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ORIGINAL ARTICLE

The Risk of Bloodstream Infection Associated with Peripherally Inserted Central Catheters Compared with Central Venous Catheters in Adults: A Systematic Review and Meta-Analysis

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BACKGROUND. Peripherally inserted central catheters (PICCs) are associated with central line–associated bloodstream infection (CLABSI). The magnitude of this risk relative to central venous catheters (CVCs) is unknown.

OBJECTIVE. To compare risk of CLABSI between PICCs and CVCs.

METHODS MEDLINE, CinAHL, Scopus, EmBASE, and Cochrane CENTRAL were searched. Full-text studies comparing the risk of CLABSI between PICCs and CVCs were included. Studies involving adults 18 years of age or older who underwent insertion of a PICC or a CVC and reported CLABSI were included in our analysis. Studies were evaluated using the Downs and Black scale for risk of bias. Random effects meta-analyses were used to generate summary estimates of CLABSI risk in patients with PICCs versus CVCs.

RESULTS. Of 1,185 studies identified, 23 studies involving 57,250 patients met eligibility criteria. Twenty of 23 eligible studies reported the total number of CLABSI episodes in patients with PICCs and CVCs. Pooled meta-analyses of these studies revealed that PICCs were associated with a lower risk of CLABSI than were CVCs (relative risk [RR], 0.62; 95% confidence interval [CI], 0.40–0.94). Statistical heterogeneity prompted subgroup analysis, which demonstrated that CLABSI reduction was greatest in outpatients (RR [95% CI], 0.22 [0.18–0.27]) compared with hospitalized patients who received PICCs (RR [95% CI], 0.73 [0.54–0.98]). Thirteen of the included 23 studies reported CLABSI per catheter-day. Within these studies, PICC-related CLABSI occurred as frequently as CLABSI from CVCs (incidence rate ratio [95% CI], 0.91 [0.46–1.79]).

LIMITATIONS. Only 1 randomized trial met inclusion criteria. CLABSI definition and infection prevention strategies were variably reported. Few studies reported infections by catheter-days.

CONCLUSIONS. Although PICCs are associated with a lower risk of CLABSI than CVCs in outpatients, hospitalized patients may be just as likely to experience CLABSI with PICCs as with CVCs. Consideration of risks and benefits before PICC use in inpatient settings is warranted.

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The use of peripherally inserted central catheters (PICCs) has grown in contemporary medical practice. Multiple reasons, including ease of insertion, numerous uses (eg, medication administration and venous access), perceived safety, and cost-effectiveness compared with other central venous catheters (CVCs), account for this popularity.[1,2] Furthermore, the proliferation of nursing-led PICC teams has made their use convenient and accessible in many settings.[3,4]

Despite these salient benefits, PICCs are also associated with central line–associated bloodstream infection (CLABSI),[1-3] a healthcare-acquired complication that prolongs hospitalization and increases cost and mortality.[4-6] Although CLABSI prevention has been a topic of national importance, ambiguity regarding the risk of PICC-related CLABSI exists. Although some evidence suggests that PICCs are associated with a lower risk of CLABSI than other devices,[7-9] other data support the contrary viewpoint.[10,11] As the use of PICCs expands to include vulnerable populations, including those that are

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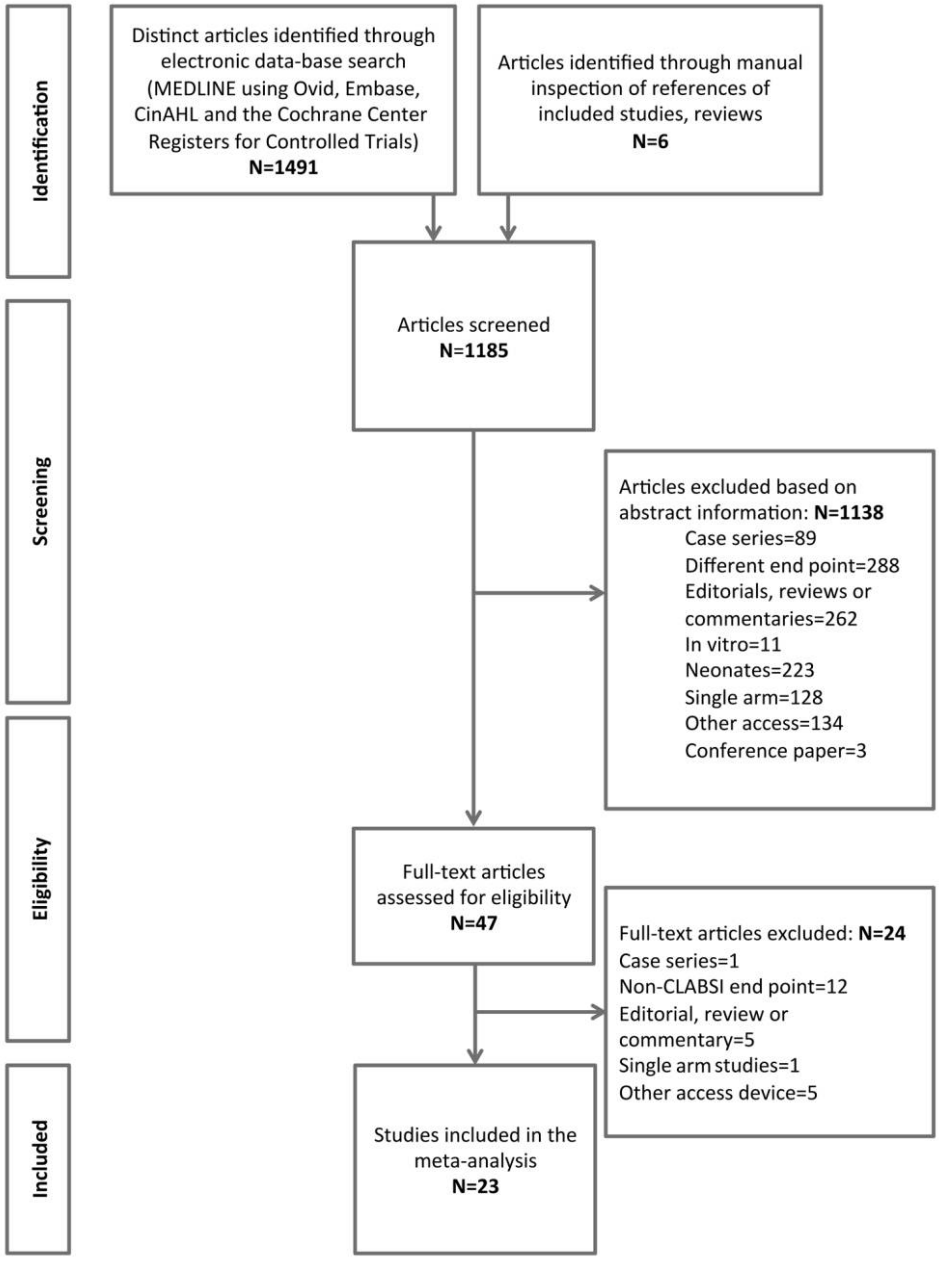

FIGURE 1. Study flow diagram. CLABSI, central line–associated bloodstream infection.

hospitalized and critically ill, determining the risk of CLABSI posed by PICCs relative to other CVCs is important for both cost and patient safety. Additionally, quantifying this risk will serve to inform clinicians when choices regarding vascular access and device selection are confronted. For these reasons, we performed a systematic review and meta-analysis of the literature. Our goal was to better understand the risk of CLABSI in patients who received PICCs compared with those who received other CVCs.

METHODS

Literature Search

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) in conducting this meta-analysis.[12] With the assistance of a medical research librarian, we performed serial literature searches for English and non-English articles. MEDLINE (via PubMed), CinAHL, Scopus, EmBASE, and Cochrane CENTRAL registry were

TABLE 1. General Characteristics and Quality of Included Studies

Study	No. of subjects	Study design	Study population	Indication for PICC	Comparator	PICC inserter/operator	CLABSI prevention	Quality of study (Downs and Black)
Al Raiy et al 2010[7]	1,260	Prospective cohort	Hospitalized patients	IV access in inpatient settings	Nontunneled catheters	Vascular access nurses and interventional radiology	NR	Low (11/24)
Alhimyary et al 1996[19]	231	Retrospective cohort	Outpatients receiving parenteral nutrition	Total parenteral nutrition	Nontunneled triple-lumen catheters	Vascular access nurses	72-hour dressing changes with povidone-iodine scrub or chlorhexidine	Low (11/24)
Cortelezzi et al 2003[20]	126	Retrospective cohort	Patients with hematogenous malignancies	Chemotherapy, antibiotics, blood products, venous access, CVP monitoring	Nontunneled and tunneled catheters	Physicians in the operating room or at the bedside	NR	Low (11/24)
Cowl et al 2000[10]	102	Randomized controlled	Inpatients receiving parenteral nutrition	Total parenteral nutrition	Nontunneled triple-lumen subclavian catheters	Physicians and vascular access nurses	Dressing changes every 3 days for subclavian and 5 days for PICC	High (14/24)
Cotogni et al 2012[21]	289	Prospective cohort	Patients with solid and hematogenous malignancies	Total parenteral nutrition	Tunneled and nontunneled catheters and ports	Vascular access nurses and surgical staff	NR	High (14/24)
Delegge et al 2005[22]	115	Retrospective cohort	Outpatients receiving parenteral nutrition	Total parenteral nutrition	Tunneled and nontunneled catheters and ports	Interventional radiology	NR	Low (10/24)
Duerksen et al 1999[23]	494	Prospective observational	In- and outpatients receiving parenteral nutrition	Total parenteral nutrition	Tunneled and nontunneled catheters	Physicians/surgical staff	Povidone/iodine dressing changes 2–3 × per week	High (12/24)
Feorance et al 2010[24]	31	Retrospective case control	Critically ill patients in a burn ICU	Venous access, antibiotics, blood products	Nontunneled triple-lumen catheters	Vascular access nurses	Dressing changes every 48 hours or sooner as needed	High (13/24)
Graham et al 1991[25]	300	Prospective cohort	Outpatients receiving home intravenous treatment(s)	Antibiotics, venous access	Tunneled and nontunneled catheters	NR	NR	Low (10/24)
Griffiths and Philpot 2002[26]	52	Retrospective cohort	Critically ill patients in an ICU setting	Venous access, antibiotics, blood products, CVP monitoring	Nontunneled catheters	Vascular access nurses	Regular care by trained nursing staff	Low (10/24)
Gunst et al 2011[9]	121	Retrospective cohort	Critically ill patients in a surgical ICU	Venous access, antibiotics, CVP monitoring	Nontunneled triple lumen catheters	Vascular access nurse	NR	High (12/24)
Lim et al 2012[27]	148	Retrospective cohort	Patients with hematogenous malignancies	Chemotherapy, antibiotics, blood products, venous access	Tunneled catheter	Vascular access nurses	Bundle practice	High (13/24)

Mollee et al 2011[28]	727	Prospective observational	Patients with solid and hematogenous malignancies	Chemotherapy, antibiotics, blood products, venous access	Tunneled and nontunneled catheters and ports	Interventional radiology	Standardized policy based on CDC guidelines and Australian nursing policies	High (12/24)
Moureau et al 2002[8]	50,470	Retrospective cohort	Outpatients receiving home intravenous treatment(s)	Home infusion needs including antibiotics, TPN, fluids and hydration	Tunneled and nontunneled catheters and ports	NR	NR	High (13/24)
Paz-Fumagalli et al 1997[29]	42	Prospective cohort	Patients with spinal cord injuries	Antibiotics, blood products, venous access, intravenous hydration	Nontunneled triple-lumen catheters	Interventional radiology	Regular care by trained nursing staff	Low (11/24)
Raad et al 1993[30]	340	Prospective cohort	Patients with malignancies receiving outpatient treatment	Chemotherapy, TPN, blood products	Tunneled and nontunneled catheters	Vascular access nurses	72-hour dressing changes with povidone-iodine scrub or chlorhexidine	High (13/24)
Schuman et al 1987[31]	669	Prospective cohort	Patients with malignancies receiving outpatient treatment	Chemotherapy, antibiotics, TPN, terminal care	Ports, tunneled catheters, and nontunneled catheters	NR	Regular care by trained nursing staff	Low (10/24)
Skaff et al 2011[11]	147	Retrospective cohort	Patients with hematogenous malignancies	Chemotherapy	Tunneled catheters	Vascular access nurses	NR	High (12/24)
Smith et al 1998[32]	838	Retrospective cohort	Hospitalized patients requiring central venous access	Venous access, antibiotics, TPN, blood products	Tunneled and nontunneled catheters and ports	Physicians/surgical staff	NR	High (12/24)
Snelling et al 2001[33]	28	Retrospective cohort	Patients with gastrointestinal cancer	Chemotherapy, venous access, antibiotics, TPN	Tunneled catheters	Physicians/surgical staff	Weekly dressing changes with chlorhexidine or povidone-iodine	Low (10/24)
Wilson et al 2012[34]	572	Retrospective cohort	Critically ill patients in a neurosurgical ICU	Venous access, antibiotics, mannitol infusion, blood products	Nontunneled triple-lumen catheters	NR	NR	High (13/24)
Worth et al 2009[35]	66	Prospective observational	Patients with hematogenous malignancies	Chemotherapy, venous access, antibiotics, TPN	Nontunneled triple-lumen catheters	Interventional radiology or surgical placement	Weekly dressing change	High (12/24)
Zhao et al 2012[13]	101	Retrospective cohort	Patients requiring home parenteral nutrition	Total parenteral nutrition	Tunneled catheters, nontunneled catheters, and ports	Interventional radiology	NR	High (12/24)

NOTE. CDC, Centers for Disease Control and Prevention; CLABSI, central line–associated bloodstream infection; CVC, central venous catheter; CVP, central venous pressure; ICU, intensive care unit; IV, intravenous; NR, not reported; PICC, peripherally inserted central catheter; TPN, total parenteral nutrition.

searched from inception using the following keywords: "PICC" or "peripherally inserted central catheter," "infection(s)," "complication(s)," "prevention," "bloodstream infection," "BSI," and "CLABSI." Boolean operators and medical subject heading terms were used to enhance electronic searches. All human studies published in full-text form were eligible for inclusion; no publication date or language restrictions were placed on searches. Additional studies of interest were identified by hand searches of bibliographies. The search was last updated on February 1, 2013.

Study Eligibility and Selection Criteria

Two authors (V.C. and J.C.O.) independently determined study eligibility. Any difference in opinion regarding eligibility was resolved through consensus.

Studies were included if they (1) involved participants 18 years of age or older and (2) systematically compared the frequency of CLABSI between PICCs and CVCs. We excluded studies that (1) involved neonates or children, because access sites and PICC types (eg, scalp veins, umbilical veins, and femoral veins) vary considerably from those in adult populations; (2) compared infection rates associated with PICCs to those associated with devices that were not CVCs (eg, peripheral intravenous catheters); and (3) were case reports, case-control studies that examined risk factors for infection, editorials, reviews, or studies that did not report CLABSI (Figure 1).

Definition of Variables and Outcomes

A CVC was defined as any central venous access device inserted into the internal jugular, subclavian, or femoral vein that terminated in the inferior vena cava or right atrium. PICCs were defined as catheters inserted in the basilic, cephalic, or brachial veins of the upper extremities with tips that terminated in the superior vena cava or right atrium; because midlines and prolines do not terminate in this position, they were not included. Venous access obtained through the external jugular vein and long-term dialysis catheters were not included. We specifically excluded dialysis catheters, because methods of infection prevention and risk factors associated with CLABSI are clinically dissimilar in this subset. Inpatient studies were defined as those in which patients remained hospitalized during the study; conversely, studies classified as outpatient were those that only involved nonhospitalized patients. Studies that featured patients who may have received a CVC or a PICC during hospitalization but were subsequently discharged from the hospital with outcome reporting after hospitalization were classified as both inpatient and outpatient. CLABSI was defined as the occurrence of bacteremia in a patient with PICCs or CVCs that was attributable to the device. The precise definition of CLABSI employed (eg, Centers for Disease Control and Prevention [CDC]/National Healthcare Safety Network [NHSN] definition, culture data, or clinical suspicion) was directly extracted from each study. Because included studies reported either the total number of CLABSI episodes or the rate of infections in PICCs or CVCs by catheter-days, we extracted data for both of these outcome measures. When available, CLABSI surveillance technique and trigger for blood culture were also abstracted from each study. If a patient received multiple devices during a study,[13,14] only the device with the index CLABSI event was included; additional events and outcomes were censored.

Data Abstraction and Validity Assessment

Data from eligible studies were abstracted using a standardized template based on the Cochrane Collaboration.[15] Data collected included information on catheter infection prevalence, duration of catheter use, type of PICC, modality of PICC insertion, number of lumens, organism cultured, method of CLABSI diagnosis (clinical vs microbiological), and infection prevention techniques used. Authors were directly contacted if relevant information was not available in published studies.

Assessment of Risk of Bias

Two authors (V.C. and J.C.O.) independently assessed the risk of study bias. Because retrospective, prospective, and randomized controlled studies met inclusion criteria, risk of bias was assessed according to the instrument developed by Downs and Black.[16] This tool encompasses 6 sections that assess reporting (total score of 11), external validity (total score of 3), internal validity or bias (total score of 7), internal validity or confounding (total score of 6), and power (total score of 2). Studies with scores of 12 or greater were considered high-quality studies.

Statistical Analysis

In studies that reported the numbers of infections in patients who received PICCs and CVCs, 2 measures were calculated. First, the relative risk (RR) of CLABSI by catheter type was determined as the ratio of cumulative risks (ie, proportion of patients with PICC-related CLABSI divided by the proportion of patients with CVC-associated CLABSI). When studies reported number of infections per catheter-days, incidence rate ratios (IRRs) of CLABSI were calculated (PICC-associated CLABSI per catheter-days divided by CVC-associated CLABSIs per catheter-days). For both RR and IRR, analyses were conducted such that values less than 1.0 were indicative of a lower risk of CLABSI with PICCs than with CVCs.

The empirical continuity correction, a pseudo-Bayesian approach, was used for studies that reported zero events in either the treatment or control groups. As described by Sweeting et al,[17] this correction is based on the pooled effect size from the studies with the events (ie, previous evidence) and is less biased than the typical 0.5 continuity correction. All meta-analyses were performed using a DerSimonian-Laird random

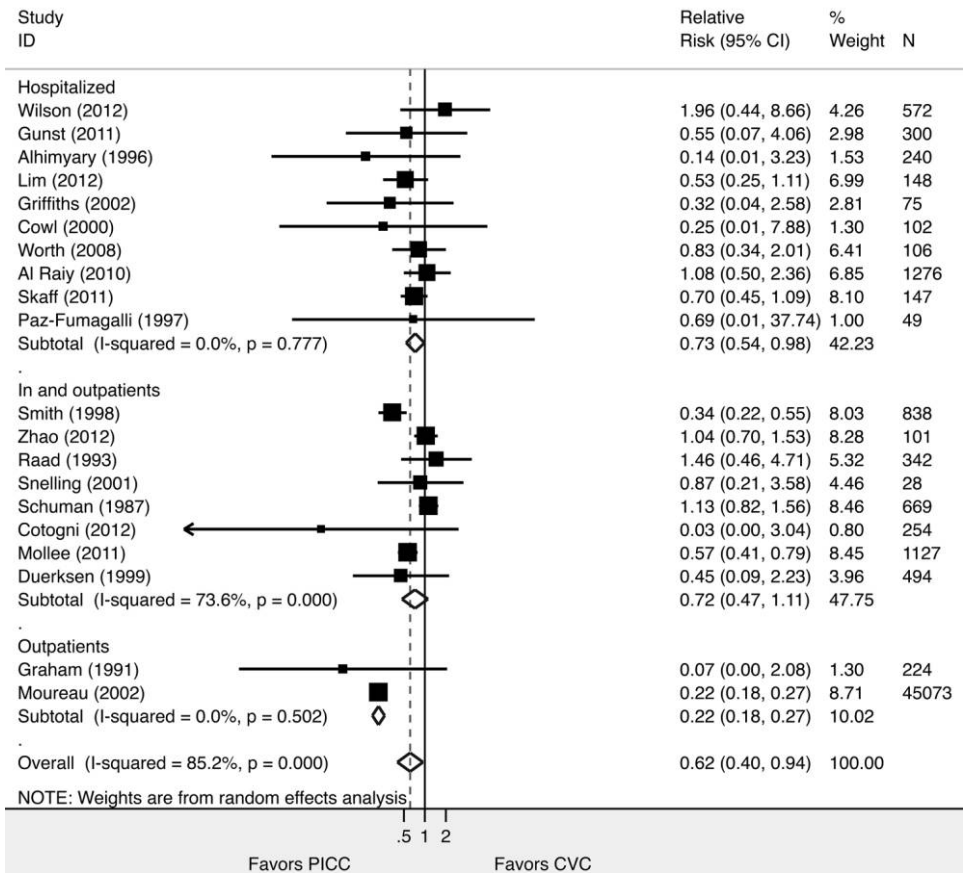

FIGURE 2. Forest plot showing relative risk of central line–associated bloodstream infection episodes with peripherally inserted central catheter (PICC) versus central venous catheter (CVC), by patient type. CI, confidence interval.

effects model. We explored heterogeneity between studies using Cochrane's Q test and the I^2 statistic, classifying heterogeneity as low, moderate, or high on the basis of an I^2 statistic of 25%, 50%, and 75% according to the method suggested by Higgins et al.[18] Publication bias for studies was assessed by visual inspection of funnel plots and Peter's test, with $P < .10$ indicative of publication bias.

A priori, we specified several additional analyses. To determine whether patient population (inpatient, outpatient, or both), patient type (patients with cancer, critically ill patients, or patients receiving total parenteral nutrition [TPN]), PICC inserter (nurse, interventional radiologist, or physician), use of ultrasound during PICC insertion, or CLABSI definition affected our conclusions, results were stratified by subgroups. Sensitivity analyses by study characteristics were performed to test the robustness of our findings. Statistical analysis was performed using Cochrane Database's Review Manager 5.1.0 and STATA MP version 11 (Stata). Statistical tests were 2-tailed with $P < .05$ considered statistically significant.

RESULTS

After the removal of duplicate entries, 1,185 unique articles were identified by our electronic search (Figure 1). Of these, 1,136 were excluded on the basis of abstract information; an additional 26 studies were excluded after full text review. Therefore, 23 unique studies involving 57,250 patients reporting the occurrence of CLABSI in patients with PICCs compared with CVCs were included in the systematic review.[7-11,13,19-35]

Among the 23 included studies, 12 were retrospective,[9,11,13,19,20,22,24,26,27,32-34] 10 prospective,[7,8,21,23,25,28-31,35] and 1 was a randomized controlled trial (Table 1).[10] Study populations were diverse and included 10 studies that involved predominantly hospitalized patients,[7,9-11,14,19,24,26,27,29,34] 9 with both inpatients and outpatients,[13,21,23,28,30-33] and 3 involving only outpatients.[8,22,25] One study did not clearly report the location of patients during treatment or device insertion.[20] Within each of these populations, unique subsets were identified. For instance, hospitalized patients included critically ill patients,[9,24,26,34] patients with cancer,[11,20,27,28,30,31,33,35] and neurosurgical patients.[34] Studies involving both inpatients and outpatients included general medical patients,[32] patients receiving parenteral nutrition,[13,23] and those undergoing cancer treatments.[11,30,31,33] Studies also varied considerably with respect to inclusion criteria: for instance, 1 study enrolled all patients who received central venous access within a specific

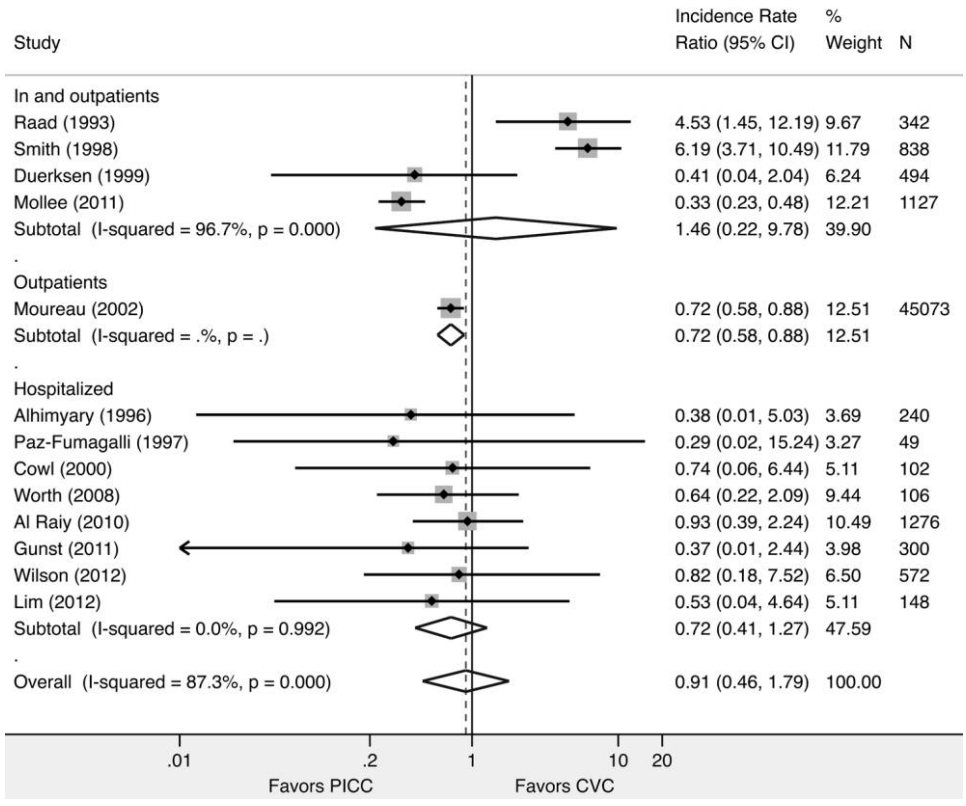

FIGURE 3. Forest plot showing incidence rate ratios of central line–associated bloodstream infection (per catheter-days) with peripherally inserted central catheter (PICC) versus central venous catheter (CVC) by patient type. CI, confidence interval.

time frame,[32] whereas 6 studies restricted inclusion to patients who received TPN.[10,13,19,21-23] No studies reported patients who received both a PICC and a CVC.

In the 20 included studies that reported numbers of CLABSI episodes in patients who received PICCs, the unweighted incidence of PICC-related CLABSI among hospitalized patients was 5.2% (76 of 1,473) versus 5.8% (76 of 1,302) in those that received CVCs. Among outpatients, the risk of CLABSI was 0.5% in patients who received PICCs (117 of 25,822) versus 2.1% (418 of 19,715) in those that received CVCs. The largest retrospective study within the systematic review had the most episodes of CLABSI in either device group.[28]

Infection Prevention Techniques and Surveillance Strategies

Infection prevention techniques were reported variably within the included studies. For example, 1 study exclusively reported using evidence-based bundled practices,[27] whereas others specifically reported weekly[33,35] or 3-day dressing changes.[19,30] Notably, the majority of included studies did not report the method of infection prevention used.[8,9,11,13,21,22,25,32,34] With respect to CLABSI definitions, 3 studies did not report a precise definition for CLABSI,[31-33] 15 used clinical findings in conjunction with culture data,[8-11,19,20,22-27,29,30,34] 1 used the National Nosocomial Infection Surveillance (NNIS) definition,[35] and 4 used the more rigorous CDC/NHSN or the NNIS definition.[7,13,21,28] With respect to triggers for microbiological evaluation, 11 reported performing cultures only in the presence of symptoms suggestive of infection,[10,13,14,21,22,26,27,36-39] 2 studies routinely cultured all catheter tips at the time of removal,[30,40] and the remainder did not specify what prompted evaluation for CLABSI.[7,19,23,29,32,34,41]

Risk of Study Bias

The median Downs and Black score for included studies was 11.3 (range, 10–14), suggesting average study quality and methodology with little between-study variation (Table 1). Cohen's interrater κ statistic for inclusion agreement and quality assessment were 0.84 and 0.80, respectively, indicative of excellent interrater agreement.

Pooled Risk of CLABSI by Infectious Episodes in PICCs versus CVCs

Twenty of the 23 included studies (n = 52,175) reported CLABSI by number of infections per person and were pooled to evaluate the risk of CLABSI in PICCs compared with

TABLE 2. Subgroup Analysis of Studies of Hospitalized Patients

Subgroup	RR (95% CI)
Base case[7,9-11,14,19,26,27,29,34]	0.73 (0.54–0.98)
Patient type	0.68 (0.48–0.96)
Cancer[11,27,35]	0.87 (0.29–2.62)
Critically ill[9,26,34]	0.19 (0.02–1.86)
Nutritionally deplete (TPN)[10]	1.07 (0.50–2.28)
Other[7,29]	
PICC inserter	
Interventional radiology[29]	0.69 (0.01–37.74)
Vascular nursing[9,11,26,27]	0.66 (0.46–0.95)
Multiple providers[7,10,35]	0.93 (0.52–1.65)
Mode of PICC insertion	
With ultrasound[27,29]	0.77 (0.32–1.83)
Without ultrasound[7,9,10]	0.85 (0.43–1.70)
Both with and without ultrasound[11,26]	0.68 (0.44–1.05)
Not reported[35]	0.83 (0.34–2.01)
Comparator type	
Nontunneled catheter[7,9,10,34,35]	0.93 (0.56–1.55)
Tunneled catheter[11,27]	0.65 (0.44–0.95)
Nontunneled and tunneled[26,29]	0.37 (0.06–2.40)
CLABSI definition	
Culture data[9-11,26,27,29,34]	0.66 (0.46–0.93)
CDC/NHSN[7]	1.08 (0.50–2.36)
NNIS definition[35]	0.83 (0.34–2.01)

NOTE. CDC, Centers for Disease Control and Prevention; CI, confidence interval; CLABSI, central line–associated bloodstream infection; NHSN, National Healthcare Safety Network; NNIS, National Nosocomial Infection Surveillance; PICC, peripherally inserted central catheter; RR, relative risk; TPN, total parenteral nutrition.

CVCs.[7-11,13,19,21,23,25-35] Within these studies, PICCs were associated with an overall lower risk of CLABSI compared with CVCs (RR [95% confidence interval (CI)], 0.62 [0.40–0.94]). However, a high degree of statistical heterogeneity was observed in the pooled data (I^2, 85.2%; Cochran's Q test statistic, 128.75; $P < .001$). Because hospitalization is known to influence the risk of CLABSI, this variable was specifically investigated as a source of heterogeneity. This approach revealed that heterogeneity in the pooled estimate existed only within studies that included both inpatients and outpatients (I^2, 73.6%), likely because of the mixed clinical characteristics in this group.[13,21,23,28,30-33] Of note, studies that exclusively included outpatients suggested that PICCs were safer than CVCs with respect to CLABSI (RR [95% CI], 0.22 [0.18–0.27]; I^2, 0%).[8,25] Although studies involving inpatients also supported this phenomenon, the effect trended toward statistical nonsignificance in this patient population (RR [95% CI], 0.73 [0.54–0.98]; I^2, 0%; Figure 2).[7,9-11,19,24,26,27,29,34]

Pooled Risk of CLABSI by Catheter-Days in PICCs versus CVCs

Thirteen of the included 23 studies ($n = 50,667$) reported CLABSI by number of infections per catheter-day.[7-10,19,23,27-30,32,34,35] Within these studies, the risk of CLABSI was similar for patients who received PICCs compared with those who received CVCs (IRR [95% CI], 0.91 [0.46–1.79]). Again, a high degree of heterogeneity was observed in the pooled data (I^2, 87.3%; Cochran's Q test statistic, 94.80; $P < .001$). As observed earlier, subgroup analysis by hospitalization status revealed that heterogeneity existed only within studies that include both inpatients and outpatients (I^2, 96.7%).[23,28,30,32] Studies that involved only hospitalized patients showed no statistical difference in the risk of CLABSI between PICCs and CVCs (RR [95% CI], 0.72 [0.41–1.27]; $I^2 = 0\%$).[7,9,10,27,29,34,35] Only 1 study included outpatients; this study suggested that PICCs were associated with lower risk of CLABSI than CVCs (IRR [95% CI], 0.72 [0.58–0.88]; Figure 3).[8]

Subgroup, Sensitivity, and Publication Bias Analyses

Because of heterogeneity in the pooled estimate and small numbers of studies involving outpatients, subgroup analyses were restricted to studies involving hospitalized patients (10 studies; $n = 2,279$; Table 2). Rates of PICC-associated CLABSI relative to CVC-associated CLABSI were similar for patients with cancer, those who were critically ill, and those requiring TPN. Meta-analytical conclusions remained robust to sensitivity testing by study design (Table 3). Visual inspection of funnel plots and Peter's test did not suggest publication bias ($P = .18$).

DISCUSSION

The prevention of CLABSI is a topic of national importance. Because most CLABSIs occur in intensive care unit (ICU) settings, much of this discourse has focused on the critically ill, for whom significant strides have been made. With the advent of interventions that include unit-based safety approaches, a technical checklist of best practices, and enhanced measurement and feedback of infection rates, significant decreases in CLABSI rates have been realized in ICUs across the United States.[42-44] Furthermore, several large-scale initiatives have reported statewide elimination of CLABSI in ICUs.[27,45,46] However, not all CVCs are equivalent with respect to the associated risk of CLABSI,[47,48] and shifts in patterns of CVC use from ICU to non-ICU settings may impact this progress.[49-51] Thus, evidence that is both device- and context-specific is needed to inform CLABSI risk and prevention.

In this systematic review and meta-analyses comparing risk of CLABSI between PICCs and CVCs, we found a 10-fold greater risk of CLABSI among hospitalized patients (5.2%) than among outpatients who received PICCs (0.5%). Additionally, hospitalized patients who underwent PICC placement experienced CLABSI rates that statistically paralleled that associated with CVCs. Conversely, outpatients experienced a lower percentage of CLABSI events with PICCs (0.5%) than with CVCs (2.1%). These findings underscore the role of patient and device factors in the development of

TABLE 3. Sensitivity Analysis

Scenario	RR (95% CI)
Base case	0.62 (0.40–0.94)
Excluding retrospective studies[7,8,10,21,23,25,28-31,35]	0.58 (0.30–1.13)
Excluding prospective studies[9-11,13,19,26,27,32-34]	0.64 (0.42–0.95)
Excluding studies of low quality[8-11,13,21,23,27,28,30,32,34,35]	0.58 (0.36–0.94)
Excluding studies in which $n > 500$[a,9-11,13,19,21,23,25-27,29,30,33,35]	0.62 (0.32–1.19)
Excluding studies published before 2005[b,7,9,11,13,21,27,28,34,35]	0.75 (0.58–0.98)

NOTE. CI, confidence interval; RR, relative risk.

[a] To assess influence of large-study effects on the pooled estimates.

[b] To account for increasing use of evidence-based bundles of infection prevention associated with insertion and catheter maintenance.

CLABSI and suggest caution when placing PICCs in hospitalized patients for inappropriate indications.

Why might PICCs pose a differential risk of infection in the inpatient setting than in the outpatient setting? CLABSIs are thought to occur by extraluminal migration of bacteria from the skin entry site, forming a critical mass at the catheter tip.[52] Because PICCs are longer in length, and bacteria have farther to travel, lower rates of CLABSI are theoretically expected. However, a considerable proportion of CLABSIs are also caused by hub manipulation, with bacteria migrating intra- rather than extraluminally. This latter route of infection is most implicated with long-term CVCs.[53] PICCs straddle the line between short- and long-term devices, such that both intra- and extraluminal routes become relevant in CLABSI related to these devices.[54,55] More frequent hub manipulation in inpatient settings than in outpatient settings may explain the increased risk of PICC-related CLABSI among hospitalized patients.

Our study has important limitations. First, we were only able to compare infections by catheter-days in 13 of the included 23 studies, a limitation that reflects the paucity of reporting of CLABSIs by catheter-days in the available literature. Second, our analyses were based on unadjusted data of rates of infection; failure to include patient- or device-level characteristics may influence our conclusions. Although the use of sensitivity and subgroup analyses helps address this problem, our findings should be interpreted with caution in this regard. Third, because the included studies did not specifically report on the use of antimicrobial catheters or practices to prevent CLABSI (eg, bundle use, site disinfection, and line-maintenance practices), we were not able to adequately address the impact of factors such as technology or infection prevention methods on PICC-related bloodstream infections.

Despite these limitations, our study also has important strengths. First, to our knowledge, this is the largest systematic review and meta-analyses specifically examining the risk of CLABSI in PICCs compared with other CVCs. Because our study specifically isolates CLABSI outcomes and characteristics associated with this event, it uniquely adds to the literature regarding PICC safety. Second, we separately analyzed CLABSI based on risk per patient, as well as CLABSI episodes per catheter-days. In doing so, we were able to assess not only CLABSI risk by exposure for groups of patients but also how CLABSI rates vary based on time-at-risk due to catheter placement. Indeed, these analyses showed that hospitalized patients who received PICCs experienced CLABSI at rates that were no different than those associated with other CVCs. In an era of escalating inpatient PICC use, this finding is timely and calls for scrutiny regarding the necessity and appropriateness of PICC insertion. Third, our study is strengthened by the inclusion of unpublished study data obtained by direct author contact.

Our findings have important implications for clinicians and policy makers. First, our study reemphasizes how the prevention of PICC-related CLABSI in hospitalized patients should be approached with the same drive, intensity, and strategic insights that have driven down CLABSI rates in ICUs. Specifically, greater use of insertion and maintenance checklists, development of appropriateness guidelines to ensure suitable placement, and timely removal of PICCs to prevent idle catheter-days are in need of greater attention in non-ICU settings.[56,57] Second, because homogenous care teams are increasingly difficult to assemble in these areas, studies that specifically assess the role of novel technologies and practices, such as chlorhexidine-impregnated site dressings or antimicrobial PICCs, are needed in the battle against CLABSI in non-ICU settings. These technological approaches may provide important layers of reinforcement against CLABSI in non-ICU settings, especially as the use of PICCs increases in these areas.[57] Third, because the risk of CLABSI associated with CVCs and PICCs appears to be similar in hospitalized patients, expansion of practices and campaigns such as hub decontamination and "scrub the hub" should specifically be targeted toward PICCs. Finally, we note that PICCs continue to appear safe in outpatient settings when used in healthier, ambulatory populations for appropriate indications. Continued efforts to educate patients on catheter care, including aseptic access, flushing techniques, and early recognition of warning signs, are important to maintain this course.

In conclusion, when placed in hospitalized patients, PICCs are associated with a risk of CLABSI that mirrors that of

CVCs. Policy and procedural oversight regarding PICC insertion and maintenance in these settings is warranted. Future studies investigating pathogenesis, insertion practice, and comparative effectiveness of prevention strategies for PICC-related CLABSI in non-ICU settings are necessary to improve patient safety.

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