

# Complication and Failures of Central Vascular Access Device in Adult Critical Care Settings

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**Objectives:** To examine the proportion and rate of central venous access device failure and complications across central venous access device types in adult intensive care.

**Data Sources:** A systematic search was undertaken in the electronic databases Cochrane Central Register of Controlled Trials (CENTRAL), Embase, U.S. National Library of Medicine National Institutes of Health (MEDLINE), and Cumulative Index to Nursing and Allied Health (CINAHL) in September 2017.

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**Study Selection:** Included studies were of observational (prospective and retrospective) or interventional design and reported central venous access device failure and complications in adult ICU settings. Studies were excluded if they were published prior to November 2006 or not reported in English. Two reviewers independently screened articles, assessed eligibility, extracted data, and assessed risk of bias.

**Data Extraction:** Data were extracted on the primary outcome, central venous access device failure, and secondary outcomes: central venous access device complications (central line-associated bloodstream infection, catheter-related bloodstream infection, catheter-related thrombosis, occlusion, catheter removal due to suspected infection, dislodgement, breakage, and local infection). Patient and device data and study details to assess the study quality were also extracted.

**Data Synthesis:** A total of 63 studies involving 50,000 central venous access devices (396,951 catheter days) were included. Central venous access device failure was 5% (95% CI, 3–6%), with the highest rates and proportion of failure in hemodialysis catheters. Overall central line-associated bloodstream infection rate was 4.59 per 1,000 catheter days (95% CI, 2.31–6.86), with the highest rate in nontunneled central venous access devices. Removal of central venous access device due to suspected infection was high (17%; 20.4 per 1,000 catheter days; 95% CI, 15.7–25.2).

**Conclusions:** Central venous access device complications and device failure is a prevalent and significant problem in the adult ICU, leading to substantial patient harm and increased health-care costs. The high proportion of central venous access devices removed due to suspicion of infection, despite low overall central line-associated bloodstream infection and catheter-related bloodstream infection rates, indicates a need for robust practice guidelines to inform decision-making surrounding removal of central venous access devices suspected of infection. (*Crit Care Med* 2018; XX:00–00)

**Key Words:** central venous access device; complications; failure; intensive care

Central venous access devices (CVADs) are a vital medical device during critical care admission to facilitate the delivery of supportive and interventional medical therapies (1). In the United States alone, more than 5 million CVADs are inserted annually (2), with 43–80% of patients in the ICU requiring central access (3). The CVAD most commonly inserted in ICU are nontunneled CVADs (NTCVADs), peripherally inserted central catheters (PICCs), and hemodialysis (4). These devices are mainly indicated for short- to medium-term duration, whereas tunneled or implanted CVAD, primarily used outside of critical care, are indicated for chronic or complex health conditions necessitating access longevity. Despite CVAD commonality in the ICU, serious patient harm, relating to insertion and management, remains prevalent (5–10).

CVAD dysfunction is caused by both infective (local tissue infections or central line-associated bloodstream infections [CLABSIs]) or mechanical (thrombotic, occlusive, or dislodgement) complications (5, 11). Infective complications are viewed as a preventable source of patient harm and have a significant impact on patients and healthcare costs (12). CVAD-associated infections are caused by translocation of bacterium and fungi either intra- or extraluminally. Excess mortality due to CLABSI is estimated at 22% (13), with each diagnosis costing U.S. \$32,000 (14), contributing to increased length of ICU admission (> 4 d) (15). Because of the severity of harm associated with CLABSI, CVADs are also frequently removed due to suspicion of infection. Early CVAD removal on sign of infection (e.g., unexplained pyrexia) is traditionally advocated, to remove the source of infection and prevent further harm (16).

Mechanical complications also cause significant CVAD dysfunction, and adverse sequelae, however, have not been the focus of global practice transformation, as seen with CLABSI. One of the most frequent and serious mechanical complications is catheter-associated venous thromboembolism (CAVTs). CAVTs are associated with significant morbidity and mortality (17) from dual sources: the increased risk of CLABSI due to microbial proliferation within the thrombus (18), and pulmonary embolism (17). Critical illness, supportive therapies, preexisting comorbidities, and catheter placement choices place patients at increased risk of CAVT development (19–21). Nonthrombotic causes of catheter occlusion, including mechanical obstruction and medication precipitate, and resultant catheter breakage, can cause treatment disruption. With the advent of light sedation and early mobilization, concern regarding the dislodgement of CVADs is rising in prominence as a serious, frequent, adverse event (22).

A systematic review of pediatric CVAD complications established 25% CVADs (95% CI, 21–29%) failed prior to completion of therapy (5). However, there is no such synthesis of CVAD data in ICU. The primary aim of this systematic review was to determine the proportion and rate of CVAD failure and complications across CVAD types in adult ICU. These data can be used by guide clinicians in benchmarking practice and informing patient safety and research priorities.

## METHODS

The review used standard methods for systematic reviews and is reported in accordance with Meta-analysis of Observational Studies in Epidemiology, where applicable (23). The review methods were prospectively registered on PROSPERO (CRD42016050292).

### Eligibility Criteria

The review included observational (prospective and retrospective cohort) studies and control groups of randomized controlled trials (RCTs) which 1) enrolled study participants 18 years old or older, 2) with CVADs in ICU, and 3) reported outcomes of interest. Types of CVAD included in the study were NTCVADs, PICCs, hemodialysis catheters, tunneled, and totally implanted vascular access device (TIVD). We excluded studies in pediatric and neonates, CVAD insertions in non-ICU clinical settings, and that did not define CVAD type. We excluded studies published prior to November 2006 as we aimed to conduct a clinically relevant and contemporaneous review. We excluded studies not published in English, due to limited access to interpreters. Abstracts were included if data were sufficient to facilitate data extraction. Study authors were contacted to seek clarification concerning review inclusion eligibility and additional data.

### Outcome Measures

The primary outcome was CVAD failure, defined as removal of CVADs before completion of therapy due to complications (5). The secondary outcomes were CVAD complications after successful CVAD insertion including CLABSI (24), catheter-related bloodstream infection (CRBSI) (12), CAVT (19), catheter removal due to suspected infection (25), occlusion, dislodgement (26), breakage (27), and local infection or phlebitis (26) (for detailed definitions, see **Supplemental Table 1**, Supplemental Digital Content 1, <http://links.lww.com/CCM/D903>).

### Search Strategy and Study Selection

A systematic search for studies reporting CVAD failure or complications was undertaken in the following electronic databases on the September 30, 2017: Cochrane Central Register of Controlled Trials, Embase, U.S. National Library of Medicine National Institutes of Health, and Cumulative Index to Nursing and Allied Health. Medical search headings were developed by healthcare librarians including “vascular access devices,” “central venous catheter,” “central venous access device,” “intensive care,” and “critical care” (for full details, see **Supplemental Table 2**, Supplemental Digital Content 2, <http://links.lww.com/CCM/D904>). Additional studies were identified through hand-searching references.

### Data Extraction and Quality Assessment

Two authors (M.T., J.S.) independently assessed titles and abstracts identified. Full texts of relevant studies were

reviewed and independently assessed for inclusion eligibility. A third author (A.U.) reviewed studies where consensus was not reached. Data extracted from included studies were number of patients, number of catheters, CVAD type, study method, frequency of CVAD failure/complications, catheter days, ICU type, and country of origin. Studies with multiple device types were split into substudies per device type. Data were extracted using a data extraction form, managed in Microsoft Excel (Microsoft, Redmond, WA).

Quality assessment tools were derived from three observational study assessment tools to comprehensively assess internal and external validity (28–30). The maximum score that each study could obtain was five (for full details, see **Supplemental Table 3**, Supplemental Digital Content 3, <http://links.lww.com/CCM/D905>).

## Data Analysis

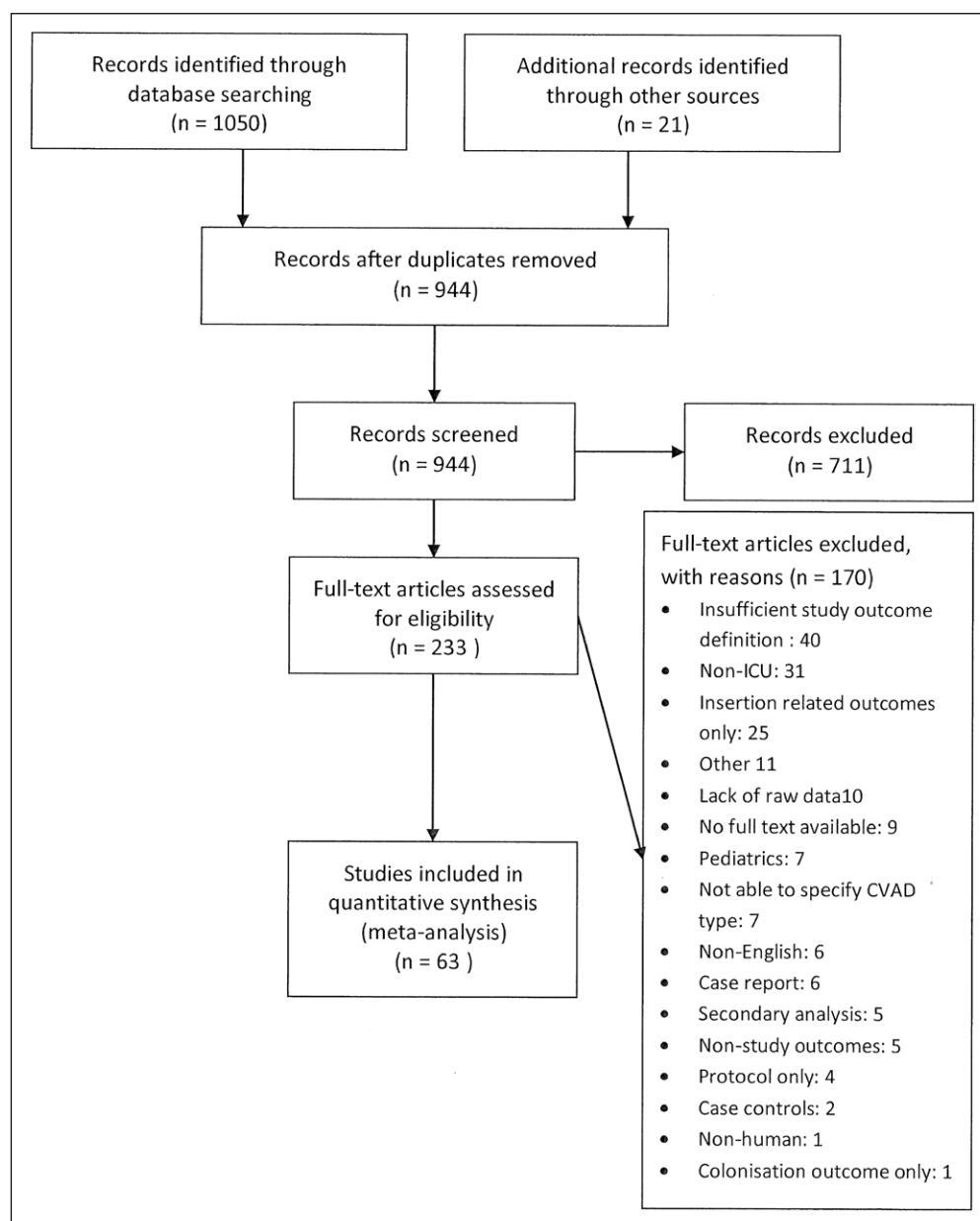
Score CIs with Freeman-Tukey double arcsine transformations were calculated for studies with dichotomous outcomes (failure/no failure), and Poisson CIs and standard errors were calculated for incidence rate (IR) outcomes. Pooled estimates were generated with random-effects meta-analysis and presented with 95% CIs. IR outcomes (continuous data) were pooled by using inverse variance with the DerSimonian and Laird method, per 1,000 catheter days and 95% CI; lower CI boundaries below zero were reported as zero. Heterogeneity between studies was assessed using the  $I^2$  statistic, categorized as low (< 25%), moderate (25–75%), or high (> 75%). Subgroup and sensitivity analyses were performed by device type, risk of bias (ROB), and study method. Statistical analysis was performed using Stata 12 (Stata Corp, College Station, TX), with statistical significance at  $p$  value of less than 0.05.

## RESULTS

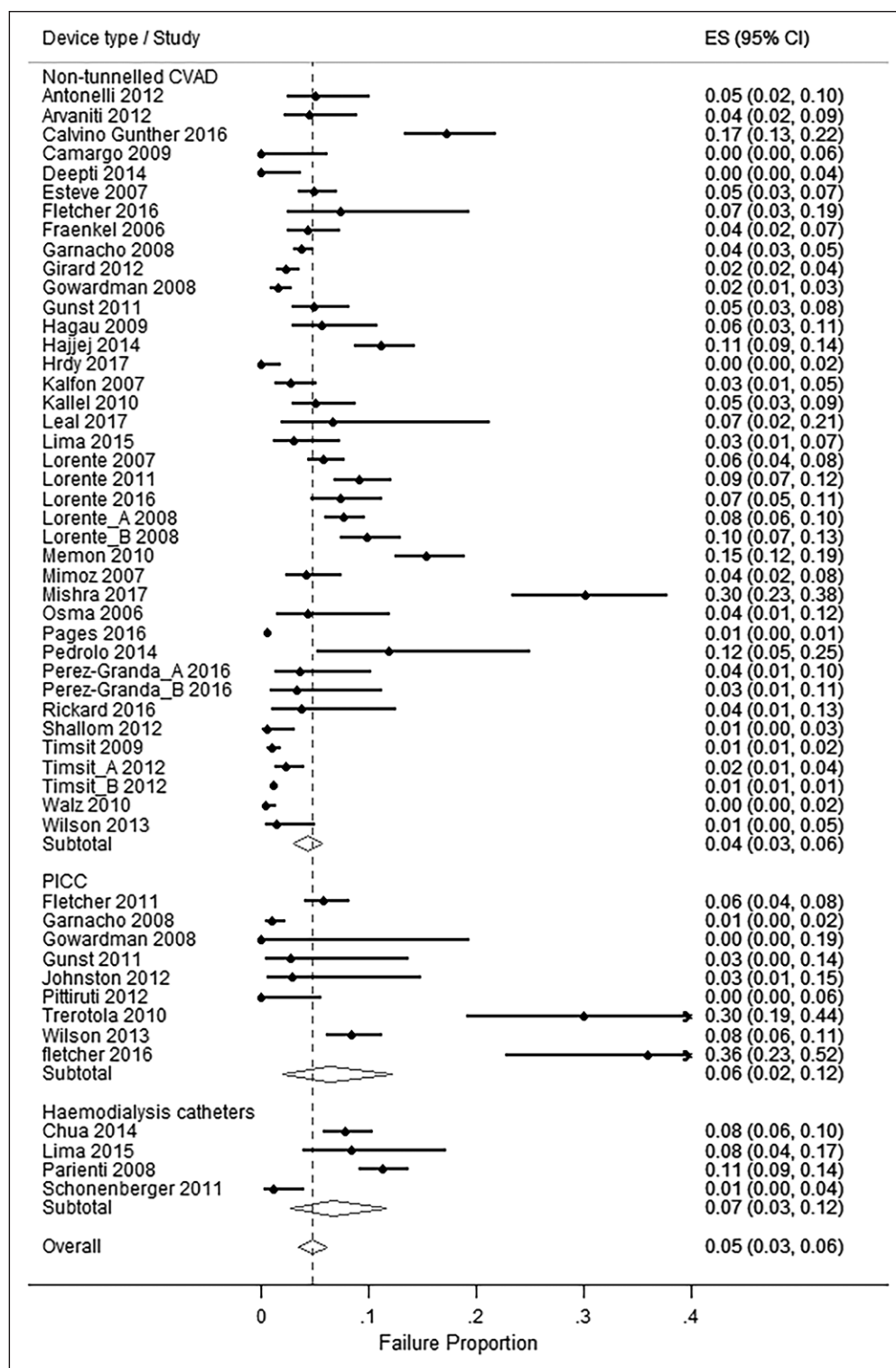
**Figure 1** displays the inclusion and exclusion processes. Electronic databases search yielded 1,048 articles, and an additional 21 studies were identified from references. Following duplicate removal, 944 titles and abstracts were screened, and 233 full texts were assessed. After exclusion of 170 articles, 63 individual studies (10 studies were split into 21 substudies, totaling 74 entries due to multiple device types) were included in the meta-analysis, containing 50,000 CVADs and 396,951 catheter days.

### Characteristics of Included Studies

Studies originated in Europe (31; 49%) (31–61), North America (12; 19%) (8, 62–72), South America (5; 8%) (22, 73–76), Oceania (6; 10%) (77–82), Asia (4; 6%) (83–86), and Middle East (5; 8%) (87–91). There were 24 RCTs (38%), 28 prospective (44%), and 11 retrospective studies (17%). As described in **Supplemental Table 4** (Supplemental Digital Content 4, <http://links.lww.com/CCM/D906>), a mix of ICU specialties were represented, with 25 studies (34%) not specifying ICU specialty.



**Figure 1.** Preferred Reporting Items for Systematic reviews and Meta Analysis flowchart of articles screened for inclusion in the systematic review. CVAD = central vascular access device.



**Figure 2.** Proportion of central vascular access device (CVAD) failure ( $n = 54$  studies). ES = effect size, PICC = peripherally inserted central catheter.

There were no studies that assessed tunneled and implanted CVADs or CVAD breakage.

**Study Quality**

The majority of studies were high quality, with 31 studies (49%) scoring five points, 25 studies (40%) with four points, and seven

studies (11%) with two to three points. Catheter days were not reported in 13 studies and were excluded from the meta-analysis reporting complications per 1,000 catheter days (22, 34, 36, 49, 55, 56, 63, 64, 67, 72, 76, 82, 85). Due to lack of consistency in outcome definitions, some study outcomes were not eligible including catheter dysfunction (34), CRBSI (73), kinking (76), fixation failure (74, 76), displacement (76), infection (22, 56), exudate (74), catheter-related infection (57–59), catheter infection (56), and local reaction (74).

**CVAD Failure**

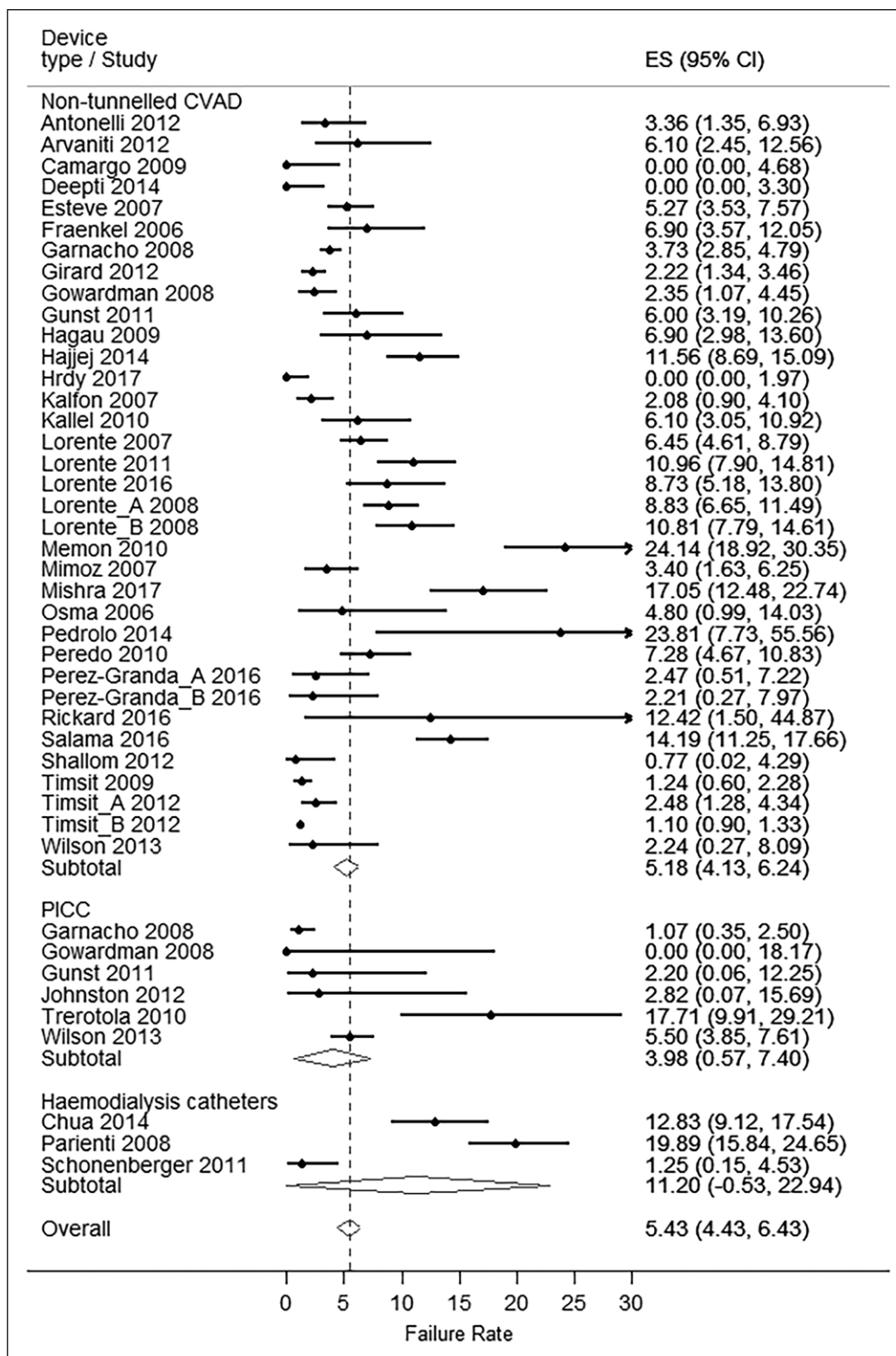
Figures 2 and 3 outline forest plots of proportion and IR of CVAD failure by CVAD type. Overall, 5% (95% CI, 3–6%) of CVADs failed before the completion of therapy (54 studies; 25,770 CVADs) at a rate of 5.43 (95% CI, 4.43–6.43) per 1,000 catheter days (44 studies; 232,001 catheter days) (Tables 1 and 2). Hemodialysis catheters had highest pooled failure proportion at 7% (95% CI, 3–12%; four studies; 1,481 CVADs) and highest pooled IR 11.2 (0–22.9) per 1,000 catheter days (three studies; 8,809 catheter days). PICCs had second highest pooled failure proportion at 6% (95% CI, 2–12%; nine studies; 1,654 CVADs) but had the lowest pooled IR 3.98 (95% CI, 0.57–7.40) per 1,000 catheter days (six studies; 13,078 catheter days). Overall, study heterogeneity reporting failure proportion was high ( $P = 95\%$ ) and for device type ( $P = 89\text{--}95\%$ ). Test for heterogeneity between subgroups

(device types) was nonsignificant ( $p = 0.40$ ) for the proportion analysis and significant for the IR analysis ( $p < 0.01$ ).

**CVAD Complication**

**NTCVAD Complications.** NTCVAD had highest proportion and IR of CRBSI (4% [95% CI, 3–5%; 32 studies; 22,784 CVADs];





**Figure 3.** Incidence rate of central vascular access device (CVAD) failure (per 1,000 catheter days) ( $n = 44$  studies). ES = effect size, PICC = peripherally inserted central catheter.

3.92 per 1,000 catheter days [95% CI, 3.11–4.74; 29 studies; 214,012 catheter days]) and CLABSI (3% [95% CI, 1–5%; 10 studies; 19,115 CVADs]; 5.28 per 1,000 catheter days [95% CI, 2.34–8.23; per 1,000 catheter days; eight studies; 139,082 catheter days]) with high heterogeneity within studies. NTCVAD also had highest proportion and IR of catheter removal due to suspected

catheter infection (20% [95% CI, 15–25%; 15 studies; 8,003 CVADs]; 23.6 per 1,000 catheter days [95% CI, 17.9–29.3; per 1,000 catheter days; 14 studies; 48,010 catheter days]) with high heterogeneity within studies. NTCVAD had highest local infection proportion (2%; 95% CI, 1–3%; six studies; 1,994 CVADs) and IR (3.01; 95% CI, 1.97–4.06; per 1,000 catheter days; three studies; 12,216 catheter days) with low to moderate heterogeneity of studies with significant effect size (**Supplemental Fig. 1**, Supplemental Digital Content 5, <http://links.lww.com/CCM/D907-legend>, Supplemental Digital Content 9, <http://links.lww.com/CCM/D911>; and **Supplemental Fig. 2**, Supplemental Digital Content 6, <http://links.lww.com/CCM/D908-legend>, Supplemental Digital Content 9, <http://links.lww.com/CCM/D911>).

**PICC Complications.** PICC had highest CAVT proportion (11%; 95% CI, 7–16%; nine studies; 1,638 CVADs), but the lowest CAVT IR of 9.31 per 1,000 catheter days (95% CI, 5.39–13.2; five studies, 12,831 catheter days) with moderate heterogeneity within studies. One study investigated PICC occlusion and reported proportion of 38% (95% CI, 24–55%; one study; 34 CVADs) and IR of 36.6 (95% CI, 15.1–58.2) per 1,000 catheter days.

**Hemodialysis Catheters Complications.** Hemodialysis catheters had the highest IR for CAVT 26.6 per 1,000 catheter days (95% CI, 0.00–80.9; two studies; 4,439 catheter days).

### Subgroup Analysis

Medical ICU had the highest proportion of NTCVAD failure (7%; 95% CI, 2–16%; six studies; 2,014 CVADs) and ICUs that did not report their ICU type had the highest IR of NTCVAD failure (7.03; 95% CI, 4.64–9.41; 10 studies; 137,235 catheter days) (**Supplemental Table 5**, Supplemental Digital Content 7,

**TABLE 1. Proportions of Central Vascular Access Device Complications Across Device Type (Subgroups) in Included Studies**

Event and CVAD Type	Studies	CVADs	Outcomes	Pooled %	95% CI
Failure					
Overall	54	25,770	1,115	5 <sup>d,e,h</sup>	3–6
NTCVAD	41	22,635	885	4 <sup>d,e</sup>	3–6
PICC	9	1,654	100	6 <sup>d,e</sup>	2–12
Hemodialysis	4	1,481	130	7 <sup>d,e</sup>	3–12
Catheter-related bloodstream infection					
Overall	40	24,865	658	3 <sup>d,e,g</sup>	2–4
NTCVAD	32	22,784	637	4 <sup>d,e</sup>	3–5
PICC	5	671	6	0 <sup>b,f</sup>	0–1
Hemodialysis	3	1,410	15	1 <sup>a,e</sup>	1–2
Central line-associated bloodstream infection					
Overall	14	20,297	405	2 <sup>d,e,h</sup>	1–4
NTCVAD	10	19,115	349	3 <sup>d,e</sup>	1–5
PICC	4	1,182	56	1 <sup>a,e</sup>	0–3
Removal of catheter due to suspected catheter infection					
Overall	19	9,306	1,527	17 <sup>d,e,g</sup>	13–22
NTCVAD	15	8,003	1,407	20 <sup>d,e</sup>	15–25
PICC	2	66	8	10 <sup>a,e</sup>	3–19
Hemodialysis	2	1,237	112	9 <sup>a,e</sup>	7–11
Catheter-associated venous thrombosis					
Overall	22	7,224	729	10 <sup>d,e,g</sup>	4–17
NTCVAD	11	4,790	547	9 <sup>d,e</sup>	1–22
PICC	9	1,638	163	11 <sup>d,e</sup>	7–16
Hemodialysis	2	796	19	1 <sup>a,e</sup>	0–2
Occlusion/blockage					
Overall	5	807	96	11 <sup>d,e,g</sup>	4–22
NTCVAD	3	702	78	8 <sup>a,e</sup>	1–20
PICC	1	34	13	38 <sup>a,e</sup>	24–55
Hemodialysis	1	71	5	7 <sup>a,e</sup>	3–15
Dislodgment/migration					
Overall	16	4,934	114	2 <sup>d,e,h</sup>	1–3
NTCVAD	13	4,759	108	2 <sup>d,e</sup>	1–3
PICC	2	104	5	2 <sup>a,e</sup>	0–7
Hemodialysis	1	71	1	1 <sup>a,f</sup>	0–8
Local infection/phlebitis					
Overall	7	2,044	44	1 <sup>c,e,h</sup>	1–3
NTCVAD	6	1,994	44	2 <sup>c,e</sup>	1–3
PICC	1	50	0	0 <sup>a,f</sup>	0–7

CVAD = central vascular access device, NTCVAD = nontunnelled CVAD, PICC = peripherally inserted central catheter.

Heterogeneity of studies: <sup>a</sup>cannot be calculated, <sup>b</sup>low (< 25%), <sup>c</sup>moderate (25–75%), or <sup>d</sup>high (> 75%).

Effect-size test: <sup>a</sup>significant or <sup>b</sup>nonsignificant.

Test for heterogeneity between subgroups: <sup>a</sup>significant or <sup>b</sup>nonsignificant.

No hemodialysis studies for central line-associated bloodstream infection and local infection/phlebitis outcomes.

**TABLE 2. Incidence Rates of Central Vascular Access Device Complications Per 1,000 Catheter Days Across Device Type (Subgroups) in Included Studies**

Event and CVAD Type	Studies	Catheter Days	Outcomes	Pooled Incidence Rate	95% CI
Failure					
Overall	44	232,001	995	5.43 <sup>d,e,g</sup>	4.43–6.43
NTCVAD	35	210,114	813	5.18 <sup>d,e</sup>	4.13–6.24
PICC	6	13,078	58	3.98 <sup>d,e</sup>	0.57–7.40
Hemodialysis	3	8,809	124	11.2 <sup>d,f</sup>	0.00–22.9
Catheter-related bloodstream infection					
Overall	36	228,999	621	3.35 <sup>d,e,h</sup>	2.67–4.03
NTCVAD	29	214,012	600	3.92 <sup>d,e</sup>	3.11–4.74
PICC	4	6,178	6	0.88 <sup>b,f</sup>	0.00–1.83
Hemodialysis	3	8,809	15	1.69 <sup>b,e</sup>	0.70–2.67
Central line-associated bloodstream infection					
Overall	10	149,018	343	4.59 <sup>d,e,g</sup>	2.31–6.86
NTCVAD	8	139,082	299	5.28 <sup>d,e</sup>	2.34–8.23
PICC	2	9,936	44	2.50 <sup>d,f</sup>	0.00–7.19
Removal of catheter due to suspected catheter infection					
Overall	18	56,274	1,270	20.4 <sup>d,e,g</sup>	15.7–25.2
NTCVAD	14	48,010	1,150	23.6 <sup>d,e</sup>	17.9–29.3
PICC	2	1,050	8	5.13 <sup>c,f</sup>	0.00–14.4
Hemodialysis	2	7,214	112	14.8 <sup>d,e</sup>	6.93–22.7
Catheter-associated venous thrombosis					
Overall	14	40,387	268	8.34 <sup>d,e,g</sup>	5.59–11.1
NTCVAD	7	23,117	146	10.2 <sup>d,e</sup>	4.36–16.0
PICC	5	12,831	103	9.31 <sup>c,e</sup>	5.39–13.2
Hemodialysis	2	4,439	19	26.6 <sup>d,f</sup>	0.00–80.9
Occlusion/blockage					
Overall	4	5,468	91	17.0 <sup>d,e,g</sup>	3.79–30.3
NTCVAD	3	5,113	78	13.1 <sup>d,f</sup>	0.00–27.0
PICC	1	355	13	36.6 <sup>a,e</sup>	15.1–58.2
Dislodgment/migration					
Overall	9	34,279	98	2.75 <sup>d,e</sup>	1.51–3.98
NTCVAD	9	34,279	98	2.75 <sup>d,e</sup>	1.51–3.98
Local infection/phlebitis					
Overall	4	13,063	39	2.45 <sup>c,e,g</sup>	0.54–4.35
NTCVAD	3	12,216	39	3.01 <sup>b,e</sup>	1.97–4.06
PICC	1	847	0	0.00 <sup>a,f</sup>	0.00–2.18

CVAD = central vascular access device, NTCVAD = nontunnelled CVAD, PICC = peripherally inserted central catheter.

Heterogeneity of studies: <sup>a</sup>cannot be calculated, <sup>b</sup>low (< 25%), <sup>c</sup>moderate (25–75%), or <sup>d</sup>high (> 75%).

Effect-size test: <sup>e</sup>significant or <sup>f</sup>nonsignificant.

Test for heterogeneity between subgroups: <sup>g</sup>significant or <sup>h</sup>nonsignificant.

No hemodialysis studies for central line-associated bloodstream infection, occlusion/blockage, dislodgement/migration, and local infection/phlebitis outcomes. No PICC studies for dislodgement/migration outcome.

<http://links.lww.com/CCM/D909>). The heterogeneity between subgroups was nonsignificant for NTCVAD failure proportion.

### Sensitivity Analysis

The results of sensitivity analysis comparing pooled proportions and IRs of CVAD failure across device types are described in **Supplemental Table 6** (Supplemental Digital Content 8, <http://links.lww.com/CCM/D910>). The proportion and IR of failure in NTCVAD was higher in the high ROB group (5% [95% CI, 3–7%; 25 studies; 17,151 CVADs]; 5.96 per 1,000 catheter days [95% CI, 4.61–7.30; 24 studies; 183,184 catheter days]) compared with the low ROB group (3% [95% CI, 1–6%; 16 studies; 5,484 CVADs]; 3.71 per 1,000 catheter days [95% CI, 1.68–5.75; 11 studies; 26,930 catheter days]).

For PICCs, the lower ROB group had higher failure proportion (8%; 95% CI, 2–16%; four studies; 1,014 CVADs vs 5%; 95% CI, 0–17%; five studies; 640 CVADs) and IR (5.50; 95% CI, 3.62–7.38 vs 3.70; 95% CI, 0.00–8.24).

## DISCUSSION

This is the first study to systematically identify and meta-analyze CVAD failure and complications across all types of CVADs in the ICU population. This study has established 5% (95% CI, 3–6%) of CVADs fail before the completion of treatment, in the adult ICU. In comparison to the review in general pediatrics (25%; 95% CI, 21–29%), our review revealed considerably lower failure (5). However, the pediatric review included predominantly long-term CVADs (58% tunneled and TIVD) (92), increasing opportunity for failure to occur. CVAD failure of 5% for adult critical care is alarming considering the type of time-sensitive treatments being disrupted (e.g., inotropic support) and the dominance of short-term CVADs.

The pooled estimates for CLABSI was 4.59 per 1,000 catheter days, which was higher than the most recent reports by ICU surveillance databases, in the United States (93) and Australian/New Zealand (94). However, in Europe, the CLABSI rate was 3.6 per 1,000 catheter days (95), and International Nosocomial Infection Control Consortium surveillance data reported 4.1 per 1,000 catheter days (96), which were similar to our result. The variance can be explained in part, as some surveillance studies did not report individual CVAD types and were not eligible for inclusion. The review also included multiple sites from lower socioeconomic levels (e.g., India and Brazil), than the Australian and U.S. databases, which is associated with higher risk of infection (97). Overall, the rate of CLABSI described in this review is much higher than the far-reaching goal of zero CLABSI proposed by Institute for Healthcare Improvement, and World Health Organization (98).

A key finding was the large number of catheters removed in ICU on suspicion of catheter infection. There is a significant practice issue with 1,527 catheter removed due to suspected infection, but only 169 emerged as confirmed CRBSI/CLABSI. A number of studies (25, 99, 100) have investigated the effects of immediate, deferred, or no removal of CVADs suspected of infection and found that there was no difference in morbidity or mortality between groups. Practice guidelines

consistently recommend using clinical judgment regarding the appropriateness of removing the catheter, if infection is evidenced elsewhere or if a noninfectious cause of fever is suspected (12). Additionally, the Infectious Diseases Society of America recommends short-term catheters should be removed if the CLABSI is due to gram-negative bacilli, *Staphylococcus aureus*, enterococci, fungi, and mycobacteria (101). However, a practice guideline specific to the management of CVADs suspected of infection in ICU has not been developed, resulting in clinicians erring toward caution, and removing CVADs early, without microbiological confirmation of CLABSI. Even with caution, many CVADs appear to be unnecessarily removed, leaving patients to experience treatment delays, and undergo additional risky insertion procedures (25, 99). The development of robust evidence and guidelines which inform clinical practice concerning the diagnosis and management of devices with suspected infection should be a priority for researchers and policy makers.

From our data, it is clear that CVAD complication risk can be device specific. PICC complications were high, particularly for CAVT, which in turn resulted in a high proportion of failure for blockage/occlusion. Consequently, PICC placement in adult ICU patients should not be viewed as less risky than NTCVAD placement and, indeed, requires vigilant monitoring and surveillance (5, 19). However, it is necessary to be cautious interpreting the CAVT results, many may have been asymptomatic only, with uncertain clinical importance.

CAVT in hemodialysis catheters is concerning, as shown by a pooled IR of 26.6 per 1,000 catheter days. Although the effect size was nonsignificant due to the inclusion of only two studies, early data indicates the possibility of harm in this population (102). Additionally, no hemodialysis catheters studies reporting CLABSI and local infection or phlebitis were identified, and only one study reported dislodgement and occlusion. There is a dearth of evidence to support hemodialysis catheter CAVT prevention practices during ICU admission (103). Research in this area is urgently required, to both provide more certain estimates of complication incidence, and inform practice development.

This review gives insights into a number of problems associated with CVAD use and provides opportunities for practice improvement. However, the review has some limitations. Due to the lack of studies reporting CVAD numbers and days, some data were not suitable for meta-analysis, which may have resulted in estimate imprecision. Consistency in reporting of such metrics needs to be prioritized by the research community, so that accurate pooled estimates can be produced. Studies that failed to specify the CVAD type were not included, and, because of this, 13 surveillance studies (91, 104–115) were ineligible. Lastly, although the pooled proportion of failure of all CVADs was homogenous, overall the meta-analysis had high heterogeneity across studies and within subgroups, especially for NTCVAD studies. This is expected due to the heterogeneous nature of critically ill patients (116). A subgroup analysis by type of ICU was attempted but could not be interpreted meaningfully due to insufficient studies. Despite these



limitations, this study provides opportunities for benchmarking in CVAD health and highlights areas requiring further investigation.

## CONCLUSIONS

This systematic review identified CVAD complications and failure are significant problems in adult ICU, and advances are necessary. Hemodialysis catheters require focused research and practice innovation, due to the paucity of evidence and potentially high complication rates. There is an urgent need for robust practice guidelines regarding the management of suspected CVAD infection to prevent unnecessary catheter removal and subsequent harm to patients.

## REFERENCES

- Loveday HP, Wilson JA, Pratt RJ, et al: Epic3: National evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *J Hosp Infect* 2014; 86(Suppl 1):S1–S70
- McGee DC, Gould MK: Preventing complications of central venous catheterization. *N Engl J Med* 2003; 348:1123–1133
- Climo M, Diekema D, Warren DK, et al: Prevalence of the use of central venous access devices within and outside of the intensive care unit: Results of a survey among hospitals in the prevention epicenter program of the Centers for Disease Control and Prevention. *Infect Control Hosp Epidemiol* 2003; 24:942–945
- Australian and New Zealand Intensive Care Society: Central Line Insertion and Maintenance Guideline, 2012. Available at: [http://www.anzics.com.au/Downloads/ANZICS\\_Insertion&maintenance\\_guideline2012\\_04.pdf](http://www.anzics.com.au/Downloads/ANZICS_Insertion&maintenance_guideline2012_04.pdf). Accessed March 14, 2018
- Ullman AJ, Marsh N, Mihala G, et al: Complications of central venous access devices: A systematic review. *Pediatrics* 2015; 136:e1331–e1344
- Eisen LA, Narasimhan M, Berger JS, et al: Mechanical complications of central venous catheters. *J Intensive Care Med* 2006; 21:40–46
- Webster CS, Merry AF, Emmens DJ, et al: A prospective clinical audit of central venous catheter use and complications in 1000 consecutive patients. *Anaesth Intensive Care* 2003; 31:80–86
- Wilson TJ, Stetler WR Jr, Fletcher JJ: Comparison of catheter-related large vein thrombosis in centrally inserted versus peripherally inserted central venous lines in the neurological intensive care unit. *Clin Neurol Neurosurg* 2013; 115:879–882
- Scott WL: Complications associated with central venous catheters. A survey. *Chest* 1988; 94:1221–1224
- Bozzetti F, Mariani L, Bertinet DB, et al: Central venous catheter complications in 447 patients on home parenteral nutrition: An analysis of over 100,000 catheter days. *Clin Nutr* 2002; 21:475–485
- Gorski LA: The 2016 infusion therapy standards of practice. *Home Healthc Now* 2017; 35:10–18
- Center for Disease Control and Prevention: Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011. Available at: <https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html>. Accessed February 1, 2018
- Rosenthal VD, Guzman S, Migone O, et al: The attributable cost, length of hospital stay, and mortality of central line-associated bloodstream infection in intensive care departments in Argentina: A prospective, matched analysis. *Am J Infect Control* 2003; 31:475–480
- Stevens V, Geiger K, Concannon C, et al: Inpatient costs, mortality and 30-day re-admission in patients with central-line-associated bloodstream infections. *Clin Microbiol Infect* 2014; 20:O318–O324
- Barnett AG, Graves N, Rosenthal VD, et al: Excess length of stay due to central line-associated bloodstream infection in intensive care units in Argentina, Brazil, and Mexico. *Infect Control Hosp Epidemiol* 2010; 31:1106–1114
- Infusion Nurses Society: Infusion therapy standards of practice. *J Infus Nurs* 2016; 39:1–169
- Burns KE, McLaren A: A critical review of thromboembolic complications associated with central venous catheters. *Can J Anaesth* 2008; 55:532–541
- Mermel LA: Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000; 132:391–402
- Chopra V, Anand S, Hickner A, et al: Risk of venous thromboembolism associated with peripherally inserted central catheters: A systematic review and meta-analysis. *Lancet* 2013; 382:311–325
- Wall C, Moore J, Thachil J: Catheter-related thrombosis: A practical approach. *J Intensive Care Soc* 2016; 17:160–167
- Higgerson RA, Lawson KA, Christie LM, et al; National Association of Children's Hospitals and Related Institution's Pediatric Intensive Care Unit FOCUS group: Incidence and risk factors associated with venous thrombotic events in pediatric intensive care unit patients. *Pediatr Crit Care Med* 2011; 12:628–634
- Lima NP, Silva GM, Park M, et al: Mobility therapy and central or peripheral catheter-related adverse events in an ICU in Brazil. *J Bras Pneumol* 2015; 41:225–230
- Stroup DF, Berlin JA, Morton SC, et al: Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283:2008–2012
- Centers for Disease Control and Prevention: Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-Central Line-Associated Bloodstream Infection). Device-associated Module BSI. 1–38]. 2017. Available at: [https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc\\_clabscurrent.pdf](https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf). Accessed January 5, 2018
- Lorente L, Martín MM, Vidal P, et al; Working Group on Catheter Related Infection Suspicion Management of GTEIS/SEMICYUC: Should central venous catheter be systematically removed in patients with suspected catheter related infection? *Crit Care* 2014; 18:564
- O'Grady NP, Alexander M, Burns LA, et al; Healthcare Infection Control Practices Advisory Committee (HICPAC): Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011; 52:e162–e193
- Alexandrou E, Spencer TR, Frost SA, et al: Central venous catheter placement by advanced practice nurses demonstrates low procedural complication and infection rates—a report from 13 years of service\*. *Crit Care Med* 2014; 42:536–543
- Hoy D, Brooks P, Woolf A, et al: Assessing risk of bias in prevalence studies: Modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012; 65:934–939
- National Heart L, and Blood Institute: Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, 2014. Available at: <https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardi-vascular-risk-reduction/tools/cohort>. Accessed June 1, 2017
- Munn Z, Moola S, Lisy K, et al: Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc* 2015; 13:147–153
- Antonelli M, De Pascale G, Ranieri VM, et al: Comparison of triple-lumen central venous catheters impregnated with silver nanoparticles (AgTive®) vs conventional catheters in intensive care unit patients. *J Hosp Infect* 2012; 82:101–107
- Arvaniti K, Lathyris D, Clouva-Molyvdas P, et al; Catheter-Related Infections in ICU (CRI-ICU) Group: Comparison of Oligon catheters and chlorhexidine-impregnated sponges with standard multilumen central venous catheters for prevention of associated colonization and infections in intensive care unit patients: A multicenter, randomized, controlled study. *Crit Care Med* 2012; 40:420–429
- Bonizzoli M, Batacchi S, Cianchi G, et al: Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. *Intensive Care Med* 2011; 37:284–289
- Günther SC, Schwebel C, Hamidfar-Roy R, et al: Complications of intravascular catheters in ICU: Definitions, incidence and severity. A randomized controlled trial comparing usual transparent dressings versus new-generation dressings (the ADVANCED study). *Intensive Care Med* 2016; 42:1753–1765
- Esteve F, Pujol M, Limón E, et al: Bloodstream infection related to catheter connections: A prospective trial of two connection systems. *J Hosp Infect* 2007; 67:30–34

36. Frizzelli R, Tortelli O, Di Comite V, et al: Deep venous thrombosis of the neck and pulmonary embolism in patients with a central venous catheter admitted to cardiac rehabilitation after cardiac surgery: A prospective study of 815 patients. *Intern Emerg Med* 2008; 3:325–330
37. Garnacho-Montero J, Aldabó-Pallás T, Palomar-Martínez M, et al: Risk factors and prognosis of catheter-related bloodstream infection in critically ill patients: A multicenter study. *Intensive Care Med* 2008; 34:2185–2193
38. Girard R, Comby C, Jacques D: Alcoholic povidone-iodine or chlorhexidine-based antiseptic for the prevention of central venous catheter-related infections: In-use comparison. *J Infect Public Health* 2012; 5:35–42
39. Hagau N, Studnicska D, Gavrus RL, et al: Central venous catheter colonization and catheter-related bloodstream infections in critically ill patients: A comparison between standard and silver-integrated catheters. *Eur J Anaesthesiol* 2009; 26:752–758
40. Johnston AJ, Streater CT, Noorani R, et al: The effect of peripherally inserted central catheter (PICC) valve technology on catheter occlusion rates—the 'ELeCTRiC' study. *J Vasc Access* 2012; 13:421–425
41. Kalfon P, de Vaumas C, Samba D, et al: Comparison of silver-impregnated with standard multi-lumen central venous catheters in critically ill patients. *Crit Care Med* 2007; 35:1032–1039
42. L'Héritau F, Olivier M, Maugat S, et al: Impact of a five-year surveillance of central venous catheter infections in the REACAT intensive care unit network in France. *J Hosp Infect* 2007; 66:123–129
43. Lorente L, Jiménez A, Castedo J, et al: Internal jugular venous catheter-related bacteremia according to central and posterior accesses. *Intensive Care Med* 2007; 33:1071–1075
44. Lorente L, Jiménez A, García C, et al: Catheter-related bacteremia from femoral and central internal jugular venous access. *Eur J Clin Microbiol Infect Dis* 2008; 27:867–871
45. Lorente L, Jiménez A, Martín MM, et al: Lower incidence of catheter-related bloodstream infection in subclavian venous access in the presence of tracheostomy than in femoral venous access: Prospective observational study. *Clin Microbiol Infect* 2011; 17:870–872
46. Lorente L, Lecuona M, Jiménez A, et al: Chlorhexidine-silver sulfadiazine- or rifampicin-miconazole-impregnated venous catheters decrease the risk of catheter-related bloodstream infection similarly. *Am J Infect Control* 2016; 44:50–53
47. Lorente L, Lecuona M, Ramos MJ, et al: The use of rifampicin-miconazole-impregnated catheters reduces the incidence of femoral and jugular catheter-related bacteremia. *Clin Infect Dis* 2008; 47:1171–1175
48. Mimoz O, Vileminey S, Ragot S, et al: Chlorhexidine-based antiseptic solution vs alcohol-based povidone-iodine for central venous catheter care. *Arch Intern Med* 2007; 167:2066–2072
49. Pages J, Hazera P, Mégarbane B, et al; 3SITES Study Group: Comparison of alcoholic chlorhexidine and povidone-iodine cutaneous antiseptics for the prevention of central venous catheter-related infection: A cohort and quasi-experimental multicenter study. *Intensive Care Med* 2016; 42:1418–1426
50. Parienti JJ, Mongardon N, Mégarbane B, et al; 3SITES Study Group: Intravascular complications of central venous catheterization by insertion site. *N Engl J Med* 2015; 373:1220–1229
51. Parienti JJ, Thirion M, Mégarbane B, et al; Members of the Cathedia Study Group: Femoral vs jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: A randomized controlled trial. *JAMA* 2008; 299:2413–2422
52. Peredo R, Sabatier C, Villagrà A, et al: Reduction in catheter-related bloodstream infections in critically ill patients through a multiple system intervention. *Eur J Clin Microbiol Infect Dis* 2010; 29:1173–1177
53. Pérez-Granda MJ, Guembe M, Cruces R, et al: Assessment of central venous catheter colonization using surveillance culture of withdrawn connectors and insertion site skin. *Crit Care* 2016; 20:32
54. Pérez-Granda MJ, Guembe M, Cruces R, et al: Vascular catheter colonization: Surveillance based on culture of needleless connectors. *Crit Care* 2016; 20:166
55. Pittiruti M, Brutti A, Celentano D, et al: Clinical experience with power-injectable PICCs in intensive care patients. *Crit Care* 2012; 16:R21
56. Ricard JD, Salomon L, Boyer A, et al: Central or peripheral catheters for initial venous access of ICU patients: A randomized controlled trial. *Crit Care Med* 2013; 41:2108–2115
57. Timsit JF, L'Héritau F, Lepape A, et al: A multicentre analysis of catheter-related infection based on a hierarchical model. *Intensive Care Med* 2012; 38:1662–1672
58. Timsit JF, Mimoz O, Mourvillier B, et al: Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med* 2012; 186:1272–1278
59. Timsit JF, Schwebel C, Bouadma L, et al; Dressing Study Group: Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: A randomized controlled trial. *JAMA* 2009; 301:1231–1241
60. Hrdy O, Strazevska E, Suk P, et al: Central venous catheter-related thrombosis in intensive care patients - incidence and risk factors: A prospective observational study. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2017; 161:369–373
61. Schönenberger M, Forster C, Siegemund M, et al: Catheter related blood stream infections in critically ill patients with continuous haemo(dia)filtration and temporary non-tunnelled vascular access. *Swiss Med Wkly* 2011; 141:w13294
62. Ajenjo MC, Morley JC, Russo AJ, et al: Peripherally inserted central venous catheter-associated bloodstream infections in hospitalized adult patients. *Infect Control Hosp Epidemiol* 2011; 32:125–130
63. Fletcher JJ, Stetler W, Wilson TJ: The clinical significance of peripherally inserted central venous catheter-related deep vein thrombosis. *Neurocrit Care* 2011; 15:454–460
64. Fletcher JJ, Wilson TJ, Rajajee V, et al: A randomized trial of central venous catheter type and thrombosis in critically ill neurologic patients. *Neurocrit Care* 2016; 25:20–28
65. Gunst M, Matsushima K, Vanek S, et al: Peripherally inserted central catheters may lower the incidence of catheter-related blood stream infections in patients in surgical intensive care units. *Surg Infect (Larchmt)* 2011; 12:279–282
66. Malinoski D, Ewing T, Bhakta A, et al: Which central venous catheters have the highest rate of catheter-associated deep venous thrombosis: A prospective analysis of 2,128 catheter days in the surgical intensive care unit. *J Trauma Acute Care Surg* 2013; 74:454–460; discussion 461–462
67. Martyak M, Kabir I, Britt R: Inpatient peripherally inserted central venous catheter complications: Should peripherally inserted central catheter lines be placed in the intensive care unit setting? *Am Surg* 2017; 83:925–927
68. Nolan ME, Yadav H, Cawcutt KA, et al: Complication rates among peripherally inserted central venous catheters and centrally inserted central catheters in the medical intensive care unit. *J Crit Care* 2016; 31:238–242
69. Ramirez C, Lee AM, Welch K: Central venous catheter protective connector caps reduce intraluminal catheter-related infection. *JAVA* 2012; 17:210–213
70. Schallom ME, Prentice D, Sona C, et al: Heparin or 0.9% sodium chloride to maintain central venous catheter patency: A randomized trial. *Crit Care Med* 2012; 40:1820–1826
71. Trerotola SO, Stavropoulos SW, Mondschein JI, et al: Triple-lumen peripherally inserted central catheter in patients in the critical care unit: Prospective evaluation. *Radiology* 2010; 256:312–320
72. Walz JM, Avelar RL, Longtine KJ, et al; 5-FU Catheter Study Group: Anti-infective external coating of central venous catheters: A randomized, noninferiority trial comparing 5-fluorouracil with chlorhexidine/silver sulfadiazine in preventing catheter colonization. *Crit Care Med* 2010; 38:2095–2102
73. Camargo LF, Marra AR, Büchele GL, et al: Double-lumen central venous catheters impregnated with chlorhexidine and silver sulfadiazine to prevent catheter colonisation in the intensive care unit setting: A prospective randomised study. *J Hosp Infect* 2009; 72:227–233
74. Pedrolo E, Danski MT, Vayego SA: Chlorhexidine and gauze and tape dressings for central venous catheters: A randomized clinical trial. *Rev Lat Am Enfermagem* 2014; 22:764–771
75. Pontes-Arruda A, Dos Santos MC, Martins LF, et al; EPICOS Study Group: Influence of parenteral nutrition delivery system on the development of bloodstream infections in critically ill patients: An international, multicenter, prospective, open-label, controlled study—EPICOS study. *JPEN J Parenter Enteral Nutr* 2012; 36:574–586

76. Leal MLM, Loyola ABAT, Hueb AC, et al: Fixation of the short-term central venous catheter. A comparison of two techniques. *Acta Cir Bras* 2017; 32:680–690
77. Chua HR, Schneider AG, Sherry NL, et al: Initial and extended use of femoral versus nonfemoral double-lumen vascular catheters and catheter-related infection during continuous renal replacement therapy. *Am J Kidney Dis* 2014; 64:909–917
78. Fraenkel D, Rickard C, Thomas P, et al: A prospective, randomized trial of rifampicin-minocycline-coated and silver-platinum-carbon-impregnated central venous catheters. *Crit Care Med* 2006; 34:668–675
79. Gowardman JR, Robertson IK, Parkes S, et al: Influence of insertion site on central venous catheter colonization and bloodstream infection rates. *Intensive Care Med* 2008; 34:1038–1045
80. Parbat N, Sherry N, Bellomo R, et al: The microbiological and clinical outcome of guide wire exchanged versus newly inserted antimicrobial surface treated central venous catheters. *Crit Care* 2013; 17:R184
81. Rickard CM, Edwards M, Spooner AJ, et al: A 4-arm randomized controlled pilot trial of innovative solutions for jugular central venous access device securement in 221 cardiac surgical patients. *J Crit Care* 2016; 36:35–42
82. Wong SW, Gantner D, McGloughlin S, et al: The influence of intensive care unit-acquired central line-associated bloodstream infection on in-hospital mortality: A single-center risk-adjusted analysis. *Am J Infect Control* 2016; 44:587–592
83. Deepti, Sinha S, Sharma SK, et al: Central venous catheter related bloodstream infections in medical intensive care unit patients in a tertiary referral centre. *Indian J Chest Dis Allied Sci* 2014; 56:85–91
84. Kujur R, Rao SM, Badwaik G, et al: Thrombosis associated with right internal jugular central venous catheters: A prospective observational study. *Indian J Crit Care Med* 2012; 16:17–21
85. Kumar A, Mehta Y, Ali T, et al: Deep vein thrombosis in medical and surgical intensive care unit patients in a tertiary care centre in North India: Incidence and risk factors. *J Anaesthesiol Clin Pharmacol* 2017; 33:181–186
86. Mishra SB, Misra R, Azim A, et al: Incidence, risk factors and associated mortality of central line-associated bloodstream infections at an intensive care unit in northern India. *Int J Qual Health Care* 2017; 29:63–67
87. Hajje Z, Nasri M, Sellami W, et al: Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit. *J Infect Chemother* 2014; 20:163–168
88. Kallel H, Damak H, Mahjoubi F, et al: Microbiological characteristics of catheter-related bacteremia in a Tunisian intensive care unit. *Tunis Med* 2010; 88:876–879
89. Memon JI, Rehmani RS, Venter JL, et al: Central venous catheter practice in an adult intensive care setting in the eastern province of Saudi Arabia. *Saudi Med J* 2010; 31:803–807
90. Osmá S, Kahveci SF, Kaya FN, et al: Efficacy of antiseptic-impregnated catheters on catheter colonization and catheter-related bloodstream infections in patients in an intensive care unit. *J Hosp Infect* 2006; 62:156–162
91. Salama MF, Jamal W, Al Mousa H, et al: Implementation of central venous catheter bundle in an intensive care unit in Kuwait: Effect on central line-associated bloodstream infections. *J Infect Public Health* 2016; 9:34–41
92. Ullman AJ, Cooke M, Kleidon T, et al: Road map for improvement: Point prevalence audit and survey of central venous access devices in paediatric acute care. *J Paediatr Child Health* 2017; 53:123–130
93. Margaret A, Edwards JR, Allen-Bridson K, et al: National Healthcare Safety Network (NHSN) report, data summary for 2013, device-associated module. *Am J Infect Control* 2015; 43:206–221
94. Australian and New Zealand Intensive Care Society: Central Line Associated Bloodstream Infection (CLABSI) Report 2015/16, 2016. Available at: <http://www.anzics.com.au/Downloads/CLABSI%20Report%202015-16.pdf>. Accessed January 1, 2018
95. European Centre for Disease Prevention and Control: Healthcare-Associated Infections Acquired in Intensive Care Units – Annual Epidemiological Report for 2015, 2017. Available at: <https://ecdc.europa.eu/en/publications-data/healthcare-associated-infections-acquired-intensive-care-units-annual>. Accessed January 8, 2018
96. Rosenthal VD, Al-Abdely HM, El-Kholy AA, et al: International Nosocomial Infection Control Consortium report, data summary of 50 countries for 2010-2015: Device-associated module. *Am J Infect Control* 2016; 44:1495–1504
97. Rosenthal VD, Jarvis WR, Jamulitrat S, et al; International Nosocomial Infection Control Members: Socioeconomic impact on device-associated infections in pediatric intensive care units of 16 limited-resource countries: International Nosocomial Infection Control Consortium findings. *Pediatr Crit Care Med* 2012; 13:399–406
98. Palomar M, Álvarez-Lerma F, Riera A, et al; Bacteremia Zero Working Group: Impact of a national multimodal intervention to prevent catheter-related bloodstream infection in the ICU: The Spanish experience. *Crit Care Med* 2013; 41:2364–2372
99. Rijnders BJ, Peetermans WE, Verwaest C, et al: Watchful waiting versus immediate catheter removal in ICU patients with suspected catheter-related infection: A randomized trial. *Intensive Care Med* 2004; 30:1073–1080
100. Deliberato RO, Marra AR, Corrêa TD, et al: Catheter related bloodstream infection (CR-BSI) in ICU patients: Making the decision to remove or not to remove the central venous catheter. *PLoS One* 2012; 7:e32687
101. Mermel LA, Allon M, Bouza E, et al: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 49:1–45
102. Napalkov P, Felici DM, Chu LK, et al: Incidence of catheter-related complications in patients with central venous or hemodialysis catheters: A health care claims database analysis. *BMC Cardiovasc Disord* 2013; 13:86
103. Zhao Y, Li Z, Zhang L, et al: Citrate versus heparin lock for hemodialysis catheters: A systematic review and meta-analysis of randomized controlled trials. *Am J Kidney Dis* 2014; 63:479–490
104. Agodi A, Auxilia F, Barchitta M, et al; GISIO: Building a benchmark through active surveillance of intensive care unit-acquired infections: The Italian network SPIN-UTI. *J Hosp Infect* 2010; 74:258–265
105. Al-Mousa HH, Omar AA, Rosenthal VD, et al: Device-associated infection rates, bacterial resistance, length of stay, and mortality in Kuwait: International Nosocomial Infection Consortium findings. *Am J Infect Control* 2016; 44:444–449
106. Latif A, Kelly B, Edrees H, et al: Implementing a multifaceted intervention to decrease central line-associated bloodstream infections in SEHA (Abu Dhabi Health Services Company) intensive care units: The Abu Dhabi experience. *Infect Control Hosp Epidemiol* 2015; 36:816–822
107. Klintworth G, Stafford J, O'Connor M, et al: Beyond the intensive care unit bundle: Implementation of a successful hospital-wide initiative to reduce central line-associated bloodstream infections. *Am J Infect Control* 2014; 42:685–687
108. Cuellar LE, Fernandez-Maldonado E, Rosenthal VD, et al: Device-associated infection rates and mortality in intensive care units of Peruvian hospitals: Findings of the International Nosocomial Infection Control Consortium. *Rev Panam Salud Publica* 2008; 24:16–24
109. Hsin HT, Hsu MS, Shieh JS: The long-term effect of bundle care for catheter-related blood stream infection: 5-year follow-up. *Postgrad Med J* 2017; 93:133–137
110. Mitharwal SM, Yaddanapudi S, Bhardwaj N, et al: Intensive care unit-acquired infections in a tertiary care hospital: An epidemiologic survey and influence on patient outcomes. *Am J Infect Control* 2016; 44:e113–e117
111. Jackson SS, Leekha S, Magder LS, et al: The effect of adding comorbidities to current centers for disease control and prevention central-line-associated bloodstream infection risk-adjustment methodology. *Infect Control Hosp Epidemiol* 2017; 38:1019–1024
112. Mehta Y, Jaggi N, Rosenthal VD, et al: Device-associated infection rates in 20 cities of India, data summary for 2004-2013: Findings of the International Nosocomial Infection Control Consortium. *Infect Control Hosp Epidemiol* 2016; 37:172–181
113. Karkhane M, Pourhoseingholi MA, Kimia Z, et al: Attitudes toward nosocomial infections associated mortality at intensive care units, and evaluation of the risk factors. *Arch Clin Infect Dis* 2016; 11:1–7

114. Li L, Fortin E, Tremblay C, et al; for SPIN-BACC: Central-line-associated bloodstream infections in Québec intensive care units: Results from the provincial healthcare-associated infections surveillance program (SPIN). *Infect Control Hosp Epidemiol* 2016; 37:1186–1194
115. Chen Y, Zhao JY, Shan X, et al; Chinese Group on Point-Prevalence Survey of Healthcare-Associated Infections: A point-prevalence survey of healthcare-associated infection in fifty-two Chinese hospitals. *J Hosp Infect* 2017; 95:105–111
116. Australian and New Zealand Intensive Care Society: ANZICS Centre for Outcome and Resource Evaluation Annual Report 2014–2015, 2016. Available at: <http://www.anzics.com.au/Downloads/ANZICS%20CORE%20Annual%20Report%202015.pdf>. Accessed January 2, 2018