REVIEW ARTICLE

# Short- and Intermediate-Term Use of Peripherally Inserted Central Catheters in Europe: A Systematic Literature Review

**Baudolino Mussa, MD**
CVC Team Torino, Department of Surgical Science, University of Turin, Turin, Italy
Corso Achille Mario Dogliotti 14, Turin, Italy
**Kim Alsbrooks, BSN, RN, RT (R), VA-BC™**
Becton Dickinson, Franklin Lakes, NJ
**Robert Hutcheson, MSc**
Certara, Montreal, QC, Canada

## Highlights

- Fifty-six studies were included in a systematic literature review.
- PICCs were compared to CICCs and PIVCs for short/intermediate-term use in Europe.
- Several efficacy and safety benefits were shown with PICCs.
- Limited evidence showed higher costs with PICCs.

## Abstract

**Aims: The aim of this systematic review is to examine the efficacy, safety, and costs associated with the short/intermediate-term use of peripherally inserted central catheters (PICCs) in comparison with centrally inserted central catheters (CICCs) and peripheral intravenous catheters (PIVCs) among adults in Europe.**

**Methods: Medline, EMBASE, Cochrane, and EconLit databases were searched for records dating from January 2000 to March 2017. Full-text versions of potentially relevant records were assessed according to prespecified inclusion and exclusion criteria.**

**Results: Of 457 identified records, 56 studies were included in the review. Data ranges for efficacy outcomes across studies did not suggest any clear advantages or disadvantages between PICCs and CICCs or PIVCs. However, individual studies reported statistically significant improvements in patient satisfaction with PICCs versus both comparators ($P < 0.001$) and fewer venipunctures for successful insertion compared with PIVCs ($P < 0.01$). Across studies, rates of removal due to complications were 3.5% to 48% with PICCs compared to 67% to 81.2% with PIVCs and 26% to 78% with CICCs. The proportion of patients reporting catheter migration/dislocation was 0% to 7.7% with PICCs compared to 9.6% to 15% with CICCs, whereas the rate of venous thrombosis was 0% to 27.2% versus 0% to 9.6%, respectively, with individual studies reporting significant differences ($P \leq 0.01$). Limited evidence showed higher costs with PICCs than with CICCs or PIVCs, but not all relevant costs were included in the analyses.**

**Conclusions: This review showed that PICCs offer several advantages compared to CICCs and PIVCs, including greater patient satisfaction, fewer complications leading to removal, and less catheter migration/dislocation, despite a moderately higher rate of venous thrombosis.**

**Keywords: Europe, PICC, CICC, PIVC, systematic review, vascular access**

Correspondence concerning this article should be addressed to robert.hutcheson@certara.com
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## Introduction

Reliable and easy venous access is essential for the safe and effective care of hospitalized patients. Venous access devices (VADs) are catheters that consist of a hub to provide access to connectors, a hollow tube divided into one or many sections (lumens), and a tip terminating within a peripheral or central blood vessel.[1] VADs can be classified as central venous access devices (CVADs), peripheral intravenous catheters (e.g., midlines or peripheral intravenous catheters [PIVCs]), or implanted ports, based on the site of entry and location of the catheter tip.[1]

CVADs allow for central access, with tip termination in the lower portion of the superior vena cava at the cavoatrial junction.[1] Centrally inserted central catheters (CICCs) are CVADs that enter directly into veins of the neck or chest. Peripherally inserted central catheters (PICCs) are CVADs that enter through peripheral veins of the upper arm but terminate in the proximity of the cavoatrial junction.[1]

PICCs are indicated for both short/intermediate- and long-term access to the central venous system.[2,3] They are used for intravenous (IV) therapy (e.g., antibiotics, total parenteral nutrition, and chemotherapy), fluid delivery, power injection of contrast media, central venous pressure monitoring, and blood sampling.[4–6] Although PICCs are recognized in Europe as effective devices for the delivery of long-term treatments of 6 months or more, there is a lack of consensus regarding their utility and advantages over CICCs and PIVCs in the short/intermediate term.[6,7]

## Aims

The aim of this systematic review is to examine the efficacy, safety, and costs associated with the short/intermediate-term (<6 months) use of PICCs among adults in Europe. The two main questions to be answered were as follows: (1) What is the extent of the available literature on short/intermediate-term PICC use among adults in Europe? and (2) What conclusions can be drawn from data in the literature about the efficacy, safety, and costs of short/intermediate-term PICC use among adults in Europe compared to CICCs and PIVCs?

## Methods

### *Data Sources*

The following electronic databases of the medical literature, scientific conference websites, and health agency/organization websites, were searched to identify relevant articles published from January 1, 2000, to March 30, 2017:

- Medline via PubMed
- EMBASE
- Cochrane Database of Systematic Reviews
- Cochrane Health Technology Assessment (HTA) Database
- Centre for Reviews and Dissemination (CRD)
- EconLit Database
- Conference abstracts from the last 2 years: NIVAS Central Venous Access Devices Symposium, French Society of Anesthesiology and Intensive Care, UK Infection Prevention Society, Vascular Access Society, Italian Gli Accessi Venosi Centrali a Lungo Termine (Long-Term Central Venous Accesses), and European Society of Intensive Care Medicine.

### *Search Strategy*

An initial screen of identified titles/abstracts and other materials from the gray literature was performed to collate a pool of potentially relevant studies. Full-text versions of potentially relevant records were then assessed according to the inclusion and exclusion criteria to determine eligibility for the review. All studies that met the set criteria were thoroughly reviewed and assessed for methodologic quality. Exclusion reasons were documented for all records screened in full text (see Figure).

The reference lists from the publications selected for inclusion and other systematic reviews and meta-analyses pertinent to the topic were screened for other potentially eligible articles.

The following steps were followed for the identification of studies:

1. The search strategy across all databases was performed by one reviewer.
2. Titles and abstracts of studies identified from the searches were screened by one reviewer based on the inclusion/exclusion criteria (level 1 screening).
3. A sample of 20% of the level 1 screening was conducted by a second reviewer to ensure that inclusion/exclusion criteria were well understood and that both reviewers were obtaining the same results. Any discrepancies were discussed until a resolution was found.
4. Full texts of studies accepted at level 1 were further reviewed by 2 analysts at level 2. If there was any uncertainty on the study relevance, a third reviewer assessed the full text, and the issue was resolved by consensus. All reasons for exclusion were documented via the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram.[8]

### *Study Selection Criteria*

The review questions were addressed in accordance with the PICOS scheme (population, intervention, comparators, outcomes, and study design) (Table 1) and the specified inclusion/exclusion criteria.[9] Studies reporting on efficacy, safety, or costs of short/intermediate-term use of PICCs for nonchemotherapy applications in Europe were included in the review.

Studies with the following were not eligible for inclusion:

- Publication date not within the specified range (January 1, 2000, to March 30, 2017)
- Patients younger than 18 years
- Relevant outcomes not reported
- Previous deep vein thrombosis (DVT) or known clotting disorder
- Improper use of PICCs
- Chemotherapy-related rationale for utilization of the PICC (to exclude patients utilizing PICCs for longer-term

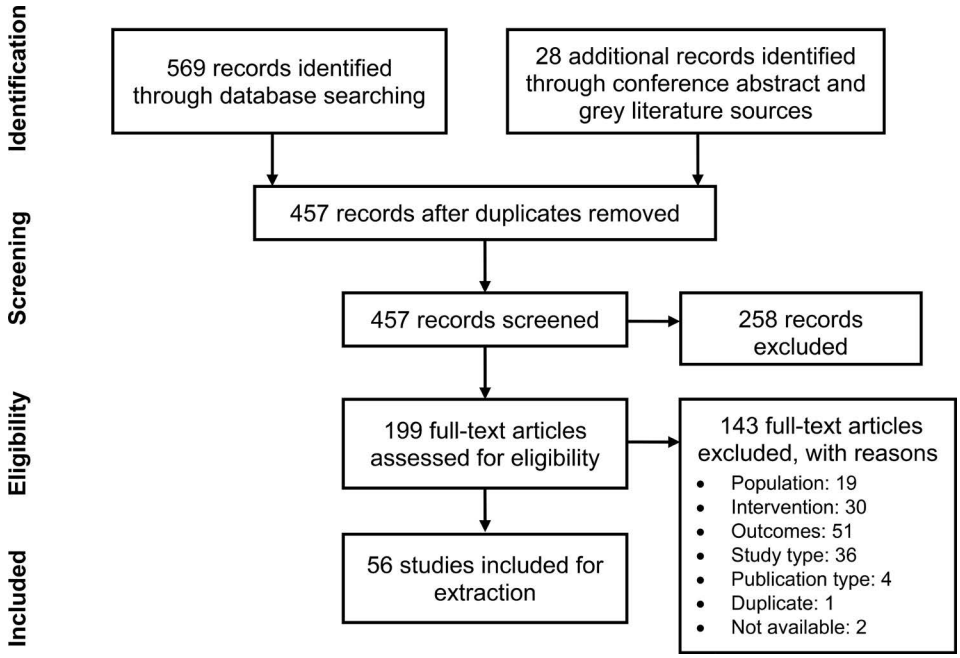


*Figure.* **PRISMA flowchart of the study selection process.**

*Table 1.* **PICOS Framework**

| | |
|---|---|
| Population | • Adults (≥18 years) who received PICCs in the short/intermediate term (<6 months) in Europe, including 28 countries in European Union, plus Norway and Switzerland |
| Intervention | • Short/intermediate-term (<6 months) use of PICCs, for nonchemotherapy |
| Comparators | • PIVCs<br>• CICCs, including tunneled and nontunneled catheters |
| Outcomes | • Efficacy<br>○ Patient comfort and satisfaction<br>○ Pain during insertion<br>○ Overall number of catheter days<br>○ Mean catheter dwell time<br>○ Placement complications<br>• Safety<br>○ Complications leading to catheter removal<br>○ Accidental catheter removal<br>○ Catheter blockage/occlusion<br>○ Catheter migration<br>○ Catheter fracture<br>○ Mechanical failure<br>○ Thrombosis/deep vein thrombosis (DVT)<br>○ Inflammation<br>○ Skin reactions<br>○ Infections<br>○ Central line–associated bloodstream infection (CLABSI)<br>○ Bleeding complications<br>• Costs<br>○ Resource utilization<br>○ Inpatient costs<br>○ Outpatient costs<br>○ Nonmedical costs |
| Study design | • Randomized controlled trials, nonrandomized controlled trials, real-world studies, reviews, HTA reports, epidemiologic studies, observational studies, patient-reported outcomes studies, registries, case studies, and cost studies |

*Table 2.* **Studies Included in This Review**

| Author (reference) | Year | Country | Study type | Interventions |
|---|---|---|---|---|
| Pirson et al[62] | 2015 | Belgium | Case study | PICC |
| Bech et al[22] | 2016 | Denmark | Retrospective, cohort study | PICC, CICC |
| Christensen et al[18] | 2014 | Denmark | Prospective study | PICC |
| Christensen et al[24] | 2016 | Denmark | Retrospective, cohort study | PICC |
| Pedersen et al[14] | 2015 | Denmark | Retrospective study | PICC, PIVC |
| Lindsay et al[63] | 2007 | Europe (unspecified) | Single-center randomized study | PICC |
| Betegnie et al[37] | 2014 | France | Retrospective study | PICC |
| Bouzad et al[23] | 2016 | France | Retrospective study | PICC |
| Cornillon et al[38] | 2017 | France | Prospective study | PICC |
| Delarbre et al[25] | 2004 | France | Retrospective study | PICC |
| Dupont et al[12] | 2015 | France | Prospective study | PICC |
| Gire et al[45] | 2015 | France | Prospective single-center study | PICC |
| Grau et al[26] | 2017 | France | Prospective cohort study | PICC |
| Juntas-Morales et al[64] | 2015 | France | Prospective study | PICC |
| Juntas-Morales et al[48] | 2017 | France | Retrospective study | PICC |
| Leroyer et al[29] | 2013 | France | Prospective study | PICC |
| Moureau et al[43] | 2010 | France | Prospective study | PICC |
| Toure et al[33] | 2015 | France | Prospective study | PICC, CICC |
| Valbousquet et al[15] | 2015 | France | Retrospective study | PICC |
| Vidal et al[35] | 2008 | France | Prospective study | PICC |
| Konstantinou et al[11] | 2013 | Greece | Prospective study | PICC, CICC |
| Konstantinou et al[65] | 2015 | Greece | Case report | PICC |
| Baldinelli et al[36] | 2015 | Italy | Prospective study | PICC |
| Bellesi et al[4] | 2013 | Italy | Prospective study | PICC |
| Bonizzoli et al[16] | 2011 | Italy | Prospective study | PICC, CICC |
| Conte et al[47] | 2015 | Italy | Prospective single-center study | PICC |
| Cotogni et al[5] | 2013 | Italy | Prospective, single-center study | PICC, CICC |
| Elli et al[13] | 2017 | Italy | Prospective study | PICC |
| Falcone et al[66] | 2017 | Italy | Retrospective, multicenter, case-control study | PICC, CICC |
| Pittiruti et al[30] | 2012 | Italy | Retrospective study | PICC |
| Salvatori et al[44] | 2016 | Italy | Retrospective study | PICC |
| Scocca et al[46] | 2008 | Italy | Prospective study | PICC |
| Sica et al[31] | 2015 | Italy | Retrospective study | PICC |
| Spaziani et al[32] | 2000 | Italy | Prospective study | PICC |

*Table 2.* ***(Continued)***

| Author (reference) | Year | Country | Study type | Interventions |
|---|---|---|---|---|
| Gerling and Feenstra[39] | 2016 | Netherlands | Case study | PICC |
| van Boxtel et al[34] | 2008 | Netherlands | Prospective study | PICC |
| Almirante et al[67] | 2012 | Spain | Surveillance study | PICC, CICC, PIVC |
| Ayuela Azcarate et al[68] | 2002 | Spain | Case report | PICC |
| Botella-Carretero et al[17] | 2013 | Spain | Prospective study | PICC, CICC |
| Hernandez et al[27] | 2011 | Spain | Cost-utility study | PICC |
| Juve[28] | 2003 | Spain | Retrospective study | PICC, CICC |
| Navarro Mediavilla et al[21] | 2015 | Spain | Retrospective study | PICC |
| Rodriguez et al[49] | 2015 | Spain | Retrospective study | PICC |
| Gardiol et al[69] | 2016 | Switzerland | Prospective study | PICC |
| Glauser et al[40] | 2016 | Switzerland | Prospective randomized controlled study | PICC |
| Periard et al[10] | 2008 | Switzerland | Single-center, randomized controlled study | PICC, PIVC |
| Barr et al[70] | 2012 | UK | Retrospective cohort study | PICC, CICC |
| El-Ghazali et al[71] | 2015 | UK | Case report | PICC |
| Griffiths and Philpot [6] | 2002 | UK | Prospective study | PICC, CICC, PIVC |
| Johnston et al[19] | 2012 | UK | Prospective study | PICC |
| Johnston et al[72] | 2013 | UK | Retrospective study | PICC |
| Johnston et al[41] | 2014 | UK | Retrospective study | PICC |
| Kumar and Amin[42] | 2004 | UK | Case report | PICC |
| Le Couteur et al[20] | 2015 | UK | Retrospective cohort study | PICC |
| Orme et al[73] | 2007 | UK | Case report | PICC |
| Parcell et al[74] | 2013 | UK | Retrospective study | PICC |

use and to focus the study on a more homogeneous population)
- Patients with stage 3b chronic kidney disease or greater (estimated glomerular filtration rate <45 mL/min)

### *Data Extraction and Analysis*

Data extraction was performed by 1 reviewer and was verified by a second reviewer. Analysis of extracted data was performed by 3 reviewers, and results were summarized in a preliminary technical report to document all findings.

## Results

### *Study Selection*

The PRISMA flowchart of the study selection process is depicted in the Figure. The searches of PubMed, EMBASE, and Cochrane Database of Systematic Reviews yielded 241, 263, and 65 relevant records, respectively, for a total of 569 records identified through database searching. Searches of the gray literature and hand searching of reference lists yielded an additional 28 records. After exclusion of duplicates, a total of 457 records were screened by title/abstract for potential eligibility, and 258 records were excluded based on title and abstract screening. A total of 199 full-text materials, including articles, reports, and conference abstracts were obtained and scrutinized against the selection criteria, of which 56 publications in full text were selected for data extraction (Table 2).

A total of 9 countries in Europe are represented by the 56 studies that were identified. Most studies were conducted in France (14 studies), followed by Italy (12 studies) and the United Kingdom (10 studies). The remaining studies were conducted in Belgium, Denmark, Greece, Netherlands, Spain, and Switzerland, and in one study (conference abstract) the country was not specified. The number of patients with a PICC in each study varied from 6 to 951. The mean patient age in the studies ranged from 18 to 70.2 years.

*Table 3.* **Summary of Efficacy Outcomes with PICCs and Comparators**

| Type of intervention | Patient comfort and satisfaction, % (*n*) | Pain during catheter insertion, % (*n*) | Number of venipunctures for catheter insertion (*n*) | Mean catheter days (*n*) | Mean catheter dwell time/ duration in days (*n*) | Placement complications, % (*n*) |
|---|---|---|---|---|---|---|
| PICC | 96.8 (1) | 0–18 (5) | 1.15*–1.16 (2) | 7.9–176.1 (6) | 9.4–127 (21) | 0–7.4 (16) |
| PIVC | 79.3 (1) | 23.4 (1) | 2.27 (1) | NR | 4.4–7.3 (2) | NR |
| CICC | NR | 12.2 (1) | 1 (1) | 22.5–98.5 (2) | 6.83–324.92 (6) | NR |

*n* = number of interventions; NR = not reported.
*Calculated as a weighted average.

### *Efficacy Outcomes*

Of the 56 studies selected for data extraction, 32 reported efficacy outcomes with PICCs alone, and 10 with PICCs versus comparators (PIVCs and CICCs). Not all studies reported all outcomes. As per the study selection criteria, comparators were considered only within the context of studies that also reported data on the use of PICCs. No separate searches for comparators were performed.

Table 3 provides a summary of the efficacy of PICCs and comparators in all studies. For each outcome, data ranges are provided, with the number of interventions (*n*) in brackets. Note that the number of interventions does not necessarily correspond to the number of studies because studies may include more than one intervention of the same type. Case studies were omitted from the summary table because single-patient studies would skew the range of results for each outcome toward either 0% or 100%. To complement the data ranges, we have also indicated throughout this article whenever a study reported a statistically significant difference between PICCs and comparators.

Patient comfort and satisfaction were reported in 2 studies. In the randomized study by Periard et al[10] comparing PICCs with PIVCs for intravenous therapy using an internally validated questionnaire, 96.8% of patients using PICCs were satisfied or very satisfied, compared to 79.3% of patients using PIVCs ($P < 0.001$). In the study by Konstantinou et al,[11] mean (SD) satisfaction score (scale 1 to 10) with PICCs was 7.78 (3.73) versus 6.59 (2.06) with CICCs in patients undergoing elective surgery or needing parenteral nutrition and infusion therapy ($P < 0.001$).

Across several studies, pain during catheter insertion was reported in 0% to 18% of patients using PICCs.[11–15] In the study by Konstantinou et al,[11] no significant difference was reported for pain during the procedure between PICCs and CICCs (7.7% vs. 12.2%, $P = 0.502$). In the study by Pedersen et al,[14] 8.7% of patients with PICCs experienced pain during insertion, compared to 23.4% of patients with PIVC lines. No statistical analysis was provided for this comparison.

None of the selected studies reported patient health-related quality of life following PICC insertion.

The study by Konstantinou et al[11] reported no significant difference between PICCs and CICCs ($P = 0.18$) in the number of venipunctures required for successful catheter insertion. However, fewer venipunctures were required with PICCs versus PIVCs in the study by Periard at al[10] for initial catheter insertion (1.16 vs. 2.27, $P < 0.01$).

The mean number of catheter days ranged between 7.9 and 176.1 days with PICCs[16–21] and was 22.5 to 98.5 days with CICCs in 2 studies.[16,17] Mean dwell time or mean catheter duration was defined as the number of days from line insertion until line removal. The reported mean catheter dwell time/duration ranged from 9.4 to 127 days with PICCs[6,10–12,15,16,18,22–35] versus 4.4 to 7.3 days with PIVCs[6,10] and 6.83 to 324.92 days with CICCs.[6,11,16,22,28,33] In 2 studies, mean catheter dwell time was significantly higher for PICCs versus CICCs ($P < 0.0001$),[11,16] whereas the opposite was true in 2 other studies ($P < 0.001$).[22,33] In the study by Periard et al[10] in patients requiring IV therapy for at least 5 days, mean catheter dwell time was significantly higher for PICCs compared to PIVCs (9.4 vs. 7.3 days, $P = 0.01$).

The percentage of patients experiencing placement complications with PICCs ranged from 0 to 7.4%.[4,12,15,21,30,31,35–44] Placement complications were not reported for comparators (CICCs and PIVCs).

### *Safety Outcomes*

Among the 56 studies selected for the review, 43 reported safety outcomes with PICCs alone, and 13 reported safety outcomes with PICCs versus comparators (PIVCs and CICCs). Table 4 summarizes the minimum and maximum values (ranges) of the safety outcomes reported with PICCs and comparators across all studies (number of interventions *n* in brackets).

The rates of removal due to complications were 3.5% to 48% with PICCs[4–6,12,14,15,20,23–27,29,32,33,35,37,38,45,46] compared to 67% to 81.2% with PIVCs[6,14] and 26% to 78% with CICCs.[5,6,33] In the study by Cotogni et al[5] in which catheters were used for home parenteral nutrition in patients with cancer, the ratio of complications leading to removal over total complications was significantly lower for PICCs versus CICCs (55% vs. 85%, $P < 0.05$).

Accidental catheter removal was reported in 1% to 8.9% of patients with PICCs across studies[4,23,26,29,31,35,44] versus 7.8% of patients with PIVCs reported in a single study that met the inclusion criteria.[14] Catheter blockage occurred in 0% to 38% of patients with PICCs[4,5,12,14,15,17,19,23,26,28,29,32–35,46,47] compared to 0% to 16% of patients with CICCs.[5,17,28,33] The proportion of patients reporting catheter migration/dislocation was 0% to 7.7% with PICCs[5,14,30,33,37] compared to 9.6% to 15% with CICCs.[5,33] In the study by Cotogni et al,[5] catheter dislocation was signifi-

*Table 4.* **Summary of Safety Outcomes Reported with PICCs, PIVCs, and CICCs: Minimum–Maximum Values Reported Across Identified Studies as % (n) Where n Is the Number of Interventions**

| Type | Complications leading to removal (*n*) | Accidental removal (*n*) | Blockage/ occlusion (*n*) | Migration (*n*) | Fracture (*n*) | Mechanical failure (*n*) | Venous thrombosis (*n*) | Inflammation (*n*) | Skin reactions (*n*) | Infections (*n*) | CLABSI (*n*) | Bleeding (*n*) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PICC | 3.5–48 (20) | 1–8.9 (7) | 0–38 (17) | 0–7.7 (5) | 0–2.1 (5) | 5–22.3 (5) | 0–27.2 (19) | 0–17 (12) | 3.2–4.5 (2) | 0–21 (18) | 0–5.7 (3) | 0–8 (8) |
| PIVC | 67–81.2 (2) | 7.8 (1) | NR | NR | NR | 16 (1) | 3.4 (1) | 17.5 (1) | 0 (1) | 0–14 (3) | NR | NR |
| CICC | 26–78 (3) | NR | 0–16 (4) | 9.6–15 (2) | 1.2 (1) | 11 (1) | 0–9.6 (4) | 0–23 (3) | NR | 0–35 (4) | NR | 0 (1) |

CLABSI = central line–associated bloodstream infections.

cantly lower with PICCs compared to CICCs (7% vs.15%, $P < 0.01$).

Rates of catheter fracture/breakage were 0% to 2.1% with PICCs across studies[4,33,35,37,47] and 1.2% with CICCs in a single study.[33] The rate of catheter mechanical failure was 5% to 22.3% with PICCs[6,15,18,27,44] and 16% and 11% in PIVCs and CICCs, respectively, in a single study.[6]

The percentage of patients experiencing venous thrombosis was 0% to 27.2% with PICCs[4,5,10,12,13,15,16,18,20,26,29,31,33,35,37,38,44,48,49] compared to 3.4% with PIVCs reported in one study[10] and 0% to 9.6% with CICCs.[5,16,17,33] In the study by Bonizzoli et al[16] in which catheters were used for prolonged IV therapy in patients discharged from the intensive care unit, rates of DVT were significantly higher for PICCs compared to CICCs (27.2% vs. 9.6% of patients or 7.7 vs. 4.4 DVTs per 1000 catheter days, $P = 0.0007$). In the study by Toure et al,[33] venous thrombosis occurred in 7.1% of patients receiving home parenteral nutrition (HPN) via PICCs, whereas no thrombosis was reported for patients with CICCs ($P = 0.01$).

Inflammation (phlebitis, edema) was reported in 0% to 17% of patients with PICCs[4,6,15,17,18,27,29,33,34,38,46,48] versus 17.5% with PIVCs reported in one study[6] and 0% to 23% with CICCs.[6,17,33] In the study by Griffiths and Philpot,[6] the number of insertion sites showing signs of phlebitis was significantly lower in critically ill patients using PICCs for venous access (17%) compared to PIVCs (65%), $P < 0.01$, but not compared to CICCs (22%).[6]

Skin reactions were reported in only 2 studies, with cellulitis occurring in 3.2% and 0% of patients with PICCs and PIVCs, respectively,[10] and edema occurring in 4.5% of patients following PICC insertion.[29]

Infections in general (sepsis, local infections, and infections at insertion site) occurred in 0% to 21% of patients with PICCs[4–6,11,13–15,18,23,26,27,33,35,37,44,47–49] versus 0% to 14% with PIVCs[6,10,14] and 0% to 35% with CVCs.[5,6,11,33] In the study by Toure et al,[33] catheter-associated infection (exit site, tunnel, or pocket infection) rate was lower in patients receiving HPN by PICCs versus CICCs (1.05 vs. 1.87 per 1000 catheter days, $P = 0.01$). Rates of central line–associated bloodstream infections (CLABSI) with PICCs were 0% to 5.7%,[12,15,26,47] and CLABSI was not assessed in the studies of PICCs and CICCs. The incidence of catheter-related bloodstream infections (CRBSI) with PICCs varied among different studies and ranged from 0 to 1.63 per 1000 catheter days.[4,5,17,22–24,31,34,38] In the study by Cotogni et al,[5] CRBSI rate was significantly lower with PICCs compared to CICCs (0 vs. 0.87 per 1000 catheter days, $P < 0.01$), and in the study by Botella-Carretero et al,[17] only PICCs, but not CICCs, showed lower CRBSI incidence than with implanted ports ($P = 0.043$). However, a higher CRBSI rate and a lower time to first CRBSI were reported for PICCs versus CICCs in a 6-year follow-up study in HPN patients (1.43 ± 0.20 vs. 0.95 ± 0.39 per 1000 catheter days, 83.91 ± 93.75 vs. 297.21 ± 386.91 days, $P < 0.001$).[22]

Rates of bleeding complications (hematomas) with PICCs ranged from 0% to 8% of patients,[4,11,13,23,26,29,30,45] and a rate of 0% for local hematomas was reported with CICCs in a single study with no significant difference compared to PICCs (2.56%, $P = 0.326$).[11]

***Cost Outcomes***

Two studies met the study selection criteria and reported cost outcomes for PICCs and their comparators. Konstantinou et al[11] reported that the mean cost of catheters was higher for PICCs versus CICCs (€250.51 vs. €35). However, the study did not consider costs of other materials, activities, complications, or length of hospital stay. The authors note that in their experience, CICCs are typically replaced more frequently than PICCs, which may have an impact on costs. The study by Periard et al[10] compared costs between PICCs and PIVCs. Overall, the cost of materials and activities was evaluated at $690 USD (*approx. €504) and $237 USD (€173) per patient for PICC and PIVC use, respectively. PICC costs included the catheter tray, sterile material for insertion, fluoroscopy, compensation of interventional radiologist, and use of the angiography suite. In both groups, costs included the material used for catheter maintenance, including dressing, valve, fixation device, material for saline flush, material for blood sampling, and nurses' salaries during catheter insertion and maintenance. The major contributors of the overall cost for PICC insertion were price of materials required for insertion ($210 USD [€153]) and angiography suite occupancy ($265 USD [€193]). Materials for catheter maintenance were $27 USD (€20) per patient in the PICC group and $18 USD (€13) in the PIVC group. Nurse time was 4.1 hours and 5.5 hours per patient for PICCs and PIVCs, respectively, corresponding to a nursing cost of $165 USD (€120) and $219 USD (€160), respectively. Although costs associated with catheter complications or differences in length of hospital stay were not factored into this analysis, the authors noted that a potential PICC advantage regarding costs may be related to an earlier hospital discharge.

## Discussion

Overall, the results of this systematic literature review demonstrate that PICCs are generally efficacious and safe to use in the short- and intermediate term (<6 months) among adults in the European setting and in some cases may be preferable to CICCs and PIVCs. However, the risk of DVT, mostly asymptomatic, was reported to be higher with PICCs than with CICCs in one study, and attention should be paid to factors that can reduce this risk.

A previous systematic literature review on the advantages and disadvantages of PICCs compared to other central venous lines including tunneled and nontunneled CICCs and venous ports covered literature from any country up to March 2011.[50] The authors noted that scientific evidence supporting a thorough comparison of PICCs with traditional central venous lines was limited. The evidence base has increased in the past 6 years, as several relevant studies have since been published. The current systematic literature review thus provides an updated perspective, focusing specifically on the use of PICCs in the short/intermediate term in the European context.

In this updated review, PICCs were associated with higher patient satisfaction than were CICCs or PIVCs in studies in which catheters were required for more than 1 week but less than 1 month. This likely relates to the more discrete nature of a PICC versus a CICC and the potential of a single PICC to accommodate all infusions and blood sampling during a hospital stay compared to several punctures that may be required with PIVCs.[10,11] Limited evidence also showed that PICCs may be associated with reduced pain compared with CICCs and PIVCs.[14] However, it should be noted that the studies did not report whether local anesthetic was used during insertion, which may have an impact on pain, ease of device positioning, and patient satisfaction. Similarly, some of the studies used nontunneled CICCs, which may have contributed to more dislocation, infection, and pain, and thus lower patient satisfaction, than if tunneled catheters had been used.

The rates of catheter removal due to complications were consistently reported to be lower for PICCs compared to CICCs and PIVCs. PICCs have a low incidence of mechanical complications that would require immediate catheter removal.[5] In this systematic literature review, catheter migration/dislocation was reported to be lower with PICCs compared to CICCs. Such complications (dislocation, external rupture) were reported to occur less with polyurethane than with silicone PICCs.[51]

Several factors may influence the risk of PICC-related venous thrombosis. Catheter size and lumen configuration are important factors influencing the risk of thrombotic complications.[52] A prospective study conducted over a period of 3 years reported that an increase in the use of single-lumen PICCs and the implementation of smaller 5 Fr triple-lumen PICCs were associated with a significant decrease in rates of DVT ($P < 0.04$).[53] Valbousquet Schneider et al[15] used smaller size PICCs (3 Fr, 20 gauge) and reported no occurrence of thrombosis among orthopedic patients on intravenous antibiotic therapy. A catheter-to-vein ratio of 45% has been reported to be optimal for reducing the risk of venous thromboembolism with PICCs, with no difference in risk when using lower ratios.[54] The use of ultrasound to assist catheter placement is also associated with a lower rate of DVT. Dupont et al[12] reported that ultrasound-guided placement of PICCs was successful in 95.6% of procedures, with no insertion complications and only 2% of patients experiencing DVT. Cotogni et al[5] used ultrasound guidance and a sutureless device for catheter insertion and reported no occurrence of DVT with PICCs, compared to 2.8% with CICCs. The catheter peripheral insertion site is also a potential contributing factor of thrombosis. Catheter insertion in the left arm was associated with increased risk of thrombosis compared with the right arm.[52] For example, in the study by Bonizzoli et al[16] in which 144 PICCs were inserted into either the left or right basilic vein, a significantly higher rate of DVT was associated with the left-side insertion (37.1% vs. 18.3%, respectively, $P = 0.0347$). Based on the anatomy of the upper venous system, venous access may be more difficult and there

*The article by Periard et al. only includes costs in USD ($). Conversion to EUR (€) was calculated using the average exchange rate for the year (2007) preceding the date of manuscript submission (February 2008), assuming that cost data was collected during 2007. The average EUR/USD exchange rate of 1.3701 for 2007 was obtained from the European Central Bank website: https://www.ecb.europa.eu/stats/policy_and_exchange_rates/euro_reference_exchange_rates/html/eurofxref-graph-usd.en.html

may be an increased potential for obstruction to flow for a central venous line located on the left side.[55] Some research suggests that the prophylactic use of anticoagulants such as low-dose warfarin may reduce the risk of catheter-related central venous thrombosis. However, there is lack of consensus in the clinical guidelines on whether anticoagulant therapy should be used for thrombosis prevention, and if so, in which patient groups. Anticoagulants are also routinely used to treat venous thrombosis after it has occurred.[3,56–58]

CRBSIs are an important source of hospital-acquired infections with high clinical and economic burden. Literature- and registry-based estimates of CRBSI during intensive care unit stays in 4 European countries (France, Germany, Italy, and the United Kingdom) indicated 8400 to 14,400 episodes, 1000 to 1584 deaths, and 15,960 to 201,600 hospital days per year, with an overall cost of €35.9 to €163.9 million.[59] The current systematic literature review uncovered conflicting results regarding rates of CRBSI in PICCs versus CICCs in Europe. In another systematic review by Maki et al[60] that was not restricted to European studies, PICCs had lower CRBSI rates than short-term noncuffed and nonmedicated central venous catheters, but had higher rates compared to PIVCs. Further studies are required to conclude the incidence of CRBSIs in PICCs versus its comparators in the European setting.

The 2 cost studies meeting the criteria of this review showed that catheter costs for PICCs are higher than for CICCs and that costs of materials and activities are higher for PICCs than for PIVCs. However, a more holistic evaluation of all incurred costs, including costs associated with treatment of complications and duration of hospital stay, should be considered when making cost comparisons. In the French study by Periard et al,[10] although PICC use was associated with higher costs compared to PIVCs, the authors note that a potential advantage with PICCs may be related to an earlier hospital discharge, which was not taken into account in this study. Another limitation was that the analysis did not include cost of catheter complications. In the current review, a comparison of safety outcomes in patients with PICCs versus PIVCs showed that patients with PICCs had fewer complications leading to removal, less catheter migration, and a lower inflammation (phlebitis) rate. In the study by Konstantinou et al,[11] although the cost of a single PICC insertion was higher than for a CICC, PICCs remained safely in the patient for a longer time (mean duration: 22.5 days), compared to CICCs (mean duration: 14.56 days), which required more frequent replacement. The cost of additional materials required to ensure maximal sterile conditions during CICC placement, as well as additional labor costs (assistants required for the placement procedure) and potentially higher risk of complications, were not taken into account and could potentially raise the total operational cost of CICCs compared to PICCs.[58] Therefore, the total costs per patient are not accurately reflected in this study. Further studies are required to assess the overall costs associated with PICCs versus comparators over the full treatment duration, with costs of all materials, labor, and complications included in the analysis.

This systematic review has some limitations. Firstly, it should be noted that there was considerable heterogeneity among included studies in terms of study size, study design, patient demographics, indication for catheter use, and definitions of measured outcomes. For this reason, a meta-analysis was not conducted. Furthermore, to limit the scope of the review and focus on PICCs, only studies that included PICCs were considered, including studies of PICCs alone without comparators. The data reported for CICCs and PIVCs in this review therefore relate only to comparisons with PICCs, despite the availability of other data in excluded studies that do not contain PICCs. The scope was further narrowed by excluding studies in which PICCs were used for chemotherapy, which helped to focus on shorter-term duration and to reduce the heterogeneity among included studies. However, the findings of this report may therefore not be applicable to the use of PICCs in chemotherapy in the short/intermediate term. Although we were able to report on statistical significance from individual studies in our review, overall efficacy and safety results and comparisons between types of catheters across studies could only be reported as ranges (minimum–maximum), as a meta-analysis was not performed. A welcome follow-up to our general and broad search would be to conduct a meta-analysis focusing on specific outcomes within the context of more focused search criteria.

## Conclusion

In conclusion, this systematic review of the European literature showed that PICCs offer several advantages compared to CICCs and PIVCs in short/intermediate-term use, including greater patient satisfaction, fewer complications leading to removal, and less catheter migration/dislocation, despite a moderately higher rate of venous thrombosis.

### *Relevance to Clinical Practice*

The findings of this review may help clinicians better understand the benefits and risks associated with the use of PICCs in the short/intermediate term, allowing them to make more informed decisions about the appropriateness of their use in different clinical scenarios. As outlined in the Infusion Nurse's Society's standards on VAD selection and placement, the appropriate type of VAD should be selected to accommodate a patient's vascular access needs based on several factors. These include prescribed therapy or treatment regimen, anticipated duration of therapy, vascular characteristics, patient age, comorbidities, history of infusion therapy, preference for VAD location, and ability and resources available to care for the device. The selected VAD should be of the smallest outer diameter with the fewest number of lumens and should be the least invasive device needed for the prescribed therapy. Peripheral vein preservation should also be considered when planning for vascular access. Selection of the most appropriate VAD should thus occur as a collaborative process among a multidisciplinary team, the patient, and the patient's caregivers.[61]

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