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

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Conflicts of interest:

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Abstract

Objective: To examine the proportion and rate of central venous access device (CVAD) failure and complications across CVAD types in adult intensive care.

Data sources: A systematic search was undertaken in the electronic databases CENTRAL, MEDLINE, CINAHL, EMBASE in September 2017.

Study selection: Included studies were of observational (prospective and retrospective) or interventional design and reported CVAD 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, CVAD failure, and secondary outcomes: CVAD complications (central line associated bloodstream infection [CLABSI], catheter related bloodstream infection [CRBSI], 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 CVADs (396,951 catheter days) were included. CVAD failure was 5% (95% CI 3-6%), with the highest rates and proportion of failure in hemodialysis catheters. Overall CLABSI rate was 4.59 per 1,000 catheter days (95% CI 2.31-6.86), with the highest rate in non-tunneled CVADs. Removal of CVAD due to suspected infection was high (17%; 20.4 per 1,000 catheter days; 95% CI 15.7-25.2).

Conclusion: CVAD complications and device failure is a prevalent and significant problem in the adult ICU, leading to substantial patient harm and increased healthcare costs. The high proportion of CVADs removed due to suspicion of infection, despite low overall CLABSI and CRBSI rates, indicates a need for robust practice guidelines to inform decision-making surrounding removal of CVADs suspected of infection.

Keywords: central venous access device, failure, complications, intensive care

Word count: 2996 words

Introduction

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 five million CVADs are inserted annually (2), with 43% to 80% of patients in the intensive care unit (ICU) requiring central access (3). The CVAD most commonly inserted in ICU are non-tunneled CVADs (NTCVADs), peripherally inserted central catheters (PICCs), and hemodialysis (HD) (4). These devices are mainly indicated for short- to medium-term duration, while 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 [CLABSI]) 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 extra-luminally. Excess mortality due to CLABSI is estimated at 22% (13), with each diagnosis costing US\$32,000 (14), contributing to increased length of ICU admission (>4 days) (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, pre-existing comorbidities and catheter placement choices place patients at increased risk of CAVT development (19-21). Non-thrombotic 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 aged 18 years or older, 2) with CVADs in ICU, and 3) reported outcomes of interest. Types of CVAD included in the study were NTCVADs, PICCs, HD catheters, tunneled and implanted

CVADs. 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), CRBSI(12), CAVT(19), catheter removal due to suspected infection(25), occlusion, dislodgement(26), breakage(27) and local infection or phlebitis(26) (see online supplement 1 for detailed definitions).

Search strategy and study selection

A systematic search for studies reporting CVAD failure or complications was undertaken in the following electronic databases on the 30 September 2017: Cochrane Central Register of Controlled Trials, EMBASE, US National Library of Medicine National Institutes of Health and Cumulative Index to Nursing and Allied Health. Medical search headings were developed by health care librarians including “vascular access devices”, “central venous catheter”, “central venous access device”, “intensive care” and “critical care” (see Online Supplement 2 for full details). Additional studies were identified through hand-searching references.

Data extraction and quality assessment

Two authors (MT, JS) independently assessed titles and abstracts identified. Full texts of relevant studies were reviewed and independently assessed for inclusion eligibility. A third author (AU) 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 sub-studies per device type. Data were extracted using a data extraction form, managed in Microsoft Excel.

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 (see Online Supplement 3 for full details).

Data analysis

Score confidence intervals (CI) 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, Texas, USA), with statistical significance at $p < 0.05$.

Results:

Figure 1 displays the inclusion and exclusion processes. Electronic databases search yielded 1048 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 (ten studies were split into 21 sub-studies, 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 Online Supplement 4, a mix of ICU specialties were represented, with 25 studies (34%) not specifying ICU specialty. 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 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), 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) (Table 1; 2). HD catheters had highest pooled failure proportion at 7% (95% CI 3-12; 4 studies; 1,481 CVADs) and highest pooled IR 11.2 (0-22.9) per 1,000 catheter days (3 studies; 8,809 catheter days). PICCs had second highest pooled failure proportion at 6% (95% CI 2-12; 9 studies; 1,654 CVADs) but had the lowest pooled IR 3.98 (95% CI 0.57-7.40) per 1,000 catheter days (6 studies; 13,078 catheter days). Overall, study heterogeneity reporting failure proportion was high ($I^2=95\%$) and for device type ($I^2=89-95\%$). Test for heterogeneity between subgroups (device types) was non-significant ($p=0.40$) 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]; 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; 8 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; 6 studies; 1,994 CVADs) and IR (3.01; 95% CI 1.97-4.06; per 1,000 catheter days; 3 studies; 12,216 catheter days) with low to moderate heterogeneity of studies with significant effect size. (See Online Supplement 5&6).

PICC complications

PICC had highest CAVT proportion (11%; 95% CI 7-16; 9 studies; 1,638 CVADs) but the lowest CAVT IR of 9.31 per 1,000 catheter days (95% CI 5.39-13.2; 5 studies, 12,831 catheter days) with moderate heterogeneity within studies. One study investigated PICC occlusion and reported proportion of 38% (95% CI 24-55; 1 study; 34 CVADs) and IR of 36.6 (95% CI 15.1-58.2) per 1,000 catheter days.

HD catheters complications

HD catheters had the highest IR for CAVT 26.6 per 1,000 catheter days (95% CI 0.00-80.9; 2 studies; 4,439 catheter days).

Subgroup analysis

Medical ICU had the highest proportion of NTCVAD failure (7%; 95% CI 2-16; 6 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; per 1,000 catheter days; 10 studies; 137,235 catheter days) (see Online Supplement 7). The heterogeneity between subgroups was non-significant 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 Online Supplement 8. 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 to 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; 4 studies, 1,014 CVADs vs 5%; 95% CI 0-17; 5 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 US (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 1000 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 US 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 non-infectious cause of fever is suspected (12). Additionally, the Infectious Diseases Society of America recommend 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 towards 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 HD catheters is concerning, as shown by a pooled IR of 26.6 per 1,000 catheter days. Although the effect size was non-significant due to the inclusion of only two studies, early data indicates the possibility of harm in this population(102). Additionally, no HD 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 HD 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.

Conclusion

This systematic review identified CVAD complications and failure are significant problems in adult ICU, and advances are necessary. HD 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.

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Figure Legend

Figure 1: PRISMA flowchart of articles screened for inclusion in the systematic review

Figure 2. Proportion of CVAD failure (n=54 studies)

CVAD: Central Vascular Access Device; ES: effect size; CI: confidence interval; PICC: peripherally inserted central catheter;

Figure 3. Incidence rate of CVAD failure (per 1000 catheter days) (n=44 studies)

CVAD: Central Vascular Access Device; ES: effect size; CI: confidence interval; PICC: peripherally inserted central catheter;

Online supplement materials

Online supplement 1: Table: Outcome definitions of CVAD complications

Online Supplement 2: Table: Search terms

Online Supplement 3: Table: Modified quality appraisal tool used in this review

Online Supplement 4: Table: Studies included, with ICU specialty and CVAD type (N=74)

Online Supplement 5: Figure: Proportion of CRBSI failure (N=40 studies)

CVAD: Central Vascular Access Devices ES: Effect Size CI: confidence intervals NTCVAD: Non-tunnelled central venous access device PICC: Peripherally inserted central catheter

Online supplement 6: Figure: Proportion of catheter removal due to suspected catheter infection (N=19 studies)

ES: Effect Size CI: confidence intervals IR: incidence rate CVAD: central venous access device PICC: Peripherally inserted central catheter

Online supplement 7: Table: Subgroup analysis: proportions and incidence rates of CVAD failure per device across ICU specialty

CVAD: Central Vascular Access Devices CI: confidence intervals IR: incidence rate NTCVAD: Non-tunnelled central venous access device PICC: Peripherally inserted central catheter HD: Haemodialysis catheter

Heterogeneity of studies can not be calculated, blow (<25%), c moderate (25%-75%), or d high (>75%).

Effect-size test e significant or f nonsignificant.

Test for heterogeneity between subgroups g significant or h nonsignificant.

Online supplement 8: Table: Sensitivity analysis: proportions and incidence rates of CVAD failure per device by ROB and prospective/retrospective studies

CVAD: Central Vascular Access Devices CI: confidence intervals IR: incidence rate NTCVAD: Non-tunnelled central venous access device PICC: Peripherally inserted central catheter HD: Haemodialysis catheter ROB: Risk of Bias

Heterogeneity of studies can not be calculated, blow (<25%), c moderate (25%-75%), or d high (>75%).

Effect-size test e significant or f nonsignificant.

Test for heterogeneity between subgroups g significant or h nonsignificant.

Online supplement 1

Table: Outcome definitions of CVAD complications

<i>CVAD-associated BSI (CLABSI):</i>	Minimum definition of laboratory-confirmed BSI that is not secondary to an infection at another body site, with a CVAD in place for more than two days on the date of event as defined by Centers of Disease Control and Prevention/ National Healthcare Safety Network (1).
<i>Catheter related BSIs (CRBSI):</i>	Minimum definition of laboratory-confirmed BSI with catheter tip cultures or by differences in growth between catheter and peripheral venipuncture blood culture specimens(2). CRBSI cases were included if the study specified that the catheters were in place more than 48 hours in addition to the CLABSI definition (3). All microbiologic methods were included.
<i>CVAD-associated thrombosis:</i>	Development of partial or complete thrombosis (symptomatic or non-symptomatic) at the CVAD site diagnosed via ultrasound (4).
<i>Catheter removal due to suspected infection:</i>	Removal of catheter due to suspected catheter infection before confirming CRBSI/CLABSI status (5).
<i>Occlusion or blockage:</i>	Partial and full blockage of the CVAD lumen or lumens (irrespective of occlusion treatment);
<i>Dislodgment or migration:</i>	Partial, complete, and/or accidental removal resulting in the CVAD tip no longer situated in the inferior or superior vena cava (6);
<i>Breakage or rupture:</i>	A visible split in CVAD material diagnosed by leakage or radiographic evidence of extravasation from a portion of the CVAD into tissue (7);
<i>Local infection and phlebitis:</i>	Exit site, entrance, and tunnel infections and phlebitis (6).

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Online Supplement 2: Table: Search terms

Search terms
<p>((("critical care"[MeSH Terms] OR ("critical"[All Fields] AND "care"[All Fields]) OR "critical care"[All Fields]) OR ("critical care"[MeSH Terms] OR ("critical"[All Fields] AND "care"[All Fields]) OR "critical care"[All Fields] OR ("intensive"[All Fields] AND "care"[All Fields]) OR "intensive care"[All Fields])) AND ("adult"[MeSH Terms] OR "adult"[All Fields])) AND ("central venous catheters"[MeSH Terms] OR ("central"[All Fields] AND "venous"[All Fields] AND "catheters"[All Fields]) OR "central venous catheters"[All Fields])) AND ("vascular access devices"[MeSH Terms] OR ("vascular"[All Fields] AND "access"[All Fields] AND "devices"[All Fields]) OR "vascular access devices"[All Fields]) AND ("2006/11/18"[PDat] : "2016/11/14"[PDat] AND "humans"[MeSH Terms] AND English[lang])</p>

Online supplement 3: Table: Modified quality appraisal tool used in this review

Questions	Yes	No	Unclear	N/A
Was the sampling frame a true or close representation of the target population? (28) i.e. (If the study has captured the whole available participants in the unit or selectively)(30)				
Were the study subjects and the setting described in detail? (30)				
Were the outcome measures clearly defined, valid, reliable (using standard criteria), and implemented consistently across all study participants? (29, 30)				
Were the study performed prospectively?				
Did the study report the outcome in catheter days?				

Online Supplement 4

Table: Studies included, with ICU specialty and CVAD type (N=74)

ICU type	NTCVAD	PICC	HD	Total
Medical	7	1	0	8
Surgical	6	1	0	7
Medical/Surgical	15	1	2	18
Neuro	3	4	0	7
Trauma	2	3	1	6
Mixed *	2	1	0	3
Not reported	19	4	2	25
Total	54	15	5	74

*Mixed: (medical or surgical ICU with neuro or trauma),

ICU: Intensive Care Unit CVAD: Central Venous Access Devices NTCVAD: Non-tunnelled central vascular access device PICC: Peripherally inserted central catheter HD: Haemodialysis catheter

Online supplement 7

Table: Subgroup analysis: proportions and incidence rates of CVAD failure per device across ICU specialty

CVAD type	Proportion of failure					Incidence rates of failure per 1000 catheter days				
	Studies	CVADs	Outcomes	Pooled %	95% CI	Studies	Catheter days	Outcomes	Pooled IR	95% CI
NTCVAD										
All ICU types	41	22,635	885	4 ^{d,e,h}	3-6	35	210,114	813	5.18 ^{d,e,g}	4.13-6.24
Medical	6	2,014	172	7 ^{d,e}	2-16	5	18,354	120	5.66 ^{d,e}	1.72-9.59
Surgical	5	698	30	4 ^{b,e}	3-6	5	7,390	30	3.55 ^{b,e}	2.02-5.08
Medical/ Surgical	13	3,693	253	3 ^{d,e}	1-5	12	41,257	251	5.16 ^{d,e}	2.98-7.35
Neuro	3	771	14	2 ^{a,e}	0-4	2	4,730	11	2.33 ^{b,e}	0.78-3.88
Trauma	0	-	-	-	-	0	-	-	-	-
Mixed	1	156	7	4 ^{a,e}	2-9	1	1,148	7	6.10 ^{a,e}	1.04-11.2
Not reported	13	15,303	409	5 ^{d,e}	3-7	10	137,235	394	7.03 ^{d,e}	4.64-9.41
PICC										
All ICU types	9	1,654	100	6 ^{d,e,g}	2-12	6	13,078	58	3.98 ^{d,e,g}	0.57-7.40
Surgical	1	37	1	3 ^{a,f}	0-14	1	455	1	2.20 ^{a,f}	0.00-8.29
Medical/Surgical	1	50	15	30 ^{a,e}	19-44	1	847	15	17.7 ^{a,e}	8.06-27.4
Neuro	4	965	78	10 ^{d,e}	3-18	2	6,748	36	4.62 ^{c,e}	0.67-8.57
Trauma	1	65	0	0 ^{a,f}	0-6	0	-	-	-	-
Not reported	2	537	6	1 ^{a,e}	0-2	2	5,028	6	1.10 ^{a,e}	0.04-2.17
HD										
All ICU types	4	1,481	130	7 ^{d,e,g}	3-12	3	8,809	124	11.2 ^{d,f,g}	0.00-22.9
Medical/ Surgical	2	674	41	6 ^{a,e}	4-7	2	4,635	41	6.90 ^{d,f}	0.00-18.2
Not reported	2	807	89	11 ^{a,e}	9-13	1	4,174	83	19.9 ^{a,e}	15.5-24.3

CVAD: Central Vascular Access Devices CI: confidence intervals IR: incidence rate NTCVAD: Non-tunnelled central venous access device PICC: Peripherally inserted central catheter HD: Haemodialysis catheter

Heterogeneity of studies ^a cannot be calculated, ^blow (<25%), ^c moderate (25%-75%), or ^d high (>75%).

Effect-size test ^e significant or ^f nonsignificant.

Test for heterogeneity between subgroups ^g significant or ^h nonsignificant.

Online supplement 8

Table: Sensitivity analysis: proportions and incidence rates of CVAD failure per device by ROB and prospective/retrospective studies

CVAD type	Proportion of failure					Incidence Rates of failure per 1000 catheter days				
	Studies	CVADs	Outcomes	Pooled %	95% CI	Studies	Catheter days	Outcomes	Pooled IR	95% CI
NTCVAD										
ROB: All	41	22,635	885	4 ^{d,e,h}	3-6	35	210,114	813	5.18 ^{d,e,h}	4.13-6.24
ROB 5	25	17,151	679	5 ^{d,e}	3-7	24	183,184	676	5.96 ^{d,e}	4.61-7.30
ROB <4	16	5,484	206	3 ^{d,e}	1-6	11	26,930	137	3.71 ^{d,e}	1.68-5.75
Study type: All	41	22,635	885	4 ^{d,e,h}	3-6	35	210,114	813	5.18 ^{d,e,g}	4.13-6.24
Prospective	38	22,115	861	4 ^{d,e}	3-6	33	207,160	793	5.17 ^{d,e}	4.09-6.25
Retrospective	3	520	24	4 ^{a,e}	1-8	2	2,954	20	5.42 ^{d,f}	0.00-11.8
PICC										
ROB: All	9	1,654	100	6 ^{d,e,h}	2-12	6	13,078	58	3.98 ^{d,e,g}	0.57-7.40
ROB 5	5	640	22	5 ^{d,f}	0-17	5	6,533	22	3.70 ^{c,f}	0.00-8.24
ROB <4	4	1,014	78	8 ^{d,e}	2-16	1	6,545	36	5.50 ^{a,e}	3.62-7.38
Study type: All	9	1,654	100	6 ^{d,e,h}	2-12	6	13,078	58	3.98 ^{d,e,g}	0.57-7.40
Prospective	6	679	36	8 ^{d,e}	0-24	5	6,533	22	3.70 ^{c,f}	0.00-8.24
Retrospective	3	975	64	4 ^{a,e}	1-9	1	6,545	36	5.50 ^{a,e}	3.62-7.38
HD										
ROB: All	4	1,481	130	7 ^{d,e}	3-12	3	8,809	124	11.2 ^{d,f}	0.00-22.9
ROB 5	0	-	-	-	-	0	-	-	-	-
ROB <4	4	1,481	130	7 ^{d,e}	3-12	3	8,809	124	11.2 ^{d,f}	0.00-22.9
Study type: All	4	1,481	130	7 ^{d,e,h}	3-12	3	8,809	124	11.2 ^{d,f,g}	0.00-22.9
Prospective	2	909	85	9 ^{a,e}	7-11	2	5,769	85	10.5 ^{d,f}	0.00-28.7
Retrospective	2	572	45	8 ^{a,e}	6-10	1	3,040	39	12.8 ^{a,e}	8.62-17.0

CVAD: Central Vascular Access Devices CI: confidence intervals IR: incidence rate NTCVAD: Non-tunnelled central venous access device PICC: Peripherally inserted central catheter HD: Haemodialysis catheter ROB: Risk of Bias

Heterogeneity of studies ^a cannot be calculated, ^blow (<25%), ^c moderate (25%-75%), or ^d high (>75%).

Effect-size test ^e significant or ^f nonsignificant.

Test for heterogeneity between subgroups ^g significant or ^h nonsignificant.

Table 1: Proportions of CVAD 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 ^{d,e,h}	3-6
NTCVAD	41	22,635	885	4 ^{d,e}	3-6
PICC	9	1,654	100	6 ^{d,e}	2-12
HD	4	1,481	130	7 ^{d,e}	3-12
CRBSI					
Overall	40	24,865	658	3 ^{d,e,g}	2-4
NTCVAD	32	22,784	637	4 ^{d,e}	3-5
PICC	5	671	6	0 ^{b,f}	0-1
HD	3	1,410	15	1 ^{a,e}	1-2
CLABSI					
Overall	14	20,297	405	2 ^{d,e,h}	1-4
NTCVAD	10	19,115	349	3 ^{d,e}	1-5
PICC	4	1,182	56	1 ^{a,e}	0-3
Removal of catheter due to suspected catheter infection					
Overall	19	9,306	1,527	17 ^{d,e,g}	13-22
NTCVAD	15	8,003	1,407	20 ^{d,e}	15-25
PICC	2	66	8	10 ^{a,e}	3-19
HD	2	1,237	112	9 ^{a,e}	7-11
Catheter Associated Venous Thrombosis					
Overall	22	7,224	729	10 ^{d,e,g}	4-17
NTCVAD	11	4,790	547	9 ^{d,e}	1-22
PICC	9	1,638	163	11 ^{d,e}	7-16
HD	2	796	19	1 ^{a,e}	0-2
Occlusion / Blockage					
Overall	5	807	96	11 ^{d,e,g}	4-22
NTCVAD	3	702	78	8 ^{a,e}	1-20
PICC	1	34	13	38 ^{a,e}	24-55
HD	1	71	5	7 ^{a,e}	3-15
Dislodgment / migration					
Overall	16	4,934	114	2 ^{d,e,h}	1-3
NTCVAD	13	4,759	108	2 ^{d,e}	1-3
PICC	2	104	5	2 ^{a,e}	0-7
HD	1	71	1	1 ^{a,f}	0-8
Local infection/ phlebitis					
Overall	7	2,044	44	1 ^{c,e,h}	1-3
NTCVAD	6	1,994	44	2 ^{c,e}	1-3
PICC	1	50	0	0 ^{a,f}	0-7

CVAD: central vascular access device; CI: confidence interval; NTCVAD: non-tunnelled central venous access device; PICC: peripherally inserted central catheter; HD: haemodialysis catheter;

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

Effect-size test: ^e significant or ^f nonsignificant.

Test for heterogeneity between subgroups: ^g significant or ^h nonsignificant.

No HD studies for CLABSI and local infection/phlebitis outcomes.

Table 2: Incidence rates of CVAD complications per 1000 catheter days across device type (subgroups) in included studies

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

CVAD: central vascular access device; CI: confidence interval; IR: incidence rate; NTCVAD: non-tunnelled central venous access device; PICC: peripherally inserted central catheter; HD: haemodialysis catheter; Heterogeneity of studies: ^a cannot be calculated, ^blow (<25%), ^c moderate (25%-75%), or ^d high (>75%). Effect-size test: ^e significant or ^f nonsignificant.

Test for heterogeneity between subgroups: ^g significant or ^h nonsignificant.

No HD studies for CLABSI, occlusion/blockage, dislodgement/migration, and local infection/phlebitis outcomes. No PICC studies for dislodgement/migration outcome.