International Journal of Nursing and Health Care Research

Moureau NL, et al. Int J Nurs Health Care Res 5: 1347

www.doi.org/10.29011/2688-9501.101347

www.gavinpublishers.com

Review Article

Integrative Review: Complications of Peripherally Inserted Central Catheters (PICC) and Midline Catheters with Economic Analysis of Potential Impact of Hydrophilic Catheter Material

Nancy L. Moureau[1*], Ellen McKneally[2], Dianna Hofbeck[3], Jamie Sharp[4], Brian Hanley[5], Vickerie Williams[6]

[1]Research Consultant, PICC Excellence, Inc, Hartwell, GA, USA

[2]Information Technology, PICC Excellence, Inc, Hartwell, GA, USA

[3]Forensic and Reimbursement Medical Specialist

[4]Registered Nurse, Intermountain Healthcare, Salt Lake City, UT, USA

[5]Vice President Research and Development, Access Vascular, Inc, Billerica, MA, USA.

[6]Director of Downstream Marketing, Access Vascular, Inc, Billerica, MA, USA.

[*]**Corresponding author:** Nancy L. Moureau, Research Consultant, PICC Excellence, Inc, Hartwell, GA, USA

Citation: Moureau NL (2022) Integrative Review: Complications of Peripherally Inserted Central Catheters (PICC) and Midline Catheters with Economic Analysis of Potential Impact of Hydrophilic Catheter Material. Int J Nurs Health Care Res 5: 1347. DOI: 10.29011/2688-9501.101347

Received Date: 29 September, 2022; **Accepted Date:** 11 October, 2022; **Published Date:** 13 October, 2022

Abstract

A literature review was conducted to evaluate the potential economic and clinical impact of hydrogel catheter materials on the incidence of catheter-related complications. Of 10,635 abstracts initially screened, 75 studies were included with 36 in outcomes, 28 for catheter materials, and 13 for economic analysis. The economic evaluation of peripherally inserted central catheters revealed a cost of $24,558 dollars for catheter-related thrombosis, $12,982 for infection, and $624 for occlusion which equate to a total national complication cost of $4.5 billion dollars annually. There was a 50% reduction in projected savings for all complications with the application of a hydrogel catheters which equated to nearly $1.8 million dollars annually for a typical 1000-bed acute care or $560,000 for a 300-bed facility. Limited clinical research on the hydrophilic catheter material suggests a remarkable and cost-effective reduction for incidence of common catheter complications. More research is needed to confirm data from existing studies.

Keywords: Peripherally inserted central catheters; Systematic review; Thrombosis; Catheter-related infection; Economic

Introduction

Most hospitalized patients receive a vascular access device (VAD) for the delivery of intravenous medications or solutions consistent with their medical treatment plan. More than 30% of those with VADs will experience a complication [1]. Millions of complications with VADs occur annually [2] ranging from catheter failure, occlusion with loss of catheter function causing delays in treatment delivery, vessel injury with catheter-related thrombosis (CRT), catheter associated bloodstream infections (CABSI) and even death [3]. Beyond patient suffering, catheter failure requiring replacement, and extended hospital length of stay (LOS), complications result in added cost to healthcare facilities

and payors [3]. Acute care facilities, by and large, are not aware of the incremental cost associated with intravenous catheter complications [4].

Standard catheters constructed of polyurethane materials are foreign to the body and can cause an immune response. Current research and development have focused on strategies, including catheter coatings, aimed at reducing the body's natural response of a fibrin coating of the catheter that contributes to complications of occlusion, thrombosis, and catheter related infection [5]. Newer hydrophilic biomaterials, used for peripherally inserted central catheters (PICC) and midline intravenous catheters (midline), may reduce the foreign body response by mimicking the body's chemistry [6]. These hydrophilic hydrogel components have the potential to eliminate many common complications resulting in cost reductions across healthcare facilities and a positive impact for the patients [7].

The aim of this research review was to identify the benchmark incidence of key complications with PICC and midline catheters to provide projections of the economic impact of catheter hydrogel material usage in reducing complications. While many factors affect the incidence of catheter complications such as the education and training of the inserter, the assessment and management of the catheter during infusions, and the adherence of blood to the catheter material, this review focused on how construction materials may contribute to complication incidence and cost.

The question remains: Are complications preventable with today's novel hydrophilic biomaterials and are they a cost-effective alternative to conventional catheters? Since there are significant complications associated with PICCs and midlines, an outcomes and cost-benefit analysis of novel catheter materials can help hospital executives make more informed decisions about catheter selection. The authors hope that this review may inspire hospital leadership to consider alternatives to standard polyurethane PICC and midline catheters with the goal of safeguarding patients by preventing clinically relevant and costly catheter complications.

Materials and Method

Design and objective

The design of this study was an integrative literature review, in which the analysis extrapolates results from qualitative, quantitative, and mixed studies integrated to develop new theories and conclusions. This integrative review adopted the preferred reporting items for systematic reviews (PRISMA) as modified and applied specifically to integrative reviews without meta-analysis [8]. The aim of this integrative research review was to quantify the incidence of the top three complication outcomes with PICC and midline catheters for thrombosis, infection, and occlusion to identify their associated costs, and project the potential economic impact of catheter hydrogel materials on reduction of catheter related complications.

Setting and population

This integrative literature review and systematic search of PICC and midline outcomes, materials and economics was performed in March 2022 by two reviewers using keywords for peer-reviewed publications accessing MEDLINE/PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, EmBASE, and Cochrane review online sources applying database-specific search strategies.

The review of literature was performed with MeSH (Medical Subject Headings National Library of Medicine) keywords. Key MeSH terms used for the search included: peripherally inserted central catheter line insertion, midline intravenous catheters, central venous catheter, vascular catheters, vascular access devices, catheter, catheterization, venous catheterization, peripheral catheterization, central venous catheter thrombosis, deep vein thrombosis, venous thrombosis, venous thromboembolism, upper extremity deep vein thrombosis, catheter related thrombosis, venous thromboembolism, catheter associated infection, catheter related infection, bloodstream infection, catheter obstruction, tissue plasminogen activator (tPA), catheter material, anti-thrombotic, antimicrobial catheter, polyurethane, silicone, hydrogel, surface modification, economic model, cost analysis, systematic review, meta-analysis, polyurethane, coated materials, biocompatible materials, surface-coated materials.

Citations were processed through Rayyan™ (http://rayyan.qcri.org, Qatar Foundation, non-profit organization in the State of Qatar) open-source document management software and EndNote™ (Endnote x20.3 PDFNet SDK© Systems, Inc. distributed by Clarivate Analytics, LLC.) software-based citation management system. Duplicate records were identified and extracted. Two authors independently reviewed the titles and abstracts to retain records meeting inclusion criteria for each category of the three outcomes, materials, and economic sections. The search was not limited by language for final publications including English. Non-English publications were manually excluded during screening. All abstracts selected by the reviewers were subjected to a full manuscript review for evaluation of inclusion criteria.

Preference in the search for outcomes of PICC and midline complication incidence was given to systematic reviews, meta-analyses, and large group research inclusive of randomized controlled trials (RCTs). Studies were excluded if the outcomes, catheter types, sample size, ages, dates, or other inclusion criteria were not met for each category. Disagreements were resolved through discussion, and through grading by a third researcher. The section narrative review of catheter materials also included research on non-human subjects.

Outcome publications were graded according to the Newcastle–Ottawa scale for quality of the evidence as recommended by the Cochrane Collaboration for included studies that were non-randomized, cohort or observational design [9]. The star rating system assigned quality based on the domains of selection of study groups, comparability of groups, and ascertainment of outcomes. Those rated receiving a star in every domain were considered of higher quality for selection inclusion and grading. Following this rating a Level of Evidence GRADE 1-5 was applied to each selected publication (Table 1) [10-45]. Inclusion and exclusion criteria apply to outcomes review.

Publication Author and Date	Research Type	Sample Size/ Catheters	Catheter Type and Material	Thrombosis	Infection	Occlusion	Quality GRADE
Al Raiy, B et al. 2010[10]	Prospective Cohort	n=622	PICC		2.1% n=13 2.3/1000 cd		2b
Bing, S et al. 2021[11]	Retrospective Cohort	n=5058 catheters	PICC n=2502 Midline n=2049 Both n=507	PICC 4% n=105 Midline 3% n=69	PICC 29% n=721 Midline 27% n=557		3b
Chopra, V, Anand, S, Hickner, A et al. 2013[12]	Systematic Review Meta-analysis	n=29,503 pts	PICC	2.7% n=797			1b
Chopra, V, Kaatz, S et al. 2019[13]	Prospective Cohort	n=1161	Midline	1.38% n=16	0.34% n=4	2.24% n=26	2b
Chopra, V, O'Horo, J et al. 2013[14]	Systematic Review Meta-analysis	n=1473	PICC		5.2% n=76		2a
Evans, RS et al. 2013[15]	Prospective Observational	n=5796	PICC	2.6% n=153 3.6/1000 cd		15.4% n=891	3b
Gonzalez, S et al. 2021[16]	Prospective Cohort	n=1142 153,191 cd	PICC	2.0% n=23 0.15/1000 cd	5.8% n=66 0.43 /1000 cd	0.9% n=10 0.06/1000 cd	2b
Greene, MT et al. 2015[17]	Retrospective Cohort	n=3790	PICC	8.4% n=208 2.75/1000 cd			2c
Hawes, M 2020[18]	Prospective Observational	n=497	Midline			2.1% n=112	3b
Jennings, K et al. 2011[19]	Retrospective Cohort	n=575	PICC		4% n=26	2% n=12	2c
Kagan, E et al. 2019[20]	Retrospective Cohort	n=5372	PICC		1.66% n=89		2c
Kim, K et al. 2020[21]	Prospective	n=1215 31,874 cd	PICC		4.4% n=54 1.69/1000 cd		3b
Kim-Saechao, S et al. 2016[22]	Retrospective Historical Cohort	n=400 3614 cd	PICC	9% n=37 10.2/1000 cd	0.2% n=5 2.2/1000 cd		3b

Koo, C et al. 2018[23]	Retrospective Cohort	n=2270	PICC	4% n=124			2c
Kramer, RD et al. 2017[24]	Systematic Review Meta-analysis	n=12,879	PICC		3.4% n=438 1.23/1000 cd		2a
Lee, J et al. 2019[25]	Prospective Cohort	n=929 17,913cd	PICCs		6.2% n=58 3.23/1000 cd		2b
Liem, TK et al. 2012[26]	Retrospective Cohort	n=2638	PICC	3.7% n=98			2c
Lisova, K et al. 2018[27]	Prospective Cohort	n=439	Midline	4.5% n=20 3.3/1000 cd			2b
Lobo, B et al. 2009[28]	Retrospective Cohort	n=954	PICC	4.89% n=38 5.1/1000 cd			2c
Lu, H, Hou, Y et al. 2021[29]	Systematic Review Meta-analysis	n=33,322	PICC n=26,422 Midline n=6900		PICC 0.48% n=127 Midline 0.58% n=40		2a
Lu, H, Yang, Q et al. 2021[30]	Systematic Review Meta-analysis	n=40,871	PICC n=33,065 Midline n=706	PICC 2.29% n=758 Midline 3.97% n=310			2a
Maki, D et al. 2006[31]	Systematic Review		PICC Midline		PICC 2.4% 2.1/1000 cd Range 0.8-2.1/1000 cd Midline 0.4% 0.2/1000 cd		2a
McDiarmid, S et al. 2017[32]	Retrospective Analysis	n=656 58,486 cd	PICC BioFlo Endexo	1.5% n=10 0.17/1000 cd	0.6% n=4 0.07/100 0cd	11.4% n=75	2c
Mushtag, A et al. 2018[33]	Retrospective Cohort	n=411	Midlines n=2	0.49%	0.2% n=1		2c
Nolan, ME et al. 2016[34]	Retrospective Cohort	n=400 1730 cd	PICC	4% n=8/200 4.6/1000cd	0.5% n=1/200 .46/1000cd		2c
Paje, D et al. 2018[35]	Prospective Cohort	n=15,397	PICC	3.2% n=362	1.1% n=177	11.6% n=1786	2b
Park, S et al. 2020[36]	Retrospective Cohort	n=1053	PICC		3.5% n=36 1.14/1000 cd		2c

Pikwer, A et al. 2012[37]	Systematic Review	n=3116	PICC	2.5% n=188 7.82/1000 cd	0.7% n=153 2.25/1000 cd	2.5% n=142 7.8/1000 cd	2a
Rabelo-Silva, ER et al. 2022[38]	Prospective Observational	n=12,725	PICC	1% n=129	0.9% n=114	2.9% n=369	3b
Schears, G et ql. 2021[39]	Systematic Review Meta-analysis	n=8174	PICC	8.9% n=727	2.12/1000 cd		2a
Scimo M et al. 2022[40]	Retrospective Cohort	n=12,687	PICC	0.83% n=105	0.1% n=13		3b
Smith, SN et al 2017[41]	Prospective Cohort	n=14,287	PICC			12% n=1,716	2b
Swaminathan, L et al. 2021[42]	Retrospective Cohort	n=10,863	PICC n=5,758 Midline n=5,105	PICC 1.5% n=86 Midline 1.4% n=74	PICC 1.6% n=93 Midline 0.4% n=19	PICC 7% n=405 Midline 2.1% n=105	2c
Tripathi, S et al. 2021[43]	Systematic Review	n=18,972	Midline	4.1% n=778	0.28/1000 cd	3.8% n=645	2a
Vaughn, V et al. 2020[44]	Prospective Cohort	n=21,653	PICC	1.7% n=386	1.1% n=236	6.5% n=1408	2b
XU, T et al. 2016[45]	Retrospective Cohort	n=406	PICC n=206 Midline n=200	PICC 1% n=2 Midline 1% n=2	PICC 2.4% n=5 Midline 2.5% n=5		2c
Pooled Incidence				PICC 3.45% 4.2/1000cd Midline 2.48%	PICC 3.47% 1.47/1000 cd Midline 3.96% 0.2/1000 cd Excluding Bing PICC 2.25% Midline .67%	PICC 8.32% Midline 3.59%	
Totals	9 Systematic 12 Prospective 15Retrospective 36 Total	Total catheters >264,606 PICC n=227,659 Midline n=36,440 Both n=507	PICC n=31 Midline n=11	24 PICC n=20 Midline n=8	27 PICC n=22 Midline n=8	13 PICC n=10 Midline n=4	

Table 1: Outcome evidence for PICC/Midline catheters; Abbreviations: cd, catheter days; midline, midline intravenous catheter; n, total number of catheters or events; PICC, peripherally inserted central catheter.

Data collection

Inclusion criteria

- PICC and/or midline catheter outcome studies
- Peer reviewed publications
- Acute care patients
- Preference for systematic reviews where adult populations predominate
- Outcome studies of adults with sample size of 300 or more for catheter thrombosis, infection, and occlusion
- Outcome and economic publications from 2000-2022
- Materials review in vivo and in vitro including animal from 1980-2022

Exclusion criteria

- Primary outpatient, home care, pediatric or cancer patient studies
- Asymptomatic thrombosis
- Cohorts or systematic reviews with sample greater than 50% for cancer, pediatric, or neonatal patients
- Urethral or jejunostomy catheters, stents, grafts, dental, or prosthetics
- Insufficient data for pooling of incidence results for outcome studies

Data analysis

Basic characteristics and outcome-specific data were extracted into SAS Institute, Inc. Microsoft® Excel® 64-bit version 2202 and Microsoft Word version 2202. The extracted information included the first author's last name, year of publication, type of research, total sample size, incidence rates of thrombosis, infection, and occlusion for PICCs and midline catheters. Extractions were completed by a single reviewer and were reviewed for accuracy by a second and third reviewer.

Catheter materials

Integrative review of catheter materials included *in vivo*, *in vitro*, and animal peer reviewed publications from 1980-2022. Catheter materials sampled with application to intravascular and biocompatible use included polyurethane and poly-derivatives, silicone, coatings, impregnations and surface modifications, polymers with hydrophilic and hydrophobic characteristics.

Economic analysis

Economic analysis was performed using PICC outcome costs published in the revised 2022 list of ICD-10 codes for PICC complications of thrombosis/deep vein thrombosis, catheter occlusion, use of thrombolytic tPA, and catheter associated infection. Literature review results were compared with ICD-10 specific complications and factored into the analysis of complication economic impact. Rates for hospital cost, diagnostic related group payments, and length of stay (LOS) attributable to complications in PICC or midline patient groups were included. Additional PICC and midline economic calculations were based on the benchmarked systematic review outcome results for incidence and published costs of complications and catheter replacement. Application of cost projections were calculated to estimate potential savings for hydrogel composite catheter material usage in dollars (USD).

The data used in the analysis was the MedPAR 2020 final data released by the Centers for Medicare and Medicaid Services (CMS) as a part of the fiscal year (FY) 2020 Final Inpatient Prospective Payment System (IPPS) rule (https://www.cms.gov/medicare/acute-inpatient-pps/fy-2022-ipps-final-rule-home-page) [45,46]. During this research, the FY2022 was the most recent MedPAR data available (https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/MEDPARLDSHospitalNational) [47].

As a first step, the MedPAR data was transformed and manipulated following the rate-setting methodology set forth by CMS in the rule. In the FY2022 final rule, CMS confirmed a policy of setting the rates based on FY2019 MedPAR data, but the proposed rule also calculated and published an "alternative" set of weights based on the FY2020 MedPAR data. Watson Policy Analysis (WPA) followed the CMS logic of the weight-setting and determined the cases and characteristics using the FY2020 data. After WPA replicated the CMS logic and policies, WPA analyzed the claims data for analysis and rate-setting. WPA also replicated the CMS logic for determination of costs of a case when CMS is determining the High-Cost Outlier. This logic was applied to the cases. The costs are the sum of estimated operating and estimated capital costs. As a part of the replication of the CMS logic, WPA used other tables and data published as a part of the rule. Using those cases expected to be used in the replication, WPA identified cases of interest. These cases had a specified ICD-10 procedure code for a PICC Insertion. The codes included here were: 02HV33Z, 05HY33Z, 05H533Z, 05H633Z, 05HM33Z, 05HN33Z, 05HP33Z, 05HQ33Z, 05HB33Z, 05HC33Z, 05HD33Z, 05HF33Z, 05H733Z, 05H833Z, 05H933Z, 05HA33Z, 06HM33Z, 06HN33Z, 06H033Z.

The diagnosis codes of interest were designated as either primary or secondary diagnosis. The diagnosis codes used for catheter related outcomes were as follows: catheter-related thrombosis T82.868A, T82.868D, T82.868S, I82.62; bloodstream infection T80.211A, T80.211D, T80.211S; catheter occlusion: 3E04317 (i.e., catheter occlusion was identified by checking the

procedure codes as opposed to the diagnosis codes). The economic analysis data elements and their source were calculated with the following inclusion/exclusion criteria:

- Diagnosis not present at time of inpatient admission
- Calculation of LOS - charges, and estimated costs
- Number of discharges
- Discharges meeting criteria for rate-setting process
- Comprised of 100% Fee-for-service inpatient discharges following data cleaning
- Basis for cost calculations
- Length of stay-Basis for total length of stay as reported in the data
- Total charges- Basis for total charges as reported in the data

ICD-10 PICC complication diagnostic codes

Thrombosis: T82.868A, D, S - Thrombosis due to vascular prosthetic devices, implants and grafts, initial encounter

Deep vein thrombosis (DVT): I82.62 - Acute embolism and thrombosis of deep veins of upper extremity

tPA: 3E04317 - Introduction of other thrombolytic into central vein, percutaneous approach

Discharges with diagnosis of DVT, Pulmonary Emboli (PE), Stroke, Acute Myocardial Infarction (STEMI) and an associated Intensive Care Unit (ICU) stay were removed to focus on catheter occlusion

Infection: T80.211A, D, S - Bloodstream infection due to central venous catheter, initial encounter.

Total cost was calculated following the methodology for estimating cost for high-cost outlier purposes through ICD-10 coding. Cost was calculated by multiplying the total charges for the claim by hospital specific cost to charge ratios released by CMS as a part of the rule. The delta represents the comparison of the average estimated cost for discharges with a PICC insertion or revision ICD-10 code, including a primary or secondary diagnosis code, for the ICD-10 diagnosis code associated with the complication (i.e., PICC with infection) and the estimated cost average for PICCs insertion or revisions with no complication diagnosis code associated. The delta resulting cost was defined as the difference or change from the ICD-10 coding PICCs with none of the complications as the base average, and the difference, combined with the event cost of the outcome. The calculation, multiplied by the benchmark incidence of complications, determined the theoretical economic benefit of a novel catheter material in preventing PICC and midline catheter complications. The average 1000 bed acute care hospital was defined as a hospital utilizing 2400 PICCs per year and 1200 midlines and the average 300 bed acute care hospital was defined as a hospital utilizing 720 PICCs and 360 midlines (number of beds x .25 x .8 x 12 = annual number of PICCs or Midlines) [48-50].

Definitions

Peripherally inserted central catheters -Venous catheter length typically 30-55cm upper extremity veins (e.g., cephalic, basilic, or brachial). Tip termination in the superior vena cava or cavo-atrial junction. Commonly inserted by PICC teams predominately nursing.

Midline catheters **-**Venous catheter length of 10-25cm inserted into upper extremity veins (cephalic, basilic, brachial), most commonly in the upper arm with catheter terminal tip in noncentral vein (brachial, axillary). Typically used for non-irritating, non-vesicant medications, and fluids when centrally placed catheters are not indicated. Radiographic confirmation not necessary for tip verification.

PICC or midline thrombosis -A broad definition of all cause catheter associated venous thrombosis was applied to include catheter related thrombosis for symptomatic thrombosis, thrombophlebitis, deep vein thrombosis, upper extremity thrombosis, venous thrombosis, and thromboembolism as they relate to PICCs and midlines.

Catheter associated infection-Infection in PICCs and midlines is defined as any primary bloodstream infection related to the catheter inclusive of catheter related bloodstream infections (CRBSI), central line associated bloodstream infections (CLABSI), catheter associated bloodstream infection (CABSI), PICC associated bloodstream infections (PABSI), or any systemic catheter associated infection not related to local skin or exit site infection.

Catheter occlusion or blockage-Inability to infuse prescribed therapy or aspirate blood from a PICC or midline as it relates to complete or partial occlusion. Documentation of thrombolytic use or administration of tPA for the purpose of declotting or occlusion resolution.

Catheter materials-PICC and midline catheter materials defined as biocompatible, urethanes, polyurethane, silicone, coated catheters, antimicrobial, antithrombotic, impregnated, hydrogel, or other polymer materials used for vascular catheters. Thermoplastic polyurethane (TPU), hydrophilic biomaterial (HBM), modified polyurethane (MPU)

Results

Results literature review

The results of literature review are displayed in the PRISMA flow chart (Figure 1). A total of 10,635 articles were initially identified

during the search and 146 other selected *via* hand search. After duplicate extraction, title and abstract screening, the reviewers evaluated full text of 2433 abstracts. Subsequently, articles were classified in three groups for outcome (n = 140), material (n = 149) and economic (n = 21) sections. Following full-text review and elimination, based on application of inclusion and exclusion criteria, a total of 75 articles were included in the integrative review, 36 for the PICC midline outcome category, 28 for materials and 13 for economic review. The outcomes publications included systematic reviews (n = 9), prospective cohort (n = 12), and retrospective cohort (n = 15) studies. A total of 31 studies for PICCs and 11 for midlines, including five studies with both PICC and midline results. PICC and midline outcome studies were further stratified into catheter related thrombosis (n = 24), infection (n = 27), and occlusion (n = 13) (Table 1). Catheter materials review results are summarized in section 3.3 below. Economic analysis included literature review, correlated with ICD-10 results (Table 2).

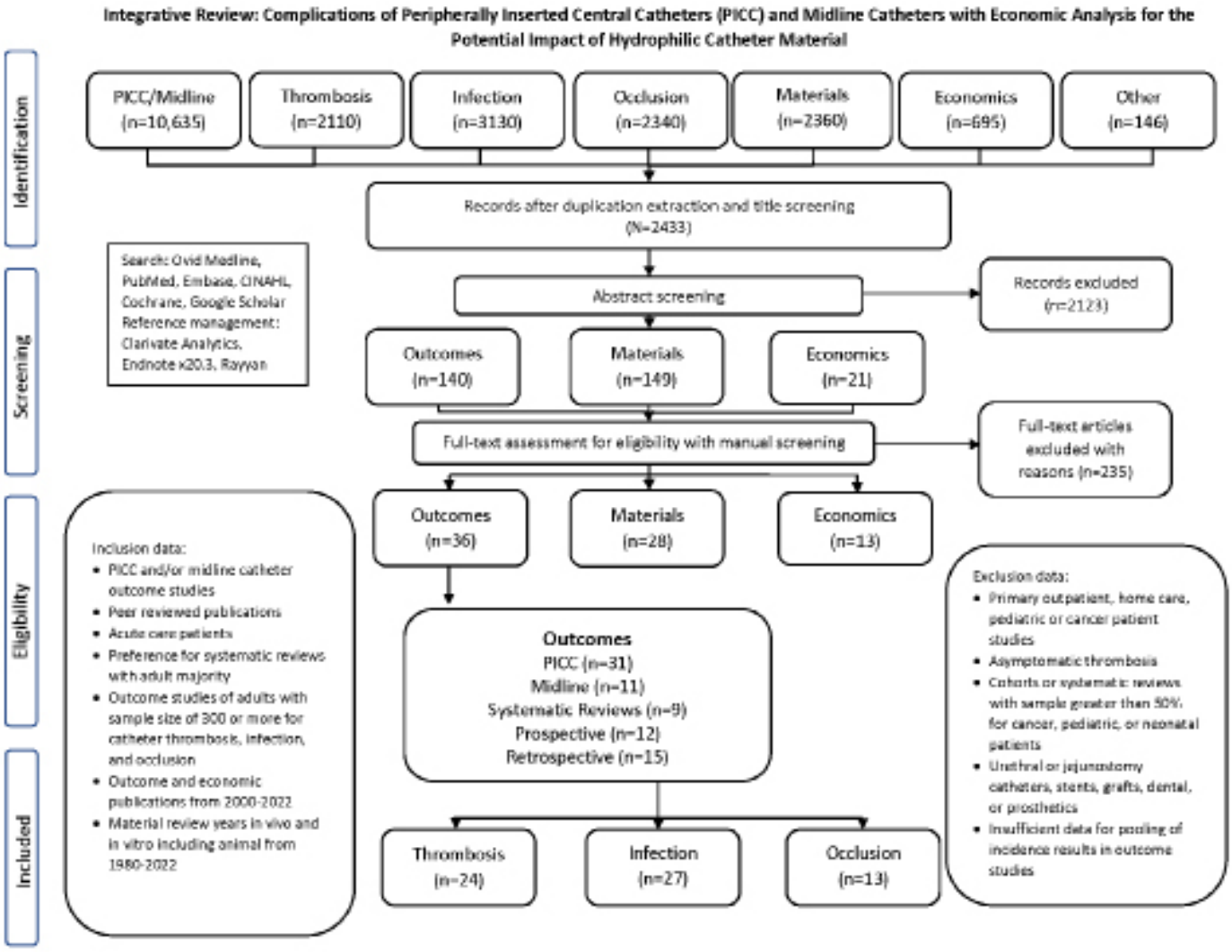

Figure 1: Flow Diagram of literature search and selection process. PRISMA Page et al. doi: 10.1136/bmj.n71. http://www.prisma-statement.org/.

Description for Diagnosis Codes Selected	Number of discharges	Length of stay (days)	Estimated cost (USD)	Estimated cost per event (USD)
01. All PICC insertions and revisions	621,469	11.1	$ 40,677	$940
02. PICC insertions or revisions with thrombosis or DVT	17,024	16.3	$ 64,294	$ 24,558
03. PICC insertions or revisions with tPA indicating occlusion	309	12.9	$ 40,360	$ 624
04. PICC insertions or revisions with infection	7760	16	$ 52,718	$ 12,982
05. PICC insertions or revisions with none of the complications	587,110	10.9	$ 39,736	Baseline

Table 2: ICD-10 report for coded outcomes with PICCs; MEDPAR Limited Data Set (LDS) - Hospital (National) FY2020 MedPAR. www.cms.gov, Center's for Medicare & Medicaid Services, https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/MEDPARLDSHospitalNational. FY 2022 IPPS Final Rule Home Page." https://www.cms.gov/medicare/acute-inpatient-pps/fy-2022-ipps-final-rule-home-page.7

Outcome incidence

The primary review of 36 outcome studies demonstrated a benchmark pooled incidence for each of the PICC and midline catheter related complications of thrombosis, infection, and occlusion [10-45]. Total catheters reported within the literature reviewed were 264,606 with 227,659 PICCs and 36,440 midlines (+205), and 507 inclusive of both catheters. Total complication events were 14,730 for an estimated incidence of 5.6%.

The pooled incidence for CRT with PICCs was 3.45% and for midlines was 2.48%. For the reviewed publications inclusive of reporting in catheter days the pooled rate for CRT in PICCs was 4.2/1000 catheter days (cd) and 3.3/1000cd for midlines.

The pooled incidence of bloodstream infections reported in the literature was 2.25% for PICCs and 0.67% for midlines (i.e., after exclusion of outlier), and per catheter days was 1.47/1000 for PICCs and 0.2/1000 for midlines (i.e., only represented in one midline study). A conservative approach was taken for the final results of infection incidence in the exclusion of the Bing et.al. study which represented an outlier for higher infection rates [11].

The pooled results for catheter occlusion incidence were 8.3% for PICCs and 3.6% for midlines. Occlusion rates were included in 13 of the published studies representing 81,105 catheters in the PICC group with 6750 reported occurrences. Within the midlines there were 6763 catheters and 243 occurrences.

Material types

The results of the materials literature review of 28 publications revealed intravascular catheters are constructed with various material types, surface modifications, coatings, impregnations, and composite polymers with physical and chemical properties that govern biocompatibility, material tensile strength, softness or hardness, chemical resistance, protein adsorption, and surface features of smoothness or irregularity [6,7,20,51-75]. Polyurethane or silicone-based catheters constitute the primary materials used in the construction of vascular access catheters. These vascular catheter materials have been in use since the 1960s providing biocompatible devices with flexibility, durability, and strength [53]. The materials have evolved from Teflon (DuPont, Wilmington, DE USA), polyurethane, and silicone catheter types to the addition of other polymers with improvements based on changes to the catheter physical and chemical properties [53]. Silicone catheters contain dimethylsiloxane as a repeated polymerized monomer unit for medical grade usage [53,65]. Silicone catheters have a higher degree of thrombogenicity with lower tensile strength and therefore are more prone to rupture, leakage, occlusion, and sepsis [58,59,63,73]. Polyurethane catheter materials, while also subject to fibrin sheath formation and embedded bacteria deposits, are available as segmented urethanes with hard and soft segments of diisocyanates and polyethers, and carbonate copolymers [53,63,64]. Polyurethanes represent a broad spectrum of physical

and chemical properties within catheter products [53,55]. Optimal features include high tensile strength, soft pliable durometer, high biocompatibility, long-term dwell, chemical resistance, and ability to maintain adequate flow with thin walls and smallest diameter [53,68].

Despite these features and advantages most polyurethane and silicone catheters are hydrophobic polymers with irregular surfaces that are highly susceptible to protein adsorption when placed into the bloodstream [55,64,65,72]. As a result, catheters present in the bloodstream automatically trigger a complex series of protein adsorption, adhesion, and activation of platelets with leukocytic blood cells promoting cellular attachment [63]. A hydrophobic or rougher surface attracts platelet adhesion, adsorbing fibrinogen [63]. As a result, catheters prepared from these materials are prone to various failure modes such as thrombosis and thrombotic occlusion [67,68]. According to Mehall et al. blood adherence to a catheter, forming a fibrin sheath, most commonly around the external catheter, promotes trapping of bacteria and colonization, enhancing the risk of catheter associated infection [63]. There are sufficiently large numbers of human studies reported in the literature indicating the foreign body response associated with polyurethane-based vascular catheters which may result in catheter failure, phlebitis, and thrombosis [32,57,76]. Polyurethane surfaces are modified with coatings or impregnation to reduce complications caused by blood or bacterial adherence [57,64,73].

Catheter manufacturers have used a range of surface modifications to address the inherent limitations of surface irregularity, hydrophobic surfaces, positive and negative ionic charges, protein adsorption, foreign body response and cellular attachment of intravascular catheters [7]. Masking the disadvantages of the hydrophobic substrate by modifying the surface of the catheter with hydrophilic coatings and impregnating the catheter with antimicrobial or thromboresistant polymer additives are some of the most common approaches [57,73]. Surface modifications have included hydrophilic and hydrophobic coatings, antimicrobial agent coatings or impregnations (e.g., antimicrobial action is surface kill or the elimination of microorganisms), antithrombotic (e.g., reducing surface attachment and formation of blood cell aggregation), or a combination, and have all been used with mixed results. Additionally, nonchemical approaches (e.g., surface topography modification, use of acoustic energy or electric current) also exist [64]. Antithrombotic coated PICCs have shown great promise in laboratory testing with 75% less thrombus accumulation on the catheter surface, however, retrospective reviews of outcomes resulted in no appreciable change in catheter occlusion, a primary measure of thrombotic deposits on the catheter surface [73].

The potential for reduced colonization on catheter surfaces with a trend toward reduction in catheter related bloodstream infections (CRBSI) was observed with antimicrobial central venous catheters and PICCs [51,63,67,73]. High quality evidence in a Cochrane review reported CRBSI reduction of 2%, and bacterial colonization down by 9% in central venous catheters [61]. In a 30-month comparator study of antimicrobial and non-antimicrobial PICCs by DeVries et al. achieved a significant reduction in PABSI with an initial rate of infection at 1.83 versus 0.62/1000 cd [52]. In another large prospective cohort study in 52 hospitals the analysis of 42,562 patients the investigators found no reduction in thrombosis, infection, or occlusion with either antimicrobial or antithrombotic PICCs [74]. In a systematic review of PICCs and central venous catheters, Slaughter et al. concluded that differences of catheter material or design did not have a significant effect on incidence of thrombosis, infection, or occlusion [69]. While antimicrobial catheter modifications in non-PICC central venous catheters have demonstrated a modest reduction in bacterial colonization and infection, the weight of evidence to support use of antimicrobial or antithrombotic coatings or impregnations in PICCS remains low [73]. Vascular catheter coatings or impregnations have not demonstrated a sufficiently durable improvement over conventional polyurethane and silicone substrates, and do not adequately address the underlying issues of surface irregularity, catheter surface conditioning, and cellular attachment that cause protein adsorption leading to thrombosis, occlusion and potentially infection [53,56,58,63,73].

Upon insertion of any intravascular catheter plasma protein adsorption immediately occurs with activation of a thrombotic cascade establishing an opportunistic relationship with bacteria that can lead to catheter related infection [63,65]. The thrombotic risk on intravascular catheters increases overtime as hydrophilic coatings wear off. Hydrophilic anti-adhesive properties applied to materials or surface modifications result in aqueous liquid activated surfaces that prevent both bacterial and blood adherence [78]. A hydrophilic layer with a negative charge is described as the smoothest surface for a catheter with smoothness attributed to the water absorbing gel-like nature of the hydrophilic material [43,55]. Aswathy et al. list the characteristics of the hydrophilic polymer as crosslinked chains that swell in response to liquid or blood as they hydrate [6].

Publications in the 1990s identified the value of hydrophilic surface coatings that addressed the issue of cellular attachment [54,58,71,72]. A product, Hydrocath (Becton Dickinson, Franklin Lakes, NJ), not currently marketed in the USA nor available as a PICC, was frequently noted in the literature was known to have a lower rate of bacterial adherence due to the hydrophilic surface coating [54,56,71]. Unfortunately, the level of adherence avoidance of this catheter was limited, reported as lasting from 72 hours up to 5 days [54]. This limited duration of cellular attachment avoidance created a challenge to develop a hydrophilic polymer that was integrated into the complete catheter material. Newer materials and

polymer composite biomaterials have been developed to solve the difficulties associated with protein adsorption, adhesion of cells and the inflammatory foreign body response [62]. By creating a super-hydrophilic biomaterial, synergistic with the body's natural chemistry, the catheter can maintain a smooth, hydrated material limiting host response by resisting cellular adherence [55,62,64].

A novel catheter product recently studied is constructed of material with hydrophilic hydrogel, rather than just a coating [62]. Mannarino et al. describe the material as a porous polyvinyl alcohol plus polyacrylic acid, and acid hydrogel, heat-treated to provide a steric barrier with crosslinking to repel protein adsorption, increase strength and surface lubricity [62]. This process established a neutralized, strongly hydrophilic surface that is highly wettable creating thromboresistance. The hydrophilic hydrogel demonstrated significant reduction in thrombus accumulation on the catheter surface, superior to standard polyurethane catheters. In the ovine portion of the study, Mannarino et al. reported prolonged durability of the hydrogel catheter at 162.5 days *in vivo* with an average of 97% reduction in platelet adhesion and tip thrombotic occlusion in comparison to other current PICC polyurethane catheters. The hydrogel composite biomaterial was processed to address the durability requirements of vascular catheters while maintaining thromboresistant clinical benefits. While no material is completely resistant to cellular adherence, the highly hydrated hydrogel material led to in vivo reductions in blood cell adherence and protein adsorption over five plus months.

Economics

The results of the economic literature review of 13 publications [15,39,41,55,77-85] provided insight into the impact of catheter complications. Due to the heterogeneity of the literature reviewed a primary focus in the analysis was given to projections based on current national complication reimbursement and coding cost. Cost associated with catheter complications were included in the economic analysis with projected PICC economic incremental expense of $24,558 USD for CRT, $12,982 for infection, and $624 for occlusion (Table 2) [46,47] midline cost estimates were not specifically available due to the nature of peripheral devices and coding, the assumption is that the costs could be comparable. Projections based on the literature review, overall PICC CRT pooled incidence of 3.45% were an estimated 34 episodes of CRT per annum for a 300-bed facility and an estimated 113 incidents per annum for a 1,000-bed facility. When factoring in ICD-10 cost estimates the CRT annual cost is projected to be over $830 thousand (K) in a 300-bed facility and over $2.7 million (M) USD for a 1,000-bed hospital.

For infection related events the PICC bloodstream pooled incidence of 2.25% and midline bloodstream infections pooled incidence of 0.67% reflects an estimated 19 episodes of infections per annum for a 300-bed facility and an estimated 62 incidences per annum for a 1,000-bed facility. When factoring in ICD-10 cost estimates the bloodstream infection annual cost is projected to be over $240K USD for a 300-bed facility and over $800K USD for a 1,000-bed hospital.

For occlusion events the PICC occlusion pooled incidence of 8.3% and midline occlusion pooled incidence at 3.6% reflects an estimated 73 episodes of occlusion per annum for a 300-bed facility or an estimated 243 episodes per annum for a 1,000-bed acute care facility. When factoring in ICD-10 cost estimates the occlusion annual cost is projected to be over $45K USD for a 300-bed facility and over $150K USD for a 1,000-bed hospital.

The application of a hydrogel PICC and Midline even with a modest 50% reduction in complications could result in savings of more than $560K USD per annum for a 300-bed acute care facility and $1.8M USD per annum for a 1,000-bed acute care facility. When factoring in the cost associated with treatment delays, catheter replacement, additional medications, extended length of stay, and other patient associated costs the savings for each acute care facility could be considerably more than these estimates.

Market research by iData estimates 2.8M PICC insertions and 1.1M midline insertions per annum [86]. When applying the reported pooled overall complication rate of 5.6% to a national view, there is an estimated total of 218,400 complications annually, with a weighted cost of $20,684 USD per episode. These cost projections equate to a total cost of complications of $4.5 billion dollars per annum nationally.

Discussion

To our knowledge, this integrative review is the first to establish complication benchmarks for PICCs and midlines while theorizing the economic impact of the application of novel composite hydrogel catheter materials. Since the publication of the landmark study highlighting the central line bundle and checklist by Pronovost et al. in 2006, much emphasis has been placed on infection prevention related to insertional practices [87]. The goal of the central line bundle and other changes in reimbursement related to CLABSI was to eliminate these catheter-related infections. Unfortunately, catheter infections still occur, and likely due in part to the characteristics of this foreign material placed into the bloodstream. Biocompatibility, blood, and bacterial adherence all play a part in the development of complications with the most serious being infection. Complications impact the delivery of treatment, patient morbidity, and add cost to healthcare systems striving for best operating efficiencies. Quantifying complication incidence and cost, while considering alternative catheter materials designed to reduce complications, may warrant a closer look at the economics associated with PICC and midline catheter materials.

Outcomes

The analysis of the literature for PICC- and midline-related outcomes of adult studies, in keeping with the inclusion criteria, established a conservative benchmark for incidence of the three complications, thrombosis, infection and occlusion as the most clinically relevant complications from a health economics perspective. With the exclusion of cancer, home care, and pediatric studies, the results were intended to project an incidence of complications occurring within the general population. The pooled results of the outcomes in the study align with other prior research on PICC-related thrombosis and infection for incidence ranges of 0-7.8% for CRT and 0-3.6% for CABSI [88-93]. The one outlier publication in our review had a significantly higher sepsis rate of 29% for PICCs and 27% for midlines and was excluded from the final pooled results to preserve a conservative approach to the incidence rating and not inflate the cost savings potential [11].

Catheter complication risk increases with poor hygienic practices, patient factors, skin, breaks in sterile technique, multiple attempts with traumatic insertions, various forms of contamination, and from lack of attention to maintenance practices [90,93,94]. Factors known to reduce complications include education and training, use of checklists, bundled practices, antimicrobial devices, disinfecting caps, and infection prevention practices [95]. With the numerous prevention strategies employed to reduce the incidence of infection and thrombosis, catheter materials are rarely mentioned other than with additional approaches for using surface modified antimicrobial or impregnated catheters [96].

Materials

Despite a small range of catheter materials currently used clinically, polyurethane materials predominate. There is no established set of hemocompatible materials or even an accepted set of principles that guide material design and selection for blood compatibility. This lack of guidance is partly due to the absence of a reliable correlation between measurable material surface properties (e.g., surface energy, wettability, and durability) and thrombosis, considered a long-standing challenge in blood contacting materials science. Historic precedent at a facility is the primary basis for material selection of most vascular access devices [70]. Considering the characteristics of ideal catheter and material components identified in the literature, high biocompatibility, resistance to protein adsorption, chemical resistance, pliability with high tensile strength, smooth surface with anti-adhesive properties, and durability with long-term dwell and maintenance of flow were the chief points [53,55,58,73]. The published studies included in the materials review varied greatly and served to inform rather than provide a means of clear evaluation of effectiveness for any one brand or type of catheter, except for the frequent mention of hydrophilic catheter and lubricity characteristics in the coated HydroCath, and composite HydroPICC and HydroMID (Access Vascular, Inc, Billerica, MA, USA) [6,54,62,74].

In relation to hydrophilic catheter performance, the most recent Bunch retrospective outcome study demonstrated differences in complication risk between polyurethane midline catheters and hydrophilic polyvinyl alcohol-based hydrogel midline catheters (HBM; HydroMID) [97]. This study compared all- cause complications for traditional or modified polyurethane (PU) and HBM catheters. he failure rate for PU was 23.8% while HBM catheters was 3.8%, a statistically significant difference ($p<.001$) representing a 84% lower midline failure rate observed in HBM compared to PU. Furthermore, there was a six-fold decrease in catheter failures for all cause complications for occlusion, phlebitis, and leakage between the two catheter types. The data analysis indicates statistically significant reductions in failure rates, upper extremity venous thrombosis, and phlebitis in the HBM group, with the polyurethane midline catheters six (6) times more likely to fail then HBM catheters. These results confirmed the catheter material performance findings described by Mannarino et al. [62]. The author also noted differences in material composition leading to positive outcomes related to the hydration status of the PU midline catheter at 2% and 35% for the HBM catheter. The higher water content of the HBM catheter was attributed to the blocking or repelling of protein surface adherence, blood and thrombus formation on the catheter.

In the body response to foreign materials, blood and tissue proteins adsorption occurs within minutes of insertion of a venous catheter, polyurethane, or silicone, PICC or midline catheter, into the bloodstream and may inhibit the function of the catheter. Biocompatibility of the material, which may prevent a foreign body response, is most successfully achieved with hydrophilic material interface between the catheter surface and the tissue reaction making the material inherently inert and closely mimicking the blood chemistry [98]. Silicone catheters have a higher risk of microorganism colonization and infection, while polyurethane catheter risk of thrombosis and occlusion are higher, with neither demonstrating physical properties of lubricity or wettability with water absorption [95,99,100]. Prevention of thrombosis, infection and catheter occlusion are high priorities for maintaining catheter function for infusion of prescribed treatment. Hydrophilic hydrogel characteristics of surface smoothness, wettability, and polymers with polyvinyl alcohol show the greatest promise as noted in the literature [6,7,54,62,73]. The HydroCath was a surface modified catheter with a hydrophilic coating [53,70]. The HydroPICC and HydroMID hydrogel catheters are not coated but are composed of a complete composite polymer that demonstrated the ideal characteristics of thromboresistance through *in vitro* and *in vivo* research [62]. The water absorptive nature of the composite, not coated, catheter material maintained a super-lubricious and hydrophilic surface making it less likely for bacterial and cellular adherence and one that did not degrade

over six months of testing in simulated *in vivo* conditions. These characteristics were verified through laboratory testing with blood-loop and micrograph investigation. Platelet adhesion was reduced by 97% in comparison with other PICC polyurethane and coated catheter products tested. Reduction of cellular adsorption with the hydrogel catheter was mainly due to the influence of the inherent protein adsorption resistance enabled by the steric barrier created at the surface of the hydrogel all which directly impact complications of both thrombosis and infection [65]. The mechanical integrity, durability and surface wettability reported on hydrophilic and hydrogel components lend support to the positive impact of reduced cellular adherence. Additional clinical research is necessary to validate the laboratory findings and demonstrate the full potential of this new biomaterial.

Economics

No study to date has combined and compared complication incidence, catheter material, and evaluation of the economic impact of an ideal catheter. Prevention practices have addressed issues of patient-related thrombotic risk and other contributing factors that increase incidence, but generally fail to include the impact of catheter materials on outcomes. Cost projections associated with PICC thrombosis from treatment delays, increased length of stay of 4-5 days, and thrombosis interventions attribute an increase of $12,317-15,973 per episode [15,71,92,101]. The health economic evaluation reflects the potential cost savings when PICC and midline complications are reduced. Furthermore, applying the complication incidence rates to the economic data assessment demonstrated the substantial cost savings that could be associated with use of catheters composed of hydrophilic hydrogel material with a lubricious surface that repelled cellular adherence, promoted host acceptance, and reduced bacteria thus limiting biofilm formation. These material features have not been economically quantified in published studies but serve as a high watermark for optimal catheter function.

While the basis of the economics for this integrative review utilized the projected ICD-10 complication rates and cost for PICCs, other research applied estimated cost for thrombosis at $9407, versus the ICD-10 rate of $24,558, for occlusion using a thrombolytic at $182.76 versus ICD-10 $624, for PICCs, and midline replacement costs at $137.70 [97,102]. Applying this replacement cost basis for midlines to the retrospective research study would result in $3039, for PU and $550, for HBM representing a six-fold cost decrease using the HBM catheter. A greater impact in the differences for PU midline versus HBM catheters is represented by the 98.1% rate of therapy completion with the hydrophilic catheter and only 69.3% therapy completion with PU midlines. Factoring in staff cost of $51.71 per hour for management of complications and midline catheter replacements would continue to add savings with each HBM catheter used.

Evaluating publications to gather, inform and assess reported incidence and better understand the relationship of catheter materials to the incidence may lead to economic improvements. With projected cost of PICC and midline complications at $4.5 billion USD per year nationally, even a modest reduction in overall complications could have a dramatic impact on cost savings. While our hypotheses are limited by the lack published research, they do highlight the need for catheter improvements, consideration for hydrogel catheter materials, and the consideration for the economic value of reducing complications. The results of this research are suggestive and serve as a basis for future studies. Future research for in vivo catheter material investigation is needed to confirm the positive impact of a hydrogel catheter material change for PICCs and midlines, the value in savings by extending the complication free dwell time, and the economic benefit to patients and healthcare facilities [103].

Limitations

This study has some important limitations. Although our integrative review pooled incidence rates for the PICC and midline catheter complications, these rates were limited by the selection of available research meeting the inclusion criteria. The review focused on PICC outcomes as primary and midlines as secondary owing to the limited research published on midlines. Publications included in the review consisted of systematic reviews, with and without meta-analyses, prospective and retrospective cohorts, and observational evidence, resulting in moderate clinical and methodological diversity, and statistical heterogeneity. Efforts were made to reduce heterogeneity through the focus on catheter types, interventions, patient study groups and specific outcomes. Material and economic literature were selected based on application to an integrative review and narrative, and do not constitute an exhaustive literature review. Consistent with the definition of an integrative review, various types of research were included with GRADE ratings evaluated as Level 2-3, and while we focused on systematic reviews to establish incidence rates, the inclusion of observational evidence is inherently more limited than Level 1 evidence. The strength of our research was the analysis from the integrative literature review providing pooled incidence benchmarks and calculated based on current ICD-10 rates of cost. Finally, we chose to be conservative in establishing incidence rates for the complications and did not include cancer studies that may have inflated the incidence results and impacted the economic analysis. While the funding source for a study does not determine the quality, results from industry-sponsored investigations must reflect cautious interpretation with heightened concern for potential bias. This integrative review serves to inform and functions as a precursor to a systematic review pending the publication of higher-level clinical research.

Conclusions

This is the first integrative review to inform PICC and midline catheter incidence of symptomatic thrombosis, infection, and occlusion with catheter material consideration and analysis of the potential economic savings associated with material change. Polyurethane and silicone irregular catheter surfaces contribute to patient complication development of thrombosis, infection, and occlusion leading to catheter dysfunction, failure and increased patient morbidity and mortality. The use of a hydrogel PICC or midline catheter in acute care, projecting a 50% reduction of complications, could result in savings of nearly $1.8M annually for a typical 1000-bed acute care facility or $560K for a 300-bed acute care facility. Maintaining a hydrated hydrophilic catheter material with a gel-like smooth surface, in contrast to polyurethane materials commonly used for these catheters, may reduce blood cell adherence, bacterial attachment and catheter complications, chipping away at the $4.5 billion-dollar projected healthcare complication cost.

Acknowledgement

The authors wish to thank Aisha Cobbs for editorial assistance, Gregory Gilbert of SigmaStats Consulting for statistical review, Gregory Watson of Watson Policy Analysis for the economic analyses, and Reba Rice the Chief Executive Officer at North Lakes Community Clinic for her review and feedback on the manuscript.

Conflict of interest

This investigation was industry sponsored by Access Vascular, Inc, (Billerica, MA, USA). The funding organization had no role in the conduct of the study, the management, interpretation of the data, or decision to submit the manuscript for publication.

Funding Statement

This investigation was industry sponsored by Access Vascular, Inc (Billerica, MA, USA). The funding organization had no role in the conduct of the study, the management, interpretation of the data, or decision to submit the manuscript for publication.

Disclosures

NM and EM are employed by PICC Excellence, Inc (Hartwell, GA, USA), with research grant support from Access Vascular, Inc (AVI). NM is sole owner of PICC Excellence, Inc., is a research consultant with AVI, and reports consulting and speaker fees from 3m, Accuvein, BBraun, Bedal, Chiesi, Civco, Cleansite, Dale Medical, Helmier, Javelin Health, IVNational, Linear Health Systems, Nexus Medical, Parker Laboratories, and Teleflex. DH is an independent economic, forensic, and reimbursement consultant. JS is employed by Intermountain Healthcare. BH and VW are employees of Access Vascular, Inc.

Author Contributions

NM designed the study. NM and EM drafted the manuscript. BH contributed to the materials review. VW coordinated and DH validated the economic analysis. JS performed grading review. NM, EM, DH, JS, BH, and VW had full access to all data in the study and take responsibility for the integrity and accuracy of the data analysis. All authors reviewed and approved the final version of the manuscript. All authors made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work. All authors were involved in the critical appraisal and contributed to the editing and final approval of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics Statement

No ethics approval was required for this integrative review of published literature.

Data Availability Statement

Because this publication was based on data extracted from previously published research, the data are available within the public domain.

References

1 Corley A, Marsh N, Ullman AJ, Rickard CM (2017) Tissue adhesive for vascular access devices: who, what, where and when?. Br J Nurs 26: S4-S17.

2 Carr PJ, Higgins NS, Cooke ML, Mihala G, Rickard CM (2018) Vascular access specialist teams for device insertion and prevention of failure, edited by Cochrane Emergency and Critical Care Group. Cochrane Database Syst Rev 3: CD011429.

3 Takashima M, Schults J, Mihala G, Corley A, Ullman A (2018) Complication and Failures of Central Vascular Access Device in Adult Critical Care Settings. Crit Care Med 46: 1998-2009.

4 Steere L, Ficara C, Davis M, Moureau N (2019) Reaching One Peripheral Intravenous Catheter (PIVC) Per Patient Visit With Lean Multimodal Strategy: the PIV5RightsTM Bundle. Journal of the Association for Vascular Access 24: 31-43.

5 Chandorkar YKR, Basu B (2019) The Foreign Body Response Demystified. ACS Biomater Sci Eng 5: 19-44.

6 Aswathy SH, Narendrakumar U, Manjubala I (2020) Commercial hydrogels for biomedical applications. Heliyon 6: e03719.

7 Gavin NC, Kleidon TM, Larsen E, O'Brien C, Ullman A, et al. (2020) A comparison of hydrophobic polyurethane and polyurethane peripherally inserted central catheter: results from a feasibility randomized controlled trial. Trials 21: 787.

8 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, et al. (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372: n71.

9 Wells G, Shea B, O'Connell D, Robertson J, Peterson J, et al. (2014) The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. Ottawa, Ontaria, Canada, Ottawa Hospital Research Institute.

10 Al Raiy B, Fakih MG, Bryan-Nomides N, Hopfner D, Riegel E, et al. (2010) Peripherally inserted central venous catheters in the acute care setting: A safe alternative to high-risk short-term central venous catheters. American Journal of Infection Control 38: 149-153.

11 Bing S, Smotherman C, Rodriguez RG, Skarupa DJ, Ra JH, et al. (2022) PICC versus midlines: Comparison of peripherally inserted central catheters and midline catheters with respect to incidence of thromboembolic and infectious complications. Am J Surg 223: 983-987.

12 Chopra V, Anand S, Hickner A, Buist M, Rogers MA, et al. (2013) Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. The Lancet 382 : 311-325.

13 Chopra V, Kaatz S, Swaminathan L, Boldenow T, Snyder A, et al. (2019) Variation in use and outcomes related to midline catheters: results from a multicentre pilot study. BMJ Qual Saf 28: 714-720.

14 Chopra V, O'Horo JC, Rogers MAM, Maki DG, Safdar N (2013) The Risk of Bloodstream Infection Associated with Peripherally Inserted Central Catheters Compared with Central Venous Catheters in Adults: A Systematic Review and Meta-Analysis. Infect Control Hosp Epidemiol. 34: 908-918.

15 Evans RS, Sharp JH, Linford LH, Lloyd JF, Woller SC, et al. (2013) Reduction of Peripherally Inserted Central Catheter-Associated DVT. Chest 143: 627-633.

16 González S, Jiménez P, Saavedra P, Macías D, Loza A, et al. (2021) Five-year outcome of peripherally inserted central catheters in adults: a separated infectious and thrombotic complications analysis. Infect Control Hosp Epidemiol 42: 833-841.

17 Greene MT, Flanders SA, Woller SC, Bernstein SJ, Chopra V (2015) The Association Between PICC Use and Venous Thromboembolism in Upper and Lower Extremities. Am J Med 128: 986-993.e1.

18 Hawes ML (2020) Assessing and Restoring Patency in Midline Catheters. J Infus Nurs 43: 213-221.

19 Jennings K, Cann T, Smyth W, Bus M (2011) Peripherally inserted central catheter complications highlight the need for ongoing support: results of a chart audit. Healthcare infection 16: 95-99.

20 Kagan E, Salgado CD, Banks AL, Marculescu CE, Cantey JR (2019) Peripherally inserted central catheter–associated bloodstream infection: Risk factors and the role of antibiotic-impregnated catheters for prevention. Am J Infect Control 47: 191-195.

21 Kim K, Kim Y, Peck KR (2020) Previous peripherally inserted central catheter (PICC) placement as a risk factor for PICC-associated bloodstream infections. Am J Infect Control 48: 1166-1170.

22 Kim-Saechao SJ, Almario E, Rubin ZA (2016) A novel infection prevention approach: Leveraging a mandatory electronic communication tool to decrease peripherally inserted central catheter infections, complications, and cost. Am J Infect Control 44 : 1335-1345.

23 Koo CM, Vissapragada R, Sharp R, Nguyen P, Ung T, et al. (2017) ABO blood group related venous thrombosis risk in patients with peripherally inserted central catheters. Br J Radiol 91:20170560.

24 Kramer RD, Rogers MAM, Conte M, Mann J, Saint S, et al. (2017) Are antimicrobial peripherally inserted central catheters associated with reduction in central line–associated bloodstream infection? A systematic review and meta-analysis. Am J Infect Control 45: 108-114.

25 Lee JH, Kim ET, Shim DJ, Kim IJ, Byeon JH, et al. (2019) Prevalence and predictors of peripherally inserted central catheter-associated bloodstream infections in adults: A multicenter cohort study, edited by Efron PA. PLoS ONE 14: e0213555.

26 Liem TK, Yanit KE, Moseley SE, Landry GJ, DeLoughery TG, et al. (2012) Peripherally inserted central catheter usage patterns and associated symptomatic upper extremity venous thrombosis. J Vascu Surg 55: 761-767.

27 Lisova K, Hromadkova J, Pavelková K, Zauška V, Havlin J, et al. (2018) The incidence of symptomatic upper limb venous thrombosis associated with midline catheter: Prospective observation. J Vasc Access 19: 492-495.

28 Lobo BL, Vaidean G, Broyles J, Reaves AB, Shorr RI (2009) Risk of venous thromboembolism in hospitalized patients with peripherally inserted central catheters. J Hosp Med 4: 417-422.

29 Lu H, Hou Y, Chen J, Guo Y, Lang L, et al. (2021) Risk of catheter‐related bloodstream infection associated with midline catheters compared with peripherally inserted central catheters: A meta‐analysis. Nurs Open 8: 1292-1300.

30 Lu H, Yang Q, Yang L, Qu K, Tian B, et al. (2022) The risk of venous thromboembolism associated with midline catheters compared with peripherally inserted central catheters: A systematic review and meta‐analysis. Nursing Open 9: 1873-1882.

31 Maki DG, Kluger DM, Crnich CJ (2006) The Risk of Bloodstream Infection in Adults With Different Intravascular Devices: A Systematic Review of 200 Published Prospective Studies. Mayo Clin Proc 81: 1159-1171.

32 McDiarmid S, Scrivens N, Carrier M, Sabri E, Toye B, et al. (2017) Outcomes in a nurse-led peripherally inserted central catheter program: a retrospective cohort study. CMAJ Open 5: E535-E539.

33 Mushtaq A, Navalkele B, Kaur M, Krishna A, Saleem A, et al. (2018) Comparison of complications in midlines versus central venous catheters: Are midlines safer than central venous lines?. Am J Infect Control 46: 788-792.

34 Nolan ME, Yadav H, Cawcutt KA, Cartin-Ceba R (2016) Complication rates among peripherally inserted central venous catheters and centrally inserted central catheters in the medical intensive care unit. J Crit Care 31: 238-242.

35 Paje D, Conlon A, Kaatz S, Swaminathan L, Boldenow T, et al. (2018) Patterns and Predictors of Short‐Term Peripherally Inserted Central Catheter Use: A Multicenter Prospective Cohort Study. J Hosp Med 13: 76-82.

36 Park S, Moon S, Pai H, Kim B (2020) Appropriate duration of peripherally inserted central catheter maintenance to prevent central line-associated bloodstream infection. PLoS ONE 15: e0234966.

37 Pikwer A, Åkeson J, Lindgren S (2012) Complications associated with peripheral or central routes for central venous cannulation. Anaesthesia 67 : 65-71.

38 Rejane Rabelo-Silva E, Lourenço SA, Maestri RN, Candido da Luz C, Carlos Pupin V, et al. (2021) Patterns, appropriateness and outcomes of peripherally inserted central catheter use in Brazil: a multicentre study of 12 725 catheters. BMJ Qual Saf 31: 652-661.

39 Schears GJ, Ferko N, Syed I, Arpino JM, Alsbrooks K (2021) Peripherally inserted central catheters inserted with current best practices have low deep vein thrombosis and central line–associated bloodstream infection risk compared with centrally inserted central catheters: A contemporary meta-analysis. J Vasc Access 22: 9-25.

40 Scimò M, Vallecorsa I, Cini A, Cabelguenne D, Piriou V (2022) Vascular access unit: Six-years experience report in France. J Vasc Access 25: 112972982210802.

41 Smith SN, Moureau N, Vaughn VM, Boldenow T, Kaatz S, et al. (2017) Patterns and Predictors of Peripherally Inserted Central Catheter Occlusion: The 3P-O Study. J Vasc Interv Radiol 28 : 749-756.e2.

42 Swaminathan L, Flanders S, Horowitz J, Zhang Q, O'Malley M, et al. (2022) Safety and Outcomes of Midline Catheters vs Peripherally Inserted Central Catheters for Patients With Short-term Indications: A Multicenter Study. JAMA Intern Med 182: 50-58.

43 Tripathi S, Kumar S, Kaushik S (2021) The Practice and Complications of Midline Catheters: A Systematic Review. Crit Care Med 49: e140-e150.

44 Vaughn VM, O'Malley M, Flanders SA, Gandhi TN, Petty LA, et al. (2020)Association of Infectious Disease Physician Approval of Peripherally Inserted Central Catheter With Appropriateness and Complications. JAMA Netw Open 3: e2017659.

45 Xu T, Kingsley L, DiNucci S, Messer G, Jeong JH, et al. (2016) Safety and utilization of peripherally inserted central catheters versus midline catheters at a large academic medical center. Am J Infect Control 44 : 1458-1461.

46 CMS FY (2022) IPPS Final Rule Home Page | CMS.

47 CMS. MEDPAR Limited Data Set (LDS) - Hospital (National) | CMS.

48 Gorski LA, Hadaway L, Hagle ME, Broadhurst D, Clare S, et al. (2021) Infusion Therapy Standards of Practice, 8th Edition Journal of Infusion Nursing 44: S1-S224.

49 Moureau NL (2019)Vessel Health and Preservation: The Right Approach for Vascular Access.

50 Chopra V, Flanders SA, Saint S, Woller SC, O'Grady NP, et al. (2015) The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): Results From a Multispecialty Panel Using the RAND/UCLA Appropriateness Method. Ann Intern Med 163: S1-S40.

51 Crnich CJ, Maki DG (2002) The Promise of Novel Technology for the Prevention of Intravascular Device–Related Bloodstream Infection. I. Pathogenesis and short-term devices. Clin Infect Dis 34: 1362-1368.

52 DeVries M, Sleweon T (2021) Bridging the gap: introduction of an antimicrobial peripherally inserted central catheter (PICC) in response to high PICC central line-associated bloodstream infection incidence. Br J Nurs 30: S16-S22.

53 Di Fiore RE (2005) Clinical and Engineering Considerations for the Design of Indwelling Vascular Access Devices - Materials and Product Development Overview, Journal of the Association for Vascular Access 10: 24-27.

54 Gatter N, Kohnen W, Jansen B (1998) In vitro efficacy of a Hydrophilic Central Venous Catheter Loaded with Silver to Prevent Microbial Colonization. Zentralbl Bakteriol 287: 157-169.

55 Greenhalgh R, Dempsey-Hibbert NC, Whitehead KA (2019) Antimicrobial strategies to reduce polymer biomaterial infections and their economic implications and considerations. International Biodeterioration & Biodegradation 136: 1-14.

56 Jansen B, Jansen S, Peters G, Pulverer G (1992) *In-vitro* efficacy of a central venous catheter ('Hydrocath') loaded with teicoplanin to prevent bacterial colonization. J Hosp Infect 22: 93-107.

57 Kleidon T, Ullman AJ, Zhang L, Mihala G, Chaseling B, et al. (2018) How Does Your PICCOMPARE? A Pilot Randomized Controlled Trial Comparing Various PICC Materials in Pediatrics. J Hosp Med 13: 517-525.

58 Kohnen W, Jansen B (1995) Polymer materials for the prevention of catheter-related infections. Zentralbl Bakteriol 283: 175-186.

59 Lacy DE, Spencer DA, Venkataraman M, Ruiz G, Weller PH (1996) Comparison of two percutaneous intravenous "midline" catheters in cystic fibrosis. J Intraven Nurs 19: 28-31.

60 Lai NM, Chaiyakunapruk N, Lai NA, O'Riordan E, Pau WSC, et al. (2018) Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults, edited by Cochrane Emergency and Critical Care Group., Cochrane Database Syst Rev 16: CD007878.

61 Maki DG, Stolz SM, Wheeler S, Mermel LA (1997) Prevention of Central Venous Catheter-Related Bloodstream Infection by Use of an Antiseptic-Impregnated Catheter: A Randomized Controlled Trial. Ann Intern Med 127: 257-266

62 Mannarino MM, Bassett M, Donahue DT, Biggins JF (2020) Novel high-strength thromboresistant poly (vinyl alcohol)-based hydrogel for vascular access applications. J Biomater Sci Polym Ed 31: 601-621.

63 Mehall JR, Saltzman DA, Jackson RJ, Smith SD (2001) Catheter Materials Affect the Incidence of Late Blood-Borne Catheter Infection. Surg Infect 2: 225-230.

64 Neoh KG, Li M, Kang ET, Chiong E, Tambyah PA (2017) Surface modification strategies for combating catheter-related complications: recent advances and challenges. J Mater Chem B 5: 2045-2067.

65 Ngo BKD , Grunlan MA (2017) Protein Resistant Polymeric Biomaterials, ACS Macro Lett 6: 992-1000.

66 Pathak R, Bierman SF, d'Arnaud P (2018) Inhibition of bacterial attachment and biofilm formation by a novel intravenous catheter material using an *in vitro* percutaneous catheter insertion model. Med Devices (Auckl) 11: 427-432.

67 Rupp ME (2005) Effect of a Second-Generation Venous Catheter Impregnated with Chlorhexidine and Silver Sulfadiazine on Central Catheter–Related Infections: A Randomized, Controlled Trial. Ann Intern Med 143: 570-580.

68 Schults JA, Kleidon T, Petsky HL, Stone R, Schoutrop J, et al. (2019) Peripherally inserted central catheter design and material for reducing catheter failure and complications, edited by Cochrane Vascular Group. Cochrane Database of Systematic Reviews 7: CD013366.

69 Slaughter E, Kynoch K, Brodribb M, Keogh SJ (2020) Evaluating the Impact of Central Venous Catheter Materials and Design on Thrombosis: A Systematic Review and Meta□Analysis. Worldviews Evid Based Nurs 17: 376-384.

70 Sukavaneshvar S (2017) Device thrombosis and pre-clinical blood flow models for assessing antithrombogenic efficacy of drug-device combinations. Adv Drug Deliv Rev 112: 24-34.

71 Tebbs SE, Sawyer A, Elliott TS (1994) Influence of surface morphology on in vitro bacterial adherence to central venous catheters. Br J Anaesth 72: 587-591.

72 Tebbs SE , Elliott TS (1994) Modification of central venous catheter polymers to prevent in vitro microbial colonisation. Eur J Clin Microbiol Infect Dis 13: 111-117.

73 Ullman AJ, Bulmer AndreWC, Dargaville TR, Rickard CM, Chopra V (2019) Antithrombogenic peripherally inserted central catheters: overview of efficacy and safety. Expert Rev Med Devices 16: 25-33.

74 Ullman AJ, Paterson RS, Schults JA, Kleidon TM, August D, et al. (2022) Do antimicrobial and antithrombogenic peripherally inserted central catheter (PICC) materials prevent catheter complications? An analysis of 42,562 hospitalized medical patients. Infect Control Hosp Epidemiol 43: 427-434.

75 Xu H, Huang Y, Jiao W, Sun W, Li R, et al. (2016) Hydrogel-coated ventricular catheters for high-risk patients receiving ventricular peritoneum shunt, Medicine 95: e4252.

76 ECRI. Polyurethane: Medical Device Material Safety Summaries - ECRI Reports | FDA.

77 Dawson RB, Moureau NL (2013) Midline Catheters: An Essential Tool in CLABSI Reduction, Infection Control Today.

78 Deutsch GB, Sathyanarayana SA, Singh N, Nicastro J (2014) Ultrasound-guided placement of midline catheters in the surgical intensive care unit: a cost-effective proposal for timely central line removal. J Surg Res 191: 1-5.

79 Horattas MC, Trupiano J, Hopkins S, Pasini D, Martino C, et al. (2001) Changing concepts in long-term central venous access: Catheter selection and cost savings, Am J Infect Control 29: 32-40.

80 Puzniak L, Gupta V, Yu KC, Ye G, Outterson K (2021) The impact of infections on reimbursement in 92 US hospitals, 2015-2018. Am J Infect Control 49 :1275-1280.

81 Royer T (2010) Implementing a Better Bundle to Achieve and Sustain a Zero Central Line-Associated Bloodstream Infection Rate. J Infus Nurs 33: 398-406.

82 Ruppert A, Steinle T, Lees M (2011) Economic burden of venous thromboembolism: a systematic review. J Med Econ 14: 65-74.

83 Steere L, Rousseau M, Durland L (2018) Lean Six Sigma for Intravenous Therapy Optimization: A Hospital Use of Lean Thinking to Improve Occlusion Management. Journal of the Association for Vascular Access 23: 42-50.

84 Steere L (2022) CLE3AR Study: 5-Year Impact of LEAN Central Venous Catheter Occlusion Management & Quality Interventions. Clin Nurse Spec 36: 92-98.

85 Wang K, Zhong J, Huang N, Zhou Y (2020) Economic evaluation of peripherally inserted central catheter and other venous access devices: A scoping review. J Vasc Access 21: 826-837.

86 iData Research, Vascular Access Devices Market Analysis | Global | 2020-2026 | MedSuite, iData Research.

87 Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, et al. (2006) An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. N Engl J Med 355: 2725-2732.

88 Balsorano P, Virgili G, Villa G, Pittiruti M, Romagnoli S, et al. (2020) Peripherally inserted central catheter–related thrombosis rate in modern vascular access era-when insertion technique matters: A systematic review and meta-analysis. J Vasc Access 21: 45-54.

89 Chen X, Liang M (2022) A Meta-Analysis of Incidence of Catheter-Related Bloodstream Infection with Midline Catheters and Peripherally Inserted Central Catheters. J Healthc Eng 12: 1-8.

90 Chopra V, Anand S, Krein SL, Chenoweth C, Saint S (2012) Bloodstream Infection, Venous Thrombosis, and Peripherally Inserted Central Catheters: Reappraising the Evidence. Am J Med 125: 733-741.

91 Chopra V, Ratz D, Kuhn L, Lopus T, Chenoweth C, et al. (2014) PICC-associated Bloodstream Infections: Prevalence, Patterns, and Predictors. Am J Med 127: 319-328.

92 Chopra V, Ratz D, Kuhn L, Lopus T, Lee A, et al. (2014) Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. J Thromb Haemost 12: 847-854.

93 Evans RS, Sharp JH, Linford LH, Lloyd JF, Tripp JS, et al. (2010) Risk of Symptomatic DVT Associated With Peripherally Inserted Central Catheters. Chest 138: 803-810.

94 Aydın H, Korfalı G, Gören S, Efe EM, Moustafa BR, et al. (2014) Risk factors for development of complication following peripherally inserted central catheters: A retrospective analysis of 850 patients. J Clin Exp Invest 5: 29-35.

95 Mingkun C, Yuxia Y, Shengyu F, Dengxu W, Min W, et al. (2019) Complications and Risk Factors of Peripherally Inserted Central Catheters: A Review. EJCBS 5: 62-65.

96 Duwadi S, Zhao Q, Budal BS (2019) Peripherally inserted central catheters in critically ill patients – complications and its prevention: A review. Int J Nurs Sci, 6: 99-105.

97 Buetti N, Marschall J, Drees M, Fakih MG, Hadaway L, et al. (2022) Strategies to prevent central line-associated bloodstream infections in acute-care hospitals: 2022 Update. Infect Control Hosp Epidemiol 43: 553-569.

98 Bunch J (2022) A Retrospective Assessment of Midline Catheter Failures Focusing on Catheter Composition. Journal of Infusion Nursing 45: 270-278.

99 Morais JM, Papadimitrakopoulos F, Burgess DJ (2010) Biomaterials/ Tissue Interactions: Possible Solutions to Overcome Foreign Body Response. AAPS J 12: 188-196.

100 Seckold T, Walker S, Dwyer T (2015) A Comparison of Silicone and Polyurethane PICC Lines and Postinsertion Complication Rates: A Systematic Review, J Vasc Access 16: 167-177.

101 Wildgruber M, Lueg C, Borgmeyer S, Karimov I, Braun U, et al. (2016) Polyurethane versus silicone catheters for central venous port devices implanted at the forearm. Eur J Cancer 59: 113-124.

102 Johansson E, Hammarskjöld F, Lundberg D, Arnlind MH (2013) Advantages and disadvantages of peripherally inserted central venous catheters (PICC) compared to other central venous lines: A systematic review of the literature. Acta Oncol 52: 886-892.

103 Carr A, Green JR, Benish E, Lanham R, Kleidon T, et al. (2021) Midline venous catheters as an alternative to central line catheter placement: a product evaluation, Br J Nurs 30 : S10-S18.