National Institute for Health and Care Excellence

# Suspected sepsis: recognition, diagnosis and early management

## [H] Evidence review for safety of peripheral administration of vasopressor

NICE guideline NG253

Evidence reviews underpinning recommendations 1.8.11 to 1.8.13 and research recommendation 5 in the NICE guideline

November 2025

Guideline version (Final)

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# Contents

# 1 Safety of peripheral administration of vasopressor

## 1.1 Review question

In people aged 16 or over with suspected sepsis, how safe is the peripheral administration of intravenous vasopressors compared to central line administration?

### 1.1.1 Introduction

Vasopressors have usually been administered via central venous access. In some areas clinical practice has started to move towards the consideration of vasopressors administration via a peripheral route where it is clinically needed, and a central line has not yet been inserted or is not available. This review explores safety outcomes when administering vasopressors peripherally in those with hypotension or experiencing shock.

### 1.1.2 Summary of the protocol

**Table 1: PICOS inclusion criteria**

| | |
|---|---|
| Population | Adults aged 16 or over who require vasoactive medication for treatment of hypotension or shock |
| Interventions | Any vasopressor delivered via peripheral venous access |
| Comparator | Any vasopressor delivered via central venous access |
| Outcomes | • Blood stream infection (dichotomous)<br>• Extravasation (dichotomous)<br>• Phlebitis (dichotomous)<br>• Bleeding (dichotomous)<br>• Occlusion (dichotomous)<br>• Mortality related to adverse events due to method vasopressor administration at 30 days (dichotomous)<br>• Serious adverse events (dichotomous) |

| | |
|---|---|
| | • Extravasation management beyond removal of cannula (dichotomous) |
| Study type | • Systematic reviews of RCTs and cohort studies<br>• RCTs<br>• Cohort studies (considered if less than 3 RCTs are found at low risk of bias, or 5 at moderate or better risk of bias) |

For the full protocol see appendix A.

### 1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

#### 1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 30 10 2024. The following databases were searched: MEDLINE (Ovid), Embase (Ovid), the Cochrane Central Register of Controlled Trials (Wiley), the Cochrane Database of Systematic Reviews (Wiley), and Epistemonikos. Full search strategies for each database are provided in Appendix B.

The searches for the cost effectiveness evidence were run on 5th November 2024. The following databases were searched: MEDLINE (Ovid), Embase (Ovid), the EconLit (Ovid), and the International HTA database (INAHTA). The validated NICE Cost Utility Filter was used on MEDLINE and Embase.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement. Further details and full search strategies for each database are provided in Appendix B.

### 1.1.4 Safety evidence

#### 1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 2751 references including 1 reference added from a separate source (see appendix B for the literature search strategy).

These 2751 references were screened at title and abstract level against the review protocol, with 2727 excluded at this level. 10% of references were screened separately by two reviewers with 98% agreement. Discrepancies were resolved by discussion.

The full texts of 24 systematic reviews, RCTs and cohort studies were ordered for closer inspection. 5 cohort studies and 1 RCT met the criteria specified in the review protocol (appendix A). For a summary of the 6 included studies see table 2.

The safety evidence study selection is presented as a PRISMA diagram in appendix C.

See section 1.1.13 References – included studies for the full references of the included studies.

#### 1.1.4.2 Excluded studies

Details of studies excluded at full text, along with reasons for exclusion are given in appendix H.

### 1.1.5 Summary of studies included in the safety evidence

### Table 2 Summary of studies included in the effectiveness evidence

| Study details | Setting/Location/ | Population | Intervention | Comparison | Outcomes | Risk of bias |
|---|---|---|---|---|---|---|
| Ricard 2013<br><br>Design: RCT<br><br>n=266 | Setting: ICU<br>Location: France | Adult ICU patients with equal central or peripheral venous access requirement. | Peripheral venous catheters (PVC) as initial venous access for any of the following:<br>• Thiopentotal,<br>• Epinephrine<br>• Norepinephrine<br>• Dopamine Dobutamine<br>• Amiodarone<br>• Vancomycin<br>• Amphotericin B<br><br>70% of patients required a vasopressor | Central venous catheters (CVC) as initial access for any of the following:<br>• Thiopentotal,<br>• Epinephrine<br>• Norepinephrine<br>• Dopamine Dobutamine<br>• Amiodarone<br>• Vancomycin<br>• Amphotericin B<br><br>70% of patients required a vasopressor | Primary outcomes: major catheter-related adverse events. Relevant for this review:<br>• Subcutaneous diffusion<br>• Phlebitis<br>• Catheter related bacteremia<br><br>Secondary outcomes:<br>• minor complications,<br>• amount of medical and paramedical time used<br>• mortality. | Moderate |
| Delaney 2020<br><br>Design: Retrospective Cohort (RCT post-hoc analysis)<br><br>n=937 | Setting: Hospital emergency department and intensive care unit<br><br>Location: Australia | Patients with early septic shock presenting to the Emergency<br>Department (ED) | Initiation of vasopressors via a peripheral venous catheter (PVC) | initiation of vasopressors via a central venous catheter (CVC) | Mortality<br>Blood stream infection<br>Bleeding<br>Catheter related SAE (serious adverse event) – necrosis | High |

| Study details | Setting/Location/ | Population | Intervention | Comparison | Outcomes | Risk of bias |
|---|---|---|---|---|---|---|
| Kilian 2022<br><br>Design: Retrospective Cohort<br><br>n=69 | Setting: Emergency department<br>Location: USA | Patients with Septic shock >18 years | Vasopressor by peripheral venous catheter | Vasopressor by central venous catheter | Mortality<br>Extravasation<br>Occlusion<br>Catheter related SAE-digital ischaemia | High |
| Munroe 2024<br><br>Design: Retrospective Cohort<br><br>n= 554 | Setting: Hospital<br><br>Location: USA | Community acquired sepsis >18 years<br><br>>99% of patients were admitted from the ED | Initial vasopressor via peripheral IV line | Initial vasopressor via central line | Mortality<br>Catheter related SAE-necrosis | High |
| Asher 2023<br><br>Design: Prospective cohort<br><br>n=139 | Setting: Intensive cardiovascular care unit (ICU)<br><br>Location: Israel | ≥18 years old and presented with hemodynamic<br>shock requiring vasopressor administration (86% cardiogenic shock, 8% septic shock) | Vasopressor by peripheral venous catheter | Vasopressor via central venous catheter | Mortality<br>Extravasation<br>Blood stream infection<br>Phlebitis<br>Bleeding<br>Catheter related SAE-necrosis | High |

| Study details | Setting/Location/ | Population | Intervention | Comparison | Outcomes | Risk of bias |
|---|---|---|---|---|---|---|
| Stolz 2022<br><br>Design: Retrospective cohort<br><br>n= 212 | Setting: ICU<br><br>Location: Australia | Critically ill patients who received vasopressors via a CVC and/or PIVC in an adult, mixed medical-surgical general intensive care unit | Vasopressor by peripheral insertion only<br><br>Vasopressor by peripheral the central | Vasopressor by central access only | Mortality<br>Extravasation<br>Blood stream infection<br>Catheter related SAE-necrosis | High |

RCT = Randomised control trial
ICU = Intensive care unit
PVC = Peripheral venous catheters
PIVC = Peripheral intravenous catheter
CVC = Central venous catheters
SAE = Serious adverse events

See appendix D for full evidence tables

### 1.1.6 Summary of the safety evidence

**Interpreting the effectiveness evidence**

For mortality outcomes the line of no effect (represented by 1.0 as mortality is a dichotomous outcomes) was used as a clinical decision threshold. The following criteria were used to interpret the effect (column of 'Interpretation of effect' below) in the summary GRADE tables with results divided into 2 groups as follows:

- The evidence showed that there is an effect if the 95% CI does not cross the line of no effect. Where there is an effect, we have stated the direction of the effect.

- The evidence could not differentiate between comparators if the 95% CI crosses the line of no effect. Where this is the case we have stated 'could not differentiate'.

Where default MIDs have been used (0.8 and 1.25) the following criteria were used to interpret the effect (column of 'Interpretation of effect' below) in the summary GRADE tables. The results were divided into 4 groups as follows:

- Where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), and the magnitude of that effect is most likely to meet or exceed the MID (i.e. the point estimate is not in the zone of equivalence). In such cases, we state that the evidence showed that there is an effect. (Where there is an effect, we will state the direction of the effect.)

- Where the data are only consistent, at a 95% confidence level, with an effect in one direction (i.e. one that is 'statistically significant'), but the magnitude of that effect is most likely to be less than the MID (i.e. the point estimate is in the zone of equivalence). In such cases, we state that the evidence showed there is an effect, but it is less than the defined MID.

- Situations where the confidence limits are smaller than the MIDs in both directions. In such cases, we state that the evidence demonstrates that there is no meaningful difference.

In all other cases, we state that the evidence could not differentiate between the comparator

**Table 3: PVC compared to CVC for vasopressor initiation in patients with sepsis – RCT evidence**

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Interpretation of effect | Certainty |
|---|---|---|---|---|---|---|---|
| **Blood stream infection (BSI) - catheter related** | | | | | | | |
| 1 | RCT | 0/128 (0.0%) | 1/137 (0.7%) | **RR 0.36** (0.01 to 8.67) | **5 fewer per 1000** (from 7 fewer to 56 more) | Could not differentiate | ⊕◯◯◯ Very low[1,2,3] |
| **Extravasation** | | | | | | | |
| 1 | RCT | 19/128 (14.8%) | 2/137 (1.5%) | **RR 10.17** (2.42 to 42.79) | **134 more per 1000** (from 21 more to 610 more). | Effect - Risk of extravasation was significantly higher for PVC compared to CVC | ⊕◯◯◯ Very low[1,2,4] |
| **Phlebitis** | | | | | | | |
| 1 | RCT | 1/128 (0.8%) | 1/137 (0.7%) | **RR 1.07** (0.07 to 16.93) | **1 more per 1000** (from 7 fewer to 116 more) | Could not differentiate | ⊕◯◯◯ Very low[1,2,3] |
| **Survival at 28 days** | | | | | | | |
| 1 | RCT | Not reported | Not reported | **HR 1.3 (0.84 to 2.01) for CVC vs PVC** | | Could not differentiate | ⊕◯◯◯ Very low[2,4] |

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Interpretation of effect | Certainty |
|---|---|---|---|---|---|---|---|
| 1. Some bias concerns, particularly because outcomes assessors were aware which patients were allocated.<br>2. Patients were selected either because they needed a vasopressor or another venotoxic drug, or an issue with PVC (either failed to insert twice or had problems with maintenance). Only 70% received vasopressors. ICU patients, not limited to sepsis patients. Unclear how many had sepsis.<br>3. Downgraded twice for imprecision as confidence interval crosses lower (0.80) and upper (1.25) default minimum important difference threshold.<br>4. Downgraded for imprecision due to very wide confidence intervals.<br><br>PVC = Peripheral venous catheter;<br>CVC = Central venous catheter | | | | | | | |

**Table 4: PVC compared to CVC for vasopressor initiation in patients with sepsis – cohort study evidence**

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator – CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Interpretation of effect | Certainty |
|---|---|---|---|---|---|---|---|
| **Blood stream infection (catheter related)** | | | | | | | |
| 3 | non-randomised studies | 3/652 (0.5%) | 2/597 (0.3%) | RR 0.49 (0.09 to 2.54) | 2 fewer per 1000 (from 3 fewer to 5 more) | Could not differentiate | ⊕◯◯◯ Very low [1,2,3] |
| **Extravasation** | | | | | | | |
| 2 | non-randomised studies | 17/263 (6.5%) | 3/49 (6.1%) | RR 0.73 (0.22 to 2.45) | 12 fewer per 1000 (from 35 fewer to 66 more) | Could not differentiate | ⊕◯◯◯ Very low [1,2,3] |
| **Phlebitis** | | | | | | | |
| 1 | non-randomised studies | 6/108 (5.6%) | 1/31 (3.2%) | RR 1.72 (0.22 to 13.77) | 23 more per 1000 (from 25 fewer to 412 more) | Could not differentiate | ⊕◯◯◯ Very low [1,2,3] |

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator – CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Interpretation of effect | Certainty |
|---|---|---|---|---|---|---|---|
| **Bleeding (catheter related)** | | | | | | | |
| 2 | non-randomised studies | 0/497 (0.0%) | 4/579 (0.7%) | RR 0.16 (0.02 to 1.38) | 6 fewer per 1000 (from 7 fewer to 3 more) | Could not differentiate | ⊕◯◯◯ Very low [1,2,3] |
| **Occlusion** | | | | | | | |
| 1 | non-randomised studies | 0/34 (0%) | 0/17 (0%) | Not estimable | **0 fewer per 1000** | No events were reported | ⊕◯◯◯ Very low[1,2,4] |
| **Mortality (all cause)** | | | | | | | |
| 5 | non-randomised studies | 311/1086 (28.6%) | 179/768 (23.3%) | RR 0.87 (0.54 to 1.42) | 30 fewer per 1000 (from 107 fewer to 98 more) | Could not differentiate | ⊕◯◯◯ Very low [2,3,5,6,7] |

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator – CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Interpretation of effect | Certainty |
|---|---|---|---|---|---|---|---|
| **Catheter related serious adverse event - skin necrosis** | | | | | | | |
| 5 | non-randomised studies | 0/1086 (0.0%) | 0/767 (0.0%) | Not estimable | **0 fewer per 1000** | No events were reported | ⊕◯◯◯ Very low[1,2,4] |

1. All studies are at high risk of bias in more than one domain. There were no adjustments for possible confounding factors.
2. Downgraded for serious indirectness. Patients in Kilian 2022 and Delaney 2020 initiated vasopressors in the ED, while Munroe 2024 included hospitalised patients and nearly all of them were admitted from the ED. The other studies-initiated vasopressors in the ICU. Downgraded if studies with vasopressor initiated in ED or usual ward setting contributed to less than 50% weight of data analysed.
3. Downgraded for serious imprecision due to very wide confidence intervals, and optimal information size (OIS) not met due to the low event rates.
4. No events were reported.
5. All studies at high risk of bias in more than one domain. Only one study reported adjusted mortality rate.
6. Most studies reported mortality at 28 or 30 days. None reported mortality attributable to adverse events or route of vasopressor management.
7. Downgraded for inconsistency as heterogeneity is high (I2 >50%).

PVC = Peripheral venous catheter;
CVC = Central venous catheter

See appendix F for full GRADE tables.

### 1.1.7 Economic evidence

A search was performed to identify published economic evaluations of relevance for this review question (See Appendix B – Literature search strategies). The search returned 523 studies, of which 523 could be excluded at title and abstract.

#### 1.1.7.1 Included studies

No economic evidence was included for this review question. See Appendix G – Economic evidence study selection.

#### 1.1.7.2 Excluded studies

All studies were excluded at the title and abstract stage.

### 1.1.8 Summary of included economic evidence

No relevant economic evidence was identified for this review question.

### 1.1.9 Economic model

This review question was not prioritised for economic modelling.

### 1.1.10 Unit costs

It is anticipated that a peripheral line may be administered by a health care assistant or a nurse depending on the setting. A more senior health care professional is required to administer a central line, which in some practices may be a junior doctor or a registrar in some centres up to a consultant in others. These costs are provided in Table .

**Table 5: Staff costs (per working hour including qualifications)**

| Resource | Unit costs | Source |
|---|---|---|
| Health care assistant (band 4) | £40 | PSSRU 2024 |
| Nurse (Band 5) | £48 | PSSRU 2024 |
| Nurse (Band 6) | £58 | PSSRU 2024 |
| Junior doctor (FY1) | £44 | PSSRU 2024 |
| Junior doctor (FY2) | £50 | PSSRU 2024 |
| Registrar | £72 | PSSRU 2024 |
| Consultant (medical) | £143 | PSSRU 2024 |

### 1.1.11 The committee's discussion and interpretation of the evidence

#### 1.1.11.1. The outcomes that matter most

The committee agreed that a reduction in all-cause mortality was the primary outcome when considering someone's initial resuscitation. When considering whether peripheral access could be used for the administration of vasopressors in patients with suspected sepsis, adverse events due to the choice of venous access is critical. This includes serious adverse events related to the method of administration such as catheter related blood stream infection, extravasation, phlebitis, bleeding, occlusion of the line and mortality at 30 days.

#### 1.1.11.2 The certainty of the evidence

The committee agreed that the certainty of the evidence for method of vasopressor administration was very low, both from the single RCT found and the pooling of results from 5 cohort studies. The evidence from the RCT was downgraded due to risk of bias and indirectness due to some concerns regarding blinding; and only 70% of participants receiving a vasopressor. In line with the protocol the study was not limited to patients with sepsis, and did not report what percentage of patients had suspected sepsis, so outcomes from this study were downgraded for indirectness in GRADE.

For the evidence from cohort studies, there was very serious risk of bias from the studies (risk of bias in patient selection and treatment allocation i.e. choice of treatment received dependent on patients initial condition, confounding bias, i.e. no adjustments of baseline imbalances, majority of patients in all studies subsequently had vasopressor administered through the CVC), indirectness (most studies carried out in the ICU, or moved patients to the ICU soon after the initiation) and imprecision (wide confidence intervals of pooled effect estimates due to relatively small sample sizes compared and low event rates).

The committee discussed the difficulties with the interpretation of the evidence as some important information affecting the risk of adverse effects and outcomes when using vasopressors peripherally were missing or not clearly reported. These outcomes included dose and rate of administration which may impact the risk and severity of adverse effects; and length of catheter remaining in place which may impact the risk of infection.

#### 1.1.11.3 Benefits and harms

When discussing the benefits and harms of administering vasopressors peripherally compared with centrally, the committee discussed the potential benefit of peripheral administration allowing vasopressors to be initiated as soon as it is required, rather than potentially being delayed due to a lack of central access. The committee also discussed that there is a potential benefit of avoiding the insertion of a CVC, as this is not a risk-free procedure, in patients who can be successfully managed with peripheral lines.

The committee discussed the risk of adverse events associated with vasopressors administered peripherally such as extravasation, phlebitis and occlusion of the line. They agreed the importance of ensuring that peripheral lines used for vasopressor administration are in sight and are monitored regularly. There is a risk of serious adverse effects such as necrosis or digital ischaemia if extravasation is not detected and addressed quickly.

#### 1.1.11.4 Cost effectiveness and resource use

No published economic evidence was available for the committee to review. The committee considered whether the recommendations could lead to resource implications. The committee considered whether there would be staffing cost differences between administering vasopressors using peripheral access as an alternative to central access. The committee agreed there would be a slight reduction in staffing costs by administering treatment using peripheral access compared to centrally because a more junior staff member can insert a peripheral venous cannula

(PVC) line and a peripheral line takes slightly less time to insert (roughly 5-10 minutes time saving). However, it was acknowledged there is considerable variation in practice as to the actual grade of staff who would be expected to deliver each method of administration. It is expected that a PVC line could be administered by either a health care assistant or a nurse (band 3-5) depending on the setting and a central line may be inserted by a junior doctor in some settings and a consultant in others.

When considering the economic implications, it is important to also consider the differences in outcomes associated with administering vasopressors either centrally or peripherally. The one randomised controlled trial which was not restricted to a population with sepsis and included other treatment options, found higher extravasation in the peripherally administered group. From the five cohort studies for either sepsis or sepsis shock no significant differences were identified for the adverse events of blood stream infection, extravasation, phlebitis, bleeding or short-term mortality. The committee discussed that treating extravasation would mostly involve removing the line, elevating the limb and considering the application of topical vasoactive agent and to administer analgesia if required based on guidance by the intensive care society (2022). Very rarely in the most severe cases there may be a need for plastic surgery to open up the skin. The committee considered this to be a very rare event and no evidence was identified for this event in the included studies.

The committee agreed that it is important not to delay the administration of vasopressors. Allowing the use of PVC when a high dependency ward is unavailable may allow for a more rapid administration. This could avoid more serious and costly consequences caused by a delay in treatment, providing the risk factors of complications (discussed in the certainty of the evidence section above) are appropriately managed.

Overall, the committee did not anticipate there to be resource implications associated with the recommendations.

#### 1.1.11.5 Other factors the committee took into account

The committee noted that the decision to initiate vasopressors should take into account the patient's overall condition and involve discussions with the patient's family members (or carers), taking into account of any possible prior wishes (such as end of life decisions), and any specialist teams currently treating the patient.

The committee acknowledged that there are other important clinical considerations which could affect the safety and effectiveness of vasopressors in patients with suspected sepsis. This includes choice of vasopressor, maximum or optimal dose that can be administered safely peripherally, appropriate monitoring strategy and other protocols related to the use of a peripheral cannula such as the length of time cannula should be left in place. The committee noted the importance of discussion with the critical care team when decisions about vasopressor initiation and possible peripheral administration are being made. Local policies could take into consideration the local resourcing situations and should be used to support the safe and effective use of peripheral vasopressor administration in patients with suspected sepsis.

The committee made a research recommendation to compare the safety and efficacy of peripheral vs centrally administered vasopressors in patients with moderate to high risk of severe illness or death based on NEWS2 score to address the gap of evidence (see Appendix I).

The committee had also noted ongoing research supported by the National Institute for Health and Care Research (NIHR) on the timing of initiation of vasopressors, the EVIS (Early Vasopressors in Sepsis) study, therefore they did not include this area in the research recommendation. Recommendations supported by this evidence review

This evidence review supports 1.8.11 to 1.8.13 in the NICE guideline and the research recommendation 5 on vasopressors. Other evidence supporting these recommendations can be found in the evidence review G: Intravenous fluids for resuscitation.

### 1.1.13 References – included studies

#### 1.1.13.1 Safety evidence

Asher, Elad, Karameh, Hani, Nassar, Hamed et al. (2023) Safety and Outcomes of Peripherally Administered Vasopressor Infusion in Patients Admitted with Shock to an Intensive Cardiac Care Unit-A Single-Center Prospective Study. Journal of clinical medicine 12(17)

Delaney, Anthony, Finnis, Mark, Bellomo, Rinaldo et al. (2020) Initiation of vasopressor infusions via peripheral versus central access in patients with early septic shock: A retrospective cohort study. Emergency medicine Australasia : EMA 32(2): 210-219

Kilian, Scott, Surrey, Aaron, McCarron, Weston et al. (2022) Vasopressor Administration via Peripheral Intravenous Access for Emergency Department Stabilization in Septic Shock Patients. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine 26(7): 811-815

Munroe, Elizabeth S, Heath, Megan E, Eteer, Mousab et al. (2024) Use and Outcomes of Peripheral Vasopressors in Early Sepsis-Induced Hypotension Across Michigan Hospitals: A Retrospective Cohort Study. Chest 165(4): 847-857

Ricard JD, Salomon L, Boyer A, Thiery G, Meybeck A, Roy C, Pasquet B, Le Mière E Dreyfuss, D. (2013) Central or peripheral catheters for initial venous access of ICU patients: a randomized controlled trial. Crit Care Med. 2013 Sep;41(9):2108-15.

Stolz, Annaliese, Efendy, Rachel, Apte, Yogesh et al. (2022) Safety and efficacy of peripheral versus centrally administered vasopressor infusion: A single-centre retrospective observational study. Australian critical care : official journal of the Confederation of Australian Critical Care Nurses 35(5): 506-511

#### 1.1.13.2 Economic

No economic studies were included for this review question.

### 1.1.14 References – other

Jones, Karen C. and Weatherly, Helen and Birch, Sarah and Castelli, Adriana and Chalkley, Martin and Dargan, Alan and Forder, Julien E. and Gao, Minyue and Hinde, Seb and Markham, Sarah and Premji, Shainur and Findlay, D. and Teo, H. (2024) Unit Costs of Health and Social Care 2023 Manual. Technical report. Personal Social Services Research Unit (University of Kent) & Centre for Health Economics (University of York), Kent, UK 10.22024/UniKent/01.02.105685.

Intensive care society (2022) Guidance for: The use of vasopressor agents by peripheral intravenous infusion in adult critical care patients

# Appendices

## Appendix A – Review protocols

**Review protocol for safety of peripherally administration of vasopressor**

| ID | Field | Content |
|---|---|---|
| 1. | Review title | Safety of peripheral administration of vasopressor in people aged 16 or over with suspected sepsis. |
| 2. | Review question | In people aged 16 or over with suspected sepsis, how safe is the peripheral administration of intravenous vasopressors compared to central line administration? |
| 3. | Objective | To determine the safety of peripheral administration of vasopressor in people aged 16 or over with suspected sepsis. |
| 4. | Searches | The following databases will be searched:<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase<br>• Epistemonikos<br>• MEDLINE<br>Searches will be restricted by:<br>• Studies published after 2010<br>• English Language<br>• Human studies<br>• Conference abstracts excluded<br>• OECD countries<br><br>The full search strategies will be reported in the final review in accordance with the PRISMA-S reporting guide. |
| 5. | Condition or domain being studied | Suspected sepsis |
| 6. | Population | Inclusion:<br>• Adults aged 16 or over who require vasoactive medication for treatment of hypotension or shock<br>Exclusion: |

| | | |
|---|---|---|
| | | • People who are or have recently been pregnant**<br>**Someone is considered to have recently been pregnant:<br>• in the 24 hours following a termination of pregnancy or miscarriage<br>• for 4 weeks after giving birth. |
| 7. | Intervention | • Any vasopressor delivered via peripheral venous access |
| 8. | Comparator | • Any vasopressor delivered via central venous access |
| 9. | Types of study to be included | • Systematic reviews of RCTs and cohort studies<br>• RCTs<br>• Cohort studies (considered if less than 3 RCTs are found at low risk of bias, or 5 at moderate or better risk of bias) |
| 10. | Other exclusion criteria | • Conference abstracts, editorials/letters<br>• Dissertations and theses<br>• Studies not published in English<br>• Pre-prints.<br>• Studies reporting data without confidence intervals or data that cannot be used to calculate confidence intervals. |
| 11. | Context | During the previous update to the Sepsis guideline published in January 2024, the guideline committee highlighted that clinical practice has moved to start vasopressors sooner or even concurrently with IV fluids, particularly in patients who are very hypotensive, as this can prevent people being given too much fluid which may worsen outcomes. Furthermore, they highlighted that a senior clinical decision maker should be able to start vasopressors using peripheral venous access without having to wait for a critical care clinician to undertake central line placement. This review explores safety outcomes when administering vasopressors peripherally in those with hypotension or experiencing shock. This review has not restricted searches to populations with suspected sepsis only as initial searches have indicated that there is limited evidence in this population; and given the changes in clinical practice regarding the use of vasopressors understanding the safety of |

| | | |
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| | | peripheral administration of vasopressor in any populations was consider useful in understanding the safety of vasopressors in populations with suspected sepsis. It is acknowledged that if a central line is available it is most likely that it will always be used and this review is focused on where there is no central access and comparative safety of utilising a peripheral line versus a central line. |
| 12. | Primary outcomes (critical outcomes) | • Blood stream infection (dichotomous)*<br>• Extravasation (dichotomous)*<br>• Phlebitis (dichotomous)*<br>• Bleeding (dichotomous)*<br>• Occlusion (dichotomous)*<br>• Mortality related to adverse events due to method vasopressor administration at 30 days (dichotomous)<br>• Serious adverse events (dichotomous)*<br>• Extravasation management beyond removal of cannula (dichotomous)*<br><br>*Where multiple time points are reported, data will be extracted for the longest time point (or up to 7 days post treatment) only." |
| 13. | Secondary outcomes (important outcomes) | None |
| 14. | Data extraction (selection and coding) | All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.<br>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.2). Study investigators may be contacted for missing data where time and resources allow.<br>Where appropriate, this review will make use of the priority screening functionality within the EPPI-reviewer software. At least 50% of the data set will |

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| | | be screened and we will stop screening after that if we screen more than 250 records without an include |
| 15. | Risk of bias (quality) assessment | Risk of bias will be assessed:<br>• Systematic reviews of RCTs and cohort studies: Risk of Bias in Systematic reviews (ROBIS)<br>• Randomised controlled trials: Cochrane risk of bias (ROB) 2 tool<br>• Cohort studies: Cochrane ROBINS-I . |
| 16. | Strategy for data synthesis | Where possible, meta-analyses will be conducted to combine the results of quantitative studies for each outcome. RCT and non-randomised comparative studies data will be pooled separately.<br><br>**Approach to meta-analysis**<br><br>Pairwise meta-analyses will be performed in Cochrane RevMan Web. A pooled relative risk will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event.<br>A pooled mean difference will be calculated for continuous outcomes (using the inverse variance method) when the same scale will be used to measure an outcome across different studies.<br>Where different studies presented continuous data measuring the same outcome but using different numerical scales these outcomes will be all converted to the same scale before meta-analysis is conducted on the mean differences. Where outcomes measured the same underlying construct but used different instruments/metrics, data will be analysed using standardised mean differences (SMDs, Hedges' g).<br>Fixed effects models will be fitted unless there is significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$, when random effects models will be used instead.<br>Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically assess the potential for publication bias.<br>**Approach to GRADE** |

<table>
<tr><td></td><td></td><td colspan="3">GRADE will be used to assess the quality of any pair-wise analysis of outcomes. Data from randomised controlled trials and non-randomised comparative studies will be initially rated as high quality where they come from:<ul><li>RCTs and systematic reviews of RCTs (where individual studies have been quality assessed using Cochrane risk of bias.</li><li>non-randomised comparative studies and systematic reviews of non-randomised studies (where individual studies have been quality assessed using the ROBINS-I assessment tool)</li></ul>The quality of the evidence for each outcome will then be downgraded or not from this starting point based on the other GRADE domains.<br>To assess imprecision, where there are no defined MIDs we will set the MID as the line of no effect for all outcomes (1.0 for dichotomous outcomes and 0 for continuous outcomes). A second decision threshold will be applied where the sample size is sufficiently small that it is not plausible any realistic effect size could have been detected.</td></tr>
<tr><td>17.</td><td>Analysis of sub-groups</td><td colspan="3">None</td></tr>
<tr><td>18.</td><td>Type and method of review</td><td colspan="3">☐ Intervention<br>☐ Diagnostic<br>☐ Prognostic<br>☐ Qualitative<br>☐ Epidemiologic<br>☐ Service Delivery<br>☒ Other: Safety</td></tr>
<tr><td>19.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>20.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>21.</td><td>Anticipated or actual start date</td><td colspan="3">October 2024</td></tr>
<tr><td>22.</td><td>Anticipated completion date</td><td colspan="3">tbc</td></tr>
<tr><td rowspan="2">23.</td><td rowspan="2">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☐</td><td>☐</td></tr>
</table>

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| | | Piloting of the study selection process | ☐ | ☐ |
| | | Formal screening of search results against eligibility criteria | ☐ | ☐ |
| | | Data extraction | ☐ | ☐ |
| | | Risk of bias (quality) assessment | ☐ | ☐ |
| | | Data analysis | ☐ | ☐ |
| 24. | Named contact | **5a. Named contact**<br>sepsisupdate@nice.org.uk<br><br>**5b Named contact e-mail**<br>sepsisupdate@nice.org.uk<br><br>**5e Organisational affiliation of the review**<br>National Institute for Health and Care Excellence (NICE) and Guideline Development Team B | | |
| 25. | Review team members | From the Centre for Guidelines:<br><br>• Guideline lead: Robby Richey<br>• Technical analyst: Anthony Gildea<br>• Technical analyst: Lee-Yee Chong<br>• Senior technical analyst: James Jagroo<br>• Health Economist: Lindsay Claxton<br>• Health Economist: Kirsty Luckham<br>• Senior Information specialist: Lynda Ayiku | | |
| 26. | Funding sources/sponsor | This systematic review is being completed by the centre for guidelines which receives funding from NICE. | | |
| 27. | Conflicts of interest | All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing | | |

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| | | with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline. |
| 28. | Collaborators | Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: tbc |
| 29. | Other registration details | N/A |
| 30. | Reference/URL for published protocol | tbc |
| 31. | Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. |
| 32. | Keywords | Sepsis, vasopressors, safety, blood stream infection, extravasation |
| 33. | Details of existing review of same topic by same authors | This is a new review question that will update Sepsis: recognition, diagnosis and early management NG51 |
| 34. | Current review status | ☒ Ongoing<br>☐ Completed but not published |

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| | | ☐ Completed and published<br>☐ Completed, published and being updated<br>☐ Discontinued |
| 35. | Additional information | N/A |
| 36. | Details of final publication | www.nice.org.uk |

# Appendix B – Literature search strategies

### Background and development

### Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches for the evidence review.

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

The MEDLINE strategies below were quality assured (QA) by a trained NICE SIS. All translated search strategies were peer reviewed by another SIS to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

### Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

### Prior work

The search terms for the sepsis population from '(A) Evidence reviews for stratifying risk of severe illness or death from sepsis' in NG51 (Jan 2024) were used to inform the population terms for the search strategy.

### Search limits and other restrictions

#### Formats

Limits were applied in adherence to standard NICE practice (as set out in the Identifying the evidence chapter of the manual) and the eligibility criteria listed in the review protocol to exclude:

- Animal studies
- Editorials, letters, news items and commentaries
- Conference abstracts and posters
- Registry entries for ongoing clinical trials or those that contain no results
- Papers not published in the English language.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:
Dickersin K, Scherer R & Lefebvre C. (1994) Systematic reviews: identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

**Date limits**
A date limit of 2010 to 2024 was applied, as stated in the review protocol.

**Search filters and classifiers**

**Effectiveness searches**
Systematic reviews filters:
Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. BMC Medical Research Methodology, 12(1), 51.

- In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.
- In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

Cohort studies terms:
Terms for cohort studies were used from the observational studies filters. The terms used for observational studies are standard NICE practice that have been developed in house.

Randomised controlled trials filters:
The MEDLINE RCT filter was McMaster Therapy – Medline - "best balance of sensitivity and specificity" version.
The standard NICE modifications were used: the MeSH heading *randomized controlled trial/*, which is equivalent *to randomized controlled trial.pt* was exploded to capture newer, narrower *terms equivalence trial/ and pragmatic clinical trial*. The free-text term *randomized.mp* was also changed to the (more inclusive) alternative *randomi?ed.mp.* to capture both UK and US spellings.
Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. *BMJ*, 330, 1179-1183.
The Embase RCT filter was McMaster Therapy – Embase "best balance of sensitivity and specificity" version.
Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *Journal of the Medical Library Association*, 94(1), 41-47.

OECD countries geographic search filters:
The OECD countries filters were used without modification: Ayiku, L., Hudson, T., Williams, C., Levay, P., & Jacob, C. (2021). The NICE OECD countries' geographic

search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association*, 109(4), 583–589.

**Cost effectiveness searches**

In line with the review protocol, the sensitive version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.
Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.
The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:
Glanville J et al. (2009) Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)
Note: Several modifications have been made to these filters over the years that are standard NICE practice.

**Effectiveness/Qualitative/Clinical/Public health/Social care searches**
**Database results**

| Databases | Date searched | Database platform | Database segment or version | No. of results downloaded |
|---|---|---|---|---|
| Cochrane Database of Systematic Reviews (CDSR) | 30th October 2024 | Wiley | Issue 10 of 12, October 2024 | 0 |
| CENTRAL | 30th October 2024 | Wiley | Issue 10 of 12, October 2024 | 873 |
| Embase | 30th October 2024 | Ovid | Embase <1974 to 2024 October 29> | 2019 |
| Epistemonikos | 30th October 2024 | Epistemonikos | Searched 30th October 2024 | 370 |
| MEDLINE ALL | 30th October 2024 | Ovid | Ovid MEDLINE(R) ALL <1946 to October 29, 2024> | 1350 |

**Search strategy history**

**Database name: MEDLINE ALL**

| **Searches** |
| --- |
| Database: Ovid MEDLINE(R) ALL <1946 to October 29, 2024><br>Search Strategy:<br>---<br>1 exp Catheterization, Peripheral/ (13761)<br>2 (peripher* or picc or piccs or piv or pivs).tw. (712715)<br>3 1 or 2 (722580)<br>4 exp Vasoconstrictor Agents/ (271207)<br>5 Receptors, Vasopressin/ (3660)<br>6 exp Antidiuretic Agents/ (37165)<br>7 (vasoconstric* or vaso-constric* or vessel* constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* antagonist* or hypertensiv* or antihypot* or anti-hypot*).tw. (267531)<br>8 (norepinephrin* or noradrenaline* or sinora*).tw. (97946)<br>9 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*).tw. (57248)<br>10 metaramin*.tw. (565)<br>11 phenylephrin*.tw. (19981)<br>12 ephedrine*.tw. (4463)<br>13 argipressin*.tw. (22)<br>14 (terlipress* or glypress*).tw. (1096)<br>15 angiotens*.tw. (128730)<br>16 or/4-15 (614336)<br>17 3 and 16 (28522)<br>18 exp Randomized Controlled Trial/ (626300)<br>19 randomi?ed.mp. (1149606)<br>20 placebo.mp. (261479)<br>21 or/18-20 (1218265)<br>22 17 and 21 (2095)<br>23 (MEDLINE or pubmed).tw. (380696)<br>24 systematic review.tw. (321753)<br>25 systematic review.pt. (277516)<br>26 meta-analysis.pt. (211004)<br>27 intervention$.ti. (223239)<br>28 or/23-27 (784774)<br>29 17 and 28 (314)<br>30 exp *Cohort Studies/ (4805)<br>31 (cohort adj (study or studies)).tw. (370885)<br>32 cohort analy$.tw. (13814)<br>33 (follow up adj (study or studies)).tw. (59159) |

| Searches |
| --- |
| 34 longitudinal.tw. (358424)<br>35 prospective.tw. (779784)<br>36 retrospective.tw. (850566)<br>37 or/30-36 (2036564)<br>38 17 and 37 (1181)<br>39 22 or 29 or 38 (3224)<br>40 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1379258)<br>41 "organisation for economic co-operation and development"/ (634)<br>42 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ |

| Searches |
| --- |
| or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3606459)<br>43 european union/ (18239)<br>44 developed countries/ (21655)<br>45 or/41-44 (3623041)<br>46 40 not 45 (1287342)<br>47 39 not 46 (3159)<br>48 limit 47 to english language (2986)<br>49 animals/ not humans/ (5237764)<br>50 48 not 49 (2801)<br>51 limit 50 to yr="2010 -Current" (1350) |

**Database name: Embase**

| Searches |
| --- |
| Database: Embase <1974 to 2024 October 29><br>Search Strategy:<br>---<br>1 exp peripheral venous catheter/ (2795)<br>2 (peripher* or picc or piccs or piv or pivs).tw. (996477)<br>3 or/1-2 (997978)<br>4 exp hypertensive agent/ (234318)<br>5 exp vasoconstrictor agent/ (318149)<br>6 exp vasopressin receptor/ (6482)<br>7 exp antidiuretic agent/ (73174)<br>8 (vasoconstric* or vaso-constric* or vessel* constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* antagonist* or hypertensiv* or antihypot* or anti-hypot*).tw. (371274)<br>9 (norepinephrin* or noradrenaline* or sinora*).tw. (115367)<br>10 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*).tw. (70772)<br>11 metaramin*.tw. (589)<br>12 phenylephrine/ (40110)<br>13 phenylephrin*.tw. (25982)<br>14 ephedrine/ (15410)<br>15 ephedrine*.tw. (5672)<br>16 argipressin*.tw. (35)<br>17 (terlipress* or glypress*).tw. (2056)<br>18 angiotensin derivative/ (1368) |

| Searches |
| --- |
| 19 angiotens*.tw. (168331)<br>20 or/4-19 (843976)<br>21 3 and 20 (41183)<br>22 random:.tw. (2137713)<br>23 placebo:.mp. (548178)<br>24 double-blind:.tw. (257256)<br>25 or/22-24 (2423852)<br>26 21 and 25 (3942)<br>27 (MEDLINE or pubmed).tw. (471294)<br>28 exp systematic review/ or systematic review.tw. (586274)<br>29 meta-analysis/ (335339)<br>30 intervention$.ti. (292722)<br>31 or/27-30 (1091702)<br>32 21 and 31 (849)<br>33 *Cohort analysis/ (49815)<br>34 cohort analy$.tw. (22319)<br>35 *Longitudinal study/ (9406)<br>36 *Retrospective study/ (40711)<br>37 *Prospective study/ (44959)<br>38 (Cohort adj (study or studies)).tw. (533914)<br>39 (follow up adj (study or studies)).tw. (77622)<br>40 longitudinal.tw. (484437)<br>41 prospective.tw. (1197264)<br>42 retrospective.tw. (1407192)<br>43 or/33-42 (3123261)<br>44 21 and 43 (2708)<br>45 26 or 32 or 44 (6617)<br>46 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or |

| **Searches** |
| --- |
| libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1822220)<br>47 exp "organisation for economic co-operation and development"/ (3211)<br>48 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3942805)<br>49 european union/ (32876)<br>50 developed country/ (36524)<br>51 or/47-50 (3978273)<br>52 46 not 51 (1659918)<br>53 45 not 52 (6445)<br>54 limit 53 to english language (6130)<br>55 nonhuman/ not human/ (5557871)<br>56 54 not 55 (5712)<br>57 limit 56 to yr="2010 -Current" (3776)<br>58 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6052334)<br>59 57 not 58 (2026)<br>60 (letter or editorial).pt. (2175646)<br>61 59 not 60 (2019) |

**Database name: CENTRAL**

| Searches |
|---|
| #1 MeSH descriptor: [Catheterization, Peripheral] explode all trees 1411<br>#2 (peripher* or picc or piccs or piv or pivs):ti,ab,kw 62146<br>#3 #1 or #2 62285<br>#4 MeSH descriptor: [Vasoconstrictor Agents] explode all trees 2301<br>#5 MeSH descriptor: [Receptors, Vasopressin] this term only 45<br>#6 MeSH descriptor: [Antidiuretic Agents] this term only 93<br>#7 (vasoconstric* or vaso-constric* or vessel* NEXT constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* NEXT antagonist* or hypertensiv* or antihypot* or anti-hypot*):ti,ab,kw 37257<br>#8 (norepinephrin* or noradrenaline* or sinora*):ti,ab,kw 9607<br>#9 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*):ti,ab,kw 12014<br>#10 metaramin*:ti,ab,kw 114<br>#11 phenylephrin*:ti,ab,kw 2612<br>#12 ephedrine*:ti,ab,kw 2567<br>#13 argipressin*:ti,ab,kw 90<br>#14 (terlipress* or glypress*):ti,ab,kw 642<br>#15 angiotens*:ti,ab,kw 17114<br>#16 {or #4-#15} 68205<br>#17 #3 and #16 3939<br>#18 "conference":pt or (clinicaltrials or trialsearch):so 784063<br>#19 #17 not #18 with Publication Year from 2010 to 2024, with Cochrane Library publication date Between Jan 2010 and Oct 2024, in Trials 873 (all CENTRAL) |

**Database name: CDSR**

| Searches |
|---|
| ID Search Hits<br>#1 MeSH descriptor: [Catheterization, Peripheral] explode all trees 1411<br>#2 (peripher* or picc or piccs or piv or pivs):ti,ab,kw 62146<br>#3 #1 or #2 62285<br>#4 MeSH descriptor: [Vasoconstrictor Agents] explode all trees 2301<br>#5 MeSH descriptor: [Receptors, Vasopressin] this term only 45<br>#6 MeSH descriptor: [Antidiuretic Agents] this term only 93<br>#7 (vasoconstric* or vaso-constric* or vessel* NEXT constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or |

| Searches |
| --- |
| antidiuret* or anti-diuret* or diuret* NEXT antagonist* or hypertensiv* or antihypot* or anti-hypot*):ti,ab,kw 37257<br>#8 (norepinephrin* or noradrenaline* or sinora*):ti,ab,kw 9607<br>#9 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*):ti,ab,kw 12014<br>#10 metaramin*:ti,ab,kw 114<br>#11 phenylephrin*:ti,ab,kw 2612<br>#12 ephedrine*:ti,ab,kw 2567<br>#13 argipressin*:ti,ab,kw 90<br>#14 (terlipress* or glypress*):ti,ab,kw 642<br>#15 angiotens*:ti,ab,kw 17114<br>#16 {or #4-#15} 68205<br>#17 #3 and #16 3939<br>#18 "conference":pt or (clinicaltrials or trialsearch):so 784063<br>#19 #17 not #18 with Publication Year from 2010 to 2024, with Cochrane Library publication date Between Jan 2010 and Oct 2024, in Trials 873 (0 CDSR) |

**Database name: Epistemonikos**

| Searches |
| --- |
| peripher* or picc or piccs or piv or pivs<br>AND<br>vasoconstric* OR vaso-constric* OR vaso constrict OR vaso constrictor OR vaso constrictors OR vaso constricted OR vaso constrictive OR vaso constrictives OR (vessel* AND constric*) OR vasoactiv* OR vaso-activ* OR vaso active OR vaso actives OR pressor* OR vasopress* OR vaso-press* OR vaso pressor OR vaso pressors OR antidiuret* OR anti-diuret* OR anti diuretic OR anti diuretics OR (diuret* AND antagonist*) OR hypertensiv* OR antihypot* OR anti-hypot* OR anti hypotensive OR anti hypotensives OR norepinephrin* OR noradrenaline* OR sinora* OR epinephrin* OR racepinephrin* OR adrenaline* OR emerade* OR jext* OR metaramin* OR phenylephrin* OR ephedrine* OR argipressin* OR terlipress* OR glypress* OR angiotens* |

**Cost-effectiveness searches**
**Database results**

| Databases | Date searched | Database platform | Database segment or version | No. of results downloaded |
| --- | --- | --- | --- | --- |
| EconLit | 5th Nov 2024 | OVID | Econlit <1886 to | 0 |

| Databases | Date searched | Database platform | Database segment or version | No. of results downloaded |
|---|---|---|---|---|
| | | | October 24, 2024> | |
| Embase | 5th Nov 2024 | Ovid | Embase <1974 to 2024 November 04> | 479 |
| INAHTA | 5th Nov 2024 | INAHTA | Searched 5th Nov 2024 | 9 |
| MEDLINE ALL | 5th Nov 2024 | Ovid | Ovid MEDLINE(R) ALL <1946 to November 04, 2024> | 240 |

**Search strategy history**

**Database name: MEDLINE ALL**

| Searches |
|---|
| Database: Ovid MEDLINE(R) ALL <1946 to November 04, 2024><br>Search Strategy:<br>---<br>1 exp Catheterization, Peripheral/ (13768)<br>2 (peripher* or picc or piccs or piv or pivs).tw. (713109)<br>3 1 or 2 (722975)<br>4 exp Vasoconstrictor Agents/ (271250)<br>5 Receptors, Vasopressin/ (3658)<br>6 exp Antidiuretic Agents/ (37172)<br>7 (vasoconstric* or vaso-constric* or vessel* constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* antagonist* or hypertensiv* or antihypot* or anti-hypot*).tw. (267617)<br>8 (norepinephrin* or noradrenaline* or sinora*).tw. (97975)<br>9 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*).tw. (57264)<br>10 metaramin*.tw. (565)<br>11 phenylephrin*.tw. (19984)<br>12 ephedrine*.tw. (4468)<br>13 argipressin*.tw. (22)<br>14 (terlipress* or glypress*).tw. (1097)<br>15 angiotens*.tw. (128792)<br>16 or/4-15 (614532)<br>17 3 and 16 (28530) |

| Searches |
| --- |
| 18 Cost-Benefit Analysis/ (96073)<br>19 Quality-Adjusted Life Years/ (17017)<br>20 Markov Chains/ (16545)<br>21 exp Models, Economic/ (16568)<br>22 cost*.ti. (153403)<br>23 (cost* adj2 utilit*).tw. (8380)<br>24 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (303785)<br>25 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (51662)<br>26 (qualit* adj2 adjust* adj2 life*).tw. (19451)<br>27 QALY*.tw. (15779)<br>28 (incremental* adj2 cost*).tw. (18892)<br>29 ICER.tw. (6772)<br>30 utilities.tw. (10162)<br>31 markov*.tw. (34299)<br>32 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (57598)<br>33 ((utility or effective*) adj2 analys*).tw. (27273)<br>34 (willing* adj2 pay*).tw. (10981)<br>35 (EQ5D* or EQ-5D*).tw. (15156)<br>36 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (4439)<br>37 (european* adj2 quality adj3 ("5" or five)).tw. (808)<br>38 or/18-37 (542480)<br>39 Economics/ (27540)<br>40 Value of life/ (5833)<br>41 exp "Costs and Cost Analysis"/ (274194)<br>42 exp Economics, Hospital/ (26028)<br>43 exp Economics, Medical/ (14451)<br>44 Economics, Nursing/ (4013)<br>45 Economics, Pharmaceutical/ (3152)<br>46 exp "Fees and Charges"/ (31557)<br>47 exp Budgets/ (14279)<br>48 budget*.ti,ab. (38464)<br>49 cost*.ti. (153403)<br>50 (economic* or pharmaco?economic*).ti. (65698)<br>51 (price* or pricing*).ti,ab. (58149)<br>52 (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. (231582)<br>53 (financ* or fee or fees).ti,ab. (176869)<br>54 (value adj2 (money or monetary)).ti,ab. (3305) |

| Searches |
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| 55 or/39-54 (789285)<br>56 "Quality of Life"/ (295843)<br>57 quality of life.tw. (419130)<br>58 "Value of Life"/ (5833)<br>59 Quality-Adjusted Life Years/ (17017)<br>60 quality adjusted life.tw. (19064)<br>61 (qaly$ or qald$ or qale$ or qtime$).tw. (15949)<br>62 disability adjusted life.tw. (6523)<br>63 daly$.tw. (5851)<br>64 Health Status Indicators/ (24150)<br>65 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (32426)<br>66 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2845)<br>67 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (8299)<br>68 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (42)<br>69 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (474)<br>70 (euroqol or euro qol or eq5d or eq 5d).tw. (18977)<br>71 (qol or hql or hqol or hrqol).tw. (81507)<br>72 (hye or hyes).tw. (77)<br>73 health$ year$ equivalent$.tw. (40)<br>74 utilit$.tw. (296835)<br>75 (hui or hui1 or hui2 or hui3).tw. (2135)<br>76 disutili$.tw. (702)<br>77 rosser.tw. (112)<br>78 quality of wellbeing.tw. (54)<br>79 quality of well-being.tw. (525)<br>80 qwb.tw. (221)<br>81 willingness to pay.tw. (9740)<br>82 standard gamble$.tw. (929)<br>83 time trade off.tw. (1471)<br>84 time tradeoff.tw. (270)<br>85 tto.tw. (1529)<br>86 or/56-85 (826547)<br>87 38 or 55 or 86 (1650135)<br>88 17 and 87 (447)<br>89 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and |

| **Searches** |
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| barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1380031)<br>90 "organisation for economic co-operation and development"/ (635)<br>91 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3607892)<br>92 european union/ (18247)<br>93 developed countries/ (21658)<br>94 or/90-93 (3624481)<br>95 89 not 94 (1288078) |

| Searches |
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| 96 88 not 95 (439)<br>97 limit 96 to yr="2010 -Current" (240)<br>98 limit 97 to english language (230) |

**Database name: Embase**

| Searches |
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| Database: Embase <1974 to 2024 November 04><br>Search Strategy:<br>---<br>1 exp peripheral venous catheter/ (2803)<br>2 (peripher* or picc or piccs or piv or pivs).tw. (996646)<br>3 or/1-2 (998151)<br>4 exp hypertensive agent/ (234469)<br>5 exp vasoconstrictor agent/ (318241)<br>6 exp vasopressin receptor/ (6480)<br>7 exp antidiuretic agent/ (73199)<br>8 (vasoconstric* or vaso-constric* or vessel* constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* antagonist* or hypertensiv* or antihypot* or anti-hypot*).tw. (371303)<br>9 (norepinephrin* or noradrenaline* or sinora*).tw. (115368)<br>10 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*).tw. (70788)<br>11 metaramin*.tw. (590)<br>12 phenylephrine/ (40139)<br>13 phenylephrin*.tw. (25987)<br>14 ephedrine/ (15428)<br>15 ephedrine*.tw. (5675)<br>16 argipressin*.tw. (35)<br>17 (terlipress* or glypress*).tw. (2055)<br>18 angiotensin derivative/ (1368)<br>19 angiotens*.tw. (168337)<br>20 or/4-19 (844214)<br>21 3 and 20 (41189)<br>22 cost utility analysis/ (13300)<br>23 quality adjusted life year/ (38719)<br>24 cost*.ti. (205694)<br>25 (cost* adj2 utilit*).tw. (13721)<br>26 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (416136) |

| Searches |
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| 27 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (71813) |
| 28 (qualit* adj2 adjust* adj2 life*).tw. (29578) |
| 29 QALY*.tw. (28965) |
| 30 (incremental* adj2 cost*).tw. (30887) |
| 31 ICER.tw. (14279) |
| 32 utilities.tw. (16157) |
| 33 markov*.tw. (43100) |
| 34 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (77482) |
| 35 ((utility or effective*) adj2 analys*).tw. (40831) |
| 36 (willing* adj2 pay*).tw. (16217) |
| 37 (EQ5D* or EQ-5D*).tw. (28858) |
| 38 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (5944) |
| 39 (european* adj2 quality adj3 ("5" or five)).tw. (1119) |
| 40 or/22-39 (682183) |
| 41 Health economics/ (36883) |
| 42 exp health care cost/ (360268) |
| 43 exp Fee/ (45826) |
| 44 exp Budget/ (35313) |
| 45 Funding/ (82670) |
| 46 budget*.ti,ab. (50561) |
| 47 cost*.ti. (205694) |
| 48 (economic* or pharmaco?economic*).ti. (81636) |
| 49 (price* or pricing*).ti,ab. (78944) |
| 50 (cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab. (314775) |
| 51 (financ* or fee or fees).ti,ab. (253480) |
| 52 (value adj2 (money or monetary)).ti,ab. (4401) |
| 53 or/41-52 (1142281) |
| 54 "Quality of Life"/ (694324) |
| 55 Quality Adjusted Life Year/ (38719) |
| 56 Quality of Life Index/ (3337) |
| 57 Short Form 36/ (43428) |
| 58 Health Status/ (161125) |
| 59 quality of life.tw. (652620) |
| 60 quality adjusted life.tw. (28906) |
| 61 (qaly$ or qald$ or qale$ or qtime$).tw. (29255) |
| 62 disability adjusted life.tw. (7814) |
| 63 daly$.tw. (7476) |

| Searches |
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| 64 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (52632)<br>65 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (3171)<br>66 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (13123)<br>67 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (75)<br>68 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (552)<br>69 (euroqol or euro qol or eq5d or eq 5d).tw. (33867)<br>70 (qol or hql or hqol or hrqol).tw. (143741)<br>71 (hye or hyes).tw. (195)<br>72 health$ year$ equivalent$.tw. (41)<br>73 utilit$.tw. (412362)<br>74 (hui or hui1 or hui2 or hui3).tw. (3438)<br>75 disutili$.tw. (1396)<br>76 rosser.tw. (148)<br>77 quality of wellbeing.tw. (81)<br>78 quality of well-being.tw. (602)<br>79 qwb.tw. (277)<br>80 willingness to pay.tw. (14486)<br>81 standard gamble$.tw. (1227)<br>82 time trade off.tw. (2179)<br>83 time tradeoff.tw. (324)<br>84 tto.tw. (2418)<br>85 or/54-84 (1425464)<br>86 40 or 53 or 85 (2566799)<br>87 21 and 86 (1242)<br>88 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ |

| Searches |
| --- |
| or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1822845)<br>89 exp "organisation for economic co-operation and development"/ (3220)<br>90 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3943283)<br>91 european union/ (32888)<br>92 developed country/ (36517)<br>93 or/89-92 (3978755)<br>94 88 not 93 (1660493)<br>95 87 not 94 (1213)<br>96 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6053309)<br>97 95 not 96 (799)<br>98 limit 97 to yr="2010 -Current" (500)<br>99 limit 98 to english language (479) |

**Database name: EconLit**

| Searches |
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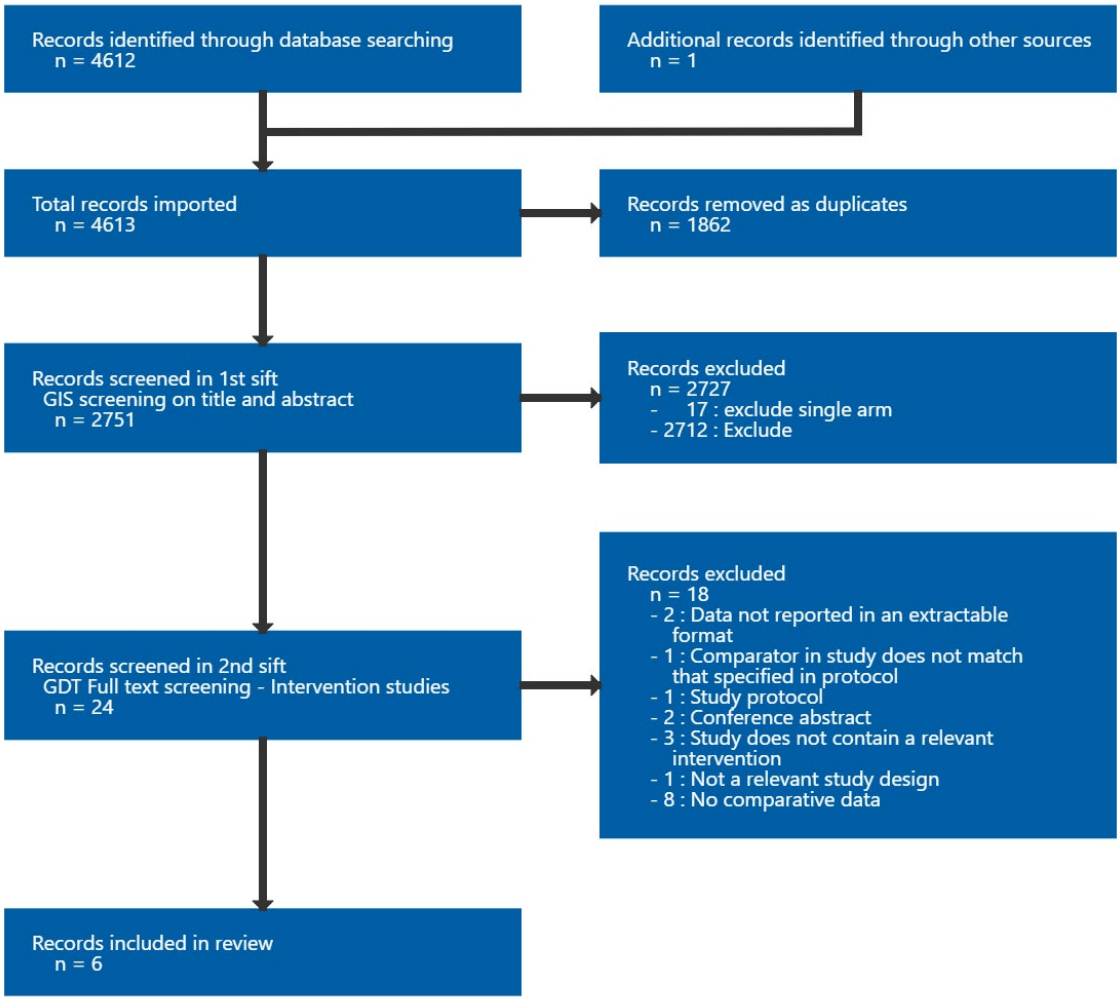
| Database: Econlit <1886 to October 24, 2024><br>Search Strategy:<br>---<br>1 [exp Catheterization, Peripheral/] (0)<br>2 (peripher* or picc or piccs or piv or pivs).tw. (5802)<br>3 1 or 2 (5802)<br>4 [exp Vasoconstrictor Agents/] (0)<br>5 [Receptors, Vasopressin/] (0)<br>6 [exp Antidiuretic Agents/] (0)<br>7 (vasoconstric* or vaso-constric* or vessel* constric* or vasoactiv* or vaso-activ* or pressor* or vasopress* or vaso-press* or antidiuret* or anti-diuret* or diuret* antagonist* or hypertensiv* or antihypot* or anti-hypot*).tw. (58)<br>8 (norepinephrin* or noradrenaline* or sinora*).tw. (2)<br>9 (epinephrin* or racepinephrin* or adrenaline* or emerade* or jext*).tw. (6)<br>10 metaramin*.tw. (0)<br>11 phenylephrin*.tw. (0)<br>12 ephedrine*.tw. (0)<br>13 argipressin*.tw. (0)<br>14 (terlipress* or glypress*).tw. (0)<br>15 angiotens*.tw. (13)<br>16 or/4-15 (77)<br>17 3 and 16 (0) |

**Database name: International HTA database**

| Searches |
| --- |
| (peripher* or picc or piccs or piv or pivs) AND (vasoconstric* OR vaso-constric* OR "vaso constrict" OR "vaso constrictor" OR "vaso constrictors" OR "vaso constricted" OR "vaso constrictive" OR "vaso constrictives" OR (vessel* AND constric*) OR vasoactiv* OR vaso-activ* OR "vaso active" OR "vaso actives" OR pressor* OR vasopress* OR vaso-press* OR "vaso pressor" OR "vaso pressors" OR antidiuret* OR anti-diuret* OR "anti diuretic" OR "anti diuretics" OR (diuret* AND antagonist*) OR hypertensiv* OR antihypot* OR anti-hypot* OR "anti hypotensive" OR anti hypotensives OR norepinephrin* OR noradrenaline* OR sinora* OR epinephrin* OR racepinephrin* OR adrenaline* OR emerade* OR jext* OR metaramin* OR phenylephrin* OR ephedrine* OR argipressin* OR terlipress* OR glypress* OR angiotens*) =9 results (limited to English and 2010+) |

# Appendix C – Safety evidence study selection



# Appendix D – Effectiveness evidence

### Asher, 2023

| | |
|---|---|
| **Bibliographic Reference** | Asher, Elad; Karameh, Hani; Nassar, Hamed; Yosefy, Chaim; Marmor, David; Perel, Nimrod; Taha, Louay; Tabi, Meir; Braver, Omri; Shuvy, Mony; Wiener-Well, Yonit; Glikson, Michael; Bruoha, Sharon; Safety and Outcomes of Peripherally Administered Vasopressor Infusion in Patients Admitted with Shock to an Intensive Cardiac Care Unit-A Single-Center Prospective Study.; Journal of clinical medicine; 2023; vol. 12 (no. 17) |

### Study details

| | |
|---|---|
| **Study type** | Prospective cohort study |
| **Study location** | Jerusalem, Israel |
| **Study setting** | Intensive cardiovascular care unit (ICCU), Shaare Zedek Medical Center |
| **Study dates** | January 2022 and December 2022 |
| **Sources of funding** | "Research received no external funding". |
| **Inclusion criteria** | Adult<br><br>Haemodynamic shock<br><br>Cardiogenic shock was defined as a systolic blood pressure (SBP) <90 mm Hg that was refractory to fluid resuscitation with clinical and laboratory evidence of end-organ dysfunction in the setting of suspected cardiac dysfunction and/or right heart catheterization with a cardiac index (CI) of ≤2.2 L/min per m2 and a pulmonary capillary wedge pressure (PCWP) of ≥15 mm Hg.<br><br>Requiring vasopressors |
| **Intervention(s)** | • Access location: proximal to the wrist<br>• Gauge size: 20G<br>• A second peripheral venous access was routinely obtained for backup and the administration of other IV drugs.<br>• "The decision to administer vasopressors via a CVC or via a PVC was made according to the discretion of the treating senior cardiologist".<br>• "...the administration of vasopressors through a peripheral line is the standard approach in our center for the initial management of patients suffering from shock."<br>• Most commonly used vasopressor: noradrenaline (103/108. 95%) |

| | |
|---|---|
| **Comparator** | • CVC was inserted under ultrasound guidance and after a strict sterile preparation technique.<br>• Access location: 14 (45%) jugular, 9 (29%) femoral and 8(26%) subclavian<br>• "...the administration of vasopressors through a peripheral line is the standard approach in our center for the initial management of patients suffering from shock. However, when additional medications with potential toxicity, multiple vasopressors, fluids at a high rate, and/or blood products are co-administered, a CVC is generally preferred."<br>• Most commonly used vasopressor: noradrenalin (27/29. 87%) |
| **Outcome measures** | Mortality<br><br>Extravasation<br><br>Blood stream infection<br><br>Phlebitis<br><br>Bleeding<br><br>Catheter related SAE-necrosis |
| **Number of participants** | 139 in included in study out of 1100 patients.<br><br>108 in PVC group, 31 in CVC group |
| **Duration of follow-up** | Not stated |
| **Loss to follow-up** | Not stated |
| **Methods of analysis** | • Categorical variables com,pared using a chi-squared test and Fisher's exact test.<br>• Student's t-test and the Mann–Whitney test were performed for the comparison of normally and non-normally distributed continuous variables, respectively.<br>• Mortality was analyzed by applying a stepwise backward Cox proportional hazards model. |

**Study arms**

**Peripheral venous catheter (PVC) (N = 108)**

**Central Venous Catheter (CVC) (N = 31)**

**Characteristics**

**Arm-level characteristics**

| Characteristic | Peripheral venous catheter (PVC) (N = 108) | Central Venous Catheter (CVC) (N = 31) |
|---|---|---|
| **Age**<br><br>Mean (SD) | 72 (12.3) | 64 (19.6) |
| **% Female**<br><br>Sample size | n = 38 ; % = 35 | n = 10 ; % = 32 |
| **BMI**<br><br>Custom value | 27 | 27 |
| **Shock type - cardiogenic**<br><br>Sample size | n = 91 ; % = 84 | n = 29 ; % = 90 |
| **Shock type - Septic**<br><br>Sample size | n = 11 ; % = 10 | n = 0 ; % = 0 |
| **Shock type (combined)**<br>Cardiogenic and septic<br><br>Sample size | n = 3 ; % = 3 | n = 2 ; % = 6 |
| **Shock type-Haemorrhagic**<br><br>Sample size | n = 3 ; % = 3 | n = 0 ; % = 0 |
| **Extravasation**<br><br>Sample size | n = 1 ; % = 1 | n = 1 ; % = 3 |

| Characteristic | Peripheral venous catheter (PVC) (N = 108) | Central Venous Catheter (CVC) (N = 31) |
|---|---|---|
| **Phlebitis**<br><br>Sample size | n = 6 ; % = 5 | n = 1 ; % = 3 |
| **Bleeding**<br><br>Sample size | n = 0 ; % = 0 | n = 1 ; % = 3 |
| **Mortality**<br>All cause- in hospital<br><br>Sample size | n = 17 ; % = 16 | n = 11 ; % = 36 |
| **Blood stream infection (BSI)**<br><br>Sample size | n = 2 ; % = 2 | n = 1 ; % = 3 |
| **Catheter related SAE- necrosis**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 |

**Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions**

| Section | Question | Answer |
|---|---|---|
| Overall bias | Risk of bias judgement | Serious<br>*(Authors state a cox proportional hazard model used for mortality but no hazard ratio or output presented from this. No evidence of adjusting for confounding factors. There was a significant age difference between the two groups with much younger participants receiving central line. The treating clinician was responsible for choosing who went into which arm based on clinical need, meaning people who had a higher degree of shock and were placed in the central arm creating selection bias.)* |
| Overall bias | Directness | Indirectly Applicable<br>*(This was a cardiogenic shock population with only a small percentage (8%) with septic shock)* |

## Delaney, 2020

| | |
|---|---|
| **Bibliographic Reference** | Delaney, Anthony; Finnis, Mark; Bellomo, Rinaldo; Udy, Andrew; Jones, Daryl; Keijzers, Gerben; MacDonald, Stephen; Peake, Sandra; Initiation of vasopressor infusions via peripheral versus central access in patients with early septic shock: A retrospective cohort study.; Emergency medicine Australasia : EMA; 2020; vol. 32 (no. 2); 210-219 |

## Study details

| | |
|---|---|
| **Secondary publication of another included study- see primary study for details** | N/A |
| **Other publications associated with this study included in review** | N/A |
| **Trial registration number and/or trial name** | Post-hoc analysis of the ARISE trial |
| **Study type** | Retrospective cohort study |
| **Study location** | Australia |
| **Study setting** | Hospital emergency department and intensive care unit |
| **Study dates** | Not specified in paper - Outlined in the ARISE trial as from October 5, 2008, to April 23, 2014. |
| **Sources of funding** | No specific funding sources for this study/post-hoc analysis but the ARISE trial was funded by the Australian National Health and Medical Research Council. NHMRC (grant 491075 and APP1021165) |
| **Inclusion criteria** | Adult<br><br>Received vasopressor within 6 hours of hospital arrival |
| **Exclusion criteria** | Admission via inter-hospital transfer |

| | |
|---|---|
| | Had a treatment limitation of no central access documented at hospital presentation<br><br>Confirmed or suspected pregnancy<br><br>Contraindication to receiving blood products<br><br>Hemodynamic instability due to active bleeding<br><br>Underlying disease process with a life expectancy < 90 days<br><br>Death deemed imminent and inevitable<br><br>Documented limitation of therapy order restricting implementation of the study protocol or aggressive care deemed unsuitable by the treating clinician<br><br>Inability to commence EGDT within one hour of randomization or deliver EGDT for 6 hours |
| **Intervention(s)** | Vasopressor administered via intravenous central venous catheter: vasopressor infusion of at least 30 minutes duration from ED presentation to 6 hours post-randomisation |
| **Comparator** | Vasopressor administered via intravenous peripheral venous catheter: vasopressor infusion of at least 30 minutes duration from ED presentation to 6 hours post-randomisation |
| **Outcome measures** | Mortality<br><br>Blood stream infection<br><br>Bleeding<br><br>Catheter related SAE-necrosis |
| **Number of participants** | • iPVC = 389<br>• iCVC = 548 |
| **Duration of follow-up** | 90 days |
| **Loss to follow-up** | Post-hoc analysis - 0 loss to follow-up. |
| **Methods of analysis** | • Between-group comparisons performed by chi-squared, t-test, or Wilcoxon rank sum test |

| | |
|---|---|
| | • 90-day mortality: Generalized estimating equations model and propensity score model |
| **Additional comments** | Adjusted results for the primary outcome of mortality at 90 days:<br>• Univariate analysis: OR 1.71 95%CI 1.28 to 2.28 (p=<0.001)<br>• Multivariable analysis: OR 1.26 95%CI 0.95 to 1.67 (p=0.11) |

### Study arms

#### intravenous Central venous catheter (iCVC) (N = 548)

Those who received a vasopressor infusion of at least 30 minutes duration from ED presentation to 6 hours post-randomisation and had the time of insertion of a CVC recorded

#### intravenous peripheral venous catheter (iPVC) (N = 389)

Initiation of vasopressors via a PVC: vasopressor infusion of at least 30 minutes duration from ED presentation to 6 hours post-randomisation - either when trial participants were recorded as commencing a vasopressor infusion prior to the time of insertion of a CVC or when no CVC was inserted prior to 6 hours post-randomisation.

### Characteristics

### Arm-level characteristics

| Characteristic | intravenous Central venous catheter (iCVC) (N = 548) | intravenous peripheral venous catheter (iPVC) (N = 389) |
|---|---|---|
| **% Female** (%)<br><br>Nominal | 39.8 | 40.1 |
| **Age**<br><br>Median (IQR) | 65.7 (53.6 to 76) | 65.4 (52.4 to 75.3) |
| **Weight (kg)**<br><br>Median (IQR) | 75 (65 to 85) | 77 (65 to 90) |

| Characteristic | intravenous Central venous catheter (iCVC) (N = 548) | intravenous peripheral venous catheter (iPVC) (N = 389) |
|---|---|---|
| **Mortality at 90 days (unadjusted)**<br><br>Nominal | 103 | 113 |
| **Mortality at 28 days (unadjusted)**<br><br>Nominal | 85 | 98 |
| **Central venous catheter related adverse events: Bleeding (unadjusted)**<br><br>Nominal | 3 | 0 |
| **Infection (unadjusted)**<br><br>Nominal | 1 | 0 |
| **Catheter related SAE- necrosis**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 |

**Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions**

| Section | Question | Answer |
|---|---|---|
| Overall bias | Risk of bias judgement | Serious<br>*(No adjustment for baseline confounding relating to outcomes outside of 90 day mortality, the majority in peripheral arm went on to receive a central line with follow up time not split accordingly or adjustments made, there was an imbalance in cointerventions (vasopressor type) across arms and there is a possibility for misclassification of the intervention given peripheral was inferred from the data rather than recorded directly.)* |
| Overall bias | Directness | Partially Applicable<br>*(Sepsis population but comparison is peripheral initiation vs central initiation, not peripheral only vs central only)* |

## Kilian, 2022

| | |
|---|---|
| **Bibliographic Reference** | Kilian, Scott; Surrey, Aaron; McCarron, Weston; Mueller, Kristen; Wessman, Brian Todd; Vasopressor Administration via Peripheral Intravenous Access for Emergency Department Stabilization in Septic Shock Patients.; Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine; 2022; vol. 26 (no. 7); 811-815 |

## Study details

| | |
|---|---|
| **Study type** | Retrospective cohort study |
| **Study location** | St Louis, USA |
| **Study setting** | Emergency department |
| **Study dates** | June 2018 to May 2019 |
| **Sources of funding** | None |
| **Inclusion criteria** | Adult<br><br>over 18 years old<br><br>Diagnosis of septic shock<br><br>Received a vasopressor |
| **Exclusion criteria** | Admission via inter-hospital transfer<br><br>History of heart failure |
| **Intervention(s)** | **Peripheral venous catheter**<br><br>Gauge size: 18 or 20<br><br>Location:<br><br>• in the antecubital fossa (AC) or more proximal in 61.9% of patients<br>• distal to the AC in 29.3% of patients<br>• location not specified in 8.8% of patients<br><br>CVC was subsequently placed<br><br>• 73.5% - in ED<br>• 14.7% - in ICU |

| | |
|---|---|
| | • 118.8 no CVC placed |
| **Comparator** | **Central Venous catheter**<br><br>17 started in ED, 18 prior |
| **Outcome measures** | Mortality<br><br>Extravasation<br><br>Occlusion<br><br>Catheter related SAE-digit ischaemia |
| **Number of participants** | 69 included, out of 136 screened<br><br>34 in PVC, 35 in CVC (17 initiated in ED, 18 existing before admission) |
| **Duration of follow-up** | Mortality followed up to 28 days. |
| **Methods of analysis** | T-test, two tailed. |
| **Additional comments** | Patients with CVC inserted before arriving in ED (n=18) were more likely to have active malignancy (44.4% vs 11.8% in those with CVC placed in ED), and had higher mortality (61.1% vs 20.6%) |

**Study arms**

**Peripheral venous catheter (PVC) (N = 34)**

**Central Venous Catheter (CVC) - started in ED (N = 17)**

CVC line started in ED

**CVC pre-existing (N = 18)**

Patients already had a CVC line

## Characteristics

### Arm-level characteristics

| Characteristic | Peripheral venous catheter (PVC) (N = 34) | Central Venous Catheter (CVC) - started in ED (N = 17) | CVC pre-existing (N = 18) |
|---|---|---|---|
| **% Female**<br><br>Sample size | n = 15 ; % = 44.1 | *empty data* | *empty data* |
| **Age**<br><br>Custom value | 64.3 | *empty data* | *empty data* |
| **Ethnicity**<br><br>Custom value | Not reported | Not reported | Not reported |
| **Active malignancy treatment**<br><br>Sample size | n = 3 ; % = 8.8 | *empty data* | *empty data* |
| **Mortality - 28 days**<br>All cause<br><br>Sample size | n = 7 ; % = 20.6 | *empty data* | *empty data* |
| **Extravasation**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 | n = 0 ; % = 0 |
| **Catheter related SAE-Digit ischaemia**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 | n = 0 ; % = 0 |
| **Occlusion**<br>Transient hypotension associated with route of administration<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 | n = 0 ; % = 0 |

### Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions

| Section | Question | Answer |
|---|---|---|
| Overall bias | Risk of bias judgement | Serious<br>*(No attempt at adjusting for differences in baseline confounding factors and no data on confounding factors that would make adverse events more likely. There was an imbalance between the groups in cointerventions (number/type of vasopressor) and time varying confounding was not addressed even though 82% or participants in peripheral arm went on to have a central line placed.)* |
| Overall bias | Directness | Partially Applicable<br>*(Although seemingly the correct population and comparison, 88.2% in peripheral arm also went on to have a central line placed)* |

### Munroe, 2024

| | |
|---|---|
| **Bibliographic Reference** | Munroe, Elizabeth S; Heath, Megan E; Eteer, Mousab; Gershengorn, Hayley B; Horowitz, Jennifer K; Jones, Jessica; Kaatz, Scott; Tamae Kakazu, Maximiliano; McLaughlin, Elizabeth; Flanders, Scott A; Prescott, Hallie C; Use and Outcomes of Peripheral Vasopressors in Early Sepsis-Induced Hypotension Across Michigan Hospitals: A Retrospective Cohort Study.; Chest; 2024; vol. 165 (no. 4); 847-857 |

### Study details

| | |
|---|---|
| **Study type** | Retrospective cohort study |
| **Study location** | Michigan, USA. |
| **Study setting** | 29 hospitals participating in the Michigan Hospital Medicine Safety Consortium’s (HMS) sepsis initiative |
| **Study dates** | November 2020-September 2022 |
| **Sources of funding** | NIH and other local hospital network grants. |
| **Inclusion criteria** | Adult<br><br>Received vasopressor within 6 hours of hospital arrival<br><br>Qualifying vasopressors: norepinephrine, epinephrine, phenylephrine, dopamine, vasopressin, and angiotensin II |

| | |
|---|---|
| | Community acquired sepsis<br><br>Hypotension |
| **Exclusion criteria** | Admission via inter-hospital transfer<br><br>Had a treatment limitation of no central access documented at hospital presentation |
| **Intervention(s)** | Initiated with a peripheral IV line<br><br>• using either a continuous or push doses |
| **Comparator** | Initiated with a Central line (CVC)<br><br>• Temporary (non-tunnelled) central venous catheter (CVC), tunnelled CVC, peripherally inserted central catheter, port, or temporary hemodialysis catheter<br>• Could be preexisting (present before hospital arrival) or new (placed after hospital arrival).<br>• Patients who received an initial vasopressor through a midline catheter, intraosseous line, or unknown route were excluded |
| **Outcome measures** | Mortality<br><br>Catheter related SAE-necrosis |
| **Number of participants** | 154, 400 in PIV initiation group, 154 in CVC initiation group |
| **Duration of follow-up** | up to 90 days for mortality |
| **Methods of analysis** | Multilevel logistic regression models<br><br>All models were adjusted for prespecified baseline patient characteristics and markers of presenting illness severity: age, admission from a post-acute care facility, hospitalization in the prior 90 days, kidney disease, liver disease, congestive heart failure, peripheral vascular disease, malignancy, BMI, lactate, creatinine, mechanical ventilation within 6 h of hospital arrival, altered mental status, and predicted mortality score, which was calculated using a logistic regression model developed and validated in the HMS sepsis cohort. |

### Study arms

### Peripheral IV (PIV) (N = 400)

| | |
|---|---|
| **Additional comments** | In the PIV initiation group,<br>• 254(62.5%) had CVC on day 1<br>• 11(2.8%) had CVC in day 2-4<br>• 135(33.8%) had no CVC by day 4 |

Vasopressors initiated with peripheral IV

### Central Line (CVC) (N = 154)

Vasopressor initiated with a CVC, either a temporary CVC, Port or PICC

### Characteristics

### Arm-level characteristics

| Characteristic | Peripheral IV (PIV) (N = 400) | Central Line (CVC) (N = 154) |
|---|---|---|
| **Age** (Median (IQR))<br><br>Custom value | 70(60-78) | 70(62-78) |
| **% Female**<br><br>Sample size | n = 192 ; % = 48 | n = 83 ; % = 53.9 |
| **Ethnicity**<br><br>Custom value | Not reported | Not reported |
| **BMI** (Median (IQR))<br><br>Custom value | 27.7 (22.5-33.2) | 28.9 (24.1-34.5) |
| **Source of admission - emergency department** (Median (IQR))<br><br>Sample size | n = 399 ; % = 99.8 | n = 153 ; % = 99.4 |
| **First level of care after ED: ICU**<br><br>Sample size | n = 366 ; % = 91.5 | n = 137 ; % = 89 |

| Characteristic | Peripheral IV (PIV) (N = 400) | Central Line (CVC) (N = 154) |
|---|---|---|
| **Mortality - 30 days** (Adjusted OR)<br>All cause<br><br>Sample size | n = 162 ; % = 40.5 | n = 75 ; % = 48.7 |
| **Mortality - 30 days** (Adjusted OR)<br>All cause<br><br>Odds ratio/95% CI | 0.76 (0.45 to 1.27) | *empty data* (*empty data* to *empty data*) |
| **Mortality - in hospital** (Adjusted OR)<br>All cause<br><br>Sample size | n = 129 ; % = 32.3 | n = 65 ; % = 42.2 |
| **Mortality - in hospital** (Adjusted OR)<br>All cause<br><br>Odds ratio/95% CI | 0.66 (0.39 to 1.12) | *empty data* (*empty data* to *empty data*) |
| **Tissue necrosis due to extravasation**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 |

### Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions

| Section | Question | Answer |
|---|---|---|
| Overall bias | Risk of bias judgement | Serious<br>*(Although some baseline confounding was adjusted for unknown confounders may be present in non-randomised studies. Time vary confounding or split follow up time was not addressed even though the majority of participants in the peripheral arm received a central line. There was an imbalance of cointerventions/different vasopressors between arms that was not adjusted for.)* |
| Overall bias | Directness | Partially Applicable<br>*(more than one-half of patients initiated on peripheral vasopressors undergoing central line placement within 1 day of hospital arrival - comparison was peripheral initiation vs central initiation, not peripheral only vs central only)* |

## Ricard, 2013

| | |
|---|---|
| **Bibliographic Reference** | Ricard JD, Salomon L, Boyer A, Thiery G, Meybeck A, Roy C, Pasquet B, Le Mière E DDD1P2; Central or peripheral catheters for initial venous access of ICU patients: a randomized controlled trial.; 2013 |

## Study details

| | |
|---|---|
| **Secondary publication of another included study- see primary study for details** | |
| **Other publications associated with this study included in review** | |
| **Trial registration number and/or trial name** | NCT00122707 |
| **Study type** | Randomised controlled trial (RCT) |
| **Study location** | France |
| **Study setting** | Three ICUs |
| **Study dates** | March 2004 to January 2006 |
| **Sources of funding** | Research program from the French Ministry of Health |
| **Inclusion criteria** | Adult<br><br>ICU patients<br><br>Require specific drugs, including vasopressors<br><br>need for specific drugs known to be veinotoxic (epinephrine: dose less than or equal to 2 mg/hr; norepinephrine: dose less than or equal to 2 mg/hr; dopamine or dobutamine: dose not exceeding 10 mg/kg/min; amiodarone: less than three ampoules [150 mg in 3 mL] per day, for an expected period |

| | |
|---|---|
| | shorter than 3 d; vancomycin: discontinuous infusion of a dose <1g/d; amphotericin B: for an expected period less than 3 d)<br><br>Experience difficulties in peripheral catheter insertion or maintenance<br><br>Define S: |
| **Exclusion criteria** | Require any drugs that is not within the specified inclusion list |
| **Intervention(s)** | • Short peripheral catheters (neither PICC nor midline catheters)<br>• 8 or 20 gauge, polyurethane catheters<br>• Changed at least every 72 hours, according to the Centers for Disease Control and Prevention recommendations for the prevention of catheter-related infections<br>• When their medical condition required it, or whenever PVC access was compromised, patients in the PVC group could have a CVC inserted, and cross over criteria defined as: either an increase in veinotoxic drug infusion rate (doses and drugs) or impossibility or great difficulties in inserting or maintaining a PVC |
| **Comparator** | • The insertion site (jugular , subclavian, femoral) was left at the clinician in charge's discretion<br>• Standard polyurethane 7F, 16 (6") or 20 cm (8"), multi-lumen (2 or 3), noncoated, nonimpregnated catheters<br>• Inserted using maximal sterile-barrier precautions including using large sterile drapes, surgical antiseptic hand wash, and use of sterile gown, gloves, mask, and cap.<br>• Removed whenever they were no longer required as recommended (18–20) and could be replaced with PVC if a venous access was still necessary. |
| **Outcome measures** | Mortality<br><br>Extravasation<br><br>Blood stream infection<br><br>Phlebitis |
| **Number of participants** | Number randomised: PVC 129, CVC 137<br><br>Number analysed: PVC 128, CVC 135 |
| **Duration of follow-up** | 28 days |
| **Loss to follow-up** | No participant was lost to follow up. |

| | |
|---|---|
| | One participant in the PVC group and two participants in the CVC group withdrew consent |
| **Methods of analysis** | Intention to treat analysis, excluding only participants who withdrew consent |

### Study arms

### Peripheral venous catheter (PVC) (N = 129)

Short peripheral catheters (neither PICC nor midline catheters)

### Central Venous catheter (N = 137)

The insertion site (jugular , subclavian , femoral) was left at the clinician in charge's discretion

### Characteristics

### Arm-level characteristics

| Characteristic | Peripheral venous catheter (PVC) (N = 129) | Central Venous catheter (N = 137) |
|---|---|---|
| **Age**<br><br>Mean (SD) | 64.8 (16) | 63.4 (15.4) |
| **Sex: Female**<br><br>Sample size | n = 43 ; % = 33.6 | n = 53 ; % = 39.3 |
| **Organ dysfunction or infection score**<br><br>Mean (SD) | 2.21 (1.07) | 2.18 (1.1) |
| **Simplified Acute Physiology Score (SAPS)**<br><br>Mean (SD) | 56.2 (21.4) | 55.9 (21.4) |
| **Mechanical ventilation**<br><br>Sample size | n = 109 ; % = 85.8 | n = 109 ; % = 80.7 |

| Characteristic | Peripheral venous catheter (PVC) (N = 129) | Central Venous catheter (N = 137) |
|---|---|---|
| **Blood stream infection**<br>Catheter related bacteraemia<br><br>No of events | n = 0 ; % = 0 | n = 1 ; % = 0.74 |
| **Extravasation**<br>Subcutaneous diffusion<br><br>No of events | n = 19 ; % = 14.84 | n = 2 ; % = 1.48 |
| **Phlebitis**<br><br>No of events | n = 1 ; % = 0.78 | n = 1 ; % = 0.74 |
| **Mortality**<br>All cause, at 28 days<br><br>Custom value | 1.3(95% CI 0.84 to 2.01) for CVC vs peripheral | *empty data* |

Some percentages and reported numbers do not tally up. Percentages calculated based on the sample sizes reported.

**Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT**

| Section | Question | Answer |
|---|---|---|
| Overall bias and Directness | Risk of bias judgement | Moderate<br>*(Some concerns around a lack of blinding so outcome assessors knew the allocation groups meaning measurement of outcomes could be subjective)* |
| Overall bias and Directness | Overall Directness | Indirectly applicable<br>*(Not a sepsis specific population and not all people received a vasopressor (70% did).)* |

**Stolz, 2022**

| | |
|---|---|
| **Bibliographic Reference** | Stolz, Annaliese; Efendy, Rachel; Apte, Yogesh; Craswell, Alison; Lin, Frances; Ramanan, Mahesh; Safety and efficacy of peripheral versus centrally administered vasopressor infusion: A single-centre retrospective observational study.; Australian critical care : official journal of the |

Confederation of Australian Critical Care Nurses; 2022; vol. 35 (no. 5); 506-511

### Study details

| | |
|---|---|
| **Study type** | Retrospective cohort study |
| **Study location** | Queensland, Australia |
| **Study setting** | ICU |
| **Study dates** | 1 April 2019 to 31 March 2020 |
| **Sources of funding** | None declared. |
| **Inclusion criteria** | Adult<br><br>ICU patients<br><br>Received a vasopressor |
| **Exclusion criteria** | Only received bolus vasopressor |
| **Intervention(s)** | Peripheral Venous Catheter (PVC)<br><br>PVC then CVC |
| **Comparator** | CVC only |
| **Outcome measures** | Mortality<br><br>Hospital mortality<br><br>Extravasation<br><br>Blood stream infection |
| **Number of participants** | 212 patients met inclusion criteria, out of 443 ICU admissions during the study period. |
| **Methods of analysis** | Fisher's exact test.<br><br>Univariate logistics regression controlling for duration of vasopressor infusion using PVC for complication rate. |

**Study arms**

**Peripheral venous catheter (PVC) only (N = 39)**

**PVC then CVC (N = 155)**

**Central Venous Catheter (CVC) (N = 18)**

**Characteristics**

**Arm-level characteristics**

| Characteristic | Peripheral venous catheter (PVC) only (N = 39) | PVC then CVC (N = 155) | Central Venous Catheter (CVC) (N = 18) |
|---|---|---|---|
| **Age** (Median (IQR))<br><br>Custom value | 68.4 (52.9-75.7) | 68.3 (53.9-76.1) | 68.5 (54.2-75.4) |
| **% Female**<br><br>Sample size | n = 18 ; % = 46 | n = 72 ; % = 46.5 | n = 9 ; % = 50 |
| **Ethnicity**<br><br>Custom value | Not stated | Not stated | Not stated |
| **BMI** (Median (IQR))<br><br>Custom value | 26.8 (24-32) | 28.7 (25-34) | 27.6 (26-30) |
| **APACHE-III score** (Median (IQR))<br><br>Custom value | 64 (43.5-76.5) | 73 (54-90) | 85.5 (56.5-100.8) |
| **Vasopressor type - noradrenaline**<br><br>Sample size | n = 14 ; % = 35.9 | n = 141 ; % = 91 | n = 16 ; % = 88.9 |
| **Extravasation** | n = 5 ; % = 12.8 | n = 16 ; % = 10.3 | n = 2 ; % = 11.1 |

| Characteristic | Peripheral venous catheter (PVC) only (N = 39) | PVC then CVC (N = 155) | Central Venous Catheter (CVC) (N = 18) |
|---|---|---|---|
| Sample size | | | |
| **Line associated bacteraemia**<br><br>Sample size | n = 0 ; % = 0 | n = 1 ; % = 0.6 | n = 0 ; % = 0 |
| **Mortality - in hospital** Adjusted OR<br><br>Odds ratio/95% CI | 1 (*empty data* to *empty data*) | 0.77 (0.21 to 2.87) | 1.89 (0.35 to 10.3) |
| **Catheter related SAE – tissue necrosis**<br><br>Sample size | n = 0 ; % = 0 | n = 0 ; % = 0 | n = 0 ; % = 0 |

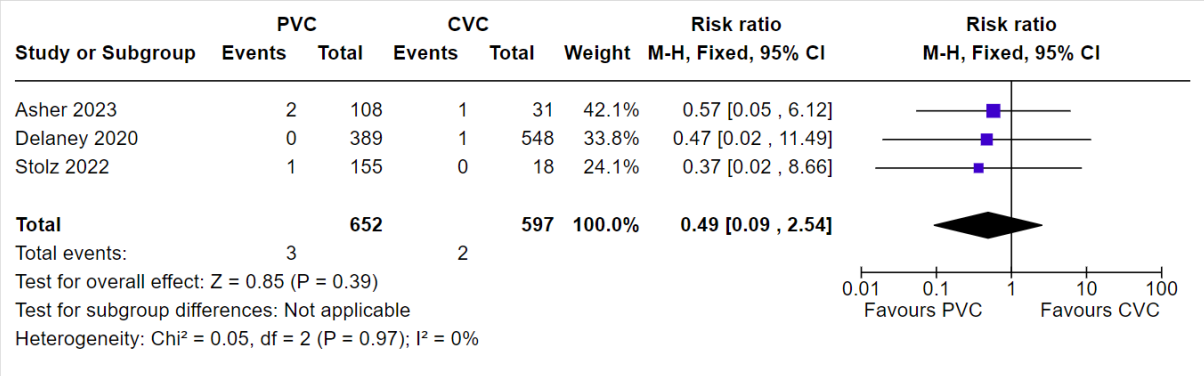
**Critical appraisal - GDT Crit App - ROBINS-I: a tool for non-randomised studies of interventions**

| Section | Question | Answer |
|---|---|---|
| Overall bias | Risk of bias judgement | Serious<br>*(Bias relating to confounding as multivariable regression not used for adverse event/safety outcomes. Some imbalances between vasopressor type and duration between arms and potential underreporting of adverse events in the peripheral arm according to the authors)* |
| Overall bias | Directness | Indirectly Applicable<br>*(Not a septic shock population specifically)* |

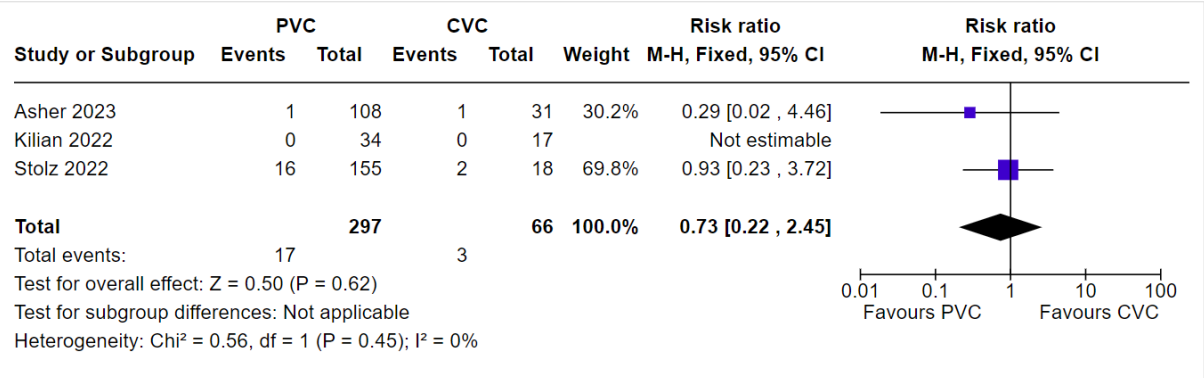
# Appendix E – Forest plots

## Forest plots for PVC vs CVC – cohort studies

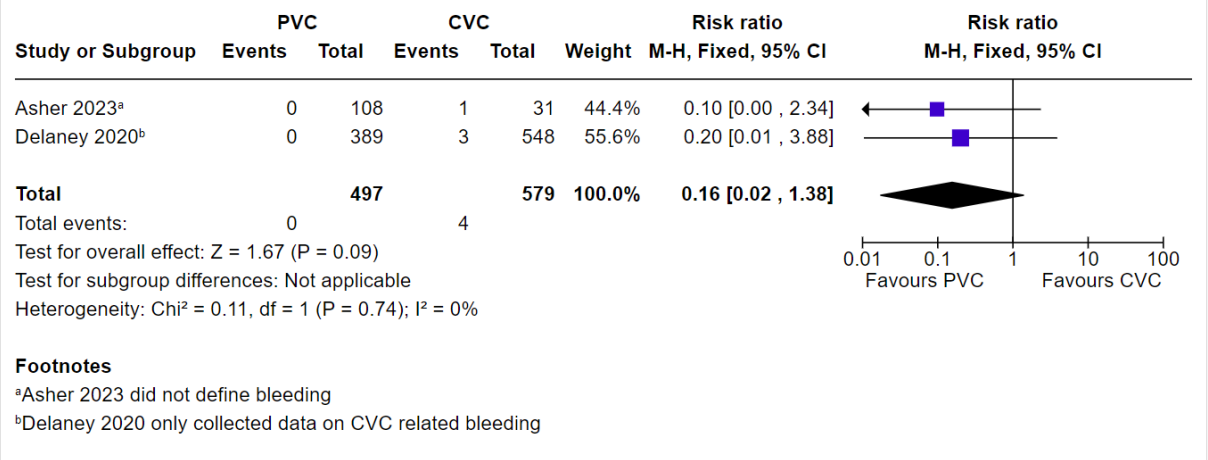
### Forest plot 1 – Blood stream infection (catheter related)




### Forest plot 2 – Extravasation



## Forest plot 3 – Bleeding

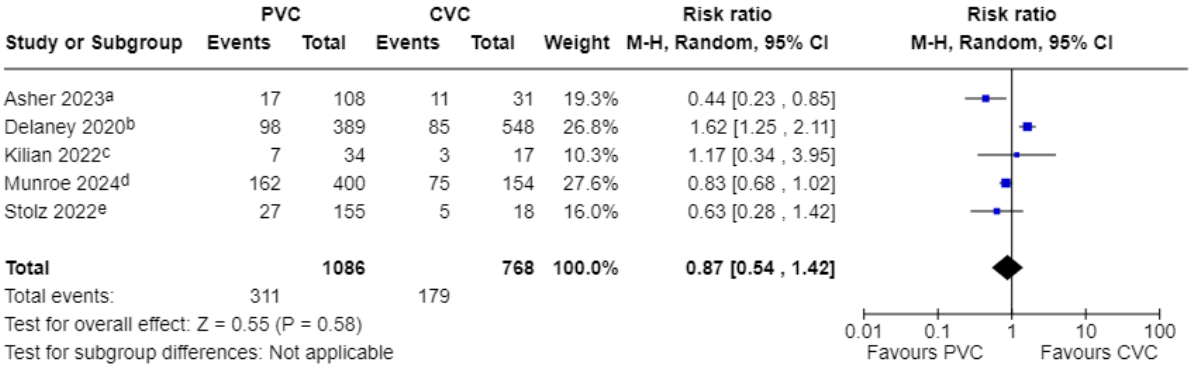



**Footnotes**

[a]Asher 2023 did not define bleeding

[b]Delaney 2020 only collected data on CVC related bleeding

## Forest plot 4 – Mortality (all cause)




**Footnotes**

[a]Asher 2023: In-hospital mortality

[b]Delaney 2020: 28-day mortality

[c]Kilian 2022: 28-day mortality

[d]Munroe 2024: 30 - day mortality

[e]Stolz 2022: In-hospital mortality

# Appendix F – GRADE tables

**Table 6: Peripheral venous catheter (PVC) compared to Central venous catheter (CVC) for vasopressor initiation in patients with sepsis – RCT evidence**

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Risk of bias | Inconsistency | Indirectness | Imprecision | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|
| **Complications - Blood Stream Infection (BSI) - catheter related** | | | | | | | | | | |
| 1[a] | RCT | 0/128 (0.0%) | 1/137 (0.7%) | **RR 0.36** (0.01 to 8.67) | **5 fewer per 1000** (from 7 fewer to 56 more) | serious[1] | not serious | very serious[2] | very serious[3] | ⊕◯◯◯ Very low |
| **Complications - Extravasation** | | | | | | | | | | |
| 1[a] | RCT | 19/128 (14.8%) | 2/137 (1.5%) | **RR 10.17** (2.42 to 42.79) | **134 more per 1000** (from 21 more to 610 more) | serious[1] | not serious | very serious[2] | serious[4] | ⊕◯◯◯ Very low |

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Risk of bias | Inconsistency | Indirectness | Imprecision | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|
| **Complications - Phlebitis** | | | | | | | | | | |
| 1[a] | RCT | 1/128 (0.8%) | 1/137 (0.7%) | **RR 1.07** (0.07 to 16.93) | **1 more per 1000** (from 7 fewer to 116 more) | serious[1] | not serious | very serious[2] | very serious[3] | ⊕◯◯◯ Very low |
| **Survival at 28 days** | | | | | | | | | | |
| 1 | RCT | Not reported | Not reported | **HR 1.3 (0.84 to 2.01) for CVC vs PVC** Not statistically significant | | not serious | not serious | very serious[2] | serious[4] | ⊕◯◯◯ Very low |

1 Some bias concerns, particularly because outcomes assessors were aware which patients were allocated.
2 Patients were selected either because they needed a vasopressor or another venotoxic drug, or an issue with PVC (either failed to insert twice or had problems with maintenance). Only 70% received vasopressors. ICU patients, not limited to sepsis patients. Unclear how many had sepsis.
3 Downgraded twice for imprecision as confidence interval crosses lower (0.75) and upper (1.25) default minimum important difference threshold.
4 Downgraded for imprecision as confidence interval crosses upper (1.25) default minimum important difference threshold.

**Reference**

a. Ricard, 2013

**Table 7: Peripheral venous catheter (PVC) compared to Central venous catheter (CVC) for vasopressor initiation in patients with sepsis – Cohort study evidence**

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Risk of bias | Inconsistency | Indirectness | Imprecision | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|
| **Blood stream infection (catheter related)** | | | | | | | | | | |
| 3[a] | non-randomised studies | 3/652 (0.5%) | 2/597 (0.3%) | RR 0.49 (0.09 to 2.54) | 2 fewer per 1000 (from 3 fewer to 5 more) | very serious[1] | not serious | serious[2] | very serious[3] | ⊕◯◯◯ Very low [1,2,3] |
| **Extravasation** | | | | | | | | | | |
| 3[b] | non-randomised studies | 17/297 (6.5%) | 3/66 (6.1%) | RR 0.73 (0.22 to 2.45) | 12 fewer per 1000 (from 35 fewer to 66 more) | very serious[1] | not serious | serious[2] | very serious[3] | ⊕◯◯◯ Very low [1,2,3] |
| **Phlebitis** | | | | | | | | | | |
| 1[c] | non-randomised studies | 6/108 (5.6%) | 1/31 (3.2%) | RR 1.72 (0.22 to 13.77) | 23 more per 1000 (from 25 fewer to 412 more) | very serious[1] | not serious | serious[2] | very serious[3] | ⊕◯◯◯ Very low [1,2,3] |

| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Risk of bias | Inconsistency | Indirectness | Imprecision | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|
| **Bleeding - catheter related** | | | | | | | | | | |
| 2[d] | non-randomised studies | 0/497 (0.0%) | 4/579 (0.7%) | RR 0.16 (0.02 to 1.38) | 6 fewer per 1000 (from 7 fewer to 3 more) | very serious[1] | not serious | serious[2] | very serious[3] | ⊕◯◯◯ Very low [1,2,3] |
| **Occlusion** | | | | | | | | | | |
| 1[e] | non-randomised studies | 0/34 (0%) | 0/17 (0%) | Not estimable | 0 fewer per 1000 | very serious[1] | not serious | serious[2] | very serious[4] | ⊕◯◯◯ Very low[1,2,4] |
| **Mortality (all cause)** | | | | | | | | | | |
| 5[f] | non-randomised studies | 311/1086 (28.6%) | 179/768 (23.3%) | RR 0.87 (0.54 to 1.42) | 30 fewer per 1000 (from 107 fewer to 98 more) | serious[5,6] | serious[7] | serious[2] | very serious[3] | ⊕◯◯◯ Very low [2,,5,6,7] |

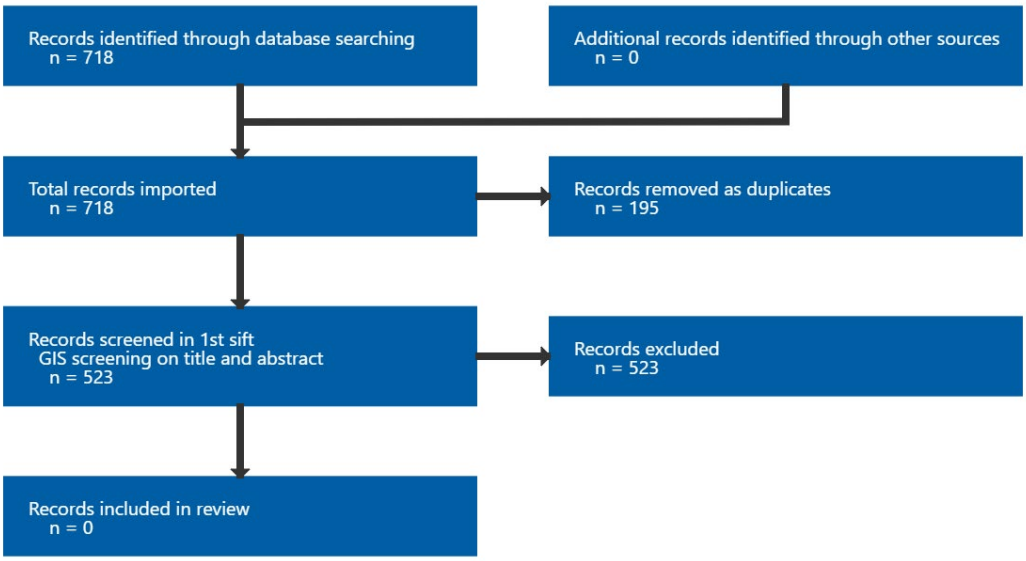
| No of studies | Study design | Intervention - PVC Number with events/number analysed | Comparator - CVC Number with events/number analysed | Effect size (risk ratio) (95% CI) | Absolute effect (95% CI) | Risk of bias | Inconsistency | Indirectness | Imprecision | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|
| **Catheter related serious adverse event - skin necrosis** | | | | | | | | | | |
| 5[g] | non-randomised studies | 0/1086 (0.0%) | 0/767 (0.0%) | Not estimable | **0 fewer per 1000** | very serious[1] | not serious | serious[2] | serious[4] | ⊕◯◯◯ Very low[1,2,4] |

1. All studies are at high risk of bias in more than one domain. There were no adjustments for possible confounding factors.
2. Patients in Kilian 2022 and Delaney 2020 initiated vasopressors in the ED, while Munroe 2024 included hospitalised patients and nearly all of them were admitted from the ED. The other studies initiated vasopressors in the ICU. Downgraded if studies with vasopressor initiated in ED or usual ward setting contributed to less than 50% weight of data analysed.
3. Downgraded for imprecision due to very wide confidence intervals, and OIS not met due to the low event rates.
4. No events were reported.
5. All studies at high risk of bias in more than one domain. Only one study reported adjusted mortality rate.
6. Most studies reported mortality at 28 or 30 days. None reported mortality attributable to adverse events or route of vasopressor management.
7. The heterogeneity is high ($I^2$ >50%).

**References:**

a. Asher, 2023; Delaney, 2020; Stolz, 2022
b. Asher, 2023; Kilian, 2022, Stolz 2022
c. Asher, 2023
d. Asher, 2023; Delaney, 2020
e. Kilian, 2022
f. Asher, 2023; Delaney, 2020; Killian, 2022; Munroe, 2024; Stolz, 2022
g. Asher, 2023; Delaney, 2020; Killian, 2022; Munroe, 2024; Stolz, 2022

# Appendix G – Economic evidence study selection



# Appendix H – Excluded studies

## Excluded studies

| Study | Reason for exclusion |
|---|---|
| Aldujeli, Ali, Haq, Ayman, Tecson, Kristen M et al. (2022) A prospective observational study on impact of epinephrine administration route on acute myocardial infarction patients with cardiac arrest in the catheterization laboratory (iCPR study). Critical care (London, England) 26(1): 393 | - Data not reported in an extractable format |
| Cape, Kari M, Jones, Laureen G, Weber, Michele L et al. (2022) Implementation of a Protocol for Peripheral Intravenous Norepinephrine: Does It Save Central Line Insertion, Is It Safe?. Journal of pharmacy practice 35(3): 347-351 | - No comparative data |
| Gershengorn, Hayley B, Basu, Tanima, Horowitz, Jennifer K et al. (2023) The Association of Vasopressor Administration through a Midline Catheter with Catheter-related Complications. Annals of the American Thoracic Society 20(7): 1003-1011 | - Study does not contain a relevant intervention |
| Kusakabe, Ayano, Sweeny, Amy, Keijzers, Gerben et al. (2021) Early vs. Late Vassopressor therapy in the Management of Patients with Sepsis and Hypotension, A Multicenter Observational Study. Archives of medical research 52(8): 836-842 | - Data not reported in an extractable format |
| Loubani, Osama M and Green, Robert S (2015) A systematic review of extravasation and local tissue injury from administration of vasopressors through peripheral intravenous catheters and central venous catheters. Journal of critical care 30(3): 653e9-17 | - Not a relevant study design *Systematic review but not of comparative studies* |
| Medlej, Kamal, Kazzi, Amin Antoine, El Hajj Chehade, Ahel et al. (2018) Complications from Administration of Vasopressors Through Peripheral Venous Catheters: An Observational Study. The Journal of emergency medicine 54(1): 47-53 | - No comparative data |

| Study | Reason for exclusion |
|---|---|
| Messina, Antonio, Milani, Angelo, Morenghi, Emanuela et al. (2021) Norepinephrine Infusion in the Emergency Department in Septic Shock Patients: A Retrospective 2-Years Safety Report and Outcome Analysis. International journal of environmental research and public health 18(2) | - No comparative data |
| Nguyen, Tammy T, Surrey, Aaron, Barmaan, Benjamin et al. (2021) Utilization and extravasation of peripheral norepinephrine in the emergency department. The American journal of emergency medicine 39: 55-59 | - No comparative data |
| Owen, Victoria S, Rosgen, Brianna K, Cherak, Stephana J et al. (2021) Adverse events associated with administration of vasopressor medications through a peripheral intravenous catheter: a systematic review and meta-analysis. Critical care (London, England) 25(1): 146 | - No comparative data |
| Powell, Sara M, Faust, Andrew C, George, Stephy et al. (2023) Effect of Peripherally Infused Norepinephrine on Reducing Central Venous Catheter Utilization. Journal of infusion nursing : the official publication of the Infusion Nurses Society 46(4): 210-216 | - Conference abstract |
| Prasanna, Nivedita, Yamane, David, Haridasa, Naeha et al. (2021) Safety and efficacy of vasopressor administration through midline catheters. Journal of critical care 61: 1-4 | - Study does not contain a relevant intervention |
| Raza, Hassan A, Nokes, Brandon T, Alvarez, Bruno et al. (2024) Use of peripherally inserted central catheters with a dedicated vascular access specialists team versus centrally inserted central catheters in the management of septic shock patients in the ICU. The journal of vascular access 25(1): 218-224 | - Study does not contain a relevant intervention |
| Ruchti, Vera Ew, Wibrow, Bradley A, Seet, Jason et al. (2021) A prospective comparison of peripheral metaraminol versus dilute noradrenaline in the intensive | - Comparator in study does not match that specified in protocol |

| Study | Reason for exclusion |
|---|---|
| care unit. Anaesthesia and intensive care 49(2): 144-146 | |
| Simkovich, S., Barnes, K., Sanghavi, K. et al. (2024) Evaluation of Compliance and Complications in a Pilot of a Protocol for the Use of Peripheral Vasopressors. Am. J. Respir. Crit. Care Med. 209 | - Conference abstract |
| Tian, David H, Smyth, Claire, Keijzers, Gerben et al. (2020) Safety of peripheral administration of vasopressor medications: A systematic review. Emergency medicine Australasia : EMA 32(2): 220-227 | - Systematic review used as source of primary studies<br><br>- No comparative data |
| Tran, Quincy K, Mester, Gaurika, Bzhilyanskaya, Vera et al. (2020) Complication of vasopressor infusion through peripheral venous catheter: A systematic review and meta-analysis. The American journal of emergency medicine 38(11): 2434-2443 | - No comparative data<br><br>- Systematic review used as source of primary studies |
| Watts, Stacey, Apte, Yogesh, Holland, Thomas et al. (2024) Randomised, controlled, feasibility trial comparing vasopressor infusion administered via peripheral cannula versus central venous catheter for critically ill adults: A study protocol. PloS one 19(5): e0295347 | - Study protocol |
| Yerke, Jason R, Mireles-Cabodevila, Eduardo, Chen, Alyssa Y et al. (2024) Peripheral Administration of Norepinephrine: A Prospective Observational Study. Chest 165(2): 348-355 | - No comparative data |

# Appendix I – Research recommendations – full details

### I 1.1 Research recommendation

In people assessed as being at moderate or high risk of severe illness or death from suspected sepsis, how safe is the peripheral administration of different infusion durations, doses and concentrations of vasopressors?

### I 1.1.1 Why this is important

Vasopressors are part of the treatment for hypotension and hypotensive shock in people with sepsis. Peripheral administration is a valuable option to have if central access is not available in a person who needs vasopressors, but there was limited evidence on the safety of peripheral administration and no evidence on dosing or concentration.

### I 1.1.2 Rationale for research recommendation

| | |
|---|---|
| Importance to 'patients' or the population | There is a lack of evidence on the safety of different infusion durations, doses and concentrations of peripherally administered vasopressors. A greater understanding of this area could be important for supporting decision making and allowing vasopressors to be initiated as soon as it is required, rather than potentially being delayed due to a lack of central access. |
| Relevance to NICE guidance | This guideline has considered vasopressors and made a recommendation for the consideration based on clinical review of peripheral vasopressor administration but more evidence is required to better understand the safety of different durations, doses and concentrations of peripherally administered vasopressor. |
| Relevance to the NHS | Whilst a recommendation has been made, more evidence is required to support clinician decision making regarding duration, dose and concentration and potentially reduce delays in administration when vasopressors could potentially benefit an individual but are delayed due to a lack of central access. |
| National priorities | Not known |
| Current evidence base | Minimal data |
| Equality considerations | None known |

### I 1.1.3 Modified PICO table

**Table title (caption style)**

| | |
|---|---|
| Population | Adults aged 16 and over with suspected sepsis (including a range of underlying infections) |
| Intervention | Any vasopressor delivered via peripheral venous access |
| Comparator | Any vasopressor delivered via central venous access |
| Outcome | • Blood stream infection<br>• Extravasation<br>• Phlebitis<br>• Bleeding<br>• Occlusion<br>• Mortality<br>• Extravasation management beyond removal of cannula |
| Study design | RCT's and well conducted cohort studies |
| Timeframe | short-term |
| Additional information | |