

CADTH Health Technology Review

Peripherally Inserted Central Catheters in Pediatric Patients Performed by Radiologists Using Fluoroscopy

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Abbreviations

AIEOP	Italian Association of Pediatric Hematology and Oncology
CVAD	central venous access device
CVC	central venous catheter
IR	interventional radiology
miniMAGIC	Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics
PICC	peripherally inserted central catheter
PICU	pediatric intensive care unit

Key Messages

- Evidence from 2 clinical studies showed that there was no difference in the rates of infection and complications between peripherally inserted central catheter (PICC) insertion at the bedside and insertion in Interventional Radiology (IR) suites. However, each of these studies focused on small subgroups of the larger pediatric population and had other methodological limitations.
- Evidence from 1 clinical study in a single quaternary, non-cardiac, pediatric intensive care unit suggested that the median time from PICC line order to successful insertion was longer for lines placed in the IR compared to at the bedside.
- Two guidelines with numerous quality limitations were identified that recommend ultrasound guidance for insertion of central venous access devices (CVAD), including PICCs: 1 was aimed at all pediatric patients and 1 was aimed at onco-hematological pediatric patients.

Context and Policy Issues

Peripherally inserted central catheters (PICC) are a type of central venous catheter that is inserted into peripheral veins in order administer medication over the intermediate to long-term (e.g., prolonged antibiotic administration).¹ Several methods exist for the insertion of PICC lines including blind insertion (using anatomic landmarks), fluoroscopy, and most commonly, ultrasound guidance.² PICC lines may be inserted by various medical personnel (e.g., nurses, non-radiologist physicians, interventional radiologists) and in various locations (e.g., at the bedside or in interventional radiology [IR] suites). The choice of insertion technique and location may depend on several factors including clinical indication (e.g., patients with critical airways could be considered for bedside placement; patients with a history of deep vein thrombosis could be considered for placement in IR),³ facility availability, personnel availability, and institutional guidelines.^{3,4}

There is varying practice with respect to PICC line insertion in the Canadian pediatric population. A review and summary of the relevant literature may help inform process decisions within Canadian health care institutions.

The aim of this report is to summarize the evidence regarding the comparative clinical effectiveness of PICC insertions performed by radiologists in IR suites, compared to nurses at the bedside, and to summarize the evidence-based guidelines regarding the optimal approach for PICC insertions in pediatric patients.

Research Questions

1. What is the comparative clinical effectiveness of peripherally inserted central catheter (PICC) insertions performed by radiologists in interventional radiology suites versus PICC insertions performed by nurses at the bedside/unit in pediatric patients?
2. What are the evidence-based guidelines regarding the optimal approach for PICC insertions in pediatric patients?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. For question 1, the main search concepts were peripherally inserted central catheters, pediatric populations, and relevant radiologic techniques. No filters were applied to this search to limit retrieval by study type. Comments, newspaper articles, editorials, and letters were excluded. For question 2, the main search concept was peripherally inserted central catheters. Search filters were applied to this search to limit retrieval to guidelines. Where possible, retrieval was limited to the human population. The searches were also limited to English-language documents published between January 1, 2015 and December 12, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Criteria	Description
Population	Pediatric patients undergoing PICC insertions
Intervention	PICC insertions performed by radiologists in IR suites using fluoroscopy for insertion guidance Include: Studies using any method of catheter tip location confirmation (e.g., fluoroscopy, X-ray, ultrasound) performed by the radiologist
Comparator	Q1: PICC insertions performed by nurses at the bedside using chest X-ray for catheter tip location confirmation Include: Studies involving nurses using no imaging (i.e., blind catheter placement) or another imaging modality (e.g., ultrasound) for insertion guidance Exclude: Studies where nurses use electrocardiograph for insertion guidance ^a Q2: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., procedure length and success rates, multiple attempts or failure to access vessel, patient satisfaction, length of sedation, risk of over-sedation and aspiration, length of hospital stay, ED visits due to cardiovascular or other adverse events, insertion site infection, catheter fracture, air embolism, catheter misplacement, repeat procedure, referral to IR after nurse-performed insertion) Q2: Recommendations regarding the optimal approach for PICC insertions in pediatric patients (e.g., performed by radiologist vs. nurse, imaging modality for catheter tip location confirmation)
Study Designs	HTAs, systematic reviews, RCTs, non-randomized studies, guidelines

ED = emergency department; HTA = health technology assessment; IR = interventional radiology; PICC = peripherally inserted central catheter; RCT = randomized controlled trial.

^aNot approved by Health Canada for this population and procedure.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published before 2015. Systematic reviews in which all relevant studies were captured in other more recent or more comprehensive systematic reviews were excluded. Primary studies retrieved by the search were excluded if they were captured in 1 or more included systematic reviews. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: the Downs and Black checklist⁵ for randomized and non-randomized studies, and the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument⁶ for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 377 citations were identified in the literature search. Following the screening of titles and abstracts, 331 citations were excluded and 46 potentially relevant reports from the electronic search were retrieved for full-text review. Ten potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 52 publications were excluded for various reasons and 4 publications met the inclusion criteria and were included in this report. These comprised 2 non-randomized studies and 2 evidence-based guidelines. Appendix 1 presents the PRISMA⁷ flow chart of the study selection.

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Two primary clinical studies^{3,4} were identified that met the inclusion criteria for research question 1 and 2 guidelines^{8,9} were identified that met the inclusion criteria for research question 2. Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Both primary clinical studies had retrospective cohort designs. The study authored by Conlon et al.³ included data from 472 PICC line placements from June 1, 2015 to May 31, 2017. The study authored by Chau et al.⁴ included data from patients who received common femoral tunnelled central venous catheters (CVC) from January 2014 to December 2015.

Both guidelines were published in 2020. The first was produced by the Italian Association of Pediatric Hematology and Oncology (AIEOP).⁸ The second is referred to as the Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics (miniMAGIC) and was produced by a group of researchers and clinicians in the US and Australia.⁹ Literature for

the AIEOP guideline was identified through 3 literature searches, each covering 1 research question; miniMAGIC was informed by a systematic review.¹⁰

To rate the quality of evidence and strength of recommendations, the AIEOP used an evidence grading system developed by the ESCMID – the European Society of Clinical Microbiology and Infectious Diseases. Each recommendation statement was assigned 1 of 3 quality levels based on the quality of the supporting evidence (where level I was “evidence from at least 1 properly designed [randomized controlled trial]” (p3)⁸ and level III was expert opinion, case studies, or reports) and a strength of recommendation (1 of 4 from A to D, where A indicates a strong recommendation for use and D represents a strong recommendation against use). The miniMAGIC guideline used the RAND/UCLA Appropriateness Method,¹¹ which resulted in clinical indications classified as “appropriate,” “uncertain,” or “inappropriate.”

The miniMAGIC recommendations were generated through a modified Delphi process. The method of recommendation development was not reported for the AIEOP document.

Country of Origin

The country of origin for the first authors of both primary clinical studies^{3,4} was the US and both studies were conducted in the US. The AIEOP guidelines⁸ are intended for Italy and the miniMAGIC guidelines⁹ are intended for Australia and the US.

Patient Population

The study authored by Conlon et al.³ included 472 PICC line placements among a retrospective cohort of patients admitted to a quaternary care, medical-surgical, pediatric intensive care unit (PICU) in the US. This was described as a large centre (n = 55 beds) with more than 3,800 admissions per year. The Chau et al.⁴ study included 244 pediatric patients (specified as those aged 0 to 18 years) who received a femoral tunnelled CVC between January 2014 and December 2015. The study population was obtained from a subset of 2,375 pediatric patients who received a PICC line during this time period. This study took place at a tertiary care pediatric hospital in the US.

The intended users of both included guidelines^{8,9} were clinicians. The target population of the miniMAGIC⁹ guideline was pediatric patients aged 0 to 18 years, who were hospitalized or in ambulatory care in Australia or the US. The AIEOP⁸ guideline was specific to pediatric onco-hematology patients.

Interventions and Comparators

Conlon et al.³ compared PICC line placement at the bedside in the PICU to placement in IR suites. This was a 2-phase study. Phase 1 involved the implementation of a quality improvement intervention that aimed to establish criteria to identify patients for bedside PICC insertion, and then implementation of a bedside PICC service in the PICU. Phase 2 aimed to increase bedside PICC service providers and evaluate the initiative’s outcomes. The bedside PICC service consisted of clinicians trained in PICC placement (2 physicians in phase 1, expanded to 4 vascular access service physicians and 1 nurse practitioner in phase 2). “Trained” was defined as the completion of more than 10 ultrasound-guided PICC placements supervised by IR physicians. PICC line insertion was guided through ultrasound. The method of tip location confirmation was not reported. Indications for bedside placement included unstable transportation and hemodynamic instability (the full list is provided in Table 2). The comparator in this study was PICC line placement in IR. Indications for insertion in IR by fluoroscopy included known history of deep vein thrombosis, history of difficult upper

extremity PICC placement, and repositioning of a PICC line using a rewiring technique. No further details were provided about the comparator.

The intervention in the Chau et al.⁴ publication was ultrasound-guided placement of primary femoral vein-tunnelled CVC at the bedside. The tip position was confirmed with ultrasound. Indications for bedside placement included unstable transportation (e.g., airway compromise). This was compared to the placement of primary femoral vein-tunnelled CVC in the IR suite, confirmed with fluoroscopy. Indications for bedside insertion in Chau et al.⁴ included unstable transportation, extracorporeal membrane oxygenation, or oscillator ventilation.

Both guidelines considered a variety of interventions. AIEOP⁸ made recommendations on the management of CVAD, indications for insertion and selection of CVADs, positioning of CVADs, infusion line management, exit/insertion site management, external and implantable CVADs, choice of and use of securement device, and recommendations on flushing and locking CVADs. miniMAGIC⁹ made recommendations on venous access device (VAD) selection characteristics and insertion technique.

Outcomes

The relevant outcomes from Conlon et al.³ included process measures (time, in hours, to PICC placement) and safety outcomes (rate per 1,000 line days of central line-associated bloodstream infections and rate per 1,000 line days of central line-associated venous thromboembolism). Two relevant outcomes were reported from Chau et al.⁴: the number and rate per 1,000 line days of central line-associated bloodstream infection (“laboratory-confirmation of bloodstream infection, central venous catheter indwelling for 48h before the bloodstream infection and without any other source of infection”⁴ [p. 809]) and the number and rate per 1,000 line days of complications. A composite complications variable, as defined by the Society of Interventional Radiology Reporting Standards for Thoracic Central Vein Obstruction,¹² was used (bleeding, malposition, symptomatic venous thrombosis, catheter occlusion, and infection). The composite complications variable was further subdivided into 2 groups: early complications (the number of complications occurring 30 days or less from time of PICC insertion) and late complications (the number of complications occurring more than 30 days after PICC insertion).

The outcomes considered in the AIEOP guideline⁸ were not explicitly described. The outcomes considered in the miniMAGIC document⁹ included device and insertion characteristics that impact the success of VAD insertion and VAD failure, as well as complications. They are listed in Table 3.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Primary Clinical Studies

The 2 primary clinical studies shared some strengths, as per the Downs and Black checklist.⁵ In terms of reporting, both of the included studies^{3,4} clearly described the objectives, the main outcomes, patient characteristics, and the main findings. Estimates of the random variability in the data were reported, adverse events were included as outcomes (both studies reported complications and/or safety outcomes), no patients were lost to follow-up, and

actual P values were reported. Regarding external validity, both studies created retrospective cohorts that comprised the entire source population (i.e., pediatric patients who received PICCs) during the study period and the study subjects were representative of the source population from which they were recruited. With respect to bias, both studies adjusted for length of follow-up (line days), the statistical tests used were appropriate, compliance with the interventions was reliable, and the outcome measures were accurate. In terms of confounding, the study subjects in the intervention and comparator groups were recruited over the same time periods and there were no patients lost to follow-up.

Both studies^{3,4} shared common limitations. These were both non-randomized studies. Study subjects were not blinded to the interventions and it is unknown whether those measuring the main outcomes were blind to the intervention. The study subjects were assigned to receive the intervention based on clinical criteria; it is unclear whether or how these clinical criteria may have affected the results in each group. Neither study presented a sample size calculation or described the clinically important differences in the main outcome measures, so it is difficult to determine whether sufficient power existed to detect differences across groups.

Differences in methodological quality were, as follows: Chau et al.⁴ described the intervention of interest, provided a small list of confounders (i.e., line days and lumen number; this may not have been complete), took place in a setting representative of the location that most pediatric patients receiving PICC lines would attend (i.e., tertiary care hospital), and made some adjustment for confounding in the analysis, whereas Conlon et al.³ did not.

The lack of randomization to the intervention and comparator groups in both these studies means that the patients in these groups may differ by important clinical or other factors and that the distribution of these factors across the 2 groups may be systematically different. Both studies^{3,4} outlined clinical criteria for receipt of PICC insertion at bedside. There was no discussion about how or whether these clinical characteristics may be associated with the measured outcomes. If an association existed, it was not adjusted for in the analyses. Lack of discussion by both authors about the impact of the clinical criteria on the selection of patients for the intervention makes interpretation of the findings difficult. Further, because sample size calculations were not provided, our confidence in the lack of statistical significance is decreased. Because no power calculation was provided, it is not possible to determine whether the lack of significant difference observed across comparisons is valid.

Guidelines

The objectives and target population were specifically described in both guidelines.^{8,9} The health questions were clear in the miniMAGIC guideline but were missing in the AIEOP document. Individuals from all relevant professional groups, views from the target population, and the target users were clearly defined in the miniMAGIC⁹ guideline but not in the AIEOP⁸ guideline. Both guidelines used systematic methods to identify evidence, but neither presented inclusion and exclusion criteria for the selection of evidence, described the strengths and limitations of the body of evidence, provided explicit links between the recommendations and the supporting evidence, had the guideline reviewed by external experts, or provided a procedure for updating the guideline. Whereas miniMAGIC⁹ described the methods for formulating the recommendations and considered the harms and benefits in formulating the recommendations, AIEOP⁸ did not. The recommendations were clearly written and easily identifiable, and different options for management were considered in both guidelines. Neither guideline included facilitators and barriers to implementation, provided

knowledge translation tools, addressed resource implications, or included monitoring criteria. It was unclear whether competing interests of the guideline development groups were addressed in both guidelines. The AIEOP⁸ includes a statement declaring that the funding bodies have not influenced the content of the guideline but miniMAGIC⁹ does not.

There were similar limitations across both included guidelines. Neither described how the strengths and limitations of the body of evidence were considered in formulation of the recommendations. However, miniMAGIC⁹ was developed using a published method – the RAND/UCLA Appropriateness Method¹¹ – and was accompanied by separate publications summarizing the systematic review¹⁰ conducted to inform these guidelines, and a methods paper.¹³ Further, the AIEOP guidelines are specific to pediatric oncology-hematology patients, which represents a subset of those of interest in the present review.

Summary of Findings

Appendix 4 presents the main study findings and authors' conclusions.

Clinical Effectiveness of PICC Insertion by Radiologists Using Fluoroscopy in Pediatric Patients

Conlon et al.³ compared PICC insertion at the bedside using ultrasound guidance by a bedside PICC service team to PICC line insertion in the IR suite using fluoroscopic guidance. The bedside PICC service was developed in 2 phases with different practitioners participating in each: phase 1 – 2 trained physicians (n = 282 PICC lines); phase 2 – 2 trained physicians plus 4 vascular access service providers and 1 nurse practitioner (n = 211 PICC lines). The method of tip confirmation at bedside was not reported.

Chau et al.⁴ compared placement of femoral-tunnelled CVC at the bedside by ultrasound guidance and tip confirmation by ultrasound to placement in the IR using fluoroscopic guidance. The health care professional inserting the catheter at bedside (e.g., nurse, physician) was not reported.

The 2 included clinical studies^{3,4} reported a total of 4 relevant outcomes.

Infection

Both studies^{3,4} reported no significant difference in the rate per 1,000 line days of central line-associated bloodstream infections between patients with PICC insertion at bedside compared to those in the IR suite. In addition, Conlon et al.³ reported no significant difference in the rate of non-mucosal barrier injury laboratory-confirmed bloodstream infection per 1,000 line days between patients with PICC insertion at bedside compared to those in the IR suite.

Venous Thromboembolism and Other Clinical Complications

Conlon et al.³ reported no significant difference in the rate of venous thromboembolism per 1,000 line days between patients with PICC insertion at bedside compared to those in the IR suite. In Chau et al.,⁴ 1.9% of bedside insertions were associated with venous thrombosis compared to 0.7% of IR insertions, but statistical significance of this comparison was not reported. Chau et al.⁴ reported that there was no significant difference in overall complications, early complications, or late complications between patients with PICC insertion at bedside compared to those in the IR suite, even after adjustment for line days and lumen number.

Process Outcomes

As per Conlon et al.,³ the median time from PICC line order to successful insertion was longer for IR placement compared to bedside.

Guidelines on PICC Insertion in Pediatric Patients

The AIEOP⁸ concluded that there is insufficient evidence to recommend 1 particular CVAD (i.e., PICC, centrally inserted central catheter or femoral-inserted central catheter). This guideline also made a strong recommendation based on level I evidence that ultrasound-guided insertion represents the standard procedure for insertion of CVADs.

The miniMAGIC⁹ considers it appropriate to insert all devices (including PICCs) by using ultrasound guidance. It also concludes that the appropriateness of electrocardiography-guided insertion of PICCs is uncertain because of limited evidence of benefit in the pediatric population.

Neither guideline provided a preferential recommendation for the location of insertion (i.e., bedside versus IR) or health care professional performing insertion (i.e., nurse versus physician).

Limitations

The 2 clinical studies had highly specialized populations³ or interventions.⁴ The patients in Conlon et al.³ were those admitted to a non-cardiac PICU (i.e., a specialized quaternary care unit). Chau et al.⁴ focused on a small subset of patients with PICC lines – those who received femoral-tunnelled CVCs. This narrow scope limits the generalizability of the findings to the broader population.

The method of tip location confirmation was either not reported³ or confirmed via ultrasound.⁴ The health care professionals performing the insertions were either not reported⁴ or included a group of professionals, of which 1 was a nurse practitioner who was involved in a subset of insertions.³ Therefore, both studies provided indirect evidence to address the research question.

Both studies reported non-significant differences between intervention and comparator groups across all clinical outcomes. However, the validity of these findings is uncertain because of the small number of outcome observations, the lack of power calculations, and limited discussion on the potential impact of confounding due to the non-randomization of patients to the intervention group.

Two guidelines were identified. The quality of the AIEOP guideline⁸ was affected by the following limitations: lack of transparency in reporting of the literature search or method of formulating recommendations, limited scope to pediatric onco-hematology patients, and specific to the Italian context.⁸ Further, neither guideline addressed the recommended location of PICC insertion or the recommended provider for insertion.

Gaps in the literature exist. No publications were identified that studied PICC insertion by radiologists using fluoroscopy as the intervention; instead, both studies were designed with PICC insertions by radiologists using fluoroscopy as the comparator. No evidence was identified that studied all PICC insertions in the general hospitalized pediatric population. There were no studies or guidelines produced in Canada, making generalizability to the context of the Canadian health care system indirect.

Conclusions and Implications for Decision- or Policy-Making

Two retrospective cohort studies^{3,4} were identified that compared PICC insertion in pediatric patients performed in IR suites versus at the bedside. Two guidelines^{8,9} were identified that addressed the optimal approach for PICC insertions in pediatric patients.

The studies summarized in this review did not report a difference in the rates of infection, venous thromboembolism, or other clinical complications between methods and locations of PICC insertion and 1 study³ reported a longer time to PICC line insertion with IR placement than with placement at the bedside. However, the identified evidence was limited in quality and quantity. It was also limited in the directness to which it addresses the research questions. It is not specific to nurses performing PICC insertions at bedside with X-ray for tip confirmation. Instead, it is general to bedside PICC insertion with ultrasound or no mention of tip confirmation.

Further, existing guidelines recommend the use of ultrasound guidance for insertion of PICC lines in pediatric patients but did not address recommendations for location of insertion or health care professional performing the insertion.

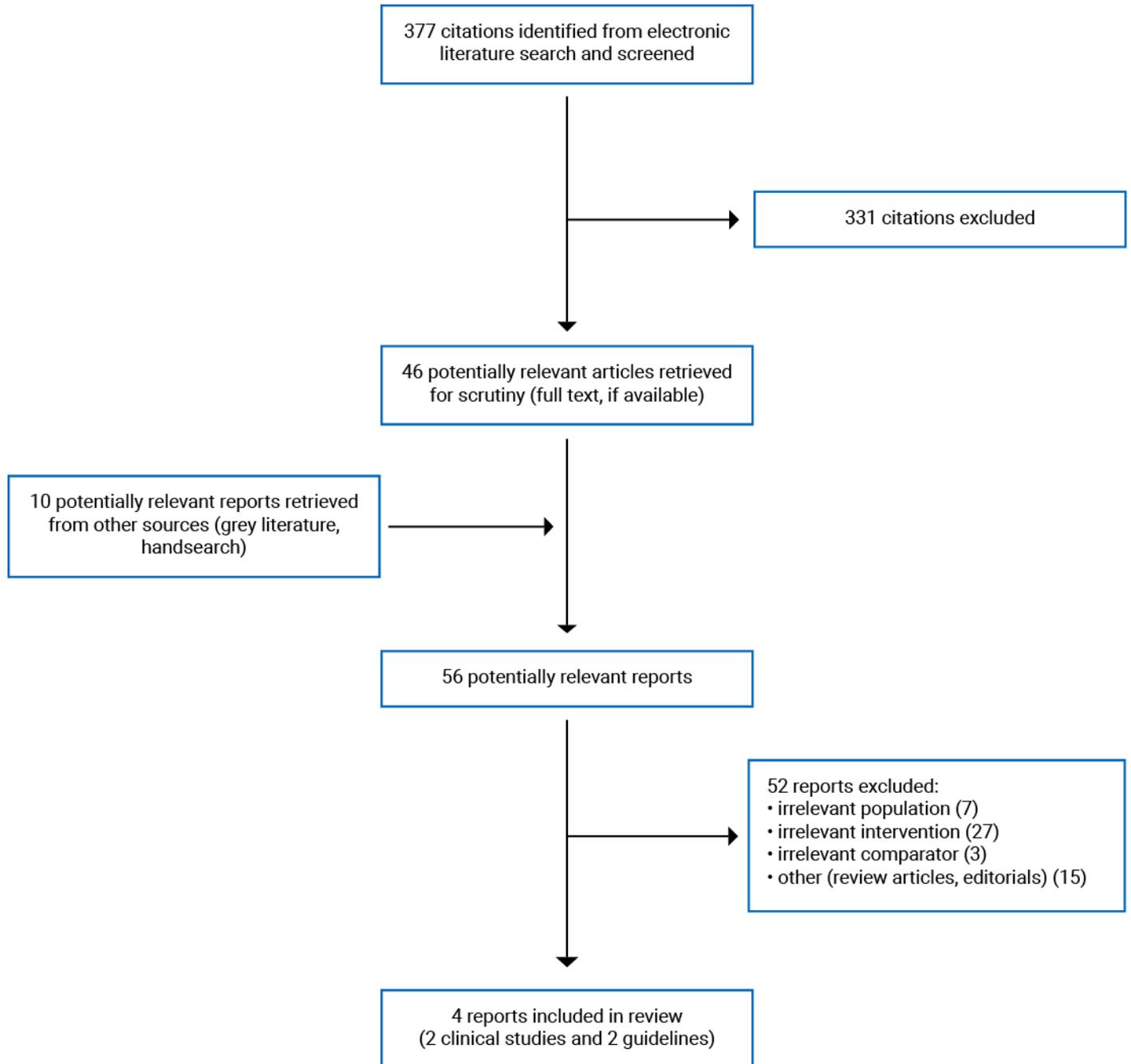
Future research should focus on a broader pediatric population, instead of population and hospital unit subgroups, to generate more generalizable results. If ethically appropriate, researchers should consider conducting randomized studies to reduce bias when comparing PICC insertion in various settings and by various health care professionals. Additional considerations beyond the evidence of clinical effectiveness and safety that may inform the choice of setting for PICC insertion may include logistical barriers and cost.

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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes
<p>Conlon et al. (2019)³ US</p> <p>Funding Sources: Children’s Hospital of Philadelphia, University of Pennsylvania National Institutes for Health, Society of Critical Care Medicine</p>	<p>Study design:Retrospective cohort study</p> <p>Setting:Single quaternary non-cardiac PICU in the US</p> <p>Objectives:</p> <ul style="list-style-type: none"> • To develop unit-specific criteria for PICC line placement and indications for bedside placement (phase 1) • To increase bedside PICC placement in the PICU (phase 2) 	<p>Patients admitted to the PICU with PICC lines</p> <p>Number of observations: N = 472 (342 IR vs. 130 bedside)</p> <p>Median age (IQR):NR for overall study population but reported separately for intervention and comparator:</p> <ul style="list-style-type: none"> • 11.3 years (5.5 to 15.6) for bedside PICC • 2.6 (0.9 to 10.3) for IR PICC 	<p>Intervention:</p> <p>PICC line placement at the bedside of PICU patients by trained providers (physicians and a nurse practitioner) using ultrasound guidance</p> <p>Indications for bedside placement:</p> <ul style="list-style-type: none"> • “presence of anticipated hemodynamic instability and/or requiring active titration or inotropes/vasopressors...” (p10)³ • “patients with existing or anticipated Critical Airway” • “patients with anticipated instability if transported on mechanical ventilation support other than ‘conventional’ support.” (p10)³ • “complex patients or [those in which the team anticipates] high risk for transport...” (p10)³ • At the request of the primary treatment team <p>Comparator:</p> <p>Other locations (including IR suite)</p> <p>Indications for insertion in IR suite by fluoroscopy:</p> <ul style="list-style-type: none"> • “known history of deep vein thrombosis in the candidate extremity in the targeted upper extremity” (p10)³ • “history of difficult upper extremity PICC placement” (p10)³ • “repositioning a PICC line using re-wiring technique” (p10)³ 	<p>Relevant outcomes:</p> <p>Process measures (time to PICC placement)</p> <p>Safety outcomes: CLABSI and central line-associated VTE</p>

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes
<p>Chau et al. (2018)⁴</p> <p>US</p> <p>Funding Source: Texas Children's Hospital</p>	<p>Study design: Retrospective cohort study</p> <p>Setting: Single tertiary hospital in the US</p> <p>Objective: To compare bedside and IR suite placement of femoral vein-tunnelled CVCs</p>	<p>Pediatric patients (0 to 18 years) that met the criteria for femoral vein-tunnelled CVC:</p> <ul style="list-style-type: none"> • “congenital cardiac patients requiring preservation of upper extremity veins, • infants younger than 6 months, or • critically ill patients unsuitable for transport to the IR suite.” (p890)⁴ <p>Number of patients: N = 244 (140 IR vs. 104 bedside)</p> <p>Age range: 1 to 3,531 days</p>	<p>Intervention: Bedside-placed primary femoral vein-tunnelled CVC. Bedside placement occurred in the ICU or ER, guided by ultrasound.</p> <p>Indications for bedside placement included “unstable transportation such as airway or cardiopulmonary compromise, extracorporeal membrane oxygenation, or oscillator ventilation.” (p890)⁴</p> <p>Comparator: Placement of primary femoral vein-tunnelled CVC in the IR suite, confirmed with fluoroscopy.</p>	<p>Relevant outcomes: Complications as defined by the Society of Interventional Radiology Reporting Standards¹²: bleeding, malposition, symptomatic venous thrombosis, and catheter occlusion. Complications assigned as early (\leq 30 days) and late ($>$ 30 days)</p> <p>Infection: laboratory-confirmation of bloodstream infection</p>

CLABSI = central line-associated bloodstream infection; CVC = central venous catheter; ER = emergency room; ICU = intensive care unit; IQR = interquartile range; IR = interventional radiology; NR = not reported; PICC = peripherally inserted central catheter; PICU = pediatric intensive care unit; vs. = versus; VTE = venous thromboembolism.

Table 3: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Italian Association of Pediatric Hematology and Oncology (2020) ⁸						
<p>Intended users: clinicians</p> <p>Target population: pediatric onco-hematology patients</p>	<p>Management of CVADs (including PICCs), indications for insertion and selection of CVADs, positioning of CVADs, infusion line management, exit/insertion site management, recommendations for external CVADs, recommendations for implantable CVADs, choice of securement device, recommendations on the use of securement devices, recommendations on flushing and locking CVADs</p>	<p>The authors did not explicitly describe the outcomes of interest.</p>	<p>3 literature searches:</p> <ul style="list-style-type: none"> • medical management of CVADs • nurse management of CVADs • insertion of CVADs and insertion-related complications <p>No information about the method of evidence synthesis was provided.</p>	<p>Evidence quality was assessed via method proposed by the European Society of Clinical Microbiology and Infectious Disease (unpublished).</p> <p>Evidence grouped into 3 quality levels: evidence from at least 1 well-designed RCT (I); evidence from at least 1 well-designed clinical trial without randomization and/or observational studies (II); expert opinion or case studies (III)</p>	<p>Recommendations were proposed by topic work groups; discussed and approved by full guideline panel. The specific method used to generate the recommendation statements (e.g., consensus, Delphi method) was not described.</p>	<p>The guideline document was reviewed by members of the AIEOP. There was no mention of external review by other experts.</p>

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
miniMAGIC (2020) ⁹						
<p>Intended users: clinicians</p> <p>Target population: pediatric patients aged 0 to 18 years (hospitalized and in ambulatory care) in Australia and the US</p>	VAD selection, characteristics, and insertion technique	<p>“Device characteristics included VAD type, device catheter-to-vein ratio, and device lumens.</p> <p>Insertion characteristics included insertion site and location and the use of vessel visualization technology.</p> <p>Complications included but were not limited to central line-associated bloodstream infection (CLABSI), VAD-associated thrombosis, occlusion, catheter dislodgement, catheter tip migration, catheter breakage or rupture, local infection, and phlebitis.” (pS244)¹⁰</p>	Systematic review with duplicate evidence screening and selection; triplicate data extraction	Duplicate quality assessment of included studies using validated tools	<p>Members of the guideline panel independently and anonymously rated clinical scenarios (n = 1,234) on a scale of 1 to 9 (1 being “harm outweighs benefit” and 9 being “benefit outweighs harm”). A second round of ratings occurred after in-person discussion (modified Delphi process). Scenarios were classified to 3 levels of appropriateness as per the RAND/UCLA method:</p> <ul style="list-style-type: none"> • “appropriate: panel median score of 7 to 9, without disagreement; • uncertain: panel median score of 4 to 6 or with disagreement regardless of median; and • inappropriate: panel median score of 1 to 3, without disagreement. • Disagreement existed if ≥ 5 panelists rated each extreme (1-3 and 7-9).” (pS271) 	<ul style="list-style-type: none"> • Internal and/or external review processes were not described.

AIEOP = Italian Pediatric Hematology Oncology Association; CVAD = central venous access device; miniMAGIC = the Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics; PICC = peripherally inserted central catheter; NR = not reported; RAND/UCLA = RAND Corporation and University of California; RCT = randomized controlled trial; VAD = venous access device.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist⁵

Strengths	Limitations
Conlon et al. (2019) ³	
<ul style="list-style-type: none"> • The study's objective and outcomes were clearly described. • The outcome measures were valid and reliable. • The patient characteristics were included. • The statistical tests used to assess the main outcomes were described and appropriate. • The main study findings were clearly described. • Estimates of the random variability in the data for the main outcomes were provided. • Actual P values were reported. • The compliance with the intervention was reliable. • The subjects were representative of, and recruited from, the source population. 	<ul style="list-style-type: none"> • The interventions were not well-described. • Potential confounders were not discussed a priori and adjustment was not made through the analyses. • The number of patients lost to follow-up (i.e., the number of patients in the retrospective cohort for which data were not available) and their characteristics were NR. • The study setting was highly specialized (PICU/quaternary setting) and not representative of the location that most of the source population would attend. • Study subjects were not randomized to the intervention group. Clinical criteria were established to assign patients to a particular bedside vs. IR PICC insertion. • Participants were not blinded. • Blinding of those measuring the main outcomes for the intervention was unable to be determined. • A sample size calculation was NR.

Strengths	Limitations
Chau et al. (2018) ⁴	
<ul style="list-style-type: none"> • The study's objective, outcomes, and interventions were clearly described. • The outcome measures were valid and reliable. • The patient characteristics were included. • The statistical tests used to assess the main outcomes were described and appropriate. • Potential confounders were described and adjustment was made through the analyses. • The main study findings were clearly described. • Estimates of the random variability in the data for the main outcomes were provided. • Actual P values were reported. • The subjects were representative of, and recruited from, the source population. • The study setting was representative of tertiary care hospitals. • The compliance with the intervention was reliable. 	<ul style="list-style-type: none"> • The number of patients lost to follow-up (i.e., the number of patients in the retrospective cohort for which data were not available) and their characteristics were NR. • Some analyses were reported in the results that were not mentioned in the methods. • Study subjects were not randomized to the intervention group and participants were not blinded. • Blinding of those measuring the main outcomes for the intervention was unable to be determined. • A sample size calculation was NR. The authors suggested that the power may have been insufficient to detect statistically significant differences in complications between the intervention and control groups.

IR = interventional radiology; NR = not reported; PICC = peripherally inserted central catheter; PICU = pediatric intensive care unit; vs. = versus.

Table 5: Strengths and Limitations of Guidelines Using AGREE II⁶

Item	Italian Association of Pediatric Hematology and Oncology (2020) ⁸	miniMAGIC (2020) ⁹
Domain 1: Scope and purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	No	Yes
3. The population (patients, public, and so forth) to whom the guideline is meant to apply is specifically described.	Yes	Yes
Domain 2: Stakeholder involvement		
4. The guideline development group includes individuals from all relevant professional groups.	Unsure	Yes
5. The views and preferences of the target population (patients, public, and so forth) have been sought.	No	Yes
6. The target users of the guideline are clearly defined.	No	Yes
Domain 3: Rigour of development		
7. Systematic methods were used to search for evidence.	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	No	No
9. The strengths and limitations of the body of evidence are clearly described.	No	No
10. The methods for formulating the recommendations are clearly described.	No	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Unsure	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	No	No
13. The guideline has been externally reviewed by experts before its publication.	No	No
14. A procedure for updating the guideline is provided.	No	No
Domain 4: Clarity of presentation		
15. The recommendations are specific and unambiguous.	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes
17. Key recommendations are easily identifiable.	Yes	Yes
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	No	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	No

Item	Italian Association of Pediatric Hematology and Oncology (2020) ⁸	miniMAGIC (2020) ⁹
20. The potential resource implications of applying the recommendations have been considered.	No	No
21. The guideline presents monitoring and/or auditing criteria.	No	No
Domain 6: Editorial independence		
22. The views of the funding body have not influenced the content of the guideline.	Yes	Unsure
23. Competing interests of guideline development group members have been recorded and addressed.	Unsure	Unsure

AGREE II = Appraisal of Guidelines for Research and Evaluation II; miniMAGIC = Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings of Included Primary Clinical Studies

Main study findings	Authors' conclusion
Conlon et al. (2019) ³	
<p>Safety outcomes: The study evaluated 130 BPS PICC lines (2,447 line days) and 342 IR PICC lines (8,270 line days) [P = NR]</p> <p>All CLABSI (includes non-MBI-LCBI)</p> <ul style="list-style-type: none"> • BPS PICC: n = 3; rate^a = 1.23 • IR PICC group: n = 18; rate^a = 2.18 • P = 0.37 <p>Non-MBI-LCBIs</p> <ul style="list-style-type: none"> • BPS PICC: n = 2; rate^a = 0.82 • IR PICC: n = 18; rate^a = 2.18 • P = 0.17 <p>VTE</p> <ul style="list-style-type: none"> • BPS PICC: n = 4; rate^a = 1.63 • IR PICC group: n = 13; rate^a: 1.57 • P = 0.91 <p>Process outcomes: “The time from order to successful PICC placement was significantly reduced in patients with BPS line placement [n = 121, median 6h (IQR 2h-23h)] compared with IR line placement [n = 326, median 34h (IQR 19h-61h); P < 0.001]” (p5)³</p>	<p>“We demonstrated that the creation and spread of a team comprised of trained physicians, nurse practitioners, and vascular access nurses specialized in bedside PICC techniques can result in a sustained increase in PICC lines placed at the bedside in critically ill children.” (p5)³</p> <p>“Process measures and balancing metrics highlight programmatic timeliness with shorter time to PICC insertion and safety with no significant difference in CLABSI and VTE rates compared to PICCs placed in IR.” (p5)³</p>

Main study findings	Authors' conclusion
Chau et al. (2018) ⁴	
<p>Distribution of catheter complications by insertion location:</p> <ul style="list-style-type: none"> • Total catheter-related complications, n/N: 14/140 (10.0%) in the IR suite group vs. 14/104 (13.5%) in the Bedside group [P = 0.55] • Early complications, n/N: 8/140 (5.7%) in the IR suite group vs. 3/104 (2.9%) in the bedside group [P = 0.44] • Late complications, n/N: 6/140 (4.3%) in the IR suite vs. 11/104 (10.6%) group in the bedside group [P = 0.07] • Rate of complications per 1,000 line days: 4.3 in the IR suite group vs. 3.6 in the bedside group [P = 0.53] • Total catheter-related infections, n/N: 7/140 (5.0%) in the IR suite group vs. 3/104 (2.9%) in the bedside group [P = 0.57] • Rate of infections per 1,000 line days: 2.1 in the IR suite vs. 0.78 in the bedside group [P = 0.14] <p>Complication and infection outcomes (P values NR)</p> <ul style="list-style-type: none"> • Total catheter-related complications, n/N: 14/140 (10.0%) in the IR suite group and 14/104 (13.3%) in the bedside group • No patients experienced bleeding in the IR suite or bedside groups • Catheter occlusion, n/N: 4/140 (2.9%) in the IR suite group and 4/104 (3.8%) in the bedside group • Malposition, n/N: 2/140 (1.4%) in the IR suite group and 5/104 (4.8%) in the bedside group • Venous thrombosis, n/N: 1/140 (0.7%) in the IR suite group and 2/104 (1.9%) in the bedside group • Infection, n/N: 7/140 (5.0%) in the IR suite group and 3/104 (2.9%) in the bedside group <p>Univariate logistic regression for complications:</p> <ul style="list-style-type: none"> • No significant difference in the odds of having bedside insertion (vs. IR suite) among those with complications (OR, 1.3; 95% CI, 0.6 to 2.9) <p>Multivariate logistic regression:</p> <ul style="list-style-type: none"> • No significant difference in the odds of having bedside insertion (vs. IR suite) among those with complications (OR, 0.8; 95% CI, 0.4 to 2.0), when adjusted for line days and lumen number 	<p>“The most common complication with IR suite placement was infection, whereas the most common complication for the bedside approach was malposition of the catheter. The total number of complications in each group was relatively low, which is why a larger sample size would be helpful to increase the power of the study.” (p893)⁴</p> <p>“We found no statistically significant differences in the total complication rate, early or late complications, or infection rate between the IR suites and bedside-placed lower extremity tunneled CVC, despite the bedside group having statistically significant longer mean line days.” (p892)⁴</p> <p>“The total complications per 1,000 line days for IR suite and bedside in this study (4.3 and 3.6, respectively) is within range of published literature for mechanical complications in all central venous access in the pediatric population 3.8–14 per 1,000 line days...” (p893)⁴</p>

BPS = bedside PICC service; CI = confidence interval; CLABSI = central line-associated bloodstream infection; CVC = central venous catheter; h = hours; IQR = interquartile range; IR = interventional radiology; non-MBI-LCBI = non-mucosal barrier injury laboratory-confirmed bloodstream infection; NR = not reported; OR = odds ratio; PICC = peripherally inserted central catheter; vs. = versus; VTE = venous thromboembolism.

⁴Rate as a measure of infections per 1,000 line days.

Table 7: Summary of Recommendations in Included Guidelines

Recommendations	Quality of evidence and strength of recommendations
Italian Association of Pediatric Hematology and Oncology (2020) ⁸	
<p>“There is not sufficient evidence to absolutely recommend one device over another... usually it is recommended to use the device with the least number of lumens...for therapeutic needs.” (p4)⁸ The authors listed PICCs, CICC, and FICCs as the “devices” covered by the guideline.</p> <p>“The ultrasound-guided technique represents the current standard for venipuncture and venous cannulation for insertion of CVAD.” (p6)⁸</p>	<p>Insufficient evidence</p> <p>Level of recommendation: Alt (Strong recommendation, with evidence from at least 1 well-designed RCT. The authors report that “t” refers to “transferred evidence...from different patient cohorts.” (p3)⁸)</p>
miniMAGIC (2020) ⁹	
<p>“...panelists rated it appropriate to insert all devices [PIVCs, PICCs and non-tunnelled CVADs] by using ultrasound guidance.” (pS279)⁹</p> <p>“...electrocardiography guided insertion of PICCs across populations was rated as uncertain because (unlike the adult population) the evidence in pediatrics for benefit of this technology is limited.” (pS280)⁹</p> <p>“Evaluation of the venous anatomy using ultrasound before placement of all central devices, and placement of VADs in neonates and pediatric patients with long-term vascular access-dependent conditions, was rated as appropriate by the panel.” (pS280)⁹</p>	<p>Appropriate (based on the RAND/UCLA levels of appropriateness)</p> <p>Uncertain (based on the RAND/UCLA levels of appropriateness)</p> <p>Appropriate (based on the RAND/UCLA levels of appropriateness)</p>

CICC = centrally inserted central catheter; CVAD = central venous access device; FICC = femoral-inserted central catheter; miniMAGIC = Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics; NR = not reported; PICC = peripherally inserted central catheter; PIVC = peripheral intravenous catheter; RAND/UCLA = RAND Corporation and University of California; RCT = randomized controlled trial; VAD = venous access device.

Appendix 5: Additional References of Potential Interest

Guidelines With Unclear Methodology

1. Queensland Health. Peripherally inserted central venous catheters (PICC). Brisbane, Queensland, Australia: Queensland Health; 2015 Jan: https://www.health.qld.gov.au/__data/assets/pdf_file/0032/444497/icare-picc-guideline.pdf. Accessed 2021 Jan 14.
 - "For potentially difficult/complicated insertions due to patient factors (e.g. impalpable vessels, morbid obesity, pre-existing injury), clinicians should consider using ultrasound guided access for PICC placement." (p4)