSI in adult ICUs. Forty-one before–after studies demonstrated consistent, beneficial results, which appeared to be more pronounced among studies implementing bundle and checklist interventions. Quality improvement interventions appeared equally effective in studies with low and high power or baseline CLABSI rate settings. The CLABSI rate reduction appears to be confirmed by the methodologically more robust interrupted time series studies. Further research should assess requirements for successful adaptation of quality improvement interventions, for example, through improvement systems, over longer follow-up periods. Studies should report before–after compliance measures, device utilization rates, and catheterization duration. These latter 2 items are necessary to assess confounding factors, because increased catheter use for shorter durations leads to intervention effect overestimations. To properly address these issues, studies need to account for the number of catheters per patient. Finally, studies should apply ITS study designs and, when introducing stepwise initiatives, enough time should be spaced between interventions to facilitate ITS analysis.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Author contributions. K. B. conceived of and designed the study; performed the search of published work, literature search, data acquisition, interpretation and synthesis, and statistical analysis; and wrote the paper. J. B. performed the statistical analysis, contributed to data interpretation, and revised the statistical portions of the report. D. Vo. substantially contributed to data analysis and interpretation and critically revised the final manuscript. S. B. designed the study; substantially contributed to the search of published work, data interpretation and synthesis; and critically revised the final manuscript. D. V. A. conceived of and designed the study; substantially contributed to data interpretation and synthesis; and critically revised the final manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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