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Quality appraisal of clinical guidelines for Peripherally Inserted Central Catheter-related thrombosis prophylaxis in patients: a systematic review

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Main text: 3927
Abstract: 337
Tables: 4
Figures: 2
Supplement tables: 7
Supplement figures: 1

Quality appraisal of clinical guidelines for Peripherally Inserted Central Catheter-related thrombosis prophylaxis in patients: a systematic review

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Disclosure/Conflicts of Interest

None.

Abstract

Introduction

PICC-related thrombosis is prone to occur, manifesting with an incidence of up to 75%. Guided by established protocols, clinical decision-making emerges as a pivotal strategy to mitigate the burden of PICC-related thrombosis. The efficacy of these guidelines, however, hinges upon the robustness of their evidentiary foundation. This article aims to conduct a meticulous evaluation of the quality of guidelines addressing the prevention of PICC-related thrombosis, with a particular emphasis on scrutinizing the strength of recommendations within the context of prophylactic measures for patients.

Methods

A systematic search of pertinent literature was conducted up to November 27, 2023. Databases such as Web of Science, Cochrane Library, PubMed, EMBASE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), China National Knowledge Infrastructure and WanFang, and nine guidelines' repositories were systematically queried. The identified guidelines underwent comprehensive appraisal utilizing the Appraisal of Guidelines for Research and Evaluation II (AGREE II). Two independent reviewers evaluated the strength of recommendations, employing a pre-defined data collection form to extract pertinent guideline characteristics.

Results

The analysis incorporated a total of eight guidelines, all rated as 'recommended' or 'recommended with modifications.' Standardized scores revealed elevated performance in the domains of Scope and Purpose, Clarity of Presentation, and Editorial Independence. Conversely, the Stakeholder Involvement and Applicability domains yielded the lowest average standardized scores. Disparities in standardized scores across guidelines were particularly evident in the domains of Rigour of Development, Stakeholder Involvement, and Applicability. The agreement between the two appraisers was almost perfect (intraclass correlation coefficients higher than 0.80). A considerable proportion of recommendations relied on evidence of low-quality or very-low-quality, in certain instances, were derived from expert opinions within working groups.

Conclusions

The study reveals that a significant portion of recommendations relies on low-quality evidence, necessitating further validation. Guideline developers are urged to prioritize methodological quality, with a specific focus on refining Stakeholder Involvement and Applicability domains. Addressing these aspects will enhance the overall quality and reliability of PICC-related thrombosis prevention guidelines.

Keywords: Peripherally Inserted Central Catheter, PICC, Catheter related thrombosis, quality in healthcare

Strengths and limitations of this study

- Our research critically evaluated the quality of guidelines for PICC-related thrombosis prevention in patients and the strength of their recommendations in PICC-related thrombosis prevention.
- Two appraisers used AGREE II, an assessment with methodological rigor and reliability, to appraise the quality of included guidelines and resolved any discrepancies by discussion.
- Our search strategy was also reproducible, however, because of language or publication restrictions, there may be a language barrier.

Introduction

Peripherally Inserted Central Catheter (PICC) has gained widespread use in clinical practice owing to its maneuverability, minimal trauma, and heightened safety attributes[1-2]. However, PICC-related thrombosis is prone to occur, stemming from factors such as unavoidable puncture injuries, toxic medication effects, and patient-specific conditions, underscores its incidence, with an incidence of up to 75%[3-4]. In recent years, the escalating utilization of PICC catheters, augmented awareness among medical professionals regarding PICC-related complications, and an elevated detection rate of asymptomatic thrombosis have collectively contributed to a steady rise in PICC-related thrombosis incidences in China[5]. This not only jeopardizes patient safety but also begets prolonged or interrupted treatment, unplanned extubation of the PICC, extended hospital stays, and increased burden on society[6-8].

It is important to emphasize that PICC-related thrombosis is preventable. Chen et al. effectively forestalled the occurrence of PICC-related thrombosis by implementing a graded nursing intervention based on risk assessment for 560 patients[9]. Similarly, Liu et al. executed ball-holding exercise training for PICC-catheterized patients, significantly reducing the incidence of PICC-related thrombosis[10]. However, the current landscape lacks clarity on the latest and most efficacious preventive measures recommended in guidelines.

Using evidence-based programs for PICC-related thrombosis can improve practice outcomes while reducing the physical, psychological, social and economic burden on individuals, families and societies. Clinical Practice Guidelines (CPGs) facilitate optimal decision-making by healthcare professionals and patients, minimizing wastage. Nonetheless, the efficacy of a CPG is contingent upon the robustness of its evidence base[11]. Therefore, an imperative exists to systematically evaluate CPGs to gauge their quality. This systematic review aims to critically appraise the quality of PICC-related thrombosis prevention guidelines and assess the strength of their recommendations.

Methods

Registry

The study adheres to the Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 statement**Error! Reference source not found.**. Additionally, it was registered in the International Prospective Registry of Systematic Reviews (PROSPERO) in December 2023 (protocol ID CRD42023495519).

Objectives

The purpose of this systematic review is to critically appraise the quality of PICC-related thrombosis prevention guidelines specific to patients. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool was used.

Data sources and search strategy

Academic databases, encompassing Web of Science, Cochrane Library, PubMed, EMBASE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Chinese databases (China National Knowledge Infrastructure and Wan Fang), were systematically searched from inception until November 27, 2023. The search strategy was tailored to the requirements of each database. Searching of reference lists from identified papers were scrutinized, and forward citation searches were performed using Google Scholar. All searches were saved in each database and imported into EndNote (V.20; Clarivate Analytics), where duplicates were removed. To supplement our database searches, we also searched guidelines repositories, including CPG Infobase: Clinical Practice Guidelines (Canadian Medical Association), the Guidelines International Network (GIN), the National Health and Medical Research Council—Australian Clinical Practice Guidelines, the National Institute for Health and Care Excellence (NICE), the National Guideline Clearinghouse (NGC), Scottish Intercollegiate Guideline Network (SIGN), New Zealand Guidelines Group (NZGG), BMJ Best Practice and Chinese guidelines repository (Yi Mai Tong). Search details are available in supplemental appendix 1.

Eligibility criteria

A complete list of inclusion and exclusion criteria is detailed in table 1.

Table 1: Inclusion and exclusion criteria

No.	Items
Inclusion criteria	
1	Published international and national guidelines on the management and/or prevention of PICC-related thrombosis
2	Published as full text
3	Guidelines published in Chinese or English
4	Most recent complete guideline (from a single working group, ie, ACCP) and any partial revisions for the guideline published thereafter
5	Include an explicit statement identifying the document as a 'guideline'
Exclusion criteria	
1	Guidelines under development
2	Guidelines were specific to one institution
3	Complete guidelines with publication dates that have been superseded by more recent complete guidelines
4	Guidelines that only cover one aspect of PICC-related thrombosis prevention (ie, anticoagulant prophylaxis)
5	Clinical practice standards, defined as a statement reached through consensus, which identifies the desired outcome. Usually used in audit as a measure of success
6	Guidelines inclusive of only one phase of care, for example, Ginzburg et al.[13] (ie, during rehabilitative therapy)

Note: ACCP, American College of Chest Physicians; PICC-related thrombosis, Peripherally

Inserted Central Catheter-related thrombosis

Data screening and extraction

Two reviewers screened titles and abstracts based on predetermined eligibility criteria. Articles that met the above inclusion and exclusion criteria were included for a second full-text screen. Conflicts were resolved through discussion or the involvement of a third reviewer. Reasons for exclusion were documented in a tabular format (supplemental appendix 2). Data extraction was independently performed using a standardized data extraction form developed based on AGREE II[14].

Quality assessment of CPGs

To evaluate the quality of pre-existing guidelines selected for guideline adaptation, two reviewers graded each guideline according to AGREE II. This instrument consists of 23 items organized into six domains. AGREE II also includes two overall assessment items for overall judgements of the practice guideline. Supplemental appendix 3 provides a brief description of each domain[15].

The 23-item AGREE II tool uses a seven-point agreement scale from 1 (strongly disagree) to 7 (strongly agree)[14]. Standardized scores for each domain were computed as (X/Y) ×100%, where X = obtained score−minimum possible score and Y = maximum possible score−minimum possible score[14]. As defined by AGREE II, we considered a CPG as 'recommended' if most items score 6 or 7 points and multidimensional evaluation is > 60%, as 'recommended with modifications' if the items scoring 6 or 7 points are similar to the items scoring 1 or 2 points, and the multidimensional evaluation is 30% to 60% and as 'not recommended' if most items score 1 or 2 points and the multidimensional evaluation is < 30%.

Before the quality appraisal using AGREE II, two reviewers completed an Online Training Tool[16] and performed calibration exercises to clarify the eligibility criteria. Following training, the two reviewers independently applied AGREE II criteria to eligible CPGs using the My AGREE PLUS online platform.[17] Our team met regularly to resolve any discrepancies in the quality appraisal. We used intraclass correlation coefficients (ICCs) to measure the agreement between the two assessors' assessment of quality (AGREE II) of included CPGs. The results were interpreted as follows: 0.00, poor agreement; 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement.[18]

Results

The electronic database search yielded 329 citations, with 14 full-text reports assessed, excluding 10 (figure 1). Guidelines repository searches retrieved 127 citations, with 13 evaluated and 4 excluded (figure 2). In total, 8 guidelines were included in the final analysis, and the detailed characteristics are shown in table 2. These CPGs were

published between 2013 and 2021. Most of the CPGs were developed in the USA (n=3),[19-21] with the remaining coming from China (n=2),[22-23] the France (n=1),[24] Europe (n=1)[25] or India (n=1)[26]. Information sources regarding where CPGs were obtained are shown in supplemental appendix 4.

Table 2 Characteristics of CPGs regarding PICC-related thrombosis prevention in patients

	ASCO 2013	ASH 2021	INS 2021	CCC-IUA 2020
Original CPG title	Central Venous Catheter Care for the Patient With Cancer: American Society of Clinical Oncology Clinical Practice Guideline	American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer	Infusion Therapy Standards of Practice, 8th Edition	Infusion catheter related venous thrombosis prevention and control China expert consensus (2020 edition)
Date published	2013	2021	2021	2020
Country of origin	USA	USA	USA	China
Objective of CPG	Guide prophylaxis and management of central venous catheter (CVC) care for patients with cancer	Guide prevention and treatment of VTE in patients with cancer	Guide patient-centered infusion care	Guide the clinical work of preventing catheter-related thrombosis
Methods used to collect/select the evidence	A targeted systematic using 2 databases	Systematic evidence reviews of topic areas	A targeted systematic using more than 9 databases	Not stated
Methods used to analyse the evidence	Not stated	The hierarchical system used to strong and conditional recommendations	The hierarchical system used to grade levels of evidence	Not stated
Ranking scheme to determine the strength of the evidence and recommendation	Not stated	Strong, conditional	I, II, III, IV, V, A/P, Committee Consensus	Not stated
Methods used to formulate the recommendations	Expert consensus	Expert consensus	Expert consensus	Expert consensus
Number of recommendations	12	34	26 recommendations in catheter-associated deep vein thrombosis	37
Method of CPG validation	External and internal peer review	External and internal peer review	External and internal peer review	External and internal peer review
Intended users	Medicaloncologists hematologist, nurses, interventional	patients, clinicians and other health care professionals	all health care settings and all populations	Clinicians and nurses

	radiologists, surgeons, infectious disease specialists, and specialized CVC care teams			
Composition of CPG working group	2 groups: 1. 15-panel members from ASCO CVC Care Expert 2. The external peer review group	3 groups: 1. 16-panel members from ASH 2. McMaster GRADE centre 3. The external peer review group	2 groups: 1. health care specialties from 17 countries around the globe 2. 120 international reviewers	2 groups: 1. 47-panel members from CCC-IUA 2. The external peer review group
Number of documents included in the appraisal	2 CPG (1360 pages); online data supplement (1359pages)	2 CPG (928 pages); online data supplement (933 pages)	1 CPG (161 pages)	1 CPG (337pages)

(continued)

	CMA 2018	ITAC-CME 2013	ESMO 2015	ISCCM 2020
Original CPG title	Chinese guidelines for the prevention and treatment of thrombotic diseases	International clinical practice guidelines for the treatment and prophylaxis of thrombosis associated with central venous catheters in patients with cancer	Central venous access in oncology: ESMO Clinical Practice Guidelines	Indian Society of Critical Care Medicine Position Statement for Central Venous Catheterization and Management 2020
Date published	2018	2013	2015	2020
Country of origin	China	France	Europe	India
Objective of CPG	Guide the diagnosis, treatment and nursing of venous thrombosis	Guide management of CRT in cancer patients	Guide management of central venous access in adult cancer patients	Guide critical care physicians and allied professionals
Methods used to collect/select the evidence	A targeted systematic using 10 databases	A targeted systematic using more than 3 databases	Not stated	A targeted systematic using 3 databases
Methods used to analyse the evidence	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence
Ranking scheme to determine the strength of the evidence and recommendation	Grade A, B, C, D; 1, 2	Grade A, B, C, D; Strong, Weak, Best clinical practice	I, II, III, IV, V; A, B, C, D, E	1, 2, 3; Useful Practice Point (UPP), Grade A, Grade B
Methods used to	Expert consensus	Expert consensus	Expert consensus	Expert consensus

formulate the recommendations				
Number of recommendations	19 recommendations in prevention	4	67	54
Method of CPG validation	External and internal peer review	External and internal peer review	External and internal peer review	External and internal peer review
Clinicians and nurses	Clinicians	Clinicians	Clinicians	Critical care physicians and allied professionals
Composition of CPG working group	3 groups: 1. Guideline development group 2. Review committee 3. External reviewer group	2 groups: 1. 24 experts from various specialties 2. The external peer review group	2 groups: 1. ESMO Guidelines Committee 2. The external peer review group	2 groups: 1. 19-panel members from ISCCM
Number of documents included in the appraisal	1 CPG (2861 pages)	2 CPG (71 pages); online data supplement (78 pages)	1 CPG (152 pages)	4 CPG (8 pages); 3 Appendices (22 pages)

Note: CVC, central venous catheter; VTE, venous thromboembolism; CRT, catheter-related thrombosis; CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

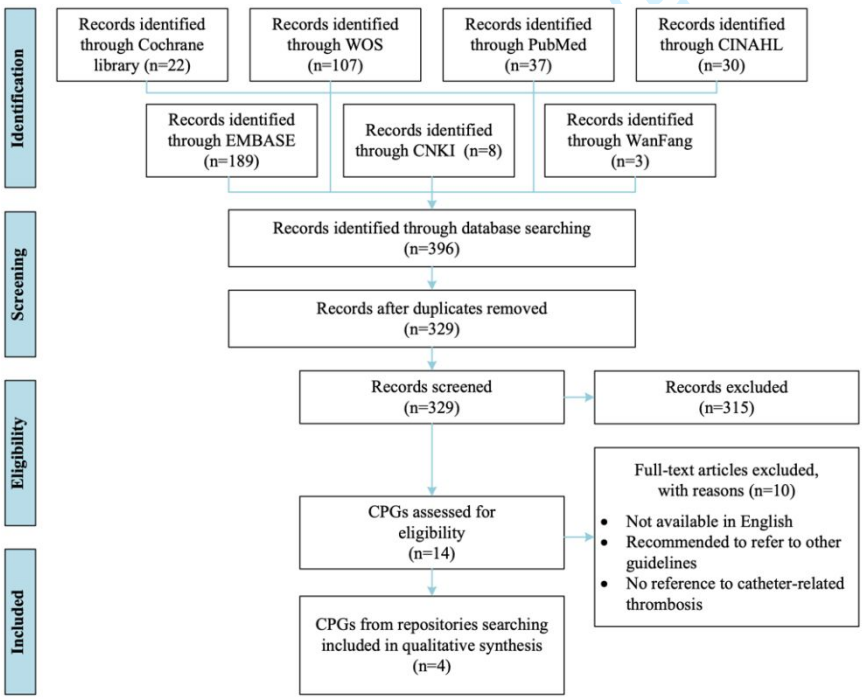

Figure 1 Search strategy for library databases (final search undertaken on 17 November 2023). CPGs, clinical practice guidelines; CINAHL, Cumulative Index of Nursing and

Allied Health Literature; WOS, Web of Science; CNKI, China National Knowledge Infrastructure.

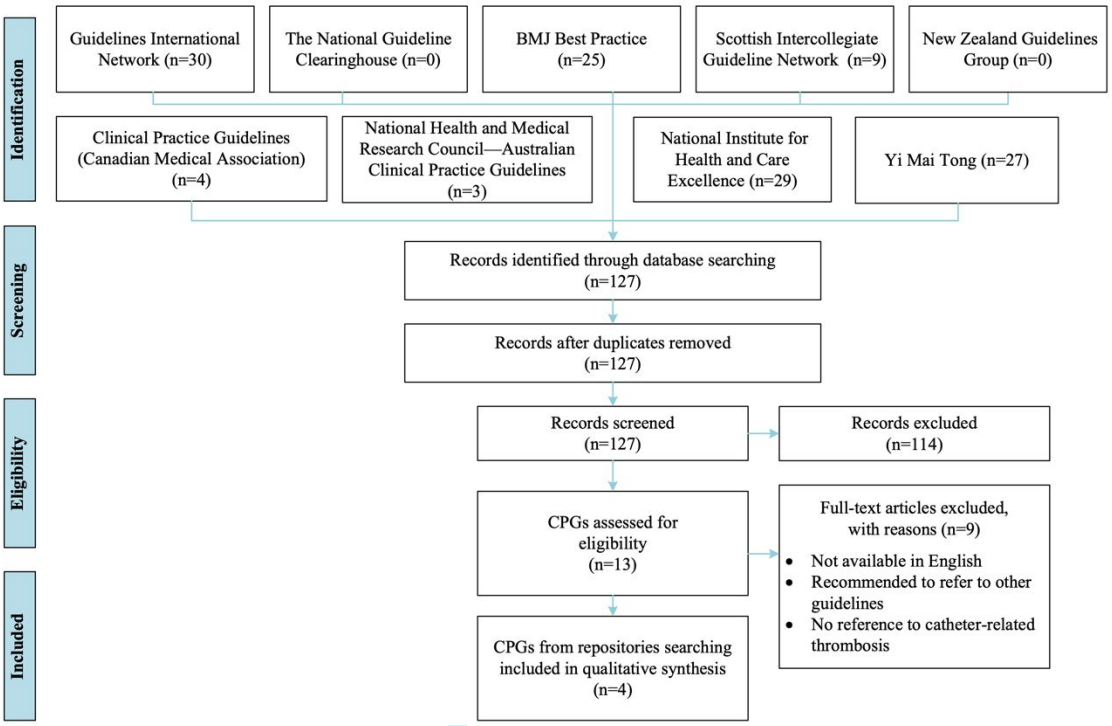

Figure 2 Search strategy for guideline repositories (final search undertaken on 17 November 2023). CPGs, clinical practice guidelines.

Two assessors appraised each CPG. The AGREE II domain scores of each guideline are presented in table 3. Detailed scoring of each AGREE II item under each domain is presented in online supplemental appendix 5. Supplementary Figure 1 shows a radar chart of the results of the guideline appraisal. The quality of the evaluated guidelines showed significant variability. The standardised scores ranged from 86% to 100% in the Scope and Purpose domain, and all CPGs scored above 80%. The standardised scores in the Stakeholder Involvement domain ranged from 58% to 83%, with all CPGs scoring above 50%. The standardised scores in the Rigour of Development domain ranged from 49% to 92%, with only one CPG scoring below 50%. The standardised scores in the Clarity of Presentation domain ranged from 89% to 97%. The standardised scores in the Applicability domain ranged from 46% to 94%, with only one CPGs scoring below 50%. The standardised scores in the Editorial Independence domain ranged from 88% to 100%. Per the quality assessment tool used in this review, 5 of the 8 included CPGs were judged to be 'recommended'. There is an almost perfect agreement between two appraisers, with the intraclass correlation coefficient (ICC) ranging from 0.886 to 0.959 (P<0.001).

Table 3 AGREE II scaled domain scores of CPGs for PICC-related thrombosis prevention in patients

	ASCO 2013	ASH 2021	INS 2021	CCC-IUA 2020	CMA 2018	ITAC-CME 2013	ESMO 2015	ISCCM 2020

1.Scope and Purpose	100%	100%	100%	89%	97%	97%	86%	92%
2.Stakeholder Involvement	81%	92%	69%	67%	69%	69%	58%	72%
3.Rigour of Development	77%	80%	85%	49%	92%	84%	66%	72%
4.Clarity of Presentation	89%	97%	97%	97%	92%	97%	97%	97%
5.Applicability	65%	94%	83%	44%	63%	54%	42%	79%
6.Editorial Independence	100%	96%	88%	88%	88%	92%	100%	100%
Recommended use of this CPG	Yes	Yes	Yes	Yes*	Yes	Yes*	Yes*	Yes
ICC (including overall CPG score)	0.906	0.876	0.937	0.921	0.886	0.952	0.959	0.958

Note: *Recommended with modifications.

Table 4 shows the levels of evidence for recommendations of PICC-related thrombosis prevention in patients, as reported in the included CPGs. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to rank recommendations.[27] Despite unanimous agreement in the recommendations for identifying and assessing risk factors, monitoring for signs and symptoms, providing non-pharmacological preventative measures, diagnose, remove the PICC against, treatment after extubation and medical personnel training, details disagree on the risk assessment tools and pharmacological choice. The Infusion Nursing Society (INS) 2021 guidelines[21] recommended the Michigan risk score for patients with PICC, but the China Medical Association (CMA) 2018 guidelines[23] recommended the Khorana score model for outpatient patients with malignancies receiving chemotherapy. The American Society of Clinical Oncology (ASCO) 2013 guidelines,[19] American Society of Hematology (ASH) 2021 guidelines[20] and International Initiative on Thrombosis and Cancer (ITAC-CME) 2013 guidelines[24] did not recommend pharmacologic prophylaxis. However, the CMA 2018 guidelines[23] recommended using LMWH or LDUH for medium and high-risk patients, and the INS guidelines[21] recommended evaluate the risks of bleeding and thrombocytopenia and the burden associated with anticoagulant management. In terms of risk assessment, pharmacologic preventative measures, diagnose and confirm PICC-related thrombosis, remove the PICC against and medical personnel training, we observed little recommendations with very low quality. The recommendations from each CPG that are informed in table 4 are detailed in supplemental appendix 6. Supplemental appendix 7 shows an explanation of the different evidence levels used across included CPGs.

Table 4 Levels of evidence for recommendations of PICC-related thrombosis

prevention in patients as reported in included CPGs

Recommendations*	ASCO 2013	ASH 2021	INS 2021	CCC-IUA 2020
1.Identify Patient risk factors	–	–	• history of thrombosis (I) • Other factors (II)	• Patients with catheterization (WG) • malignant tumors, chemotherapy and surgery (WG)
2.Identify catheter related risk factors	–	–	• catheter-to-vessel ratio prior to insertion no more than 45% ratio (A/P) • place small-diameter catheters (II) • catheter tip location (A/P)	• the smallest external diameter (WG) • catheter tip location (WG)
3. Identify operator risk factors	–	–	• Evaluate the need and appropriateness of PICC catheter exchange (V) • Catheter removal and replacement in a new site are associated with a high risk (IV)	• Repeated puncture and withdrawal of catheter (WG) • Non-standard rushed, sealing tube operation can increase the risk (WG)
4. Risk assessment of patients with PICC	–	–	when choosing and inserting a PICC (I)	–
5. Consider use of a risk scoring system	–	–	the Michigan Risk Score (III)	–
6. Monitor for signs and symptoms	–	–	Measuring arm circumference (IV)	–
7. Pharmacologic preventative measures for PICC-related thrombosis	Not to use as preference (WG)	• not using parenteral thromboprophylaxis (Low) • not using oral thromboprophylaxis (Low)	• Use LMWH (I) • Use enoxaparin not increased risk of bleeding (IV)	–
8. Non-pharmacological preventative measures for PICC-related thrombosis	flushing with saline as preference (WG)	–	handgrip exercise (IV)	• handgrip exercise (WG) • providing appropriate and adequate nursing care (WG)
9. Diagnose and confirm PICC-related thrombosis	–	–	Doppler ultrasound as preference (II)	Doppler ultrasound as preference (WG)

10. Remove the PICC against	–	–	Do not remove when the catheter is correctly positioned, functional, and necessary for infusion therapy. (II)	–
11. Treatment after extubation	–	–	• Anticoagulation therapy was given for at least 3 months after extubation (II) • Use LMWH as preference (I)	–
12. Medical personnel training	–	–	–	Establishing education and training systems (WG)

(Continued)

Recommendations*	CMA 2018	ITAC-CME 2013	ESMO 2015	ISCCM 2020
1.Identify Patient risk factors	–	–	–	–
2.Identify catheter related risk factors	–	catheter tip location (Grade 1A)	–	catheter tip location (A, 2)
3. Identify operator risk factors	–		–	assess knowledge and compliance (A, 1)
4. Risk assessment of patients with PICC	VTE risk assessment with a central venous catheter (2B)	–	–	–
5. Consider use of a risk scoring system	using the Khorana score model (1B)	–	–	–
6. Monitor for signs and symptoms	–	–	–	–
7. Pharmacologic preventative measures for PICC-related thrombosis	• Not use for low-risk patients (2B) • Use LMWH or LDUH as preference for medium and high risk (2 B)	Not to use as preference (Grade 1A)	–	–
8. Non-pharmacological preventative measures for PICC-related thrombosis		–	flushing with saline as preference (I, C)	providing appropriate and adequate nursing care (B, 2)
9. Diagnose and confirm PICC-related thrombosis	–	–	Doppler ultrasound as preference (III, A)	Doppler ultrasound as preference (B, 2)

10. Remove the PICC against	–	–	–	No need to extubate (A, 2)
11. Treatment after extubation	–	–	–	–
12. Medical personnel training	–	–	–	• Establishing education and training systems (A, 1) • Establishing Credentialing process (B, 2)

Note: CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Discussion

To our knowledge, this is the first systematic quality appraisal of CPGs for PICC-related thrombosis prevention in patients, with recognition of eight guidelines. Overall, the quality of all incorporated guidelines was deemed acceptable, evaluated as either 'recommended' or 'recommended with modifications.' Despite consistency in recommendations across the included CPGs, they employed diverse classification systems to indicate levels of evidence. Discrepancies in preferred pharmacological prophylaxis (such as low molecular weight heparin (LMWH), direct oral anticoagulants (DOACs), or no drug prophylaxis) could be attributed to variations in data availability from trials and the timing of approval by regulatory agencies. It's noteworthy that a substantial proportion of recommendations relies on low-quality or very-low-quality evidence, or even on expert opinions from working groups, suggesting uncertain clinical significance. Therefore, advocating for high-quality randomized controlled trials is imperative to reinforce the evidence base and potentially enhance the cost-effectiveness of treatment.[28] Additionally, in terms of non-pharmacological prevention, very few strong recommendations were identified, indicating a lack of robust evidence. These findings would explain why PICC-related thrombosis prophylaxis is still not routinely administered as guideline recommended in most hospitals.[29-30] It is worth noting that as the first line of defense in the prevention of PICC-related thrombosis, dynamic and accurate risk assessment is crucial. However, current guidelines do not provide detailed descriptions of the timing of risk assessment and specialized assessment tools for PICC-related thrombosis prevention.[21-23] Therefore, Future research should delve into these aspects to refine risk assessment specificity, facilitating clinical prevention and enhancing assessment accuracy.

The standardised scores varied between different domains. The Scope and Purpose, Clarity of Presentation, and Editorial Independence domains exhibited relatively high

standardized scores. In contrast, the Stakeholder Involvement, Rigor of Development, and Applicability domains demonstrated considerable variations among the CPGs. Our results are consistent with the results of other CPG quality appraisal focusing on different clinical topics.[31-32] Marked improvements in CPG development methodology over the past decade may have a role in explaining the variance scores. Moreover, guideline development should be carried out according to the formulated plan, such as the WHO Guideline Development Handbook.[33] It is also recommended to report methodological details for clinical guideline development based on AGREE II.[34]

We found that the domains of Stakeholder Involvement and Applicability were marked with the lowest standardized scores, which may be factors influencing implementation. This is consistent with the findings of Wang et al.[35] Stakeholder involvement focuses on gaining support from a strong collaborative multidisciplinary network and obtaining the needs of all the potential users.[36] Indeed, a multidisciplinary approach to PICC-related thrombosis prevention involving key stakeholders is essential for putting recommendations into practice. However, only two CPGs included patients and their representatives in guideline development, and corresponding suggestions have not been clearly shown.[19-20] In addition, the content of patient/family education was also neglected in existing guidelines. Evidence-based medicine highlights the importance of patient- centered communication.[37] Patient values and preferences should be taken into account, and the pros and cons of these options should be discussed with the patient.[38] Therefore, guideline developers should consider the involvement and engagement of patients and the public in future CPG updates.

Guideline applicability is exceptionally critical for implementation. However, there is a lack of consensus on how CPG should be done in practice. Only three CPGs appraise the barriers and facilitators to guideline implementation and provide strategies to improve guideline uptake.[19-21] Putting recommendations into practice is always challenging. Examples of multiple evidence-based implementation strategies for preventing PICC-related have been evaluated, such as computerized reminder systems, education, audit and feedback, and distribution of guidelines.[39] We call researchers to add the Improve CPG Implementation domain as one of the pillars in guideline development.

This review has some strengths and weaknesses. The search strategy, developed collaboratively, was reproducible and aligned with systematic review standards. However, language or publication restrictions may have led to missing certain CPGs. The inclusion of guidelines spanning 2013 (ASCO and ITAC-CME) to 2021 (ASH and INS) raises concerns about obsolescence based on evolving evidence. CPGs that are ‘recommended’ based on the AGREE II scoring could be obsolete if the CPGs are derived from outdated evidence. Therefore, some caution is warranted here. Lastly, two appraisers used AGREE II, an assessment with methodological rigorous and

reliability, to appraise the quality of included guidelines and resolved any discrepancies by discussion. Although the appraisers were inexperienced in guideline evaluation, all had completed the AGREE II online training. Besides, the team members met weekly online to discuss progress and problems. And six of our group members have attended the Joanna Briggs Institute (JBI) evidence-based medicine training courses.

Conclusions

In summary, recommendations for PICC-related thrombosis prevention predominantly rely on evidence of inadequate quality, necessitating further validation. Guideline developers should intensify focus on methodological rigor, especially in the Stakeholder Involvement and Applicability domains. Moreover, considerations for improving CPG implementation and sustainability should be integral to future guideline development efforts.

Supplementary Material

Supplementary Table 1 PRISMA checklist
Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients
Appendix 2: Excluded studies and reason
Appendix 3: Definitions of AGREE II domains
Appendix 4: Summary of sources where CPGs were obtained
Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients
Appendix 6: Specific recommendations across all CPGs that informed in Table 4
Appendix 7: Evidence level systems used across CPGs
Supplementary Figure 1 The AGREE II domain scores of each guideline

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Supplementary Material

Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients
Appendix 2: Excluded studies and reason
Appendix 3: Definitions of AGREE II domains
Appendix 4: Summary of sources where CPGs were obtained
Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients
Appendix 6: Specific recommendations across all CPGs that informed in Table 4
Appendix 7: Evidence level systems used across CPGs
Supplementary Figure 1 The AGREE II domain scores of each guideline

Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients

Web of Science search performed on 27 November 2023

#	Query
1	TS=(practice guideline* OR clinical guideline* OR consensus OR practice pattern* OR best practice*)
2	TS=(venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT)
3	TS=(peripherally inserted central catheter* OR PICC*)
4	1 AND 2 AND 3

Cochrane Library search performed on 27 November 2023

#	Query
1	MeSH descriptor: [Practice Guideline] explode all trees
2	MeSH descriptor: [Consensus] explode all trees
3	MeSH descriptor: [Practice Patterns, Nurses'] explode all trees
4	MeSH descriptor: [Practice Patterns, Physicians'] explode all trees
5	(practice guideline*):ti,ab,kw OR (clinical guideline*):ti,ab,kw OR (consensus):ti,ab,kw OR (practice pattern*):ti,ab,kw OR (best practice*):ti,ab,kw
6	1 OR 2 OR 3 OR 4 OR 5
7	MeSH descriptor: [Venous Thrombosis] explode all trees
8	MeSH descriptor: [Venous Thromboembolism] explode all trees
9	MeSH descriptor: [Upper Extremity Deep Vein Thrombosis] explode all trees
10	(venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT):ti,ab,kw
11	7 OR 8 OR 9 OR 10
12	MeSH descriptor: [Catheterization, Peripheral] explode all trees
13	(peripherally inserted central catheter*):ti,ab,kw OR (PICC*):ti,ab,kw
14	12 OR 13
15	6 AND 11 AND 14

PubMed search performed on 27 November 2023

#	Query
1	Search:((((("Practice Guidelines as Topic"Mesh]) OR "Practice Guideline" [Publication Type]) OR "Consensus"[Mesh])OR"Practice Patterns, Nurses'"[Mesh]) OR "Practice Patterns, Physicians'[Mesh]
2	Search: ((((practice guideline*[Title/Abstract]) OR (clinical guideline*[Title/Abstract])) OR (consensus[Title/Abstract])) OR (practice pattern*[Title/Abstract])) OR (best practice*[Title/Abstract])
3	1 OR 2
4	Search: (("Venous Thrombosis"[Mesh]) OR "Venous Thromboembolism"[Mesh]) OR "Upper Extremity Deep Vein Thrombosis"[Mesh]
5	Search: (((((venous thrombo*[Title/Abstract]) OR (vein thrombo*[Title/Abstract])) OR

	(catheter related thrombo*[Title/Abstract])) OR (CRT[Title/Abstract])) OR (VTE[Title/Abstract])) OR (UEDVT[Title/Abstract])
6	4 OR 5
7	Search: "Catheterization, Peripheral"[Mesh]
8	Search: (peripherally inserted central catheter*[Title/Abstract]) OR (PICC*[Title/Abstract])
9	7 OR 8
10	3 AND 6 AND 9

EMBASE search performed on 27 November 2023

#	Query
1	'practice guideline'/exp OR 'consensus'/exp OR 'nursing practice'/exp OR 'clinical practice'/exp
2	'practice guideline*':ab,ti OR 'clinical guideline*':ab,ti OR consensus:ab,ti OR 'clinical practice':ab,ti OR 'best practice*':ab,ti OR 'nursing practice':ab,ti
3	1 OR 2
4	'vein thrombosis'/exp OR 'venous thromboembolism'/exp OR 'catheter thrombosis'/exp
5	'venous thrombo*':ab,ti OR 'vein thrombo*':ab,ti OR 'catheter related thrombo*':ab,ti OR crt:ab,ti OR vte:ab,ti OR 'upper extremity deep vein thrombosis':ab,ti OR uedvt:ab,ti
6	4 OR 5
7	'peripherally inserted central venous catheter'/exp
8	'peripherally inserted central catheter*':ab,ti OR picc*:ab,ti
9	7 OR 8
10	3 AND 6 AND 9

CINAHL search performed on 27 November 2023

#	Query
1	(MH "Practice Guidelines") OR (MH "Consensus")
2	TI (practice guideline* OR clinical guideline* OR consensus OR clinical practice OR best practice* OR nursing practice) OR AB (practice guideline* OR clinical guideline* OR consensus OR clinical practice OR best practice* OR nursing practice)
3	1 OR 2
4	(MH "Venous Thromboembolism") OR (MH "Venous Thrombosis") OR (MH "Catheter-Related Thrombosis") OR (MH "Upper Extremity Deep Vein Thrombosis")
5	TI (venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT) OR AB (venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT)
6	4 OR 5
7	(MH "Peripherally Inserted Central Catheters")
8	TI (peripherally inserted central catheter* OR PICC*) OR AB (peripherally inserted central catheter* OR PICC*)
9	7 OR 8
10	3 AND 6 AND 9

CNKI search performed on 27 November 2023

#	Query
1	SU=('静脉血栓栓塞症'+'深静脉血栓'+'导管相关性血栓')*('外周穿刺中心静脉导管'+'外周中心静脉导管置管'+'中心静脉通路装置'+'PICC')*('指南'+'共识')
2	Language=中文
3	1 AND 2

WanFang search performed on 27 November 2023

#	Query
1	主题:("静脉血栓栓塞症"+"深静脉血栓"+"导管相关性血栓")*("外周穿刺中心静脉导管"+"外周中心静脉导管置管"+"中心静脉通路装置"+"PICC")*("指南"+"共识")
2	语言：中文
3	1 AND 2

Appendix 2: Excluded studies and reason

	Author (year)	Title	Reason(s) for exclusion
1	Bierman S. (2016)	AAGBI safe vascular access guidelines II	This is an interpretation of a guideline on PICC-related thrombosis, not a guideline.
2	Brewer C. (2012)	Reducing upper extremity deep vein thrombosis when inserting PICCs	This is a less narrative summary of evidence on reducing PICC-associated thrombosis, not a guideline.
3	Delluc A, et al. (2015)	Catheter-related thrombosis: Unresolved issues	This is a review summarizing the unresolved issues of catheter-related thrombosis, not a guideline.
4	Desruennes E, et al. (2018)	Central venous access for cancer chemotherapy	Not in English.
5	Evans RS, et al. (2013)	Reduction of peripherally inserted central catheter-associated DVT	This is a single-center study of catheter-versus-PICC-associated thrombosis, not prevention, and is not a guideline.
6	Geerts W (2014)	Central venous catheter-related thrombosis	This article focuses on recent evidence of catheter-related thrombosis, ongoing controversies, and practical ways to reduce the burden of CVC-related thrombosis. It is not a guideline.
7	Macmillan T, et al. (2018)	SecurAcath for Securing Peripherally Inserted Central Catheters: A NICE Medical Technology Guidance	The article is one among the series of NICE Medical Technology Guidance summaries. It is not a guideline.
8	Maynard G. (2014)	Upper extremity deep vein thrombosis: A call to arms	This is a review of catheter-related deep venous thrombosis of the upper extremity, not a guideline.
9	Meyer M B (2011)	Managing Peripherally Inserted Central Catheter Thrombosis Risk: A Guide for	This is a retrospective study of PICC-associated thrombosis. It is not a guideline.

		Clinical Best Practice	
10	Yuen HLA, et al. (2021)	Upper Extremity Deep Vein Thrombosis: Current Knowledge and Future Directions	The current research progress and prospect of catheter-related thrombosis were reviewed.
11	American Society of Anesthesiologists, ASA (2019)	Practice Guidelines for Central Venous Access 2020: An Updated Report by the American Society of Anesthesiologists Task Force on Central Venous Access.	This recommendation for prevention of catheter-related infections and mechanical trauma or injury does not address catheter-related thrombosis.
12	ASCO (2019)	Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update	For Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer, catheter-related thrombosis was not involved.
13	American Society of Anesthesiologists, ASA (2018)	American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients	This article mainly focuses on the drug prevention of VTE in hospitalized and non-hospitalized medical patients, and does not involve the content of catheter-related thrombosis.
14	Clinical Practice Guidelines, Canadian Medical Association (2018)	Central venous catheter-related deep vein thrombosis	Provides guidance for the prevention of catheter-related thrombosis, not a guideline.
15	NICE (2020)	Venous thromboembolic diseases: diagnosis, management and thrombophilia testing	The diagnosis and management of VTE are not concerned with the prevention of catheter-associated thrombosis.
16	American Society of Anesthesiologists, ASA (2018)	American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism	The diagnosis of VTE is described only, but catheter-related thrombosis is not mentioned.
17	American Society of	American Society of Hematology 2019	For prevention of vte in hospitalized patients surgeons

	Anesthesiologists, ASA (2018)	guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients	not involved catheter-related thrombosis.
18	Chinese Society of Clinical Oncology, CSCO (2019)	Tumor related prevention and treatment guidelines for venous thromboembolism (2019 edition)	Prophylaxis of catheter-related thrombosis was not covered.
19	Fu QN, et al. (2020)	Clinical Practice Recommendation of Chinese Expert Consensus on Venous Thrombosis associated with Infusion catheterization	This article is a guideline interpretation.

Appendix 3: Definitions of AGREE II domains

Domain 1 - Scope and Purpose: This domain is concerned with the overall aim(s) of the guideline, the specific health question(s) it attempts to address, and the target population(s) that the guideline focusses on (items 1-3).

Domain 2 - Stakeholder Involvement: This domain focuses on the extent to which the guideline was developed by the appropriate stakeholders and consequently, how well the guideline represents the views of its' intended users (items 4-6).

Domain 3 - Rigour of Development: This domain relates to the processes used to gather and synthesize evidence that underpins the guideline, the methods used to formulate recommendations, and the process for updating the guideline (items 7-14).

Domain 4 - Clarity of Presentation: This domain focusses on the language, structure, and format of the guideline (items 15-17).

Domain 5 - Applicability: This domain pertains to the likely barriers and facilitators to guideline implementation, strategies to improve and monitor guideline uptake, and the resource implications of applying the guideline (item 18-21).

Domain 6 - Editorial Independence: This domain is concerned with the formulation of recommendations not being unduly biased with competing for interest, such as funding, personal gain or ghost writing (items 22-23).

Overall assessment: This is a rating of the overall quality of the guideline, based on the judgement of guideline appraisers, and dictates whether the appraiser would recommend the use of the guideline in practice.

Appendix 4: Summary of sources where CPGs were obtained

CPG Document	Link to document
ASCO 2013	https://guidelines.ebmportal.com/central-venous-catheter-care-patient-cancer-american-society-clinical-oncology-clinical-practice
ASH 2021	https://www-ncbi-nlm-nih-gov-443.webvpn.cams.cn/pmc/articles/PMC7903232/pdf/advancesADV2020003442C.pdf
INS 2021	https://www-embase-com-443.webvpn.cams.cn/search/results?subaction=viewrecord&id=L633948335&from=export
CCC-IUA 2020	https://link.cnki.net/doi/10.19538/j.cjps.issn1005-2208.2020.04.03
CMA 2018	https://oss.wanfangdata.com.cn/file/download/perio_zhyx201836002.aspx
ITAC-CME 2013	https://linkinghub-elsevier-com-s.webvpn.cams.cn/retrieve/pii/S1538-7836(22)05263-1
ESMO 2015	https://linkinghub-elsevier-com-s.webvpn.cams.cn/retrieve/pii/S0923-7534(19)47179-2
ISCCM 2020	https://www-ncbi-nlm-nih-gov-443.webvpn.cams.cn/pmc/articles/PMC7085816/pdf/ijccm-24-S6.pdf

CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients

Section	Item	ASCO 2013		ASH 2021		INS 2021		CCC-IUA 2020		CMA 2018		ITAC-CME 2013		ESMO 2015		ISCCM 2020	
		A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2
Scope and Purpose	1	7	7	7	7	7	7	6	7	7	7	7	7	5	6	7	7
	2	7	7	7	7	7	7	6	5	7	7	6	7	6	6	6	5
	3	7	7	7	7	7	7	7	7	6	7	7	7	7	7	7	7
Stakeholder Involvemen	4	7	5	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	5	5	4	5	6	2	1	2	1	2	2	2	1	2	2	2	2
	6	7	7	7	7	7	7	6	7	7	6	7	7	5	4	7	7
Rigour of Development	7	5	6	5	4	7	7	2	1	7	7	6	7	2	1	7	7
	8	6	6	2	2	2	1	2	4	4	2	7	7	2	3	2	1
	9	2	1	7	7	6	5	2	2	7	7	7	7	7	7	5	6
	10	6	5	7	7	7	7	3	4	7	7	6	5	6	6	6	6
	11	6	5	7	7	7	7	6	6	7	7	7	7	7	7	7	7
	12	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	13	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	14	7	7	6	4	7	7	2	1	7	7	2	1	2	1	2	1
Clarity of Presentation	15	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	16	6	7	7	6	6	7	7	7	7	7	7	6	7	7	7	7
	17	6	5	7	7	7	7	7	6	6	5	7	7	7	6	7	6
Applicability	18	7	7	5	6	7	7	4	3	4	3	4	3	3	4	3	4
	19	4	3	7	7	7	7	2	2	7	7	6	7	2	2	7	7
	20	7	7	7	7	4	5	6	6	6	5	5	5	6	6	6	5
	21	2	2	7	7	5	6	2	4	2	4	2	2	2	3	7	7
Editorial Independence	22	7	7	7	6	5	6	7	7	6	5	7	7	7	7	7	7
	23	7	7	7	7	7	7	5	6	7	7	6	6	7	7	7	7
Overall Assessment	OA1	6	6	6	6	6	7	4	4	6	6	5	5	4	5	6	6
	OA2	Yes	Yes	Yes	Yes	Yes	Yes	Yes*	Yes*	Yes	Yes	Yes*	Yes*	Yes*	Yes*	Yes	Yes

*Recommended with modifications.

Appendix 6: Specific recommendations across all CPGs that informed in Table 4

Recommendations identified in Table 4	Corresponding recommendation from each of the included CPGs
1. Identify Patient risk factors	*INS 2021:* • Older age (>60 years), malignancy, diabetes mellitus, obesity, chemotherapy administration, thrombophilia (eg, Factor V Leiden, protein C deficiency, protein S deficiency), critical illness, and history of thrombosis are identified in multiple studies as significant risk factors. (I) • Other cited risk factors include presence of adult/ pediatric chronic diseases including inflammatory bowel disease, congenital heart disease, sickle cell disease, end-stage renal failure, surgery/trauma patients, pregnancy, hyperglycemia in nondiabetic children in critical care; history of prior CVADs; repeated PICC insertion in the same arm in pediatric patients. (II) *CCC-IUA 2020:* • Patients with catheterization are often in special disease-related states, and these states are highly overlapping with high risk factors for venous thrombosis, such as surgery, malignant tumors, and prolonged bed rest. (WG) • Malignant tumor patient is one of the important people use infusion catheter, malignant tumor. The risk of VTE is significantly increased in patients with malignant tumors, and the risk may be increased by chemotherapy and surgery. (WG)
2.Identify catheter related risk factors	
• **Catheter diameter selection**	*INS 2021:* • Measure the catheter-to-vessel ratio prior to insertion; ensure minimally no more than 45% ratio. (A/P) • Avoid placement of multilumen PICCs unless necessary for patient infusion requirements; place small-diameter catheters; small-diameter catheters (eg, 4 Fr) are associated with reduced risk of CA-DVT; in adults CA-DVT developed more rapidly with 5 Fr and 6 Fr PICCs when compared to small-diameter PICCs. (II) *CCC-IUA 2020:* • On the premise of meeting the treatment needs, the infusion device with the smallest external diameter, the least number of lumen

	and the least trauma should be selected. (WG)
• **Catheter tip position**	*INS 2021:* • Ensure proper placement of all CVAD tips in the lower third of the superior vena cava (SVC) or cavoatrial junction as tips located in the mid-to- upper portion of the SVC are associated with greater rates of DVT. (A/P) *CCC-IUA 2020:* • Under the same circumstances, the risk of thrombosis is lower if the catheter tip is located in the subclavian vein than in the proximal part of the basilic vein. (WG) • *ITAC-CME 2013:* • Catheters should be inserted on the right side, in the jugular vein, and the distal extremity of the central catheter should be located at the junction of the superior vena cava and the right atrium (Grade 1A). *ISCCM 2020:* • We recommend IJ and SCV catheter tip should be placed in the lower one-third of the SVC near the SVC/RA junction (A, 2).
3. Identify operator risk factors	*INS 2021:* • Evaluate the need and appropriateness of PICC catheter exchange; an association between CA-DVT and PICC exchange was reported in a retrospective study. (V) • Catheter removal and replacement in a new site are associated with a high rate of new-site CA-DVT. (IV) *CCC-IUA 2020:* • Repeated puncture and withdrawal of catheter during catheterization can aggravate intimal injury and increase the risk of thrombosis. (WG) • Non-standard rushed, sealing tube operation can increase the thrombotic wind duct loss risk. (WG)

	ISCCM 2020: • We recommend that a mechanism should be in place to assess knowledge and compliance with guidelines of all the personnel involved in care related to CVC (A, 1)
4. Risk assessment of patients with PICC	*INS 2021:* • Employ risk reduction interventions when choosing and inserting a PICC; while PICCs have been associated with higher rates of deep vein thrombosis (DVT) than other CVADs, the risk of CA-DVT was not increased when compared to non-PICC CVADs when smaller diameter and single-lumen PICCs were placed. (I) *CMA 2018:* • VTE risk assessment is recommended for patients with a central venous catheter (2B).
5. Consider use of a risk scoring system	
• **Using Michigan Risk Score**	*INS 2021:* • Consider use of a risk scoring system when evaluating PICC placement; the Michigan Risk Score identified risk for PICC-associated CA-DVT based on 5 risk factors: history of DVT, a multilumen PICC, active cancer, presence of another CVAD at the time of PICC insertion, and white blood cell count greater than 12 000. There was a 5-fold greater risk for CA-DVT for those patients in the highest risk class as compared to those at the lowest risk. (III)
• **Using Khorana score model**	*CMA 2018:* • VTE risk assessment using the Khorana score model is recommended for outpatient patients with malignancies receiving chemotherapy. (1B)
6. Monitor for signs and symptoms	
• **Measuring arm circumference**	*INS 2021:* • Measure baseline circumference of the extremity with a PICC or a midline catheter upon insertion, noting location for future measurements and assess circumference when edema or signs and symptoms of DVT present, noting the location and characteristics of edema; a 3-cm increase in midarm circumference in adults with PICCs was associated with CA-DVT. (IV)
7. Pharmacologic preventative measures for PICC-related thrombosis	
• **Not to use as**	*ASCO 2013:*

preference	• The use of systemic anticoagulation (war-farin, low–molecular weight heparin [LMWH], unfractionated heparin) has not been shown to decrease the incidence of catheter- associated thrombosis, and therefore, routine prophylaxis with anti- coagulants is not recommended for patients with cancer with CVCs. (WG) *ASH 2021:* • For patients with cancer and a central venous catheter (CVC), the ASH guideline panel suggests not using parenteral thromboprophylaxis (conditional recommendation, low certainty in the evidence of effects ⊕OO). • For patients with cancer and a CVC, the ASH guideline panel suggests not using oral thromboprophylaxis (conditional recommendation, low certainty in the evidence of effects ⊕⊕OO). *CMA 2018:* • Routine pharmacologic prophylaxis is not recommended for low-risk patients (2B). *ITAC-CME 2013:* • Use of anticoagulation for routine prophylaxis of CRT is not recommended (Grade 1A).
• **Use LMWH or LDUH as preference**	*CMA 2018:* • Medium and high risk patients without anticoagulation taboo, suggest using LMWH or LDUH (2 B).
• **Use LMWH**	*INS 2021:* • Low-molecular-weight heparin (LMWH) was associated with a reduction in symptomatic CA-DVT for patients with cancer; however, the effect of LMWH on mortality is inconclusive; evaluate the risks of bleeding and thrombocytopenia and the burden associated with anticoagulant management vs the benefit of reducing CA-DVT risk. (I) • Hospitalized pediatric patients with inflammatory bowel disease treated with an anticoagulant prophylaxis protocol (enoxaparin) upon PICC placement had a decreased risk of CA-DVT with no increased risk of bleeding. (V)
8. Non-pharmacological preventative measures for PICC-related thrombosis	

• **handgrip exercise**	*INS 2021:* • Consider upper extremity exercise to reduce venous stasis; handgrip exercise using an elastic ball 3 or 6 times per day for 3 weeks was associated with a lower incidence of ultrasound-confirmed CA-DVT in patients with cancer who had a PICC; more research is needed for postinsertion nursing interventions. (IV) *CCC-IUA 2020:* • When conditions permit, the use of nonpharmacological measures for thromboprophylaxis is encouraged, including early mobilization of the catheterization limb, normal daily activities, appropriate limb exercise and adequate hydration. (WG)
• **flushing with saline as preference**	*ASCO 2013:* • Routine flushing with saline of the CVC to prevent fibrin buildup is recommended. (WG) *ESMO 2015:* • Intermittent flushing with heparin is a standard practice in the maintenance of CVC patency. However, when compared with 0.9% normal saline flushing, no differences in thrombosis rates were found (I, C)
• **providing appropriate and adequate nursing care**	*ISCCM 2020:* • We suggest providing appropriate and adequate nursing care to improve CVC-related outcomes. (B, 2) *CCC-IUA 2020:* • For patients with high risk of thrombosis, it is still necessary to take corresponding preventive measures against VTE risk. (WG)
9. Diagnose and confirm PICC-related thrombosis	
• **Doppler ultrasound as preference**	*INS 2021:* • Diagnose and confirm CA-DVT using color-flow Doppler ultrasound by the presence of at least 2 of the following: noncompressability of the vein, abnormal color Doppler vein pattern, and/or IV filling defect. Venography with contrast injection may also be used to assess more proximal veins (eg, brachiocephalic) that are obscured by the clavicle or ribs. (II) *CC-IUA 2020:*

	• Doppler ultrasound is the first choice, which can indicate the location and range of CRT. (WD) *ESMO 2015:* • Although venography is considered the gold standard for the diagnosis of CRT, Doppler ultrasound is usually carried out (III, A). *ISCCM 2020:* • We suggest that ultrasound guidance can be used for early identification of mechanical complication (B, 2).
10. Remove the PICC against	
• **Do not remove catheter unless necessary**	*INS 2021:* • Do not remove a CVAD in the presence of CA-DVT when the catheter is correctly positioned, functional, and necessary for infusion therapy. (II) *ISCCM 2020:* • We recommend prompt removal of CVC when it is not essential (A, 2).
11. Treatment after extubation	
• **Anticoagulation therapy was given for at least 3 months after extubation**	*INS 2021:* • Treat CA-DVT with anticoagulant medication for at least 3 months after CVAD removal. For CVADs with a longer dwell time, continue the treatment for as long as the CVAD is in situ; catheter-directed thrombolysis may be of benefit to patients with severe symptoms, thrombus involving most of the axillary/subclavian vein, with symptoms for less than 14 days, good functional status, life expectancy greater than 1 year, and low risk for bleeding. (II)
• **Use LMWH as preference**	*INS 2021:* • For patients with cancer and CA-DVT, LMWH is recommended; for patients who do not have cancer, dabigatran, rivaroxaban, apixaban, or edoxaban is recommended over vitamin K antagonists (eg, warfarin). (I)
12. Medical personnel training	
• **Establishing education and**	*CCC-IUA 2020:* • Standardized placement, use and maintenance of catheters and professional nursing teams are important prerequisites to reduce

training systems	catheter-related complications, including thrombosis. (WG) *ISCCM 2020:* • We recommend that a healthcare education and training program should be in place when CVCs are inserted and maintained for overall quality improvement (A, 1)
• **Establishing Credentialing process**	*ISCCM 2020:* • We suggest providing appropriate and adequate nursing care to improve CVC-related outcomes (B, 2)

CVADs, Central Venous Access Devices; CA-DVT, catheter-associated deep vein thrombosis; CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Appendix 7: Evidence level systems used across CPGs

Evidence Levels	CPG Working Group
ASCO 2013/ CCC-IUA 2020	
WG	Recommendations based on expert opinion/consensus by the working group.
ASH 2021	
strong	-For patients: most individuals in this situation would want the recommended course of action, and only a small proportion would not.
	-For clinicians: most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.
	-For policy makers: the recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.
	-For researchers: the recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.
conditional	-For patients: the majority of individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences.
	-For clinicians: recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with their values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences.
	-For policy makers: policymaking will require substantial debate and involvement of various stakeholders. Performance measures about the suggested course of action should focus on whether an appropriate decision-making process is duly documented.
	-For researchers: this recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations that determined the conditional (rather than strong) recommendation will help to identify possible research gaps.

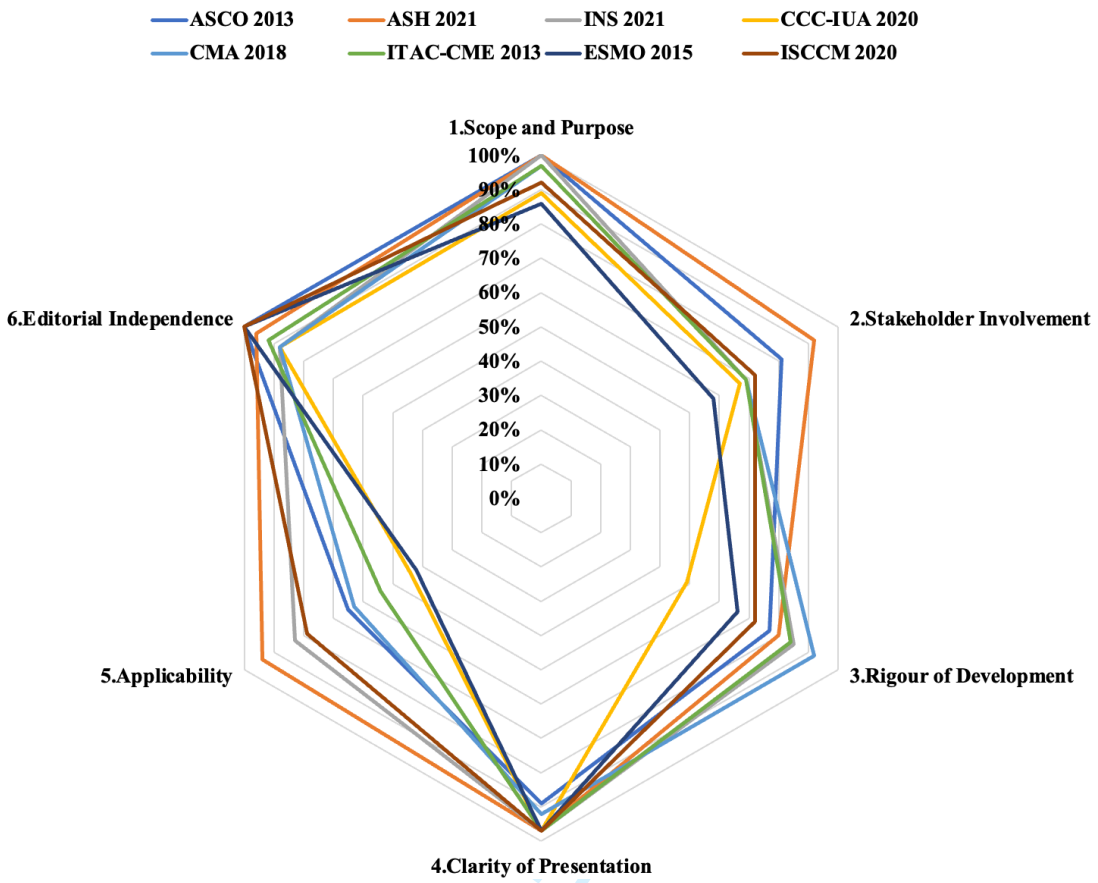
INS 2021	
I	Meta-analysis, systematic literature review, guideline based on randomized controlled trials (RCTs), or at least 3 well-designed RCTs.
II	Two well-designed RCTs, 2 or more well-designed, multicenter clinical trials without randomization, or systematic literature review of varied prospective study designs.
III	One well-designed RCT, several well-designed clinical trials without randomization, or several studies with quasi-experimental designs focused on the same question. Includes 2 or more well-designed laboratory studies.
IV	Well-designed quasi-experimental study, case control study, cohort study, correlational study, time series study, systematic literature review of descriptive and qualitative studies, narrative literature review, or psychometric study. Includes 1 well-designed laboratory study.
V	Clinical article, clinical/professional book, consensus report, case report, guideline based on consensus, descriptive study, well-designed quality improvement project, theoretical basis, recommendations by accrediting bodies and professional organizations, or manufacturer recommendations for products or services. This also includes a standard of practice that is generally accepted but does not have a research basis (e.g., patient identification).
A/P	Evidence from anatomy, physiology, and pathophysiology as understood at the time of writing.
Committee Consensus	Review of evidence, discussion, and committee agreement for a Practice Recommendation. Used when there is insufficient or low-quality evidence to draw a conclusion.
CMA 2018	
High (A)	Further research is very unlikely to change our confidence in the estimate of effect
Moderate (B)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low (C)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low (D)	Any estimate of effect is very uncertain
Recommendation (1)	Interventions clearly have more benefits than harms
Suggestions (2)	Interventions may have more benefits than harms
Not suggestions	Interventions may do more harm than good or pros and cons of relationship is not clear

(2)	
Not recommended (1)	Interventions clearly do more harm than good
ITAC-CME 2013	
Strong (Grade 1 Guideline)	The panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects
Weak (Grade 2 Guideline)	The panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but is not confident
Best clinical practice (Guidance)	In the absence of any clear scientific evidence and because of undetermined balance between desirable and undesirable effects, judgment was based on the professional experience and consensus of the international experts within the working group
ESMO 2015	
I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta- analyses of well-conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, experts opinions
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, ...), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended
ISCCM 2020	

1	Evidence from ≥1 good quality and well-conducted randomized control trial(s) or meta-analysis of RCT's
2	Evidence from at least 1 RCT of moderate quality, or well-designed clinical trial without randomization; or from cohort or case-controlled studies
3	Evidence from descriptive studies, or reports of expert committees, or opinion of respected authorities based on clinical experience
Useful Practice Point (UPP)	Not backed by sufficient evidence; however, a consensus reached by the working group, based on clinical experience and expertise
Grade A	Strong recommendations to do (or not to do) where the benefits clearly outweigh the risk (or vice versa) for most, if not all patients
Grade B	Weak recommendations, where benefits and risk are more closely balanced or are more uncertain

CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Supplementary Figure 1 The AGREE II domain scores of each guideline



CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

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Quality appraisal of clinical guidelines for Peripherally Inserted Central Catheter-related thrombosis prophylaxis in patients: a systematic review

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Disclosure/Conflicts of Interest

None.

Abstract

Objectives To evaluate and analyze the quality of clinical practice guidelines for Peripherally Inserted Central Catheter related thrombosis (PICC-related thrombosis) to identify the most current and effective prophylactic measures recommended in the guidelines.

Design Scoring and analysis of the guidelines using the AGREE II.

Data sources Cochrane Library, PubMed, EMBASE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Chinese databases (China National Knowledge Infrastructure and Wan Fang) and the relevant websites of the guideline were searched through 8 August 2024.

Eligibility criteria for selecting studies Studies that primarily clinical practice guidelines on the prevention of PICC-related thrombosis were included.

Data extraction and synthesis Two reviewers independently screened the searched items and extracted data and scored documents using Appraisal of Guidelines for Research and Evaluation II (AGREE II). Findings were summarized in Grading of Recommendation, Assessment, Development and Evaluation (GRADE) evidence profiles and synthesized qualitatively.

Results
The analysis incorporated a total of nine guidelines, all rated as 'recommended' or 'recommended with modifications'. Standardized scores revealed elevated performance in the domains of Scope and Purpose, Clarity of Presentation, and Editorial Independence. Conversely, the Stakeholder Involvement and Applicability domains yielded the lowest average standardized scores. Disparities in standardized scores across guidelines were particularly evident in the domains of Rigour of Development, Stakeholder Involvement, and Applicability. The agreement between the two appraisers was almost perfect (intraclass correlation coefficients higher than 0.80). A considerable proportion of recommendations relied on evidence of low-quality, in certain instances, were derived from expert opinions within working groups.

Conclusions
The review reveals that a significant portion of recommendations relies on low-quality evidence. Guideline developers are urged to prioritize methodological quality, with a specific focus on refining Stakeholder Involvement and Applicability domains. Addressing these aspects will enhance the overall quality and reliability of PICC-related thrombosis prevention guidelines. One potential way to mitigate these challenges is to endorse a standardized approach to guideline development and to synthesize reliable clinical evidence to reduce variation in recommendations.

Keywords: Peripherally Inserted Central Catheter, PICC, Catheter related thrombosis, quality in healthcare

Strengths and limitations of this study

- This systematic review used a comprehensive search for Clinical Practice Guidelines on the prevention of PICC-related thrombosis.
- Two appraisers used AGREE II, an assessment with methodological rigor and reliability, to appraise the quality of included guidelines and resolved any discrepancies by discussion.
- Caution is warranted in interpreting the AGREE II results, as the AGREE framework assigns equal weighting to all six domains, irrespective of their individual significance.
- We used the Grading of Recommendation, Assessment, Development and Evaluation approach to evaluate and summarize the strength and quality of the evidence.

Introduction

Peripherally Inserted Central Catheter (PICC) has obtained widespread use in clinical practice owing to the maneuverability, minimal trauma, and heightened safety attributes[1-3]. However, PICC-related thrombosis is prone to occur, stemming from factors such as unavoidable puncture injuries, toxic medication effects, and patient-specific conditions, underscores its incidence. The incidence of PICC-related thrombosis varied between 2.3% and 71.9% due to differences in study population, testing modality and threshold for diagnosis, of which 94.5% were asymptomatic[4-5]. In recent years, a steady rise in the incidence rate of PICC-related thrombosis has been attributed to the escalating utilization of PICC lines, augmented awareness among medical professionals regarding PICC-related complications, and an elevated detection rate of asymptomatic thrombosis[6]. This not only jeopardizes patient safety but also begets prolonged or interrupted treatment, unplanned extubation of the PICC, extended hospital stays, and increased burden on society[7-9].

It is important to emphasize that some interventions can reduce the occurrence of PICC-related thrombosis[10]. One study effectively forestalled the occurrence of PICC-related thrombosis by implementing a graded nursing intervention based on risk assessment for 560 patients[11]. Similarly, Liu et al. executed ball-holding exercise training for PICC-catheterized patients, significantly reducing the incidence of PICC-related thrombosis[10]. However, the current landscape lacks clarity on the latest and most efficacious preventive measures recommended in guidelines.

Using evidence-based programs for PICC-related thrombosis can improve practice outcomes while reducing the physical, psychological, social and economic burden on individuals, families and societies. Clinical Practice Guidelines (CPGs) facilitate optimal decision-making by healthcare professionals and patients, minimizing wastage. Nonetheless, the efficacy of a CPG is contingent upon the robustness of its evidence base[12]. Therefore, an imperative exists to systematically evaluate CPGs to gauge their quality. This systematic review aims to critically appraise the quality of PICC-related thrombosis prevention guidelines and assess the strength of their recommendations.

Methods

Registry

The review followed Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[13] and used the recommended Grading of Recommendation, Assessment, Development and Evaluation (GRADE) process[14] to summarize findings. Additionally, it was registered in the International Prospective Registry of Systematic Reviews (PROSPERO) in December 2023 (protocol ID CRD42023495519).

Objectives

The purpose of this systematic review is to critically appraise the quality of PICC-related thrombosis prevention guidelines specific to patients. The Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool was used.

Data sources and search strategy

Academic databases, encompassing Cochrane Library, PubMed, EMBASE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Chinese databases (China National Knowledge Infrastructure and Wan Fang), were systematically searched from inception until 8 August 2024. The search strategy was tailored to the requirements of each database. Searching of reference lists from identified papers were scrutinized, and forward citation searches were performed using Google Scholar. All searches were saved in each database and imported into EndNote (V.20; Clarivate Analytics), where duplicates were removed. To supplement our database searches, we also searched guidelines repositories, including CPG Infobase: Clinical Practice Guidelines (Canadian Medical Association), the Guidelines International Network (GIN), the National Health and Medical Research Council—Australian Clinical Practice Guidelines, the National Institute for Health and Care Excellence (NICE), the National Guideline Clearinghouse (NGC), Scottish Intercollegiate Guideline Network (SIGN), New Zealand Guidelines Group (NZGG), BMJ Best Practice and Chinese guidelines repository (Yi Mai Tong). Search details are available in supplemental appendix 1.

Eligibility criteria

A complete list of inclusion and exclusion criteria is detailed in table 1.

Table 1: Inclusion and exclusion criteria

No.	Items
Inclusion criteria	
1	Published international and national guidelines on the management and/or prevention of PICC-related thrombosis
2	Most recent complete guideline (from a single working group, ie, ACCP) and any partial revisions for the guideline published thereafter
3	Include an explicit statement identifying the document as a 'guideline'
Exclusion criteria	
1	Guidelines under development
2	Guidelines were specific to one institution
3	Complete guidelines with publication dates that have been superseded by more recent complete guidelines
4	Clinical practice standards, defined as a statement reached through consensus, which identifies the desired outcome. Usually used in audit as a measure of success
5	Guidelines inclusive of only one phase of care, for example, Ginzburg et al.[15] (ie, during rehabilitative therapy)

Note: ACCP, American College of Chest Physicians; PICC-related thrombosis, Peripherally

Inserted Central Catheter-related thrombosis

Data screening and extraction

Two reviewers screened titles and abstracts based on predetermined eligibility criteria. Articles that met the above inclusion and exclusion criteria were included for a second full-text screen. Conflicts were resolved through discussion or the involvement of a third reviewer. Reasons for exclusion were documented in a tabular format (supplemental appendix 2). Data extraction was independently performed using a standardized data extraction form developed based on AGREE II[16].

Quality assessment of CPGs

To evaluate the quality of pre-existing guidelines selected for guideline adaptation, two reviewers graded each guideline according to AGREE II. This instrument consists of 23 items organized into six domains. AGREE II also includes two overall assessment items for overall judgements of the practice guideline. Supplemental appendix 3 provides a brief description of each domain[17].

The 23-item AGREE II tool uses a seven-point agreement scale from 1 (strongly disagree) to 7 (strongly agree)[16]. Standardized scores for each domain were computed as (X/Y) ×100%, where X = obtained score−minimum possible score and Y = maximum possible score−minimum possible score[16]. As defined by AGREE II, we considered a CPG as 'recommended' if most items score 6 or 7 points and multidimensional evaluation is > 60%, as 'recommended with modifications' if the items scoring 6 or 7 points are similar to the items scoring 1 or 2 points, and the multidimensional evaluation is 30% to 60% and as 'not recommended' if most items score 1 or 2 points and the multidimensional evaluation is < 30%.

Before the quality appraisal using AGREE II, two reviewers completed an Online Training Tool[18] and performed calibration exercises to clarify the eligibility criteria. Following training, the two reviewers independently applied AGREE II criteria to eligible CPGs using the My AGREE PLUS online platform.[19] Our team met regularly to resolve any discrepancies in the quality appraisal. We used intraclass correlation coefficients (ICCs) to measure the agreement between the two assessors' assessment of quality (AGREE II) of included CPGs. The results were interpreted as follows: 0.00, poor agreement; 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement.[20]

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Results

After removal of duplicates 272 citations were screened for the electronic database, with 13 full-text reports assessed and 5 included (figure 1). Guidelines repository searches retrieved 151 citations, with 16 evaluated and 4 included (figure 2). Ultimately, 9 guidelines were included in the final analysis, and the detailed characteristics are shown in table 2. These CPGs were published between 2013 and 2024. Most of the CPGs were developed in the USA (n=3),[21-23] with the remaining coming from China (n=3),[24-26] France (n=1),[27] Europe (n=1)[28] or India (n=1)[29]. Information sources regarding where CPGs were obtained are shown in supplemental appendix 4.

Table 2 Characteristics of CPGs regarding PICC-related thrombosis prevention in patients

	ASCO 2013	ASH 2021	INS 2024
Original CPG title	Central Venous Catheter Care for the Patient With Cancer: American Society of Clinical Oncology Clinical Practice Guideline	American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer	Infusion Therapy Standards of Practice, 9th Edition
Date published	2013	2021	2024
Country of origin	USA	USA	USA
Objective of CPG	Guide prophylaxis and management of central venous catheter (CVC) care for patients with cancer	Guide prevention and treatment of VTE in patients with cancer	Guide patient-centered infusion care
Methods used to collect/select the evidence	A targeted systematic using 2 databases	Systematic evidence reviews of topic areas	A targeted systematic using more than 9 databases
Methods used to analyse the evidence	Not stated	The hierarchical system used to strong and conditional recommendations	The hierarchical system used to grade levels of evidence
Ranking scheme to determine the strength of the evidence and recommendation	Not stated	Strong, conditional	I, II, III, IV, V, A/P, Committee Consensus
Methods used to formulate the recommendations	Expert consensus	Expert consensus	Expert consensus
Number of recommendations	12	34	46 recommendations in catheter-associated thrombosis
Method of CPG	External and internal	External and internal	External and internal

validation	peer review	peer review	peer review
Intended users	Medicaloncologists hematologist, nurses, interventional radiologists, surgeons, infectious disease specialists, and specialized CVC care teams	patients, clinicians and other health care professionals	all health care settings and all populations
Composition of CPG working group	2 groups: 1. 15-panel members from ASCO CVC Care Expert 2. The external peer review group	3 groups: 1. 16-panel members from ASH 2. McMaster GRADE centre 3. The external peer review group	2 groups: 1. health care specialties from 12 countries around the globe 2. 144 international reviewers
Number of documents included in the appraisal	2 CPG (1360 pages); online data supplement (1359pages)	2 CPG (928 pages); online data supplement (933 pages)	1 CPG (180 pages)

(continued)

	CCC-IUA 2020	CMA 2018	IITC-CNA 2022
Original CPG title	Infusion catheter related venous thrombosis prevention and control China expert consensus (2020 edition)	Chinese guidelines for the prevention and treatment of thrombotic diseases	Clinical Nursing Practice Guidelines for Common Complications of Intravenous Catheters
Date published	2020	2018	2022
Country of origin	China	China	China
Objective of CPG	Guide the clinical work of preventing catheter-related thrombosis	Guide the diagnosis, treatment, and nursing of venous thrombosis	Guide patient-centered infusion care
Methods used to collect/select the evidence	Not stated	A targeted systematic using 10 databases	A targeted systematic using 14 databases
Methods used to analyse the evidence	Not stated	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence
Ranking scheme to determine the strength of the evidence and recommendation	Not stated	Grade A, B, C, D; 1, 2	I, II, III, IV, V; Grade A, B, C, D

Methods used to formulate the recommendations	Expert consensus	Expert consensus	Expert consensus
Number of recommendations	37	19 recommendations in prevention	57
Method of CPG validation	External and internal peer review	External and internal peer review	External and internal peer review
Intended users	Clinicians and nurses	Clinicians	Clinicians and nurses
Composition of CPG working group	2 groups: 1.47-panel members from CCC-IUA 2.The external peer review group	3 groups: 1.Guideline development group 2.Review committee 3.External reviewer group	2 groups: 1.23-panel members from IITC-CAN 2.External reviewer group
Number of documents included in the appraisal	1 CPG (337 pages)	1 CPG (2861 pages)	1 CPG (2381 pages)

(continued)

	ITAC-CME 2022	ESMO 2015	ISCCM 2020
Original CPG title	2022 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer, including patients with COVID-19	Central venous access in oncology: ESMO Clinical Practice Guidelines	Indian Society of Critical Care Medicine Position Statement for Central Venous Catheterization and Management 2020
Date published	2022	2015	2020
Country of origin	France	Europe	India
Objective of CPG	Guide management of catheter related thrombosis (CRT) in cancer patients	Guide management of central venous access in adult cancer patients	Guide critical care physicians and allied professionals
Methods used to collect/select the evidence	A targeted systematic using more than 3 databases	Not stated	A targeted systematic using 3 databases
Methods used to analyse the evidence	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence	The hierarchical system used to grade levels of evidence
Ranking scheme to determine the strength of the	Grade A, B, C, D; Strong, Weak, Best clinical practice	I, II, III, IV, V; A, B, C, D, E	1, 2, 3; Useful Practice Point (UPP), Grade A, Grade B

evidence and recommendation	(guidance)		
Methods used to formulate the recommendations	Expert consensus	Expert consensus	Expert consensus
Number of recommendations	41	67	54
Method of CPG validation	External and internal peer review	External and internal peer review	External and internal peer review
Clinicians and nurses	Clinicians	Clinicians	Critical care physicians and allied professionals
Composition of CPG working group	2 groups: 1.19 experts from various specialties 2.87 international reviewers	2 groups: 1.ESMO Guidelines Committee 2.The external peer review group	2 groups: 1.19-panel members from ISCCM 2.The external peer review group
Number of documents included in the appraisal	2 CPG (334 pages); online data supplement (123 pages)	1 CPG (152 pages)	4 CPG (8 pages); 3 Appendices (22 pages)

Note: CVC, central venous catheter; VTE, venous thromboembolism; CRT, catheter-related thrombosis; CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Two assessors appraised each CPG. The AGREE II domain scores of each guideline are presented in table 3. Detailed scoring of each AGREE II item under each domain is presented in online supplemental appendix 5. Supplementary Figure 1 shows a radar chart of the results of the guideline appraisal. The quality of the evaluated guidelines showed significant variability. The standardized scores ranged from 86% to 100% in the Scope and Purpose domain, and all CPGs scored above 80%. The standardized scores in the Stakeholder Involvement domain ranged from 58% to 92%, with all CPGs scoring above 50%. The standardized scores in the Rigour of Development domain ranged from 49% to 94%, with only one CPG scoring below 50%. The standardized scores in the Clarity of Presentation domain ranged from 89% to 97%. The standardized scores in the Applicability domain ranged from 42% to 94%, with only one CPGs scoring below 50%. The standardized scores in the Editorial Independence domain ranged from 88% to 100%. Per the quality assessment tool used in this review, 6 of the 9 included CPGs were judged to be ‘recommended’. There is an almost perfect agreement between two appraisers, with the intraclass correlation coefficient (ICC) ranging from 0.876 to 0.968 (P<0.001).

Table 3 AGREE II scaled domain scores of CPGs for PICC-related thrombosis prevention in patients

	ASCO 2013	ASH 2021	INS 2024	CCC-IUA 2020	CMA 2018	IITC-CNA 2022	ITAC-CME 2022	ESMO 2015	ISCCM 2020
1.Scope and Purpose	100%	100%	100%	89%	97%	89%	97%	86%	92%
2.Stakeholder Involvement	81%	92%	69%	67%	69%	58%	89%	58%	72%
3.Rigour of Development	77%	80%	85%	49%	92%	74%	85%	66%	72%
4.Clarity of Presentation	89%	97%	97%	97%	92%	89%	100%	97%	97%
5.Applicability	65%	94%	83%	44%	63%	48%	63%	42%	79%
6.Editorial Independence	100%	96%	92%	88%	88%	92%	92%	100%	100%
Recommended use of this CPG	Yes	Yes	Yes	Yes*	Yes	Yes*	Yes	Yes*	Yes
ICC (including overall CPG score)	0.913	0.876	0.942	0.919	0.887	0.968	0.923	0.957	0.958

Note: *Recommended with modifications.

Table 4 shows the levels of evidence for recommendations of PICC-related thrombosis prevention in patients, as reported in the included CPGs. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach[30] was used to rank recommendations. Despite unanimous agreement in the recommendations for identifying and assessing risk factors, monitoring for signs and symptoms, providing non-pharmacological preventative measures, diagnose, remove the PICC against, treatment after diagnosis and medical personnel training, details disagree on the risk assessment tools and pharmacological choice. The Infusion Nursing Society (INS) 2024 guidelines[23] recommended the Caprini Risk Assessment Model and the Michigan risk score for patients with PICC, but the China Medical Association (CMA) 2018 guidelines[25] recommended the Khorana score model for outpatient patients with malignancies receiving chemotherapy. The American Society of Clinical Oncology (ASCO) 2013 guidelines,[21] American Society of Hematology (ASH) 2021 guidelines[22] and International Initiative on Thrombosis and Cancer (ITAC-CME) 2022 guidelines[27] did not recommend pharmacologic prophylaxis, and the INS 2024 guidelines[23] notes that recommendations for pharmacologic prophylaxis have not been established for all patient populations but should be guided by individual patient risk. However, the CMA 2018 guidelines[25] recommended using LMWH or LDUH for medium and high-risk patients. In terms of risk assessment, pharmacologic preventative measures, diagnose and confirm PICC-related thrombosis, remove the PICC against

and medical personnel training, we observed little recommendations with relatively low quality. The recommendations from each CPG that are informed in table 4 are detailed in supplemental appendix 6. Supplemental appendix 7 shows an explanation of the different evidence levels used across included CPGs.

Table 4 Levels of evidence for recommendations of PICC-related thrombosis prevention in patients as reported in included CPGs

Recommendations*	ASCO 2013	ASH 2021	INS 2024
1.Identify Patient risk factors	–	–	• History of thrombosis (I) • Other factors (II)
2.Identify catheter related risk factors	–	–	• Catheter-to-vessel ratio prior to insertion no more than 45% ratio (II) • Place small-diameter catheters (I) • Catheter tip location (A/P)
3. Identify operator risk factors	–	–	• Use a bundled approach for PICC insertion (II) • Consider tunneling PICCs (III) • Use ultrasound for accurate insertion(V) • Use electrocardiography for PICC tip location (III)
4. Risk assessment of patients with PICC	–	–	• When choosing and inserting a PICC (I)
5. Consider use of a risk scoring system	–	–	• The Caprini Risk Assessment Model (IV) • The Michigan Risk Score (IV)
6. Monitor for signs and symptoms	–	–	• Measuring arm circumference (IV)
7. Pharmacologic preventative measures for PICC-related thrombosis	• Not to use as preference (WG)	• Not using parenteral thromboprophylaxis (Low) • Not using oral thromboprophylaxis (Low)	• Guided by individual patient risk (I)
8. Non-pharmacological preventative measures for PICC-related thrombosis	• Flush with saline as preference (WG)	–	• Handgrip exercise (III)

9. Diagnose and confirm PICC-related thrombosis	–	–	Doppler ultrasound as preference (II)
10. Remove the PICC against	–	–	• Do not remove when the catheter is correctly positioned, functional, and necessary for infusion therapy (I)
11. Treatment after diagnosis	–	–	• Anticoagulant medication for at least 3 months after diagnosis (IV)
12. Medical personnel training	–	–	• Ensure that the selected VAD is inserted by staff with specific training, using vascular visualization (II)

(Continued)

Recommendations*	CCC-IUA 2020	CMA 2018	IITC-CNA 2022
1.Identify Patient risk factors	• Patients with catheterization (WG) • Malignant tumors, chemotherapy and surgery (WG)	–	–
2.Identify catheter related risk factors	• The smallest external diameter (WG) • Catheter tip location (WG)	–	–
3. Identify operator risk factors	• Repeated puncture and withdrawal of catheter (WG) • Non-standard rushed, sealing tube operation can increase the risk (WG)	–	–
4. Risk assessment of patients with PICC	–	• VTE risk assessment with a central venous catheter (2B)	–
5. Consider use of a risk scoring system	–	• The Khorana score model (1B)	–
6. Monitor for signs and symptoms	–	–	–
7. Pharmacologic	–	• Not use for low-risk	–

preventative measures for PICC-related thrombosis		patients (2B) • Use LMWH or LDUH as preference for medium and high risk (2 B)	
8. Non-pharmacological preventative measures for PICC-related thrombosis	• Handgrip exercise (WG) • Providing appropriate and adequate nursing care (WG)	–	• Non-pharmacological measures (V, B) • providing appropriate and adequate nursing care (II, A)
9. Diagnose and confirm PICC-related thrombosis	• Doppler ultrasound as preference (WG)	–	• Doppler ultrasound as preference (I, A) • Not to routine use Doppler ultrasound (IV, D)
10. Remove the PICC against	–	–	• Extractions consider the actual situation (II, B)
11. Treatment after diagnosis	–	–	• Routine anticoagulation before removal (IV, B) • Further assessed for appropriate interventions (I, A)
12. Medical personnel training	• Establishing education and training systems (WG)	–	–

(Continued)

Recommendations*	ITAC-CME 2022	ESMO 2015	ISCCM 2020
1.Identify Patient risk factors	–	–	–
2.Identify catheter related risk factors	• Catheter tip location (Grade 1B)	–	• Catheter tip location (A, 2)
3. Identify operator risk factors		–	• Assess knowledge and compliance (A, 1)
4. Risk assessment of patients with PICC	–	–	–
5. Consider use of a risk scoring system	–	–	–
6. Monitor for signs and symptoms	–	–	–
7. Pharmacologic preventative measures for PICC-related thrombosis	• Not to use as preference (Grade 1A)	–	–
8. Non-pharmacological	–	• Flushing with saline as preference (I, C)	• providing appropriate and adequate nursing care

preventative measures for PICC-related thrombosis			(B, 2)
9. Diagnose and confirm PICC-related thrombosis	–	• Doppler ultrasound as preference (III, A)	• Doppler ultrasound as preference (B, 2)
10. Remove the PICC against	–	–	• No need to extubate (A, 2)
11. Treatment after diagnosis	• Use LMWHs for a minimum of 3 months (guidance)	–	–
12. Medical personnel training	–	–	• Establishing education and training systems (A, 1) • Establishing Credentialing process (B, 2)

Note: CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Discussion

To our knowledge, this is the first systematic quality appraisal of CPGs for PICC-related thrombosis prevention in patients, with recognition of nine guidelines. Overall, the quality of all incorporated guidelines was deemed acceptable, evaluated as either 'recommended' or 'recommended with modifications'. We summarized all key recommendations about PICC-related thrombosis prophylaxis, and compared and visualized the difference among them, providing a concise but informative overview for clinicians and researchers.

Most of the guidelines included in the study tend not to recommend the routine use of pharmacological prophylaxis of PICC-related thrombosis. Despite consistency in recommendations across the included CPGs, they employed diverse classification systems to indicate levels of evidence. Discrepancies in preferred pharmacological prophylaxis (such as low molecular weight heparin (LMWH), direct oral anticoagulants (DOACs), or no drug prophylaxis) could be attributed to variations in data availability from trials and the timing of approval by regulatory agencies. The latest guidelines state that prophylactic anticoagulation for catheter related thrombosis prevention have not been established for all patient populations but should be guided by individual patient risk.[23] This may indicate that the choice of whether or not to use pharmacological

prophylaxis for PICC-related thrombosis based on risk assessment in the future.[31] It may be a trend for future research. It is noteworthy that a substantial proportion of recommendations relied on low-quality or very-low-quality evidence, or even on expert opinions from working groups, suggesting uncertain clinical significance. Therefore, advocating for high-quality randomized controlled trials is imperative to reinforce the evidence base and potentially enhance the cost-effectiveness of treatment.[32]

Additionally, regarding non-pharmacological prevention, only a very limited number of strong recommendations could be found, which implies the absence of solid evidence. It was worth noting that current updated guidelines were more inclined to recommend non-pharmacological prophylaxis, such as INS 2024, which specifies the frequency and duration of handgrip exercises (3 or 6 times per day for 3 weeks). [23-24,26] These findings would account for the fact that prophylaxis for PICC-related thrombosis is still not routinely implemented as per guideline recommendations in most hospitals..[33-34] However, there were no clear criteria for the number and the duration of each set of handgrip exercises. Therefore, a large randomized controlled trial could be conducted in the future to develop a standardized content of handgrip exercises. It was also worth noting that as the first line of defense in the prevention of PICC-related thrombosis, dynamic and accurate risk assessment is crucial. However, current guidelines did not provide detailed descriptions of the timing of risk assessment and specialized assessment tools for PICC-related thrombosis prevention.[23-25] Therefore, Future research should delve into these aspects to refine risk assessment specificity, facilitating clinical prevention and enhancing assessment accuracy.

We found that standardized scores for different domains varied across the nine guidelines included. The Scope and Purpose, Clarity of Presentation, and Editorial Independence domains exhibited relatively high standardized scores. In contrast, the Stakeholder Involvement, Rigor of Development, and Applicability domains demonstrated considerable variations among the CPGs. Our results are consistent with the results of CPG quality evaluations for other clinical topics.[35-36] This suggests that improvements in these areas may improve the consistency of the guidance provided. With significant improvements in CPG development methods over the past decade, differences between existing clinical practice guidelines can be explained in part by guideline development methodology. Therefore, guideline development should be based on developed standards (e.g., the WHO Manual for Guideline Development[37]) in conjunction with the methodological details of the AGREE II Reporting Clinical Guideline Development.[17]

We discovered that the Stakeholder Involvement and Applicability domains had the lowest standardized scores, which might be factors affecting implementation. This is in consistent with the findings of Wang et al.[38] Stakeholder involvement centers on obtaining support from a robust collaborative multidisciplinary network and getting the requirements of all potential users.[39] Truly, a multidisciplinary approach to

preventing PICC-related thrombosis, which involves key stakeholders, is crucial for implementing recommendations. However, only two CPGs incorporated patients and their representatives in guideline development, and relevant suggestions were not clearly presented.[21-22] In addition, the content of patient/family education was also neglected in existing guidelines. Evidence-based medicine emphasizes the significance of patient-centered communication.[40] Patient with PICC-line may have some concerns about non-pharmacological prophylaxis for thromboprophylaxis, such as the fear of catheter dislodgement and displacement due to activity, which may affect quality of life. Consequently, Patients' values and preferences should be considered, and the advantages and disadvantages of these choices should be discussed with patients.[41]

The low score for Guideline applicability mainly reflects the lack of description of the barriers to implementation. However, there is little consensus on how to carry out CPG in practice. Only three CPGs assess the barriers and facilitators to guideline implementation and offer strategies to enhance guideline uptake.[21-23] Whilst these may add to the usefulness of the guidelines, it is unclear to what extent they actually improve the implementation of the recommendations. Multiple evidence-based implementation strategies have been evaluated to prevent PICC-related issues.[42] We urge guide developers to consider the Improve CPG Implementation domain as one of the development objectives.

This review has some strengths and limitations. Our assessment is based on what guideline organizations reported. The search strategy, which was developed collaboratively, was reproducible and aligned with systematic review standards. The inclusion of guidelines spanning 2013 (ASCO) to 2024 (INS) raises concerns about obsolescence based on evolving evidence. CPGs that are ‘recommended’ according to the AGREE II scoring might be out-of-date if they are based on obsolete evidence. Thus, some caution is necessary here. Lastly, two appraisers utilized AGREE II, an assessment with methodological rigor and reliability, to assess the quality of the included guidelines and settle any disparities through discussion. Six members of our group have taken part in the evidence-based medicine training courses offered by the Joanna Briggs Institute (JBI). This participation has equipped them with valuable skills and knowledge in evidence-based practice, enhancing the quality and credibility of our research.

Conclusions

In summary, the current guidelines for PICC-related thrombosis require significant improvements in methodological quality. They showed inconsistencies in some recommendations, highlighting the need for standardized guideline development and high-quality evidence synthesis. Guideline developers should intensify focus on methodological rigor, especially in the Stakeholder Involvement and Applicability domains. Moreover, the existing guidelines need to be further clarified in the areas of

risk assessment (including tools and timing of assessment, etc.), pharmacological prevention, and non-pharmacological prevention. High-quality randomized controlled studies are urgently needed to address these issues in the future.

Figure legend

Figure 1 Search strategy for library databases (final search undertaken on 8 August 2024). CPGs, clinical practice guidelines; CINAHL, Cumulative Index of Nursing and Allied Health Literature; CNKI, China National Knowledge Infrastructure.

Figure 2 Search strategy for guideline repositories (final search undertaken on 8 August 2024). CPGs, clinical practice guidelines.

Supplementary Material

Supplementary Table 1 PRISMA checklist
Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients
Appendix 2: Excluded studies and reason
Appendix 3: Definitions of AGREE II domains
Appendix 4: Summary of sources where CPGs were obtained
Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients
Appendix 6: Specific recommendations across all CPGs that informed in Table 4
Appendix 7: Evidence level systems used across CPGs
Supplementary Figure 1 The AGREE II domain scores of each guideline

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Supplementary Material

Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients
Appendix 2: Excluded studies and reason
Appendix 3: Definitions of AGREE II domains
Appendix 4: Summary of sources where CPGs were obtained
Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients
Appendix 6: Specific recommendations across all CPGs that informed in Table 4
Appendix 7: Evidence level systems used across CPGs
Supplementary Figure 1 The AGREE II domain scores of each guideline

Appendix 1: Searching strategies for CPGs on PICC-related thrombosis prevention in patients

Cochrane Library search performed on 8 August 2024

#	Query
1	MeSH descriptor: [Practice Guideline] explode all trees
2	MeSH descriptor: [Consensus] explode all trees
3	MeSH descriptor: [Practice Patterns, Nurses'] explode all trees
4	MeSH descriptor: [Practice Patterns, Physicians'] explode all trees
5	(practice guideline*):ti,ab,kw OR (clinical guideline*):ti,ab,kw OR (consensus):ti,ab,kw OR (practice pattern*):ti,ab,kw OR (best practice*):ti,ab,kw
6	1 OR 2 OR 3 OR 4 OR 5
7	MeSH descriptor: [Venous Thrombosis] explode all trees
8	MeSH descriptor: [Venous Thromboembolism] explode all trees
9	MeSH descriptor: [Upper Extremity Deep Vein Thrombosis] explode all trees
10	(venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT):ti,ab,kw
11	7 OR 8 OR 9 OR 10
12	MeSH descriptor: [Catheterization, Peripheral] explode all trees
13	(peripherally inserted central catheter*):ti,ab,kw OR (PICC*):ti,ab,kw
14	12 OR 13
15	6 AND 11 AND 14

PubMed search performed on 8 August 2024

#	Query
1	Search:((((("Practice Guidelines as Topic"Mesh]) OR "Practice Guideline" [Publication Type]) OR "Consensus"[Mesh])OR"Practice Patterns, Nurses'"[Mesh]) OR "Practice Patterns, Physicians'[Mesh]
2	Search: ((((practice guideline*[Title/Abstract]) OR (clinical guideline*[Title/Abstract])) OR (consensus[Title/Abstract])) OR (practice pattern*[Title/Abstract])) OR (best practice*[Title/Abstract])
3	1 OR 2
4	Search: (("Venous Thrombosis"[Mesh]) OR "Venous Thromboembolism"[Mesh]) OR "Upper Extremity Deep Vein Thrombosis"[Mesh]
5	Search: (((((venous thrombo*[Title/Abstract]) OR (vein thrombo*[Title/Abstract])) OR (catheter related thrombo*[Title/Abstract])) OR (CRT[Title/Abstract])) OR (VTE[Title/Abstract])) OR (UEDVT[Title/Abstract])
6	4 OR 5
7	Search: "Catheterization, Peripheral"[Mesh]
8	Search: (peripherally inserted central catheter*[Title/Abstract]) OR (PICC*[Title/Abstract])
9	7 OR 8
10	3 AND 6 AND 9

EMBASE search performed on 8 August 2024

#	Query
1	'practice guideline'/exp OR 'consensus'/exp OR 'nursing practice'/exp OR 'clinical practice'/exp
2	'practice guideline*':ab,ti OR 'clinical guideline*':ab,ti OR consensus:ab,ti OR 'clinical practice':ab,ti OR 'best practice*':ab,ti OR 'nursing practice':ab,ti
3	1 OR 2
4	'vein thrombosis'/exp OR 'venous thromboembolism'/exp OR 'catheter thrombosis'/exp
5	'venous thrombo*':ab,ti OR 'vein thrombo*':ab,ti OR 'catheter related thrombo*':ab,ti OR crt:ab,ti OR vte:ab,ti OR 'upper extremity deep vein thrombosis':ab,ti OR uedvt:ab,ti
6	4 OR 5
7	'peripherally inserted central venous catheter'/exp
8	'peripherally inserted central catheter*':ab,ti OR picc*:ab,ti
9	7 OR 8
10	3 AND 6 AND 9

CINAHL search performed on 8 August 2024

#	Query
1	(MH "Practice Guidelines") OR (MH "Consensus")
2	TI (practice guideline* OR clinical guideline* OR consensus OR clinical practice OR best practice* OR nursing practice) OR AB (practice guideline* OR clinical guideline* OR consensus OR clinical practice OR best practice* OR nursing practice)
3	1 OR 2
4	(MH "Venous Thromboembolism") OR (MH "Venous Thrombosis") OR (MH "Catheter-Related Thrombosis") OR (MH "Upper Extremity Deep Vein Thrombosis")
5	TI (venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT) OR AB (venous thrombo* OR vein thrombo* OR catheter related thrombo* OR CRT OR VTE OR UEDVT)
6	4 OR 5
7	(MH "Peripherally Inserted Central Catheters")
8	TI (peripherally inserted central catheter* OR PICC*) OR AB (peripherally inserted central catheter* OR PICC*)
9	7 OR 8
10	3 AND 6 AND 9

CNKI search performed on 8 August 2024

#	Query
1	(主题: '静脉血栓栓塞症'+'深静脉血栓'+'导管相关性血栓') AND (主题: '外周穿刺中心静脉导管'+'外周中心静脉导管置管'+'中心静脉通路装置'+'PICC') AND (主题: '指南'+'共识')
2	Language=中文
3	1 AND 2

WanFang search performed on 8 August 2024

#	Query
1	题名或关键词:(静脉血栓栓塞症 or 深静脉血栓 or 导管相关性血栓) and 题名或关键词: (外周穿刺中心静脉导管 or 外周中心静脉导管置管 or 中心静脉通路装置 or PICC) and 题名或关键词: (指南 or 共识)
2	语言：中文
3	1 AND 2

Appendix 2: Excluded studies and reason

	Author (year)	Title	Reason(s) for exclusion
1	Bierman S. (2016)	AAGBI safe vascular access guidelines II	This is an interpretation of a guideline on PICC-related thrombosis, not a guideline.
2	Brewer C. (2012)	Reducing upper extremity deep vein thrombosis when inserting PICCs	This is a less normative summary of evidence on reducing PICC-associated thrombosis, not a guideline.
3	Delluc A, et al. (2015)	Catheter-related thrombosis: Unresolved issues	This is a review summarizing the unresolved issues of catheter-related thrombosis, not a guideline.
4	International Society on Thrombosis and Haemostasis, ISTH (2014)	Catheter-associated deep vein thrombosis of the upper extremity in cancer patients: guidance from the SSC of the ISTH	Provides guidance for the prevention of catheter-related thrombosis in cancer patients, not a guideline.
5	Evans RS, et al. (2013)	Reduction of peripherally inserted central catheter-associated DVT	This is a single-center study of catheter-versus-PICC-associated thrombosis, not prevention, and is not a guideline.
6	J A Capdevila (2016)	2016 Expert consensus document on prevention, diagnosis and treatment of short-term peripheral venous catheter-related infections in adult	The consensus focuses on indications for intravenous catheter placement, catheter maintenance and registration, and diagnosis and treatment of catheter-related infections. It was excluded due to the absence of content dealing with catheter-related thrombosis.
7	Macmillan T, et al. (2018)	SecurAcath for Securing Peripherally Inserted Central Catheters: A NICE Medical Technology Guidance	The article is one among the series of NICE Medical Technology Guidance summaries. It is not a guideline.
8	Maynard G. (2014)	Upper extremity deep vein thrombosis: A call to arms	This is a review of catheter-related deep venous thrombosis of the upper extremity, not a guideline.

9	Meyer M B (2011)	Managing Peripherally Inserted Central Catheter Thrombosis Risk: A Guide for Clinical Best Practice	This is a retrospective study of PICC-associated thrombosis. It is not a guideline.
10	Infusion Nursing Society, INS (2021)	Infusion Therapy Standards of Practice, 8th Edition	An updated version is available.
11	American Society of Anesthesiologists, ASA (2019)	Practice Guidelines for Central Venous Access 2020: An Updated Report by the American Society of Anesthesiologists Task Force on Central Venous Access.	This recommendation for prevention of catheter-related infections and mechanical trauma or injury does not address catheter-related thrombosis.
12	ASCO (2019)	Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update	For Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer, catheter-related thrombosis was not involved.
13	American Society of Anesthesiologists, ASA (2018)	American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients	This article mainly focuses on the drug prevention of VTE in hospitalized and non-hospitalized medical patients, and does not involve the content of catheter-related thrombosis.
14	International Initiative on Thrombosis and Cancer, ITAC-CME (2013)	International clinical practice guidelines for the treatment and prophylaxis of thrombosis associated with central venous catheters in patients with cancer	An updated version is available.
15	National Institute for Health and Care Excellence,NICE (2020)	Venous thromboembolic diseases: diagnosis, management and thrombophilia testing	The diagnosis and management of VTE are not concerned with the prevention of catheter-associated thrombosis.
16	American Society of Anesthesiologists, ASA (2018)	American Society of Hematology 2018 guidelines for management of venous	The diagnosis of VTE is described only, but catheter-related thrombosis is not mentioned.

		thromboembolism: diagnosis of venous thromboembolism	
17	American Society of Anesthesiologists, ASA (2019)	American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients	For prevention of in hospitalized patients surgeons not involved catheter-related thrombosis.
18	Chinese Society of Clinical Oncology, CSCO (2019)	Tumor related prevention and treatment guidelines for venous thromboembolism (2019 edition)	Prophylaxis of catheter-related thrombosis was not covered.
19	Fu QN, et al. (2020)	Clinical Practice Recommendation of Chinese Expert Consensus on Venous Thrombosis associated with Infusion catheterization	This article is a guiding interpretation.
20	Clinical Practice Guidelines (Canadian Medical Association) (2020)	Central venous catheter-related deep vein thrombosis	This article provides guidance for the prevention of catheter-related thrombosis and is not a guideline .

Appendix 3: Definitions of AGREE II domains

Domain 1 - Scope and Purpose: This domain is concerned with the overall aim(s) of the guideline, the specific health question(s) it attempts to address, and the target population(s) that the guideline focusses on (items 1-3).

Domain 2 - Stakeholder Involvement: This domain focuses on the extent to which the guideline was developed by the appropriate stakeholders and consequently, how well the guideline represents the views of its' intended users (items 4-6).

Domain 3 - Rigour of Development: This domain relates to the processes used to gather and synthesize evidence that underpins the guideline, the methods used to formulate recommendations, and the process for updating the guideline (items 7-14).

Domain 4 - Clarity of Presentation: This domain focusses on the language, structure, and format of the guideline (items 15-17).

Domain 5 - Applicability: This domain pertains to the likely barriers and facilitators to guideline implementation, strategies to improve and monitor guideline uptake, and the resource implications of applying the guideline (item 18-21).

Domain 6 - Editorial Independence: This domain is concerned with the formulation of recommendations not being unduly biased with competing for interest, such as funding, personal gain or ghost writing (items 22-23).

Overall assessment: This is a rating of the overall quality of the guideline, based on the judgement of guideline appraisers, and dictates whether the appraiser would recommend the use of the guideline in practice.

Appendix 4: Summary of sources where CPGs were obtained

CPG Document	Link to document
ASCO 2013	https://guidelines.ebmportal.com/central-venous-catheter-care-patient-cancer-american-society-clinical-oncology-clinical-practice
ASH 2021	https://www-ncbi-nlm-nih-gov-443.webvpn.cams.cn/pmc/articles/PMC7903232/pdf/advancesADV2020003442C.pdf
INS 2021	https://www-embase-com-443.webvpn.cams.cn/search/results?subaction=viewrecord&id=L633948335&from=export
CCC-IUA 2020	https://link.cnki.net/doi/10.19538/j.cjps.issn1005-2208.2020.04.03
CMA 2018	https://oss.wanfangdata.com.cn/file/download/perio_zhyx201836002.aspx
IITC-CNA 2022	https://rs.yiigle.com/cmaid/1410887
ITAC-CME 2013	https://linkinghub-elsevier-com-s.webvpn.cams.cn/retrieve/pii/S1538-7836(22)05263-1
ESMO 2015	https://linkinghub-elsevier-com-s.webvpn.cams.cn/retrieve/pii/S0923-7534(19)47179-2
ISCCM 2020	https://www-ncbi-nlm-nih-gov-443.webvpn.cams.cn/pmc/articles/PMC7085816/pdf/ijccm-24-S6.pdf

CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Appendix 5: AGREE II scaled item scores of CPGs for PICC-related thrombosis prevention in patients

Section	Item	ASCO 2013		ASH 2021		INS 2024		CCC-IUA 2020		CMA 2018		IITC-CNA 2022		ITACC-CHE 2022		ESMO 2015		ISCCM 2020	
		A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2	A1	A2
Scope and Purpose	1	7	7	7	7	7	7	6	7	7	7	7	7	7	7	5	6	7	7
	2	7	7	7	7	7	7	6	5	7	7	6	6	6	7	6	6	6	5
	3	7	7	7	7	7	7	7	7	6	7	6	6	7	7	7	7	7	7
Stakeholder Involvemen	4	7	5	7	7	7	7	7	7	7	7	5	5	7	7	7	7	7	7
	5	5	4	5	6	2	1	2	1	2	2	1	2	5	5	2	2	2	2
	6	7	7	7	7	7	7	6	7	7	6	7	7	7	7	5	4	7	7
Rigour of Development	7	5	6	5	4	7	7	2	1	7	7	7	7	7	7	2	1	7	7
	8	6	6	2	2	2	1	2	4	4	2	1	2	5	6	2	3	2	1
	9	2	1	7	7	6	5	2	2	7	7	7	7	7	7	7	7	5	6
	10	6	5	7	7	7	7	3	4	7	7	7	7	7	7	6	6	6	6
	11	6	5	7	7	7	7	6	6	7	7	6	6	7	7	7	7	7	7
	12	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	13	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	14	7	7	6	4	7	7	2	1	7	7	1	1	5	6	2	1	2	1
Clarity of Presentation	15	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	16	6	7	7	6	6	7	7	7	7	7	6	7	7	6	7	7	7	7
	17	6	5	7	7	7	7	7	6	6	5	5	6	7	7	7	6	7	6
Applicability	18	7	7	5	6	7	7	4	3	4	3	4	3	4	3	3	4	3	4
	19	4	3	7	7	7	7	2	2	7	7	5	6	6	7	2	2	7	7
	20	7	7	7	7	4	5	6	6	6	5	4	5	7	7	6	6	6	5
	21	2	2	7	7	5	6	2	4	2	4	2	2	2	2	2	3	7	7
Editorial Independence	22	7	7	7	6	6	6	7	7	6	5	7	7	6	6	7	7	7	7
	23	7	7	7	7	7	7	5	6	7	7	6	6	7	7	7	7	7	7
Overall Assessment	OA1	6	6	6	6	6	7	4	4	6	6	5	5	6	6	4	5	6	6
	OA2	Yes	Yes	Yes	Yes	Yes	Yes	Yes*	Yes*	Yes	Yes	Yes*	Yes*	Yes	Yes	Yes*	Yes*	Yes	Yes

*Recommended with modifications.

Appendix 6: Specific recommendations across all CPGs that informed in Table 4

Recommendations identified in Table 4	Corresponding recommendation from each of the included CPGs
1. Identify Patient risk factors	*INS 2024:* ➓ Malignancy (type of cancer, tumor size, and characteristics), diabetes mellitus, obesity, chemotherapy administration, thrombophilia (eg, Factor V Leiden, protein C deficiency, protein S deficiency), critical illness, and personal and family history of thrombosis. (I) ➓ Other risk factors include SARS-CoV 2 virus infection (COVID-19), patient age (but vary widely per study and population risks), pregnancy, elevated triglycerides, elevated low-density protein, ethnicity (higher risk reported in Black or African Americans), reduced functional capacity (as measured by Eastern Oncology Cooperative Group [ECOG] scoring), readmission to the hospital shortly after central vascular access device (CVAD) insertion, inadequate hydration and nutrition, non-O blood types, and blood transfusions. (I) *CCC-IUA 2020:* ➓ Patients with catheterization are often in special disease-related states, and these states are highly overlapping with high risk factors for venous thrombosis, such as surgery, malignant tumors, and prolonged bed rest. (WG) ➓ Malignant tumor patient is one of the important people use infusion catheter, malignant tumor. The risk of VTE is significantly increased in patients with malignant tumors, and the risk may be increased by chemotherapy and surgery. (WG)
2.Identify catheter related risk factors	
➓ **Catheter diameter selection**	*INS 2024:* ➓ Use the smallest diameter, least number of lumens possible to deliver the required infusion therapy. (I) ➓ In a meta-analysis of PICC-related outcomes, optimal insertion techniques and use of single-lumen, smaller diameter PICCs reduced PICC-related DVT risk to a rate comparable to other CVADs. (I) ➓ Measure the catheter-to-vessel ratio prior to insertion; ensure no more than 45% ratio. (II) *CCC-IUA 2020:*

	⓾ On the premise of meeting the treatment needs, the infusion device with the smallest external diameter, the least number of lumen and the least trauma should be selected. (WG)
⓾ **Catheter tip position**	*INS 2024:* ⓾ Position the tip of a CVAD in the lower third of the superior vena cava (SVC) or upper third of the right atrium (RA) at or near the cavoatrial junction (CAJ) for adults and children. For lower body insertion sites, position the CVAD tip in the inferior vena cava (IVC) above the level of the diaphragm. (A/P) ⓾ For lower body insertion sites, position the CVAD tip in the inferior vena cava (IVC) above the level of the diaphragm. (IV) *CCC-IUA 2020:* ⓾ Under the same circumstances, the risk of thrombosis is lower if the catheter tip is located in the subclavian vein than in the proximal part of the basilic vein. (WG) ⓾ *ITAC-CME 2022:* ⓾ Catheters should be inserted on the right side, in the jugular vein, and the distal extremity of the central catheter should be located at the junction of the superior vena cava and the right atrium (Grade 1B). *ISCCM 2020:* ⓾ We recommend IJ and SCV catheter tip should be placed in the lower one-third of the SVC near the SVC/RA junction (A, 2).
3. Identify operator risk factors	*INS 2024:* ⓾ Use a bundled approach for PICC insertion, including systematic ultrasound evaluation and identification of optimal area for placement, insertion methods that reduce vascular trauma, optimal tip placement verification, optimal catheter-to-vein ratio, and use of smallest diameter/fewest number of lumens. (II) ⓾ Consider tunneling PICCs. A single-center, randomized, controlled, nonblinded, prospective trial demonstrated tunneled PICCs had a lower incidence of venous thrombosis and lower costs of catheter maintenance compared to nontunneled PICCs. (III) ⓾ Reduce thrombotic risk with arterial catheter insertion and management through use of ultrasound for accurate insertion, optimization

	of the catheter entry angle and length within the artery, catheter securement and stabilization, and frequent monitoring of circulatory status. (V) ➓ The use of electrocardiography to confirm appropriate PICC tip positioning has been associated with reduced thrombotic risk. (III) *CCC-IUA 2020:* ➓ Repeated puncture and withdrawal of catheter during catheterization can aggravate intimal injury and increase the risk of thrombosis. (WG) ➓ Non-standard rushed, sealing tube operation can increase the thrombotic wind duct loss risk. (WG) *ISCCM 2020:* ➓ We recommend that a mechanism should be in place to assess knowledge and compliance with guidelines of all the personnel involved in care related to CVC (A, 1)
4. Risk assessment of patients with PICC	*INS 2024:* ➓ Evaluate the risk of CAT during the process of VAD selection with careful consideration of patient vasculature, urgency and type of treatment required, and patient preference and functional needs (including laterality). (I) *CMA 2018:* ➓ VTE risk assessment is recommended for patients with a central venous catheter (2B).
5. Consider use of a risk scoring system	
➓ **Using Caprini Risk Assessment Model**	*INS 2024:* ➓ The Caprini Risk Assessment Model may have predictive value for PICC-related thrombosis, especially in high-risk patients. The Caprini score, however, was found to have moderate sensitivity and low specificity, possibly leading to overdiagnosis. (IV)
➓ **Using Michigan Risk Score**	*INS 2024:* ➓ Machine learning predictive techniques using genotypes may assist in identifying patients at high risk for PICC-related thrombosis. (IV)
➓ **Using Khorana**	*CMA 2018:*

score model	❿ VTE risk assessment using the Khorana score model is recommended for outpatient patients with malignancies receiving chemotherapy. (1B)
6. Monitor for signs and symptoms	
❿ **Measuring arm circumference**	*INS 2024:* ❿ Monitor for signs, symptoms, and potential consequences of CAT; recognize that CA-DVT often does not produce overt signs and symptoms. Clinical signs and symptoms are related to obstruction of venous blood flow and may include, but are not limited to, pain/edema/erythema in the extremity, shoulder, neck, or chest, and engorged peripheral veins of the extremity. (IV) ❿ Measure baseline circumference of the extremity with a PICC or a midline catheter upon insertion, noting location for future measurements to ensure consistent measurement. Assess circumference when edema or signs and symptoms of DVT present, noting the location and characteristics of edema. A 3-cm increase in mid-arm circumference in adults with PICCs was associated with CA-DVT. (IV) ❿ Recognize post-thrombotic syndrome as a potential long-term consequence of CA-DVT characterized by chronic pain, swelling, and skin changes. (II)
7. Pharmacologic preventative measures for PICC-related thrombosis	
❿ **guided by individual patient risk**	*INS 2024:* ❿ Recommendations for prophylactic anticoagulation for CA-DVT prevention have not been established for all patient populations but should be guided by individual patient risk. (I) a. VTE prophylaxis is recommended during cancer treatment requiring CVAD insertion and has not been associated with a risk of major bleeding. (I) b. The role of pharmacologic VTE prophylaxis is unclear in pediatric patients but has been associated with decreased CAT risk without increased bleeding risk in specific pediatric populations. (II)
❿ **Not to use as preference**	*ASCO 2013:* ❿ The use of systemic anticoagulation (war-farin, low–molecular weight heparin [LMWH], or unfractionated heparin) has not been shown to decrease the incidence of catheter- associated thrombosis, and therefore, routine prophylaxis with anti- coagulants is not recommended for patients with cancer with CVCs. (WG) *ASH 2021:*

	❿ For patients with cancer and a central venous catheter (CVC), the ASH guideline panel suggests not using parenteral thromboprophylaxis (conditional recommendation, low certainty in the evidence of effects ⊕OOO). ❿ For patients with cancer and a CVC, the ASH guideline panel suggests not using oral thromboprophylaxis (conditional recommendation, low certainty in the evidence of effects ⊕⊕OO). *CMA 2018:* ❿ Routine pharmacologic prophylaxis is not recommended for low-risk patients (2B). *ITAC-CME 2022:* ❿ Use of anticoagulation for routine prophylaxis of catheter-related thrombosis is not recommended (Grade 1A).
❿ **Use LMWH or LDUH as preference**	*CMA 2018:* ❿ Medium and high risk patients without anticoagulation taboo, suggest using LMWH or LDUH (2 B).
8. Non-pharmacological preventative measures for PICC-related thrombosis	
❿ **handgrip exercise**	*INS 2024:* Consider upper extremity exercise to reduce venous stasis; handgrip exercise using an elastic ball 3 or 6 times per day for 3 weeks was associated with a lower incidence of ultrasound-confirmed CA-DVT in patients with cancer who had a PICC. Further research is needed to identify postinsertion nursing interventions that reduce thrombotic risk (III). *CCC-IUA 2020:* ❿ When conditions permit, the use of nonpharmacological measures for thromboprophylaxis is encouraged, including early mobilization of the catheterization limb, normal daily activities, appropriate limb exercise, and adequate hydration. (WG) *IITC-CNA 2022:* ❿ Physical prophylaxis can be used to reduce thrombosis, and the use of non-pharmacological measures to prevent thrombosis is encouraged when conditions permit (V, B).

❿ **flushing with saline as preference**	*ASCO 2013:* ❿ Routine flushing with saline of the CVC to prevent fibrin buildup is recommended. (WG) *ESMO 2015:* ❿ Intermittent flushing with heparin is a standard practice in the maintenance of CVC patency. However, when compared with 0.9% normal saline flushing, no differences in thrombosis rates were found (I, C)
❿ **providing appropriate and adequate nursing care**	*ISCCM 2020:* ❿ We suggest providing appropriate and adequate nursing care to improve CVC-related outcomes. (B, 2) *CCC-IUA 2020:* ❿ For patients with high risk of thrombosis, it is still necessary to take corresponding preventive measures against VTE risk. (WG) *IITC-CNA 2022:* ❿ The principles of aseptic operation should be strictly adhered to during puncture and maintenance to reduce the chance of central venous catheter infection (II, A).
9. Diagnose and confirm PICC-related thrombosis	
❿ **Doppler ultrasound as preference**	*INS 2024:* ❿ Diagnose and confirm CA-DVT using color-flow Doppler ultrasound by the presence of at least 2 of the following: an echogenic mass in the venous structure assessed; noncompressibility of the vein, abnormal color Doppler vein pattern, and/or vein filling defect. Venography with contrast injection may also be used to assess more proximal veins (eg, brachiocephalic) that are obscured by the clavicle or ribs. (II) *CC-IUA 2020:* ❿ Doppler ultrasound is the first choice, which can indicate the location and range of CRT. (WG) *ESMO 2015:*

	❿ Although venography is considered the gold standard for the diagnosis of CRT, Doppler ultrasound is usually carried out (III, A). *ISCCM 2020:* ❿ We suggest that ultrasound guidance can be used for early identification of mechanical complication (B, 2). *IITC-CNA 2022:* ❿ The occurrence of catheter-related venous thrombosis can be assessed by observation, measurement and questioning of the patient's complaints and by colour Doppler imaging methods (I, A).
❿ **Not to routine use Doppler ultrasound**	*IITC-CNA 2022:* ❿ Based on the available evidence, the use of Doppler ultrasound to screen all patients for catheter-related venous thrombosis is not recommended (IV, D).
10. Remove the PICC against	
❿ **Do not remove catheter unless necessary**	*INS 2024:* ❿ Evaluate the need and appropriateness of PICC exchange. PICC exchange was independently associ- ated with a twofold greater risk of thrombosis in a retrospective study. However, this risk may have been influenced by the fact that patients who experienced exchanges were more likely to have had multilumen PICCs. (IV) ❿ Do not remove a CVAD in the presence of CA-DVT when the catheter is correctly positioned, functional, and necessary for infusion therapy. The decision to remove a CVAD should be made based on the individual patient's characteristics, symptoms, and imaging. (I) ❿ Carefully consider the need to retain or remove an implanted port at the conclusion of chemotherapy, evaluating the patient risks and need for further therapy. (V) *ISCCM 2020:* ❿ We recommend prompt removal of CVC when it is not essential (A, 2). *IITC-CNA 2022:*

	❿ Symptomatic thrombosis should be retained or the timing of extubation should be considered in the light of the degree of dependence on the catheter for treatment, the likelihood of re-establishing venous access, and the progression of the thrombus (II, B).
11. Treatment after diagnosis	
❿ **Anticoagulation therapy was given for at least 3 months after extubation**	*INS 2024:* ❿ Treat CA-DVT with anticoagulant medication for at least 3 months after diagnosis. For CVADs with a longer dwell time, continue the treatment for as long as the CVAD is in situ; unfractionated heparin infusion or catheter-directed thrombolysis may be of benefit to patients with severe symptoms. (IV) *ITAC-CME 2022:* ❿ For the treatment of symptomatic catheter-related thrombosis in patients with cancer, anticoagulant treatment is recommended for a minimum of 3 months; in this setting, LMWHs are suggested. Direct comparisons between LMWHs and VKAs have not been made in this setting (guidance). *IITC-CNA 2022:* ❿ When catheter removal is warranted, it should be preceded by routine anticoagulation according to the occurrence of thrombus and ultrasound screening for thrombus before removal (IV, B)
❿ **further assessed for appropriate interventions**	*IITC-CNA 2022:* ❿ After thrombosis has occurred, the patient's risk factors for catheter-related venous thrombosis should be further assessed for appropriate interventions (I, A).
12. Medical personnel training	
❿ **Establishing education and training systems**	*CCC-IUA 2020:* ❿ Standardized placement, use and maintenance of catheters and professional nursing teams are important prerequisites to reduce catheter-related complications, including thrombosis. (WG) *ISCCM 2020:* ❿ We recommend that a healthcare education and training program should be in place wherever CVCs are inserted and maintained for

	overall quality improvement (A, 1)
❿ **Establishing Credentialing process**	*INS 2024:* ❿ Ensure that the selected VAD is inserted by staff with specific training, using vascular visualization. (II) *ISCCM 2020:* ❿ We suggest providing appropriate and adequate nursing care to improve CVC-related outcomes (B, 2)

CVADs, Central Venous Access Devices; CA-DVT, catheter-associated deep vein thrombosis; CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Appendix 7: Evidence level systems used across CPGs

Evidence Levels	CPG Working Group
ASCO 2013/ CCC-IUA 2020	
WG	Recommendations based on expert opinion/consensus by the working group.
ASH 2021	
strong	-For patients: most individuals in this situation would want the recommended course of action, and only a small proportion would not.
	-For clinicians: most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.
	-For policy makers: the recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.
	-For researchers: the recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.
conditional	-For patients: the majority of individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences.
	-For clinicians: recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with their values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences.
	-For policy makers: policymaking will require substantial debate and involvement of various stakeholders. Performance measures about the suggested course of action should focus on whether an appropriate decision-making process is duly documented.
	-For researchers: this recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations that determined the conditional (rather than strong) recommendation will help to identify possible research gaps.

INS 2024	
I	Meta-analysis, systematic literature review, guideline based on randomized controlled trials (RCTs), or at least 3 well-designed RCTs.
II	Two well-designed RCTs, 2 or more well-designed, multicenter clinical trials without randomization, or systematic literature review of varied prospective study designs.
III	One well-designed RCT, several well-designed clinical trials without randomization, or several studies with quasi-experimental designs focused on the same question. Includes 2 or more well-designed laboratory studies.
IV	Well-designed quasi-experimental study, case control study, cohort study, correlational study, time series study, systematic literature review of descriptive and qualitative studies, narrative literature review, or psychometric study. Includes 1 well-designed laboratory study.
V	Clinical article, clinical/professional book, consensus report, case report, guideline based on consensus, descriptive study, well-designed quality improvement project, theoretical basis, recommendations by accrediting bodies and professional organizations, or manufacturer recommendations for products or services. This also includes a standard of practice that is generally accepted but does not have a research basis (e.g., patient identification).
A/P	Evidence from anatomy, physiology, and pathophysiology as understood at the time of writing.
Committee Consensus	Review of evidence, discussion, and committee agreement for a Practice Recommendation. Used when there is insufficient or low-quality evidence to draw a conclusion.
CMA 2018	
High (A)	Further research is very unlikely to change our confidence in the estimate of effect
Moderate (B)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low (C)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low (D)	Any estimate of effect is very uncertain
Recommendation (1)	Interventions clearly have more benefits than harms
Suggestions (2)	Interventions may have more benefits than harms
Not suggestions	Interventions may do more harm than good or pros and cons of relationship is not clear

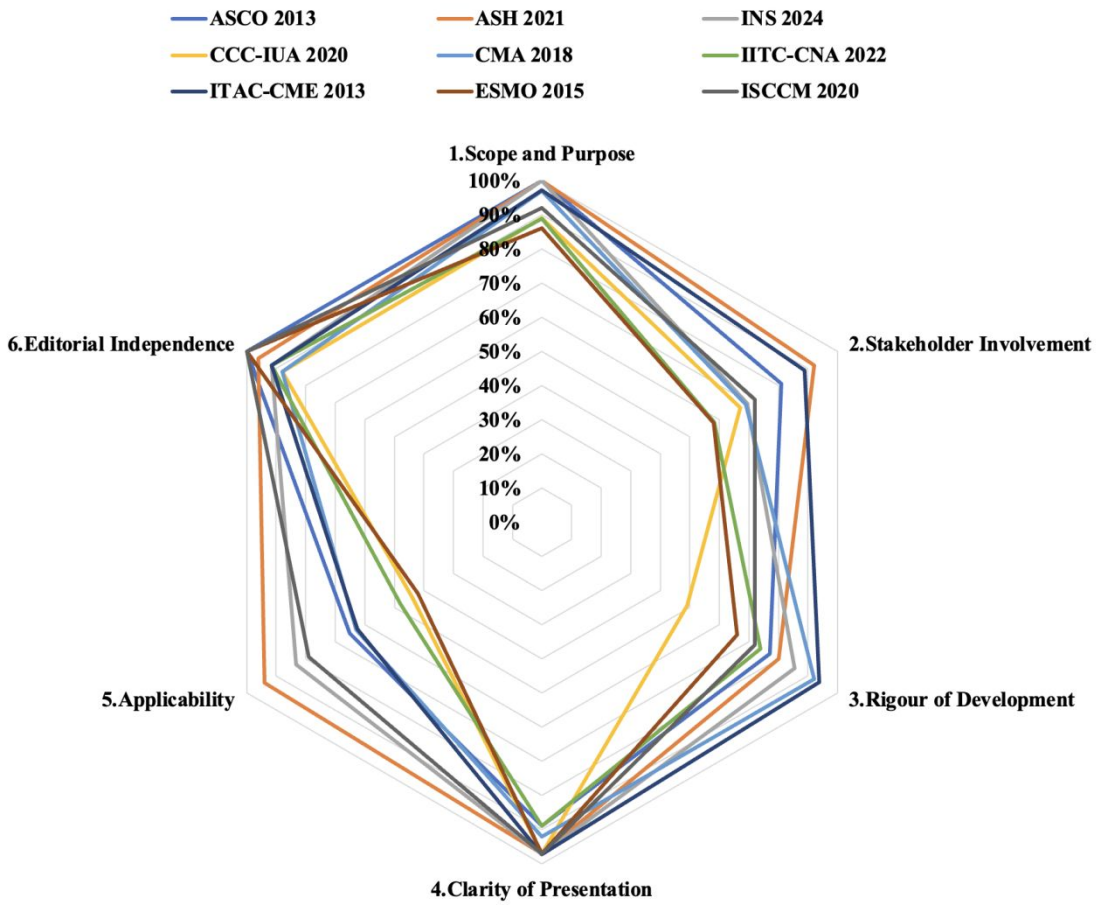
(2)	
Not recommended (1)	Interventions clearly do more harm than good
ITAC-CME 2022	
High (A)	further research is very unlikely to change our confidence in the estimate of effect
Moderate (B)	further research is likely to have an important impact on our confidence in the estimate of effect and could change the estimate
Low (C)	further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low (D)	any estimate of effect is very uncertain
Strong (Grade 1)	The panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects
Weak (Grade 2)	The panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but is not confident
Best clinical practice (Guidance)	In the absence of any clear scientific evidence and because of undetermined balance between desirable and undesirable effects, judgment was based on the professional experience and consensus of the international experts within the working group
IITC-CNA 2022	
I	Meta-analysis, systematic literature review, guideline based on randomized controlled trials (RCTS), or at least 3 well-designed RCTs.
II	Two well-designed RCTs, 2 or more well-designed, multicenter clinical trials without randomization, a systematic literature review of varied prospective study designs.
III	One well-designed RCT, several well-designed clinical trials without randomization, or several studies with quasi-experimental designs focused on the same question. Includes 2 or more well-designed laboratory studies.
IV	Well-designed quasi-experimental study, case control study, cohort study, correlational study, time-series study, systematic literature review of descriptive and qualitative studies, narrative literature review, or psychometric study. Includes 1 well-designed laboratory study.
V	Clinical article, clinical/professional book, consensus report, case report, guideline based on consensus, descriptive study, well-designed quality improvement project, theoretical basis, recommendations by accrediting bodies and professional organizations, or manufacturer recommendations for products or services.

	This also includes a standard of practice that is generally accepted but does not have a research basis (e.g., patient identification).
A	Evidence is highly effective and can be recommended to all clinical staff.
B	Evidence is valid and can be recommended to clinical staff.
C	the evidence is valid under certain conditions and the findings should be applied with caution.
D	Evidence validity is quite limited, valid only within a narrow range, and application is more restricted.
ESMO 2015	
I	Evidence from at least one large randomised controlled trial of good methodological quality (low potential for bias) or meta- analyses of well-conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, experts opinions
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, ...), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended
ISCCM 2020	
1	Evidence from ≥1 good quality and well-conducted randomized control trial(s) or meta-analysis of RCT's
2	Evidence from at least 1 RCT of moderate quality, or well-designed clinical trial without randomization; or from cohort or case-controlled studies
3	Evidence from descriptive studies, or reports of expert committees, or opinion of respected authorities, based on clinical experience
Useful Practice Point (UPP)	Not backed by sufficient evidence; however, a consensus reached by the working group, based on clinical experience and expertise

Grade A	Strong recommendations to do (or not to do) where the benefits clearly outweigh the risk (or vice versa) for most, if not all patients
Grade B	Weak recommendations, where benefits and risk are more closely balanced or are more uncertain

CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.

Supplementary Figure 1 The AGREE II domain scores of each guideline



CPGs, clinical practice guidelines; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; INS, Infusion Nursing Society; CCC-IUA, Chinese Chapter Congress of the International Union of Angiology; CMA, China Medical Association; IITC-CNA, Intravenous Infusion Therapy Committee of Chinese Nursing Association; ITAC-CME, International Initiative on Thrombosis and Cancer; ESMO, European Society for Medical Oncology; ISCCM, Indian Society of Critical Care Medicine.