NHS National Services Scotland

Quality Improvement Tool (QIT) Literature Review

Insertion and Maintenance of Central Venous Catheters (CVC)

Version 1.0
30 December 2022

ARHAI Scotland
Antimicrobial Resistance and Healthcare Associated Infection

Key Information

Document title:	Quality Improvement Tool Literature Review – Insertion and Maintenance of Central Venous Catheters (CVC)
Date published/issued:	**30 December 2022**
Date effective from:	**30 December 2022**
Version/issue number:	1.0
Document type:	Literature review
Document status:	Final

Document information

Document information	Description
Description:	This literature review examines the extant scientific literature on the insertion and maintenance of central venous catheters (CVCs) in the health and care setting.
Purpose:	To inform the Quality Improvement Tool on Insertion and Maintenance of CVCs in order to facilitate the prevention and control of healthcare associated infections in Scottish health and care settings.
Target Audience:	All staff involved in the insertion and maintenance of CVCs in Scotland.
Update/review schedule:	Updated as new evidence emerges with changes made to recommendations as required. Review will be formally updated every 3 years with next review in 2025.
Cross reference:	National Infection Prevention and Control Manual
Update level:	Practice – Evidence for paediatric and neonatal populations have been included. Additional recommendations have been added. Research – Further research required for CVC dressings in paediatric and neonatal populations; glove use during specific CVC care procedures; and CVC care in the primary or community setting.

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Version history

This literature review will be updated in real time if any significant changes are found in the professional literature or from national guidance/policy.

Version	Date	Summary of changes
1.0	December 2022	The Insertion and Maintenance of Central Venous Catheters (CVCs) literature reviews for Adults (V3.0 Sep 2014) and Neonates (V1.0 Sep 2017) were amalgamated and updated using a two-person methodology. Objectives have been added to address evidence on both insertion and maintenance of CVCs.

Approvals

Version	Date Approved	Name
1.0	December 2022	NPGE Working Group, CIPC Working Group and Perinatal Network

Contents

1. Objectives

The aim is to review the extant scientific literature regarding insertion and maintenance of CVCs in health and care settings to inform an evidence-based CVC insertion and maintenance Quality Improvement Tool (QIT) and recommendations for practice.

The specific objectives of the review are to determine:

1.1 Insertion of Central Venous Catheters

- What are the indications for CVC insertion?
- What administrative and clinical checks should be in place prior to insertion?
- How should hand hygiene be performed, what product should be used?
- When should hand hygiene be performed throughout the procedure?
- What Personal Protective Equipment (PPE) should be worn and when?
- How should the environment be prepared prior to insertion?
- How should equipment be prepared prior to insertion?
- How should the insertion site be prepared?
- What required standard or best practice technique should be used for insertion?
- What type of dressing should be used to cover the catheter site?

1.2 Maintenance of Central Venous Catheters

- What administrative and clinical checks should be in place for maintenance of CVCs?
- When should hand hygiene be performed when accessing/administering medication/ throughout the process of maintenance?
- How and when should hand hygiene be performed, what product should be used?

- What PPE should be worn and when?
- How should the CVC access site be maintained?
- When should removal of CVCs be considered?

2. Methodology

This targeted literature review was produced using a defined two-person systematic methodology as described in the National Infection Prevention and Control Manual:Development Process.

This review considered relevant literature for neonatal, paediatric, and adult populations covering the general types of CVCs including peripherally inserted central catheters (PICCs), non-tunnelled CVCs (also known as percutaneous and non-cuffed CVCs), tunnelled CVCs (also called Hickman lines) and totally implantable devices (also known as implanted ports). Midline catheters, although not considered CVCs, are also included in this review as their insertion and maintenance should be carried out in accordance with CVC guidance.

In addition, the following were considered out of scope for this review:

- Catheter design
- Emergency insertion of CVCs
- Antimicrobial impregnated catheters
- Prophylactic use of antimicrobials
- Flushing technique
- Flush and lock solutions
- Administration sets including blood administration sets
- Studies focusing on procedural aspects of CVC insertion and maintenance
- Alcohol based caps for passive disinfection of catheter hubs

- Chlorhexidine bathing in ICU patients with CVCs
- Individual evidence pertaining exclusively to non-infectious complication risks

There are a number of factors related to healthcare delivery that were not within the remit of this review. This includes assessing that staff are appropriately trained and competent in all aspects of the insertion and management of CVCs, using an approved educational package and that they complete the required competencies and accreditation according to health and care setting policy. The overall approach to the delivery of healthcare is supported by patient safety and improvement approaches and organisational readiness. These recommendations are considered alongside clinical requirements. The appropriateness of any CVC infection prevention activities should be evaluated alongside other clinical risks and contraindications. Manufacturer's guidance and where appropriate, local or national clinical guidance should also be followed.

3. Discussion

3.1 Implications for practice: Insertion of Central Venous Catheters

What are the indications for CVC insertion?

See Appendix 3 for definitions of non-tunnelled CVCs, tunnelled CVCs, peripherally inserted central catheters (PICCs), totally implantable devices, neonatal umbilical venous catheters (UVCs) and midline catheters.

No evidence from primary studies was included in this review to inform on the correct indications for CVC use however, five guidelines and nine expert-consensus guidance documents outlined the considerations for indications and contraindications.[1-14] This included that CVCs are used for patients requiring repeated administration of medication, chemotherapy, fluids, parenteral nutrition, blood products, and can be inserted for dialysis and frequent blood sampling.[1, 7-10]

Infusates which require use of central vascular catheters

Within one National Institute of Health and Care Excellence (NICE) guideline as well as three expert opinion documents, there was broad agreement that intravenous infusions which are not suitable for a short peripheral vascular catheter (PVC), should be delivered via a CVC (excluding midlines).[3, 7, 9, 10] These included continuous vesicant drugs, such as chemotherapy[7, 9, 10] vasopressor drugs[10, 12] and infusates with extreme pH or unsuitable osmolality.[7, 10, 12] However, the Infusion Nurses Society (INS) Standards emphasised that time-critical, lifesaving therapies should not prevent PVC insertion until a CVC can be inserted.[10] Both the US-based Infusion Nurses Society (INS) standards in 2011 and the Royal College of Nursing (RCN) Standards for Infusion Therapy stated that fluids with pH <5 or >9, as well as fluids of >900 mOsm/L osmolarity should be administered via a CVC.[9, 10] One UK NICE guideline on adult nutrition support recommended that CVCs should be used for certain parenteral nutrition formulations - with attention to the pH, tonicity and long-term compatibility of the product.[3] The RCN and INS Standards were more explicit; stating that parenteral nutrition and other products with >10% dextrose and >5% protein should be administered using a CVC.[9, 10] Separately, NICE guidelines for neonatal parenteral nutrition recommended CVCs should be selected over PVCs for the administration of parenteral nutrition in neonates, regardless of concentration/formulation.[4]

Anticipated duration of use

Duration was reported as a primary reason for selection of a CVC for infusion therapy. There was evidence from four guidelines, and two expert-consensus guidance that CVCs should be the preferred option for long-term intravenous access, including intermittent long-term access required for some chronic conditions.[1-4, 9, 10] The 2020 NICE guidelines on neonatal parenteral nutrition stated that CVCs are the preferred vascular device, however PVCs may be used if it would avoid a delay in starting, or avoidance of interruptions to therapy, where a duration of <5 days is expected, or where a CVC is impractical.[4] Additionally, the RCN and INS Standards stated that CVCs should be considered when expected duration is longer than indicated for PVCs.[9, 10] There was disagreement among guidelines and expert guidance documents on the recommended maximum duration for different CVC types. While this is due to the requirement for more primary research on the selection of different CVC types,[10] this was also a reflection of the need for wider clinical assessment when selecting a specific CVC.

Evidence on duration for different CVC types:

- **Non-tunnelled CVCs:** Non-tunnelled (standard) CVCs were described as short-term - for anticipated duration 7-10 days, according to RCN and epic3.[1, 9] NICE guidance on parenteral nutrition in adults stated CVCs may be considered for duration <30 days.[3] Meanwhile, US-based guidance on dialysis, noted that temporary non-tunnelled CVCs for haemodialysis should be limited to <14 days.[5]

- **UVCs:** Healthcare Infection Control Practices Advisory Committee (HICPAC) guidelines recommend umbilical venous catheters for no longer than14 days.[2]

- **PICCs:** A peripherally inserted central catheter (PICC) was described as a medium to longer-term option. The epic3 team described the typical PICC duration as 4 weeks to 6 months;[1] while NICE guidelines on parental nutrition in adults recommended PICCs be considered >14 days expected duration. Meanwhile, CDC guidelines stated that, like midline catheters, PICCs should be considered for peripheral access >6 days.[2]

- **Tunnelled CVCs:** Skin-tunnelled CVCs are recommended for longer-term, continuous access. There was consensus by epic3, RCN and INS standards that tunnelled CVCs should be considered for anticipated duration >4 weeks, and, provided no complications, may be kept in place for months and years if required.[1, 9, 10] NICE guidance on parenteral nutrition in adults recommended tunnelled CVCs when access for >30 days is required.[3] Tunnelled CVCs are also routinely recommended under specific conditions for short and long-term haemodialysis.[5]

- **Totally implantable ports:** Like tunnelled CVCs, totally implantable ports are an option for long-term duration, when access over months or years is anticipated, and are preferred for intermittent access.[1]

- **Midline catheters:** Where therapy is compatible with peripheral access, epic3 and RCN guidance stated that midline catheters are typically chosen for a duration of 1-4 weeks,[1, 9] while the INS standards, and Centers for Disease Prevention and Control (CDC) guidelines stated that midlines should be considered when anticipated duration is 5-14 days,[10] or exceeding 6 days,[2] respectively.

Minimum essential number of ports or lumens

Multi-lumen CVC devices may be used for concurrent administration and medications, as well as parenteral nutrition, and haemodynamic monitoring among critically ill patients.[1] However, both epic3 and two guidelines from the CDC have recommended that CVCs should be of single lumen configuration unless additional therapies are required, and multiple-lumen CVCs should not be routinely placed unless required.[1, 2, 6] While guidelines have stated there is strong evidence for the recommendation based on several randomised controlled trials (RCTs), the trials were very dated, and some studies failed to demonstrate a difference in the rate of catheter-related bloodstream infections (CRBSIs). The epic3 guidelines authors noted that patients requiring multi-lumen catheters tend to be more severely ill, which was a confounder for risk of colonisation and CRBSI, in the evidence base.[1] Additionally, CDC guidelines for NICU patients with umbilical venous catheters supported this recommendation but highlighted this was based on low quality evidence, and was at risk of bias due to confounders.[6] Six expert opinion guidance documents also made this recommendation.[7-12] No primary or secondary studies were identified in this review for inclusion on this topic. The rationale for this additional infection risk by the guidelines teams was both the increased trauma at the insertion site, as well as the additional manipulation require to operate the device.[1, 11] Two expert-guidance documents from the UK-based Association of Anaesthetists, as well as the US Association for Professionals in Infection Control and Epidemiology (APIC), also stated that the smallest diameter devices capable of delivering the required therapy should be selected to minimise vein trauma.[7, 12]

Use of a dedicated lumen for parenteral nutrition

In 2011, the CDC stated in guidelines for prevention of intravascular catheter-related infections, that the use of a designated lumen for parenteral nutrition was an unresolved issue.[2] However, since this time, epic3 and NICE guidelines as well as two expert opinion guidance documents have stated that parenteral nutrition or any other lipid-based solution should be given via a dedicated lumen.[1, 3, 9, 12] Only one guidelines document cited evidence for this; epic3 cited one very dated, observational study which reported that the use of a dedicated lumen or single lumen device reduced the risk of CR-BSI.[1] Additionally, there were also very low quality, observational studies that reported parenteral nutrition as a risk factor for major infections, which were excluded in this review due to insufficient quality and confounding bias. However, the use of a dedicated lumen for parenteral nutrition is a well-established clinical practice, and further studies would likely be considered impractical.

Multifactorial indications for CVCs

Due to the vast differences in patient populations, required therapies, and clinical needs of individual patients, clinical judgement on indications for use is required. Four guidelines and five expert-based guidance documents stated that selection of CVC type involves a clinical assessment of the individual patient and should not be based on reduction of infection risk alone.[2-4, 6, 7, 9, 10, 12, 13]

There was consensus in the evidence base that the following should be considered:

- the intended purpose, duration and appropriate route of access of therapy[2-4, 7, 9, 10, 12, 13]
- consideration of the patient's age, diagnoses, severity of illness,[9, 12] medical history, and vascular condition[7, 9, 10, 12]
- consideration of the patient's history of intravascular devices[9, 10]
- the risk to benefit ratio associated with both infectious and non-infectious complications
- operator experience[2, 7, 12]
- staff resource and ability to care for the device[7, 10]

What administrative and clinical checks should be in place prior to insertion?

CVCs, like other invasive indwelling devices, can result in serious catheter-related bloodstream infections (CRBSIs), and are especially dangerous due to their direct access to the central vasculature of the patient.[1, 7, 11] Skin microorganisms that colonise catheter hubs and the skin adjacent to the insertion site are the source of most CRBSIs; these organisms can migrate along the surface of the catheter lumen to enter the bloodstream.[1, 7, 11] Coagulase-negative staphylococci such as *Staphylococcus epidermidis* are commonly implicated microorganisms as well as *S. aureus*, *Candida* species, and enterococci.[1, 7, 11] CVCs can also become extrinsically contaminated via the hands of healthcare workers or caregivers when touching the catheter hub during essential care interventions. Other less common sources of CRBSI include contamination of the infusate,[1, 7] or from the carriage of organisms through the bloodstream from remote sources of local infection (such as pneumonia), resulting in seeding of the indwelling catheters, also known as hematogenous spread.[7, 11] A large proportion of patients

who require CVCs will be more susceptible to infection, including patients undergoing chemotherapy, or long-term treatment such as renal dialysis, immunosuppressed patients and those in intensive care units (ICUs).[1, 7-10]

The use of CVCs is an essential clinical requirement for certain patient populations. The invasive nature of these devices along with the vulnerability of the patients and the often prolonged duration of use increases the risk of CRBSIs. In 2018, 5% of healthcare associated infections in Scottish ICUs were CVC-related infections; with an estimated 1.6 central-line associated bloodstream infections per 1,000 catheter-days.[15]

Staff education

According to the Infection Prevention and Control Quality Standards, set out by NICE, healthcare organisations should have written protocols to ensure specified procedures are completed in order to minimise the risk of infection during the care of CVCs.[16] Two UK guidelines (epic3 and NICE CG32),[1, 3] a US guideline from the CDC,[2] as well as five expert-led guidance documents[8, 9, 14, 17, 18] provided clear consensus that only staff trained and assessed as competent in CVC-related IPC practices should be involved in the insertion and care of CVCs. Expert-led guidance included the Royal College of Nursing Standards for Infusion Therapy,[9] the UK Government/UK Kidney Patient Safety Committee Dialysis Guidance,[17] the Paediatric Chief Pharmacists Group,[18] as well as a clinician-led UK guidance document by Bishop et al.,[8] and a US-based guidance document by the Society for Hospital Epidemiology of America (SHEA).[14]

Review of the necessity and indications for a CVC

There was agreement across three guideline documents, including NICE,[3, 4] and the CDC,[2] as well as six expert opinion pieces,[7, 9, 10, 12-14] on conducting a clinical assessment to review the necessity and indication for a CVC, prior to its insertion. No primary studies were included. Expertise included the Association of Anaesthetists of Great Britain and Ireland,[12] the Royal College of Nursing,[9] the Infection Prevention Society,[13] and three US-based organisations; SHEA,[14] the Association for Professionals in Infection Control and Epidemiology (APIC),[7] and the US Infusion Nurses Society.[10] The evidence varied in detail, with many overlapping sources cited throughout the literature base. However, there was consensus that prior to insertion, staff should conduct a clinical assessment to check the following:

- there is a genuine need for the CVC [2, 9, 13, 14]
- its intended purpose [2, 7, 9, 10, 12]

- its expected duration [2, 9, 12, 13]
- whether therapy could be delivered via an alternative route (for example a peripherally inserted device) [3, 4, 9, 13]

The Royal College of Nursing Infusion Therapy Standards also recommended a review of the CVC device against the same criteria 48 hours post-insertion.[9] The US-based SHEA guidance noted that whilst reviewing the necessity for CVC utilisation prior to insertion may reduce CRBSIs, there are also corresponding risks associated with selecting an alternative intravascular catheter which should be considered.[14] Seven guidance documents,[7-10, 14, 17, 19] as well as the epic3 guideline,[1] emphasised that prior to insertion of a CVC, patients and caregivers should receive education on the indications for a CVC (see section: patient education).

How should hand hygiene be performed, what product should be used?

Three guidance documents outlined that for insertion of CVCs, a maximum reduction of microbial counts on the hands is necessary, and therefore surgical hand antisepsis should be performed.[10, 20, 21] Guidance from the WHO, the Association for Safe Aseptic Practice, and the Infusion Nurses Society recommend that surgical hand antisepsis should be performed prior to insertion to reduce cross-transmission risk, and to mitigate against any potential breaches/tears in sterile gloves during the procedure.[10, 20, 21] The surgical hand antisepsis technique aims not only to remove transient microorganisms but to reduce resident microorganisms on the skin.[1, 2, 20] This necessitates that products used for surgical hand antisepsis have a broad spectrum of action.[20] Both alcohol-based hand rubs and liquid soap, used with water, are presented as accepted products for surgical hand antisepsis across the literature.[1, 2, 9, 14, 20]

Further information and recommendations on surgical hand antisepsis can be found in the NIPCM.

When should hand hygiene be performed throughout the procedure?

No primary evidence was identified related to when hand hygiene should be performed. Guidelines by the NICE-accredited epic3 team,[1] World Health Organization (WHO)[20] and the CDC,[2, 22] as well as three expert opinion-based guidance documents,[9, 10, 21, 22] produced recommendations on when hand hygiene is required for CVC insertion. Expertise included the Association for Safe Aseptic Practice, the Infusion Nurses Society, and the Royal College of Nursing. There was consensus that hand hygiene should be performed before carrying out a clean/aseptic procedure such as inserting an invasive device.

Additionally, it is consistently recommended across the evidence that hand hygiene should be performed before and after contact with blood and body fluids, and before donning and after doffing gloves and other PPE items.[1, 2, 9, 10, 20, 22] This includes mention of the WHO 5 moments for hand hygiene by The Association for Safe Aseptic Practice.[21] It is also stated across the evidence that the use of gloves during procedures does not remove the need for effective hand hygiene to be performed.[1, 9, 14, 20]

Surgical hand antisepsis is a routinely accepted procedure applied where maximal barrier precautions (MBPs) are in place, and is performed immediately before donning sterile PPE (for example gloves and gown).[1, 2, 9, 10, 20, 21] This is consistent with the current recommendations of the NIPCM relating to surgical hand antisepsis and general hand hygiene. More information on hand hygiene can be found within the NIPCM hand hygiene literature reviews

What Personal Protective Equipment (PPE) should be worn and when?

No primary research was identified for inclusion that assessed the scientific effectiveness of PPE during CVC insertion for this research question. However, there was strong agreement across four guideline documents,[1, 2, 20, 23] (WHO, CDC, Loveday *et al.* and NICE), and six expert opinion pieces (CDC,[22] RCN,[9] Infusion Nurses Society,[10] SHEA[14], Association for Safe Aseptic Practice (ASAP)[21] and the Association of Anaesthetists of Great Britain and Ireland (AAGBI)[12]), that single-use sterile gloves should be worn for insertion of CVCs, including PICCs and midline catheters, as part of maximal sterile barriers. This is due to the requirement for direct contact with sterile parts during CVC insertion.[1] The WHO also stated that in addition to sterility, surgical gloves which differ in thickness, elasticity and strength compared to other medical gloves, should be selected.[20] Both WHO and the INS Standards state that sterile gloves should fit appropriately and extend to cover the wrists of gowns.[10, 20] WHO also included guidance on the

correct way to don surgical sterile gloves in relation to maintaining aseptic technique, and donning of other PPE.[20] The Aseptic Non Touch Technique (ANTT®) Framework recommends a risk assessment to assess the complexity of a procedure and subsequent technical difficulty to achieve asepsis. Complex and straightforward procedures are termed 'surgical-ANTT' and 'standard-ANTT', respectively. Sterile gloves are therefore indicated for surgical-ANTT procedures such as CVC insertion.[21] Risk assessment based on risk of transmission/contamination, patient care activity taking place, and suitability of specific items of PPE is also recommended by Loveday *et al.* as part of the epic3 guidance.[1]

The INS Standards and RCN also recommended eye protection to protect from potential blood/body fluid splash or spray during CVC insertion.[9, 10] Additionally, PPE risk assessment is required as per Health and Safety legislation; the Health and Safety at Work etc. Act (1974),[24] and the Control of Substances Hazardous to Health 2002 Regulations (as amended),[25] as well as the Personal Protective Equipment at Work (Amendment) Regulations 2022.[26]

Two guidelines and two expert-led guidance documents recommended maximum sterile barrier (MSB) precautions during insertion and defined this as the wearing of sterile gloves, sterile gown, surgical mask and cap, together with the use of a full body sterile drape (similar to the drapes used in the operating room) during the insertion of CVC.[1, 2, 9, 12] CDC guidelines cited three studies which suggested that maximal sterile barrier (MSB) precautions during insertion had been associated with reduced colonisation of CVCs.[2] However the studies had limitations, including the use of bundled interventions for assessment and all three included studies were very dated. The epic3 guideline group also included a systematic review on educational interventions to improve hand hygiene as supporting indirect evidence that MSB during CVC insertions may delay colonisation time, and reduce rates of healthcare associated infections (HAIs) compared to less stringent barriers.[1] The guideline group also balanced the lack of adverse patient reactions and relative low cost of MSB precautions, with the high preventative impact of reducing CRBSIs.[1]

How should the environment be prepared prior to insertion?

No primary studies or direct evidence from guidelines were identified to inform this research question. However two expert opinion-based guidance documents stated that CVCs are routinely inserted in designated, specialised areas, such as operating rooms, theatres, ICUs, or radiology suites, where a high standard of asepsis can be maintained.[8, 12] The epic3 guidance team stated that although it is assumed that CVCs inserted in operating theatres pose a lower

risk of infection than those inserted on inpatient wards or other patient care areas, two prospective studies suggest that the difference in risk of infection depended largely on the magnitude of barrier protection used (for instance maximal barrier precautions) during catheter insertion, rather than the surrounding environment (for instance ward vs operating theatre).[1] However, the guidelines group made no recommendation as to setting for insertion.

In hospital, the care environment has been associated with transmission of HAIs, via contact with contaminated surfaces at sites close to the patient. As part of standard principles for preventing healthcare-associated infections, the epic3 guideline recommended that the hospital environment must be visibly clean; free from non-essential items and equipment, dust and dirt; and acceptable to patients, visitors and staff.[1] This is a requisite of best practice in NHSScotland as laid out in Healthcare Improvement Scotland's (HIS) IPC Standards 2022.[27, 28] Management of environmental controls/risks has also been repeatedly cited as a core part of aseptic technique, including as part of the standardised ANTT® [11, 21] The US-based Joint Commission guidance on reducing central line-associated bloodstream infections (CLABSIs) stated this includes keeping doors closed during operative procedures, minimising traffic into and out of operating rooms, and excluding unnecessary personnel during procedures.[11]

Further guidance and recommendations on cleaning the environment including blood and body fluid spillages can be found in the NIPCM systematic literature reviews: Safe Management of the Care Environment (Environmental Decontamination) and Management of blood and body fluid spillages in health and care settings.

How should equipment be prepared prior to insertion?

There was a paucity of primary research to inform this research question. UK Legislation and mandatory standards from HIS were included, as well as two guidelines, and six expert opinion documents.[1, 2, 9-12, 14, 21, 27, 29] Both CDC and NICE guidelines strongly recommend the use of a full body/large sterile drapes during CVC insertion; this was based on expert opinion of the groups as well as observational evidence consisting of bundled interventional studies on maximal sterile barrier precautions.[1, 2] Expert guidance from the Infusion Nurses Society (INS) recommend that, a form of aseptic technique known as surgical-ANTT®, where all sterilised or aseptic procedural equipment, handled with sterile gloves, should be placed upon the drape to ensure asepsis.[10] The ANTT® framework defines this as the "Critical Aseptic Field". This ensures asepsis of all equipment that will come into contact with the patient at insertion site, and thus prevents a route for transmission of pathogens onto or into the patient.[10, 21] All

equipment should be single-use, where possible.[9, 10] Sterile, single-use equipment for contact with the patient must not be reused and reuse is prohibited in UK legislation (MHRA).[9, 10, 29] The RCN and INS Standards recommend sterile items should be inspected for product integrity, cleanliness and expiry date; defective items should be reported, through local organisational policies, to the Scottish Incident Reporting and Investigation Centre (IRIC) and MHRA as the regulatory authority of medical devices.[9, 10] Four expert-guidance documents recommended the use of designated carts and/or kits (either bought as kits or pre-prepared by staff), with essential equipment for insertion, as well as procedures for re-stocking, to ensure equipment is readily available and easily accessible for CVC insertions.[10-12, 14] The Associations of Anaesthetists of Great Britain and Ireland also suggested a specialist trolley should be on stand-by for difficult insertions, with additional or replacement items.[12]

How should the insertion site be prepared?

CRBSIs/infections can originate from migration of organisms from the patient's skin at the insertion site, from the hands of healthcare workers, or via cross transmission from the surface of personal protective equipment (PPE).[1, 2] Antisepsis of the insertion site is therefore crucial in minimising the risk of microbial seeding of the external surface of the CVC as it is inserted and migration of these organisms down the lumen post–insertion; such migration can lead to biofilm formation, ultimately resulting in infection.[1, 2, 7] This has been correlated to the density of the microbial contamination at the insertion site.[1]

Adults and paediatric patients:

Effectiveness of antiseptic products

Two guidelines, one systematic review of RCTs and three primary studies, including an RCT and two observational studies were included in this review that provided evidence on skin preparation prior to insertion of CVCs; for adult and paediatric patients.[1, 2, 30-33]

Both epic3 and CDC guidelines stated that skin should be decontaminated at the insertion site with chlorhexidine and allowed to dry before inserting a CVC.[1, 2] The NICE-accredited epic3 team recommend a single-use application of 2% chlorhexidine gluconate in 70% isopropyl alcohol, while the CDC stated >0.5% chlorhexidine was adequate. The epic3 guideline group cited indirect evidence from another NICE guideline, assessing skin antisepsis during insertions of PVCs, and dressing changes of CVCs, as well as several RCTs related to both CVCs and arterial catheters; and a meta-analysis - this was the same primary evidence cited by CDC.[1, 2]

The epic3 guideline concluded there was indirect evidence that chlorhexidine in alcohol may be more effective than povidone-iodine (PVI) in alcohol.[1] While evidence was graded as high, this was based on indirect and imprecise data, from studies using heterogenous concentrations/preparations of chlorhexidine, PVI, and alcohol. With respect to the use of chlorhexidine, various concentrations (0.5% to 4%), bases (alcohol versus aqueous solutions) and comparator solutions were used in studies, limiting the conclusions. More research is also needed regarding the role of an alcohol base in relation to the efficacy of chlorhexidine versus an aqueous base.

Similarly, a Cochrane systematic review in 2016 examined skin antisepsis at insertion and during care for reducing CVC-related infections.[30] The study included 12 studies with a total of 3,446 catheters; the majority related to adults in ICUs, haematology, oncology or general wards. Many studies took place pre-2000. The authors appraised the evidence as very low quality due to uncertainty, confounding and lack of adequate statistical power. Pooled analysis of four studies (1,436 catheters) indicated there was very low quality evidence that chlorhexidine may reduce catheter-related BSI compared with povidone-iodine (RR 0.64, (95% CI 0.41, 0.99); equivalent to absolute risk reduction of 2.3%, (95% CI 0.06 to 3.7%). All comparison groups used 10% povidone-iodine, except one (5%). The review also pooled data from across five studies (1,533 catheters) which demonstrated there was a significant risk reduction in catheter colonisations associated with chlorhexidine versus povidone iodine, (RR 0.68, 95% CI 0.56 to 0.84) (absolute risk reduction of 8%). The remaining head to head comparisons in the review provided insufficient data.[30] A high quality RCT (also included in the Cochrane review), compared 0.1% octenidine in propanol versus 74% ethanol, for skin preparation of non-tunnelled CVCs in haematology patients.[31] This study reported a significant reduction in colonisation but not catheter-associated bloodstream infections, associated with 0.1% octenidine.

Two observational studies were also considered for inclusion in this review, however, for both, results were limited by confounding bias, and require cautious interpretation.[32, 33] One non-randomised cross-over trial investigated 0.05% chlorhexidine versus 10% povidone-iodine, and reported a slight increase in CRBSIs and proportion of positive blood culture samples associated with 0.05% chlorhexidine that were not statistically significant.[32] The use of blood culture data by this study is limited by the potential bias of contaminants.[32] Another retrospective, observational study, published in 2018, on chemotherapy patients demonstrated a significant reduction in CVC colonisation associated with 1% chlorhexidine in 70% alcohol versus povidone iodine.[33] Infectious complications were significantly lower in the chlorhexidine

group compared to the povidone group. Additionally, 0/52 patients experienced a CRBSI in the chlorhexidine group compared to 12/63 in the povidone-iodine group (p=0.003).

Overall, this review identified low quality, imprecise and highly heterogeneous evidence supporting the use of chlorhexidine over povidone-iodine for reducing risk of colonisation and potentially catheter-related bloodstream infections prior to insertion. The majority of the evidence related to adults and data on paediatric patients was not reported separately. Across the evidence, concentrations of chlorhexidine ranged from 0.05% to 2% chlorhexidine vs predominantly 10% povidone-iodine solution.

Chlorhexidine tolerability

Chlorhexidine containing products carry a risk of allergy including anaphylaxis.[34]

For patients with sensitivity to chlorhexidine, epic3 recommend povidone iodine in alcohol should be used.[1] CDC guidance stated in 2011 that tincture of iodine (an iodophor) or 70% alcohol can be used as alternative.[2]

Single-use application method

As recommended by epic3, and other UK expert opinion guidance, a single-use application should be used.[10, 12, 32] Stock solutions of aqueous chlorhexidine used for skin antisepsis during CVC procedures were previously linked to a hospital outbreak of *Burkholderia cepacia* complex bacteraemia.[35] This review identified no specific studies or evidence with respect to technique for application or specifically on drying times, however povidone-iodine is known to have a longer drying time. While the manufacturers' instructions should be followed for skin antisepsis products, one expert guidance recommended that the applicator should be swept back and forth repeatedly, for 30-60 seconds.[19] The INS Standards reinforced that skin antisepsis should only be performed on skin that is visibly clean; otherwise skin should be first cleansed with soap and water, and dried, prior to this step.[10]

Neonates:

Effectiveness of antiseptic products

In 2021, the CDC produced specialised guidelines for prevention of CLABSIs in NICU patients, and conditionally recommended consideration of chlorhexidine in alcohol for skin antisepsis in neonatal intensive care unit (NICU) patients in whom "the benefits are judged to outweigh the potential risks".[6] However, this recommendation was based on a single pilot RCT (also included here and discussed below)[36]. The guideline group stated that gestational age, chronologic age,

and skin maturity should be considered for determining eligible patients. Meanwhile, both general CDC guidelines by O'Grady et al. in 2011,[2] and the US-based INS Standards[10] do not recommend a specific antiseptic agent for skin preparation in neonates, including for umbilical venous catheters. The INS standards reported that studies have not established a superior antiseptic agent for neonates.[10] In this present review, two RCTs, conducted in Ireland and the US, were identified which investigated the use of 2% chlorhexidine and 10% povidone iodine for skin antisepsis in critically ill or premature neonates in reducing colonisations and infections, and both trials demonstrated a lack of statistical power to detect a difference.[36, 37]

Single-use, sterile application method:

The INS standards also recommended a single-use and sterile applicator should be used, containing sterile solution, for performing skin antisepsis in neonates.[10]

Adverse events associated with antiseptic products on neonatal skin

In neonates, chlorhexidine has been associated with skin irritation such as dermatitis and chemical burns; guidelines produced by the CDC (O'Grady et al. 2011) stated that safety was an unresolved issue for infants aged <2 months.[2] However, recent CDC guidelines and two RCTs provide cautious evidence regarding the safe use of chlorhexidine for skin antisepsis in neonates.[6, 36-38] The CDC guidelines by Bryant et al. stated that 2% chlorhexidine is conditionally recommended as the preferred antiseptic agent, provided an individual risk assessment is conducted.[6] The Society for Hospital Epidemiology of America (SHEA) produced a companion article for these guidelines and recommended based on expert opinion that for infants born at <28 weeks' gestation (extremely preterm infants) an aqueous form of chlorhexidine should be considered.[38] Additionally, across two trials, there was a low incidence of skin reactions/dermatitis reported for patients in the chlorhexidine[37] and povidone-iodine groups,[36, 37] all of which resolved without further treatment. It was also reported in two expert guidance documents that rinsing with sterile water may prevent any chemical burns associated with chlorhexidine.[38] Guidance by SHEA recommended temporary use of povidone-iodine or reduced concentration of chlorhexidine in cases of chlorhexidine-related severe dermatitis.[38]

The systemic absorption of antiseptic products is also a reported concern among neonates. In the pilot RCT by Garland et al., detectable levels of systemic chlorhexidine were reported in serum samples of neonates receiving skin antisepsis for PICCs; (range 13-100 ng mL^{-1}).[36] Expert guidance by SHEA reported that evidence from a single non-inferiority trial identified percutaneous absorption of both 1% and 2% aqueous chlorhexidine solutions in 59 neonates.[38] Meanwhile, Kieran et al. reported that routine thyroid-stimulating hormone (TSH) biomarkers

were significantly increased in 12 neonates, all from the povidone-iodine arm of the trial, with eight neonates requiring further treatment.[37] Study authors acknowledged that while causality was a possibility via iodine interference with the underdeveloped thyroid of neonatal patients, further research is required. Both CDC guidelines and the INS Standards have stated that tincture of iodine (but not povidone-iodine) should be avoided due to the deleterious effects on the neonatal thyroid gland.[2, 10]

NOTE: MHRA notice – All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. Any incidents should be reported to IRIC and MHRA.[34]

What required standard or best-practice technique should be used for insertion?

Selection of insertion site

Adults: Non-tunnelled CVCs can be placed in the subclavian, internal jugular or femoral veins, however, there have been numerous scientific studies aimed at evaluating the different infection risks associated with each site. Two guidelines, one high quality systematic review and one RCT examining the risks from different insertion sites in non-tunnelled CVCs of adult patients were included to answer this research question.[1, 2, 39, 40] CDC guidelines by O'Grady et al., found there was sufficient evidence to recommend that, unless medically contraindicated, (e.g. for haemodialysis) the subclavian site should be used in preference to the jugular or femoral sites for non-tunnelled catheter placement.[2] However grading of the evidence was stronger for avoidance of the femoral site, compared to a preference of the subclavian site. According to the guidelines, the femoral site has been associated with higher colonisation rates; and, in some studies, higher rates of bloodstream infections. The epic3 guideline group recommended that, unless contraindicated, the upper extremity should be selected for non-tunnelled catheter placement (that is avoidance of the femoral site).[1] The guideline group cited data from a meta-analysis (excluded from this review due to quality issues), that reported no significant differences in infection risk between insertion sites across eight cohort studies and two trials of mainly ICU patients however, the authors failed to address any methodological quality and risk of bias from studies. One high quality Cochrane systematic review updated in 2012, cited evidence from a single high quality multi-centre trial of 270 critically ill adults in ICUs which indicated that the femoral site was associated with increased colonisations (14% patients vs 2%) and complications (22% patients vs 2%) compared to the subclavian site in the short-

term.[39] However, the trial is quite dated (published in 2001) and may be less generalisable to settings where quality improvement bundles have been successful in reducing infectious complications.[39]

Further RCTs are required on indication of insertion site for reducing infection and complication risks on wider patient groups. Due to the established practice of recommending against the femoral site, observational studies are often unable to correct for this intrinsic indication bias in their analyses. Guideline recommendations by the CDC by O'Grady in 2011 and the epic3 group in 2014 emphasise that the selection of CVC insertion site should be a pragmatic decision based on a clinical assessment, weighing the risks of infection and mechanical complications, and operator experience.[1, 2] Other factors should be taken into account including patient comfort, the ease by which asepsis can be maintained during the procedure and throughout aftercare, and site distance from open wounds/burns.[1, 2] This further highlights the importance of a clinical risk assessment prior to insertion.

In summary, there is a high to moderate quality of scientific evidence that the subclavian site should be selected for non-tunnelled CVCs in adults wherever possible, except where contraindicated (such as for haemodialysis) however, a thorough risk assessment and clinical judgement is needed to determine optimal site for each patient.

Neonates: In neonates, the upper or lower limb, umbilical cord or the scalp can be used as CVC insertion sites. Two US-based guidelines and four observational studies were assessed to inform this research question, including for both tunnelled, non-tunnelled and PICC insertion site placements in neonates.[2, 6, 41-44] Unlike for adults, there were no guidelines that recommended an optimal insertion site in neonatal populations. Two guidelines by the CDC judged that the benefit-harm assessment for different insertion sites in neonates was unclear.[2, 6] Evidence cited by guidelines generally included low quality, inconsistent results from observational studies. For non-tunnelled CVCs in neonates, one retrospective study reported that internal jugular inserted CVCs were associated with increased risk of infection, colonisation and obstruction/kinking compared to subclavian inserted CVCs.[44] In this study 29% of internal jugular and 15% of subclavian inserted CVCs were removed due to complications ($p<0.01$). In another study, site of tunnelled CVCs were compared; these catheters were only inserted in neonates who had a PICC placement failure.[43] Researchers found that neonates who had a tunnelled CVC inserted in the neck location via surgery under general anaesthetic (74% internal jugular; 24% subclavian, 2% external jugular vein) were found to have a higher risk of CRBSI, accidental

removal and complications compared to younger, more premature neonates who had CVC inserted in the NICU under local anaesthetic, into the saphenous vein through the groin.[43]

There was similar limited evidence related to neonatal infection risk from insertion sites of PICCs. CDC NICU guidance in 2021 stated there was limited data suggesting adverse events associated with PICCs in upper extremity sites; however this was confounded by clinicians' difficulties in accessing a suitable vein for insertion in this population; as well as the preference to choose non-femoral sites (indication bias).[6] Based on expert opinion, the authors stated that the femoral site insertions and their dressings may be more difficult to keep clean and dry than upper extremity sites. Two observational studies were included. One study found non-significant trend towards increased risk for upper extremity sites (7.1 CRBSIs per 1,000 vs 4.8 per 1,000 in lower extremity sites); with a shorter time to complication than lower extremity sites.[42] Another study reported no significant difference in complication rates between scalp, upper and lower extremity PICC sites.[41]

NICU guidelines by the CDC concluded that choice of insertion site be based on clinical needs of the patient and not solely on infection risk.[6] There is insufficient evidence to inform a recommendation on optimum catheter insertion site in neonates to reduce infection risk. The evidence from observational studies is limited, heterogeneous and at times conflicting. Higher quality randomised trials are required to provide further clarity on this issue.

Aseptic technique throughout insertion procedure

There was limited evidence from three guideline groups and three expert-based guidance documents related to the best practice technique for CVC insertions.[1, 2, 10, 11, 21, 23] No primary or secondary studies were identified for this research question.

As defined by the ANTT® framework, 'aseptic technique' is a set of specific practices and procedures used to assure asepsis and prevent the transfer of potentially pathogenic microorganisms to key-parts (for example syringe cap or needle cover) or key-sites/critical sites on the body (for example an open wound and insertion sites for invasive medical devices) or to sterile equipment/devices.[21] It involves the protection of key-parts and key-sites from contamination from microorganisms during the procedure. Both epic3 and CDC guidelines recommend that aseptic technique should be used for insertion of a CVC.[1, 2] However the epic3 guideline authors recommend surgical asepsis, which is a more complex process than medical aseptic technique; including maintaining an aseptic environment.[1] This recommendation is based on established best practice and therefore classed as expert opinion. Neither guideline

group discussed the clinical evidence to support a single approach or methodology involved. Intervention studies relating to aseptic technique tend to be focused on quality improvement and are usually bundled and compliance focused.[1] Surgical aseptic technique is a broad term for the collective actions which prevent cross-transmission of microorganisms; including sterility of equipment combined with a non-touch technique; ensuring critical parts that must remain sterile throughout the procedure are not compromised and use of appropriate hand hygiene and PPE (for example surgical scrub, sterile gloves).[1, 10, 21] CVC insertion protocols including aseptic technique procedures should be set out in local organisational policies.[9] The ANTT® is a framework that standardises the procedures for maintaining aseptic technique,[10, 21] ANTT® is considered by NICE as an accepted example of aseptic technique for vascular access.[23] The US-based Infusion Nurses Society recommends ANTT® as best practice example of a clinical framework for aseptic technique; two expert guidance documents also recommended that when adherence to aseptic technique cannot be assured, the catheter should be replaced as soon as possible, preferably within 48 hours.[10, 11]

Patient education in aseptic technique and catheter care

Seven guidance documents,[7-10, 14, 17, 19] as well as two UK NICE guidelines,[1, 23] were suitable to inform on the content of patient education. These included the indications for use, education in managing the device, as well as the risks and physical signs and symptoms of infections, complications and adverse events. According to SHEA, patient education should include comprehensive verbal and written information.[14] This is particularly important where a long-term CVC will remain in place outside of an acute care setting or where patients are discharged home with CVCs in situ.[1, 7, 17] UK NICE guidelines, the US-based APIC guidance and INS standards recommended that prior to discharge from hospital, patients and/or their caregivers should be taught any IPC-related device management techniques they need to care for the CVC, which should be in accordance with local policies. Patients/caregivers should also be taught how to recognise signs/symptoms of a complication and what to do/who to contact; discharged patients should have a clear pathway for accessing health care services, where required.[7, 9, 10, 19, 23]

Documentation of CVC insertion

The use of CVC bundles and their associated checklists are an internationally recognised measure of reducing CRBSIs and other complications, in both ICU and non-ICU settings, through standardisation of practice, and improving adherence to these standards.[2, 7, 9, 10] Furthermore, adherence to ARHAI Scotland's evidence-based recommendations for

CVC insertion and maintenance is a requisite of safe, high-quality care across NHSScotland, as set out in Scottish Government CEL 19(2013).[45] CVC insertion checklists and care bundles, alongside surveillance and audit, allow analysis of data to adjust and improve systems, performance and outcome.[1, 20] Accurate record keeping of patient care is a professional and legal requirement for clinicians and registered nurse practitioners; (as per GMC/NMC).
Three CVC-related expert guidance documents made specific recommendations regarding best practice on the documentation required in patient records when a CVC is inserted; the Royal College of Nursing, US-based Infusion Therapy Standards of Practice, as well as a 2010 Confidential Enquiry into parenteral nutrition in hospitalised patients in the UK (England, Wales and Northern Ireland).[9, 10, 46] These included: the indications for CVC insertion, the date and time of insertion, details of insertion technique, imaging and tip position, the number of attempts, the clinician performing insertion, as well as the clinicians responsible for ongoing care of the device. Additionally, documentation should include the details of the CVC (make, lot/batch, size/gauge, length, number of lumen, and expiry date), and other equipment used, the condition of skin at insertion site, details on the dressing, securement, and other site care, as well as patient information. This may include any adverse events; discomfort/pain, and vital signs where appropriate, as well as provision of patient education.[10, 46] The INS Standards also highlighted that additional documentation is required for both PICCs and midline CVCs; where details on the external and internal catheter length; and circumference of the extremity are used in clinical evaluation of possible complications (for example oedema, DVT).[10] Adverse events including serious adverse events associated with the catheter are required to be reported to the healthcare organisation; care team; management personnel; as well as IRIC and the MHRA (where appropriate).[10] Two guidance groups also highlighted that breaches of aseptic technique should also be documented.[10, 11]

What type of dressing should be used to cover the catheter site?

This review identified 18 studies in total on this topic including five systematic reviews/ meta-analyses,[47-51] four randomised controlled trials (RCTs),[52-55] one before and after study,[56] as well as three guidelines [1, 2, 23, 57] and five expert-opinion based guidance documents.[5, 9, 10, 14, 38]

Until 2016/2017, two major guidelines groups recommended that a sterile, transparent, semipermeable polyurethane dressing should be used to cover the insertion site; however O'Grady et al. stated that sterile gauze could also be selected based on preference.[1, 2] Unlike gauze, transparent polyurethane dressings allow for inspection of the catheter site and the

material is permeable to water vapour and oxygen, while remaining impermeable to microorganisms.[1] Based on the clinical expertise of guideline groups, there was agreement that where there is bleeding at the insertion site, or where there is profuse perspiration in the patient, a sterile gauze dressing is preferred – with immediate replacement of the dressing as soon as possible, when bleeding has stopped, or within 24 hours.[1, 2, 23]

This review identified two meta-analyses including a Cochrane review, which pooled trial data comparing sterile gauze dressings (secured with tape) to adhesive transparent polyurethane film dressings and reported no clear difference in risk of CRBSIs,[50] and catheter-related infections.[47] Both reviews and guidelines reported serious flaws in the evidence base, including inconsistency and imprecision; no studies related to insertion sites that were bleeding or oozing.[1, 2, 23, 47, 50, 58]

Chlorhexidine-impregnated dressings

Adults: There were two guideline documents, three systematic reviews and meta-analyses, as well as three RCTs, and one before and after study included in this review on the effectiveness of chlorhexidine-impregnated dressings in adults.[1, 2, 49-51, 54-59] Chlorhexidine-impregnated dressings are designed to continually release chlorhexidine at the CVC insertion site for the local reduction and inhibition of bacterial skin colonisation.[1, 58] In the epic3 guidelines, the use of chlorhexidine-impregnated dressings are recommended for consideration as a strategy to reduce CRBSIs.[1, 58] In 2017, the CDC guidelines updated their guidance to provide new recommendations regarding chlorhexidine-impregnated dressing types.[57] Both guidelines were in agreement that, for adults, a 2% chlorhexidine-impregnated sponge or gel dressings can help to reduce the risk of catheter-related bloodstream infections. The CDC guidelines stated this was based on high quality evidence from five trials comparing chlorhexidine-impregnated sponge (n=4) and gel (n=1) to a standard transparent adhesive dressing in reducing CRBSIs.[57] Following appraisal, two of these were included in this review, and three were excluded. epic3 guidelines also cited evidence from two reviews, three RCTs, (two of which were included in this review)[54, 59] and an economic evaluation, which indicated that chlorhexidine-impregnated sponge or gel CVC dressings reduced CRBSIs in adults.[58] The Cochrane meta-analysis by Ullman et al.[50] in 2015 reported a non-significant reduction in CRBSIs associated with chlorhexidine-impregnated dressings compared with standard polyurethane dressings. The results spanned five trials (4,876 patients), with a pooled Relative Risk (RR) of 0.65 (95% CI 0.40, 1.05), p=0.08); the evidence was rated as moderate quality evidence. Two later systematic reviews and meta-analyses with similar objectives and search periods showed similar findings; Puig-Asensio et al. in 2020 reported in their meta-analysis there was a

significant reduction in the proportion of CRBSIs (from 3.2% to 2.0%) in the chlorhexidine-impregnated dressings group compared to a combined control group of standard polyurethane dressings (17/20 studies), gauze (2/20), and no dressing (1 study).[49] Subgroup analyses showed this remained significant for adults using short-term CVCs (RR 0.63; 95% CI, 0.51, 0.77), but not for other CVC types or age groups (paediatric or neonatal patients). This was consistent with findings by Wei et al. in 2019 who pooled heterogeneous trial data that indicated a significant decrease in incidence of CRBSIs for chlorhexidine-impregnated dressings, (Odds Ratio (OR) 0.60 (95% CI 0.42, 0.85), as well as a reduction in catheter colonisation (OR 0.46 (95% CI 0.36, 0.58)).[51] However, across all three reviews, the quality of studies was poor with high clinical heterogeneity. Many trials were funded by the manufacturers of the dressings. Another important consideration is that chlorhexidine dressings require less frequent dressing changes in accordance with the manufacturer's guidelines; Puig Asensio et al. stratified results by dressing change frequency.[49] Studies reporting similar change frequencies in the intervention and control groups favoured the chlorhexidine dressing (12 studies (RR 0.58 (95% CI 0.42, 0.82) while for five studies, where dressings were changed ≤ 3 days in the control groups, and seven days in the chlorhexidine group; the effect difference was attenuated (5 studies RR 0.73 (0.46, 1.14).

A large block randomised trial by Timsit et al. in 2012, took place at 12 adult ICU sites in France, and examined chlorhexidine gel dressings compared with two types of standard dressings; the results were generalisable to critically ill adults receiving short-term catheterisation (median six days).[54] Additionally, 18% of patients had septic shock as the reason for admission. The study reported a 73% reduction in major catheter-related infections, (HR 0.27 (95% CI 0.11, 0.66) and 70% reduction in CRBSIs (HR 0.30, (0.10, 0.92) associated with the gel dressing; and a 50% reduction in catheter colonisations (Hazard Ratio (HR) 0.50 (0.34, 0.75). The trial had several limitations to its generalisability; such as different practices and skin antiseptic agents /practices used compared to current practice in NHSScotland.[54] Another trial by Ruschulte et al. took place in two High Dependency Units (HDUs) in Germany, 2009, and also found significant reductions in CVC-related infections among 601 chemotherapy patients, falling from 11% to 6%, RR 0.54 (0.31, 0.84), when a chlorhexidine sponge dressing was compared to standard sterile transparent dressing.[59] Conversely, in 2019, researchers in China conducted an RCT which reported no significant differences in the mean central-line associated bloodstream infections between chlorhexidine-containing dressings and a control group receiving a standard dressing.[55] However, the study was likely underpowered, since the few events took place during the follow up period.[55] It should be noted that all three RCTs overlapped with the included meta-analyses.[54, 55, 59] Overall, most of the evidence related to

effectiveness of chlorhexidine dressings included critically ill adults receiving short-term catheterisation. One before and after study examined use of chlorhexidine-impregnated dressings in the longer-term, outpatient setting.[56] This study, set in the USA, examined catheter-related bloodstream infections in patients with tunnelled CVCs for haemodialysis, with 5847 total dialysis sessions under study. The researchers reported no difference in the rate of bloodstream infections per 1,000 dialysis sessions.

It should be noted that chlorhexidine has some contraindications and been associated with risk of allergic reaction including anaphylaxis.[34] All primary studies were required to exclude patients with a known allergy to chlorhexidine. Two included studies reported adverse reactions to chlorhexidine.[54, 56] The RCT by Timsit et al. reporting significantly more cases of severe contact dermatitis (22 patients vs 5 in control ($p<0.001$), but no systemic adverse reactions.[54] Across all ages, there was no evidence related to the clinical impact of chlorhexidine dressings on the development of antiseptic resistance which is unknown.

Paediatric patients: There were two guidelines, one systematic review and two RCTs included which investigated chlorhexidine-impregnated dressings in paediatric patients.[1, 2, 49, 52, 53, 57, 58] The CDC stated in its 2017 updated guidelines on intravascular catheter-related infections that the use of chlorhexidine-based dressings in patients <18 years were an unresolved issue due to a lack of sufficient evidence on their efficacy.[57] This guidance cited evidence from three RCTs in ICU patients <18 years, suggesting no difference between chlorhexidine dressings and standard dressing or sterile gauze. Following critical appraisal, two of these were included in this review.[52, 53] This evidence was rated very low quality, and studies were described as likely underpowered. The systematic review and meta-analysis by Puig Asensio included a meta-analysis of four studies of paediatric populations, and found that chlorhexidine dressings did not significantly reduce CRBSIs; (pooled RR 0.71 (0.33, 1.50). One of the RCTs included paediatric ICU patients in Turkey, where efficacy of chlorhexidine-dressings was compared to gauze dressings; 63% patients were <1 year old, and the mean duration of catheterisation was 14 days.[52] Results demonstrated that compared to sterile dressings, chlorhexidine based dressings were associated with no differences in CRBSIs, colonisations, or local catheter site infections all of which were very rare events overall.[52] Another trial set in a paediatric cardiac ICU investigated the proportion of positive microbiological culture from CVC tips and segments removed from 145 patients aged 0-18 years, and found a significant reduction in CVC colonisations for chlorhexidine versus standard dressings (11 vs 21 patients, $p=0.04$), without adjustment for confounders.[53] Bloodstream infections were too rare an event in the study period to allow comparison of dressing types (seven BSIs overall).[53] Further, well-powered RCTs in

paediatric populations are required to assess the use of chlorhexidine-impregnated dressings. According to CDC and epic3 guidelines, a sterile, transparent semipermeable dressing is sufficient in paediatric patients[1, 57, 58] there is moderate quality, consistent evidence that chlorhexidine-based dressings are not associated with added benefits such as reduced CRBSIs, and therefore, no recommendation can be made regarding their use in children.

Neonates: There was broad agreement across one guideline group, a Cochrane systematic review and expert guidance that chlorhexidine dressings should not be used in neonatal patients.[38, 48, 57] The CDC strongly recommended against the use of chlorhexidine containing dressings in premature neonates, due to the risk of serious adverse skin reactions, particularly in extremely low birth weight neonates, based on moderate quality evidence.[57] A Cochrane review conducted in 2016 was in broad agreement with the guidelines, reporting an increased risk of contact dermatitis, with no reduction in CRBSI rates associated with use of chlorhexidine dressings in neonates.[48] The Society of Hospital Epidemiology produced a white paper in 2022 on practical approaches to reducing central-line associated bloodstream infections in NICUs. This latest guidance remained in agreement with the CDC 2017 guidelines; that the benefits of chlorhexidine dressings have not been demonstrated in NICU patients, and are associated with increased risk of contact dermatitis.[38, 57] However, SHEA recommended they may be considered where other interventions have failed to reduce CLABSIs in NICU patients, in infants ≥28 weeks gestation and ≥7 days of age.[38] Furthermore, SHEA cautioned that adverse reactions may not be visible underneath the sponge section of the dressing and pressure over the sponge should be avoided. There was no evidence related to dressings for specific CVC types, including umbilical venous catheters.

Overall, for evidence related to dressing types, there was considerable overlap in the included studies of all four systematic reviews[48-51], while across primary studies, there was considerable clinical heterogeneity.[52-56, 59] However, moderate quality evidence for the potential benefits of chlorhexidine-based dressings was generalisable to adults requiring temporary, short term non-tunnelled CVCs in hospital, taking into account issues such as patient tolerance and preference. For children, there is moderate quality, but consistent evidence that there is no difference between a sterile, transparent semipermeable dressing and chlorhexidine-based dressings. For neonatal patients, there was moderate quality evidence that chlorhexidine-based dressings should not be used.

According to the Royal College of Nursing, and the US Infusion Nurses Society Standards on infusion therapy, while the benefit of certain dressing types should be balanced against the risk of adverse effects, other criteria for consideration include: CVC type, insertion site, the expected

duration of the CVC, patient characteristics, including skin conditions, or any known allergies or sensitivities, the patient size, patient preference, as well as cost, sterility, wear time, and ease of use of the dressing.[9, 10]

NOTE: MHRA notice – All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. Any incidents should be reported to IRIC and MHRA.[34]

3.2 Implications for practice: Maintenance of Central Venous Catheters

What administrative and clinical checks should be in place for maintenance of CVCs?

Regular review of clinical requirement

It is well established that one of the most effective ways of reducing the risk of CRBSIs is by removal of the CVC when no longer clinically indicated, through the regular evaluation of the ongoing clinical need for catheterisation.[1, 2] There is clear consensus in the evidence that ongoing monitoring of the continuing clinical requirement of the CVC is vital – both CDC guidelines, the epic3 team, NICE Quality Standards, as well as five expert guidance documents stated that this should be conducted and recorded at least daily, in addition to when accessing or caring for the device.[1, 2, 7, 9-11, 14, 16] Additionally, review of the CVC may be required on a more regular basis, depending on the clinical situation of the individual patient.[2, 10]

Furthermore there was evidence that during this check, and at any point during care or access of the device, the dressing should be inspected to ensure it remains intact, is not visibly soiled or damp, and does not require a scheduled dressing change (see section: dressing changes, under objective 'How should the CVC access site be maintained?').[1, 2, 6, 9, 10] The INS Standards also recommended that the entire infusion system is routinely assessed for system integrity, infusion accuracy, and identification of complications and expiration dates of the infusate, dressing, and administration set.[10]

While, CVCs are more commonly used in hospitals and ICUs, patients with CVCs in situ can also be found in wider health and care settings, such as outpatient, ambulatory care, long-term care, and home settings.[1, 7, 17, 19] In home care and outpatient settings, a regular clinical review

of the need for the CVC and other routine assessments can be conducted during visits/clinical sessions, depending on patient factors.[5, 10, 17] Patients can also be educated on the maintenance of CVCs, including the need for daily inspection of the insertion site, as well as signs and symptoms of complications.[1, 7, 10, 17, 19]

Physical examination of the insertion site and surrounding area

There was consensus that a physical examination of the insertion site should also be conducted as part of the regular review of the CVC, in order to detect complications as soon as possible.[1, 2, 5, 9, 16, 17, 19] The CDC recommended that assessment of the CVC occurs daily by visual inspection, and by palpation through the intact transparent dressing.[2] According to epic3 guideline and three guidance documents, PICCs and midlines should be inspected for phlebitis using the Visual Infusion Phlebitis score.[1, 9, 16, 19] Guidance also recommended that patients should be encouraged to report any changes in their catheter site or any new discomfort.[2, 10, 19] According to the CDC guidelines, where there is tenderness or pain, the dressing should be removed and the insertion site visually inspected.[2] INS Standards also recommended that for midline catheters, increased inspection may be required for intermittent infusions of known irritants and vesicants which may cause complications.[10] The US-based Kidney Disease Outcome Quality Initiative (KDOQI) guidelines for vascular access in haemodialysis patients recommended that staff perform a basic medical history focused on signs and symptoms of CVC-related complications, in addition to a physical examination of the catheter, exit site, tunnel, and surrounding area at each catheter dressing change or dialysis session.[5]

When should hand hygiene be performed when accessing/administering medication/throughout the process of maintenance?

While no primary evidence was included, there was consensus across three guidelines and three expert-led guidance that while surgical antisepsis is required prior to insertion, standard hand hygiene (that is hand rubbing with ABHR or hand washing if visibly soiled) should be performed to decontaminate hands immediately before and after accessing the CVC line/site for standard or usual care procedures throughout its care and maintenance – including: access for infusion/medicine administration, dressing changes, or contact through palpation with the insertion site.[2, 20, 22, 23] The World Health Organization (WHO) Guidelines on Hand Hygiene in Health Care (2009)[20] clearly describe the indications for hand hygiene and present these within the WHO ‘My 5 Moments for Hand Hygiene’ approach, including emphasising the importance of performing hand hygiene before clean/aseptic procedures to prevent healthcare-associated

infections. These 5 Moments are widely promoted within NHSScotland and hand hygiene performance is audited against these Moments. As part of Moment 2 (before aseptic procedures), WHO strongly emphasises that hand hygiene should be performed before, during and after and as required throughout all handling of invasive device for patient care – regardless of whether or not gloves are worn. WHO also emphasise the need for hand hygiene when/if moving from a contaminated body site to another body site during care of the same patient.

For further guidance and recommendations on when to undertake Hand Hygiene and the use of Gloves, see the NIPCM systematic literature reviews Hand Hygiene: Hand washing, hand rubbing and indications for hand hygiene and Personal Protective Equipment (PPE): Gloves.

Hand hygiene is also a key safeguard of medical aseptic technique during routine care of CVCs.[21] The ANTT® framework is a best-practice example that is used for standardisation of aseptic technique, and outlines that prior to conducting a procedure, the healthcare worker should conduct a risk assessment, as to whether standard/medical or surgical aseptic technique is required. Clinical judgement should be used in the event that a CVC in situ required more complex or extended-duration procedures.

How should hand hygiene be performed, what product should be used?

There were no primary studies related to hand hygiene for care and maintenance of CVCs identified for this research question. Guidance by World Health Organization described how standard hand hygiene should be performed with an alcohol-based hand rub (ABHR) for at least 20 seconds as the gold standard for hand hygiene.[20] This is in alignment with hand hygiene recommendations in the NIPCM, which apply in all health and care settings in NHSScotland.[28] According to the NIPCM, while use of ABHR is the preferred method, hands should be washed with soap and water when organically soiled, including visibly dirty, visibly contaminated with blood or other body fluids, or if a patient is suspected or confirmed as having a known gastrointestinal infection (for example norovirus or a spore forming organism such as *Clostridioides difficile*). Hands should be washed with soap and water if ABHR is unavailable.

For further guidance and recommendations on Hand Hygiene, see the NIPCM systematic literature reviews Hand Hygiene: Hand washing, hand rubbing and indications for hand hygiene and Hand Hygiene Products.

What PPE should be worn and when?

No primary studies of sufficient quality were identified for inclusion in this evidence. Most guidance documents were vague in detail as to the PPE requirements for specific routine procedures during CVC care and maintenance. The decision to wear PPE and selection of PPE during CVC maintenance should be based on risk assessment of the procedure required was cited across two guidance documents; the epic 3 and NICE guidelines [1, 23] and two expert opinion document; the Association for Safe Aseptic Practice and the RCN. [9, 21] However, RCN adds that appropriate PPE should be used as per local policy.

There was some disagreement over the choice between sterile and clean gloves during access. The CDC guidelines by O'Grady in 2011, recommended that either clean or sterile gloves should be selected for dressing changes on intravascular devices,[2] however the epic3 team stated that as part of general asepsis, sterile gloves should be donned for contact with susceptible sites or clinical devices, but did not specify for routine dressing changes.[1]. However, together with NICE guidelines for IPC in primary care, the ANTT® framework and the INS Standards for infusion therapy, epic3 guidelines stated that sterile gloves are required for procedures that require any direct contact with sterile sites.[1, 10, 21, 23]. However, CDC guidelines to prevent and control CLABSI in NICU patients do not make a recommendation as they state that this remains an unresolved issue. [6]

The World Health Organization and RCN stated that sterile gloves should be used 'when performing vascular access and procedures', and 'any site care of CVCs', respectively.[9, 20] However, WHO also recommended that gloves are not indicated for 'any vascular line manipulation in absence of blood leakage'.[20] The INS Infusion Therapy Standards recommended sterile gloves be selected based on risk assessment but gave several examples (sterile gloves during any insertion site palpation, and for implanted ports, prior to insertion of non-coring needle, non-sterile gloves typically for infusion therapy, phlebotomy). The RCN Standards alongside epic3 and NICE recommended that glove selection will be based on several factors: the procedure being undertaken and any technical difficulties involved, any direct contact with susceptible sites or clinical devices, the risks involved and the local organisational policies and procedures in place.[9, 23, 58] As described in WHO hand hygiene guidance, single-use clean gloves are required where contact with blood or body fluid or contact with non-intact skin is expected.[20, 28] Finally, although the ANTT® framework recommends the use of sterile gloves for access to sterile sites, for instance the insertion site, it also stipulates

that non-sterile gloves are sufficient for standard-ANTT if a procedure can be performed without touching the CVC insertion site or sterile devices that come into contact to sterile sites.[21]

The epic3 guidelines and RCN Standards for Infusion Therapy recommended disposable plastic aprons should be worn for all infusion procedures due to the risk of contact with blood /body fluid and/or contamination of uniform.[9, 58] There was no further evidence included on other individual components of PPE to be donned for maintaining or accessing CVCs.

Overall, the evidence directly related to CVCs or intravascular devices included mainly expert-based guidance and was found to be vague in detail. Based on the principles of aseptic technique, sterile gloves should be selected for dressing changes, and where the procedure involves direct contact with key parts of the CVC, or the insertion site. For infusion therapy, or procedures where no contact with sterile sites is required, there is consensus in the literature that the decision to use or wear PPE (gloves, gowns, plastic aprons, masks/face-shields and eye protection) should be based on an assessment of the risks associated with a specific care activity and should consider whether there is a risk of contact or exposure to blood and/or body fluids, secretions and/or excretions, non-intact skin.

Further precautions may be required for specific care activities or procedures. Information on these can be found in the following sections on 'How should the CVC access site be maintained?' and 'When should removal of CVCs be considered?'

For further Guidance on PPE recommendations for standard infection prevention and control, see the NIPCM systematic literature reviews: Gloves; Aprons and Gowns; Eye/Face Protection.

How should the CVC access site be maintained?

Aseptic technique for care of CVCs

Three guidelines agreed that aseptic technique should be maintained during accessing or caring for CVCs (epic3, CDC guidelines by O'Grady and NICE guidelines).[1, 2, 23] Aseptic technique can be further broken down into surgical asepsis which is required for complex, invasive medical procedures such as insertion of CVCs, and medical or standard aseptic technique which may be applicable for care and access of CVCs. Standard asepsis described by epic3 guidelines as the application of standard principles of infection prevention, including decontaminating hands, use of PPE, maintaining an aseptic area, and not touching susceptible sites or the surface of invasive devices.[1] While guidelines did not specify whether surgical or

standard/medical aseptic technique should be used, expert opinion by the INS standards stated either one should be selected based on the ability of the healthcare worker to prevent touching sterile sites and invasive parts.[10] Additionally, the NICE guidelines in IPC for primary and community care and INS standards recommended based on expert opinion that the ANTT® framework is a best practice example of standardised technique, which is widely used in community settings.[10, 23] The principles of ANTT® include a preliminary risk assessment by the healthcare worker on the correct selection of either surgical or medical asepsis for the procedure at hand. However the INS standards suggested that for CVC care and maintenance procedures which are relatively straight-forward, standard-ANTT should be used, and provided the following example scenarios including: accessing and changing a needleless connector, flushing, locking, administration set preparation and change, medication administration and wound care.[10]

This review identified one retrospective before and after study in Australia which attempted to compare the effectiveness of ANTT versus a sterile technique during routine changing of needle-less connectors as part of CVC maintenance.[61] The study included 150 bone marrow transplant recipient inpatients, who received either ANTT care using non-sterile clean gloves without a sterile field, or care using a sterile technique (described as use of sterile dressing pack including gloves and sterile field, and using sterile gauze to hold lumens). However, the study was underpowered to report any differences in primary outcomes, and additionally represents a bundled intervention. Research on the individual components of aseptic technique during care of CVCs was not identified.

Single-use product for 'scrub the hub'

There is substantial evidence that CVC access ports, hubs and needle-less connectors become contaminated with microorganisms and require thorough disinfection prior to, and after access to CVCs. This is important in order to prevent transfer of organisms to intraluminal parts of the CVC, and to prevent potential biofilm formation.[2] The CDC guidelines recommend to 'minimise contamination risk by scrubbing the access port with an appropriate antiseptic (chlorhexidine, povidone iodine, an iodophor or 70% isopropyl alcohol) and accessing the port only with sterile devices'.[2] The guidelines stressed that time spent applying the disinfectant in addition to chosen disinfection solutions may be important to effectiveness. Two US-based guidance documents (SHEA and INS) recommended 70% alcohol or alcohol-based chlorhexidine be used; but there was inconsistency as to the duration of scrubbing ports in order to optimise decontamination; SHEA stated a minimum of 5 seconds of applied mechanical friction, while US INS standards stated 5-15 seconds.[10, 38] In the UK, epic3 guidelines, along with the Royal College of Nursing

recommended a single-use application of 2% chlorhexidine gluconate in 70% isopropyl alcohol, with 15 seconds active scrubbing, followed by drying time prior to access.[1, 9] This was based on expert consensus of the guideline group; as well as indirect evidence from experimental studies. The guideline group identified no RCTs comparing the efficacy of different methods of decontaminating ports and hubs prior to access. This review identified four before and after studies assessing 'scrub the hub' policies – all of which related to paediatric and neonatal units.[62-65] One study in Sweden compared a 15 second duration of scrubbing the hub to a single swipe with 5% chlorhexidine in alcohol over 25-month inpatient period on the incidence of coagulase-negative *Staphylococci* sepsis.[62] Researchers reported a reduction from 1.5% to 0% in the intervention phase; but this did not reach statistical significance. Three before and after studies compared 2% chlorhexidine in alcohol wipes to using alcohol wipes alone, and found reductions in confirmed septicaemia and CRBSIs.[63-65] However, all three studies were subject to confounding bias; in two of the studies, authors noted that additional quality improvements in hand hygiene were ongoing, as well as some clinical differences between the patient groups in the intervention and control periods.

For those with chlorhexidine intolerance, epic3 guidelines stated that povidone-iodine should be selected.[1] However, according to INS standards, this has a longer drying time (up to 6 minutes) making it less preferable in a busy clinical setting.[10] INS standards also recommended disinfection of surfaces before and after each access, including between subsequent entries of medication in a single session to remove organic and inorganic debris, although this was not addressed in the primary evidence. Four guidance groups emphasised the importance of checking compatibility of connectors/parts with disinfection agents, via manufacturer's directions.[2, 9, 10, 23] NICE guidance recommended consideration of an aqueous solution of chlorhexidine gluconate where alcohol is not permitted by the catheter manufacturer's recommendations.[23]

Dressing changes

Adults and paediatric patients: If the dressings are non-intact or have become loosened, this increases the risk of microorganisms gaining entry via the CVC. There is consensus from four guidelines that CVC dressings should be changed when the dressing is compromised, including damp, loosened or visibly soiled, as soon as possible; CDC, epic3, NICE quality standards and the INS.[1, 2, 10, 16] This includes any lifting of the sides, other signs of detachment, or where there is a loss of skin integrity below the dressing.[10] Expert opinion guidance from the Kidney Outcome Quality Initiatives (KDOQI) in the US recommended that changing dressing should be based on the clinician's discretion and best clinical judgment, with a minimum of once weekly.[66]

There was some disagreement for short-term CVC gauze dressings, with CDC stating these should be routinely changed every 2 days for gauze dressings,[2] epic3 recommended as soon as possible (through change to semipermeable dressings),[1] and NICE guidelines on IPC in primary and community care recommended changing every 24 hours.[23] However, all three guidelines recommended that semipermeable polyurethane dressings and chlorhexidine-impregnated dressings should be changed every 7 days.[1, 2, 23] The NICE guidelines on IPC in primary and community care cited one study of very low quality which found that polyurethane dressings changed once per week as opposed to twice per week were associated with decreased inflammation; although results were of "uncertain clinical importance".

One systematic review and meta-analysis was identified for this review which reported no significant difference in infection rate according to frequency of dressing change when using semipermeable dressings -the analysis compared a dressing change frequency of 10-15 days with a more frequent group of 2-5 days.[47] The pooled relative risk (RR) was 1.04, (95% CI 0.67, 1.61). However, the review reported the risk of skin irritation was reduced with longer intervals between changes (10-15 days vs 2-5 days) (RR 0.71, (95% CI 0.052, 0.96)).

Three guidelines (epic3, CDC guidelines by O'Grady and NICE guidelines) recommended that standard dressings used on tunnelled or implanted CVC sites should be changed no more than once per week (unless the dressing is soiled or loose), until the insertion site has healed.[1, 2, 23] There was no recommendation by CDC regarding the necessity for any dressing on well-healed exit sites of long-term cuffed and tunnelled CVCs,[2] while epic3 stated these dressings may no longer be required.[1] Expert guidance by the Infusion Nurses Society recommended that for implanted ports, dressing should be changed every seven days, and if gauze is needed over non-coring needles and access sites, a dressing change every two days is recommended.[10] Meanwhile, the Royal College of Nursing stated a kit should be used to improve standardisation of the procedure.[9] The RCN also recommended that dressing change frequency and procedures should be laid out in organisational policies. Any dressing changes are required to be documented and the dressing labelled with date and time, with care taken to avoid placement of any labels over the insertion site.[9, 10]

There was no separate evidence of sufficient quality identified to inform dressing changes in paediatric patients.

Neonatal patients: There is consensus from two expert guidance documents that no scheduled dressing change should be performed for neonatal patients.[10, 38] Instead, the US-based SHEA

guidance for prevention of central line-associated bloodstream infections in NICUs, as well as the INS standards both recommended that dressings should only be changed as required per patient, due to clinical indications, or where the dressing is compromised (for example soiled, damp or loose).[38] SHEA stated this was regardless of gestational or chronological age, or birth weight, to prevent or reduce skin damage and skin barrier breakdown associated with each dressing change.[38] Additionally, guidance by the US National Association of Neonatal Nurses stated that neonatal dressing changes should be performed using sterile technique.[60] Care should also be taken not to damage the skin at the site during removal of the existing dressing.[60]

Skin antisepsis during dressing changes and prior to access

Three guidelines (epic3, NICE and CDC) recommend that the insertion site should be prepared with antiseptic agent and allowed to dry prior to every dressing change, or prior to accessing the device.[1, 2, 23] The NICE guidelines on IPC for primary and community settings discussed the evidence for skin antisepsis specifically during ongoing care and maintenance of CVCs.[23] The group reported that on the balance of highly uncertain, very low quality evidence across five trials, chlorhexidine gluconate in alcohol was the most effective choice; the guidelines also noted that using the same antiseptic/disinfectant as used in scrubbing the connector hubs could help reduce the chance of confusion around which solution to use in community or home care settings.[23] These trials were not included in the present review due to low quality (n=3), the dated nature of the research (n=1) or due to the inclusion of arterial catheters (n=1). The guidelines referred to the CDC recommendation of using >0.5% concentration, however acknowledged that further research on the optimal concentration was required. The importance of checking compatibility of connectors/ parts with skin antiseptic agents via manufacturer's directions was also emphasised in guidelines.[2, 9, 10, 23]

The effectiveness and potential side effects of skin antiseptic agents are also described in the discussion for insertion of CVCs (skin antisepsis prior to insertion). This evidence remains directly applicable to skin antisepsis during ongoing care and dressing changes, with the exception of neonatal patients receiving umbilical venous catheters (UVCs). These catheters are short-term (≤7 days) and routine dressing changes are not indicated; no evidence related to skin antisepsis post-insertion was identified, except in one RCT, where if a change of dressing was required, the investigators cleansed the site with sterile saline, followed by drying with sterile gauze.[37] The evidence on skin antisepsis specifically related to UVCs was insufficient and expert clinical judgement should be used, weighing benefits with potential risks.

Continued patient education

Three guidelines and one expert guidance documents were identified which recommend follow-up training and support should be made available to patients with CVCs and their carers, as part of their care plan.[3, 4, 10, 23] Particularly for discharged patients, this should include proper care of the CVC, and precautions for prevention of infections including dressing care, aseptic technique, hand hygiene, and self-monitoring for signs and symptoms of infection and any impact on aspects of daily living.

NOTE: MHRA notice- All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. Any incidents should be reported to IRIC and MHRA.

When should removal of CVCs be considered?

Adults and paediatric patients: Three guideline groups, (epic3, the CDC and the US-based KDOQI Vascular access guidelines for haemodialysis)[1, 2, 66], as well as expert opinion-based guidance from the UK (RCN, AAGBI)[9, 12] and the USA (INS, SHEA) provided consistent but low quality evidence related to CVC removal in adults.[10, 38] Both epic3 and CDC guidelines strongly recommended the prompt removal of CVCs where they are no longer essential.[1, 2] Both guidelines also recommended that CVCs, including PICCs, should **not** be routinely replaced as a strategy to prevent CRBSIs. This was based on very dated evidence from three trials and one meta-analysis. Two trials compared a scheduled CVC replacement at day seven with removal when clinically indicated, while one trial compared replacement at day three versus clinical need, and found routine change was not associated with CRBSIs.[1, 2] This evidence was in agreement with various multidisciplinary expert-based guidance documents, including: RCN, and INS Infusion therapy standards, SHEA and AAGBI guidance.[9, 10, 12, 14] In addition, both the CDC and the UK Royal College of Nursing stated that midline catheters should also only be replaced when there is a specific clinical indication or according to manufacturer's instructions, and that the optimal duration of midline catheters was unknown.[2, 9] For tunnelled CVCs, the US KDOQI Clinical Practice guidelines for vascular access for haemodialysis recommended, based on expert opinion, that tunnelled CVCs which were in use for haemodialysis are not associated with a maximum upper duration limit, but that regular evaluation should determine if the CVC remains the most appropriate dialysis access option.[66] Further evidence related to optimal duration/removal of CVCs in adults was not identified. There was no separately reported evidence for paediatric patients.

Neonates: This review identified two CDC guidelines (O'Grady et al and Bryant et al)[2, 6] and two primary studies (Butler-O'Hara et al and Milstone et al)[67, 68] that related to CVC removal in neonates. Two CDC guidelines recommended both UVCs and PICCs be removed as soon as possible and when no longer needed due to concerns regarding increasing risk of CRBSIs in neonates.[2, 6] CDC guidance on NICU patients by Bryant et al. based this recommendation on very low quality evidence from nine observational studies which showed a positive correlation of PICC-related infections with increasing dwell time.[6] One of these studies was included in the ARHAI review below, the remaining eight were excluded due to quality issues (n=6), lack of generalisability to NHSScotland settings (n=1), or were dated (n=1). Both included guideline groups were unable to identify an optimal maximum duration of PICCs in neonates due to imprecision and heterogeneity in studies, therefore clinical judgment should be used for individual neonates who have an ongoing CVC need. A large observational study published in 2013 provided evidence that increased PICC dwell time was associated with increasing risk of central line-associated bloodstream infections in 3,967 NICU patients in the USA.[68]

For umbilical venous catheters, the CDC guidelines by O'Grady et al. in 2011 recommended that UVCs may be used for up to 14 days if managed aseptically.[2] Meanwhile, CDC guidelines by Bryant et al. recommended that UVCs should be considered for removal at or before seven days dwell time and a peripherally inserted central catheter (PICC) or other long-term central venous catheter inserted, in NICU patients requiring long-term central venous access.[6] Evidence included one RCT and three observational studies. These were appraised by ARHAI during this review; the RCT and one observational study were sufficient quality and included below. The block-randomised trial compared UVC duration for 210 premature neonates.[67] In the short-term group, UVCs were removed before 10 days, where they were then indicated to receive PICCs if necessary (n=106) while in the long-term group, the UVCs could be used until day 28 (n=104). The overall rate of catheter-related sepsis was 20% in long-term patients versus 13% in the short-term group (p=0.17) however the study was statistically underpowered.[67] Meanwhile, a prospective observational study in two NICUs in the USA over a ten year period examined the trend in the dwell time until CLABSI in 19 neonates – they found that the CLABSI incidence rose from 4% of all events by Day 14, up to 17% by Day 18; representing a steep increase. However, the units also had a policy of replacement of UVC with a PICC device after days 5-7, which limited interpretation of results from those with UVCs remaining in situ.[69] There are a number of potentially confounding factors associated with different insertion sites and catheter dwell times; the type of catheter required is intrinsically linked to patient factors that may increase or decrease risk of CRBSI, for example an umbilical

catheter is typically placed within the first week of birth when infants may be at a higher risk for infection. It is therefore difficult to compare outcomes in UVCs with those for PICCs, which may be in situ longer and in older (more than seven days old) infants. Overall, for neonatal patients, there was moderate quality evidence that while CVCs should be removed as soon as clinically indicated and/or no longer necessary – for UVCs specifically, these should be clinically assessed after one week in situ, to consider replacement with a PICC. The evidence was imprecise on this exact number of days, (ranging between five and 14), which will be dependent on patient risk factors and aseptic management of the device. Further research was needed to identify a maximum duration of PICCs in neonatal patients.

4. Implications for Research

Generally, there was a lack of high-quality primary research examining specific components of CVC insertion and maintenance bundles. Much of the evidence was excluded due to use of multiple interventions as part of quality improvement tools. Due to the clinical heterogeneity among the population using CVCs, there was a lack of generalisability from trials from across various health and care settings, age ranges, and medical specialties. Many included studies had similar limitations relating to confounding and indication bias, particularly for paediatric and neonatal populations. Much of the evidence for some recommendations therefore came from expert opinion of clinicians, especially for some well-established practices/clinical techniques, for example hand hygiene and individual components of PPE, where trials may be unethical/impractical and indirect evidence was used.

The evidence related to dressing type (such as chlorhexidine-impregnated dressings) was over-generalisable towards critically ill adults in ICU, and therefore this limited extrapolation of their effectiveness outside this population and setting.

In some trial data, CRBSIs or other measurements were very rare outcomes, which meant that well-conducted trials were too underpowered to detect meaningful differences. There was heterogeneity in outcome measures including catheter related infections with or without bacteraemia, sepsis, CRBSIs and use of surveillance data, and studies used different denominators.

For CVC maintenance, it was not clear or specific in the evidence base, where sterile versus non-sterile gloves should be selected due to a lack of high-quality randomised control trials. Furthermore, the individual components of aseptic technique requires further research to take account of the little data on longer-term primary, community, or home-based CVC care.

5. Recommendations

This review makes the following recommendations based on an assessment of the extant scientific literature on the insertion and maintenance of Central Venous Catheters (CVCs) in the health and care setting.

5.1 Recommendations for Insertion of Central Venous Catheters

What are the indications for CVC insertion?

CVCs are frequently inserted for the repeated administration of intravenous therapy (IV) such as fluids, medication, chemotherapy, parenteral nutrition or blood products and can be inserted for dialysis and frequent blood sampling.

(No recommendation)

CVCs are indicated for infusates that are unsuitable for peripheral vascular catheterisation and when extended or intermittent vascular access is required.

(Category C recommendation)

Central venous catheter (CVC) is the preferred route for the administration of neonatal parenteral nutrition, however peripheral vascular access may be considered if:

- it would avoid a delay or interruption to parenteral nutrition
- short-term use of peripheral venous access is anticipated, for example less than five days
- central venous access is impractical

(Category C recommendation)

The CVC with the minimum essential number of ports or lumens should be selected and the smallest diameter capable of delivering the required therapy.

(Category C recommendation)

A single or dedicated lumen is recommended for parenteral nutrition or any other lipid-based solution.

(Category C recommendation)

CVC type should not be based on reduction of infection risk alone. The CVC type should be selected based on clinical judgement, with consideration of the following:

- the intended purpose, duration and appropriate route of access for therapy
- consideration of the patient's age, diagnoses, severity of illness, medical history and vascular condition
- consideration of the patient's history of intravascular devices
- the risk to benefit ratio associated with both infectious and non-infectious complications
- operator experience
- staff resource and ability to care for the device

(Category C recommendation)

What administrative and clinical checks should be in place prior to insertion?

CVCs should only be inserted when there is a clear clinical indication for their use. A clinical review of the necessity and indication for CVC use should be conducted and documented prior to insertion.

(Category C recommendation)

When should hand hygiene be performed throughout the procedure?

For CVCs (including midline and PICC catheters), surgical hand antisepsis should be performed immediately before donning maximal sterile barrier precautions.

(Category C recommendation)

Surgical hand antisepsis should be conducted according to recommendations set out in the NIPCM.

(Category C recommendation)

For more information, see NIPCM systematic literature review 'Surgical hand antisepsis in the clinical setting'.

What Personal Protective Equipment (PPE) should be worn and when?

Ensure that maximal sterile barrier precautions are used by healthcare workers, including headwear, fluid-resistant surgical mask (FRSM), sterile gown and sterile gloves.

(Category B recommendation)

How should the environment be prepared prior to insertion?

The environment should be suitable for maintaining aseptic conditions and surfaces should be decontaminated appropriately in accordance with the NIPCM prior to CVC insertion. The environment should be visibly clean, free from non-essential items and equipment and have adequate lighting and privacy.

(Category C recommendation)

How should equipment be prepared prior to insertion?

All sterilised or aseptic procedural equipment should be handled with sterile gloves.

(Category B recommendation)

Sterile items should be inspected for product integrity, cleanliness, and an expiry date.

(Category C recommendation)

How should the insertion site be prepared?

For adults, ensure that a single-use application of 2% chlorhexidine** in 70% isopropyl alcohol is used for skin preparation of the insertion site and allowed to dry in accordance with manufacturer's instructions, before CVC insertion.

(Category B recommendation)

Chlorhexidine** should be avoided in patients susceptible to skin irritation and an appropriate alternative antiseptic used (such as 10% povidone-iodine).

(Category B recommendation)

For paediatric patients, ensure that single-use application of an appropriate antiseptic (based on individual patient clinical assessment) is used for skin preparation of the insertion site and allowed to dry in accordance with manufacturer's instructions before CVC insertion.

(Category C recommendation)

For neonates, ensure that single-use, sterile application of an appropriate antiseptic (based on individual patient clinical assessment) is used for skin preparation of the insertion site and allowed to dry in accordance with manufacturer's instructions before CVC insertion.

(Category A recommendation)

** **Note:** All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. View **MHRA alert**.

What required standard or best practice technique should be used for insertion?

For adults, use a subclavian site for insertion of non-tunnelled CVCs unless clinically contraindicated. The femoral site should be avoided where possible.

This recommendation does not replace the need for undertaking a thorough clinical assessment to determine optimal CVC placement for each patient.

(Category A recommendation)

For paediatric patients and neonates, there was insufficient evidence to inform a recommendation regarding insertion site. Local policies should be followed.

(No recommendation)

Ensure that maximal sterile barrier precautions are used by healthcare workers. This applies to both PPE and application of a full sterile body drape to ensure surgical asepsis.

(Category B recommendation)

Ensure that surgical aseptic technique is maintained throughout insertion of CVCs.

(Category C recommendation)

Patient education should be provided on the indications and management of CVCs, risks and physical signs/symptoms of infections, complications and adverse events.

(Category C recommendation)

What type of dressing should be used to cover the catheter site?

Ensure that a sterile, transparent, semi-permeable dressing is used to cover the catheter site.

(Category B recommendation)

A sterile gauze dressing may be used if the patient has profuse perspiration or if the catheter insertion site is bleeding or oozing. Gauze dressings prevent visual observation of the insertion site and should be replaced with a sterile, transparent semipermeable dressing as soon as possible for example when bleeding/oozing has resolved.

(Category C recommendation)

For adults, consider using a chlorhexidine-impregnated** sponge or gel dressing to cover the catheter site. Chlorhexidine-impregnated dressings should be avoided in patients susceptible to skin irritation.

(Category A recommendation)

For premature neonates, avoid the use of chlorhexidine-impregnated** dressings in view of the associated risk of with contact dermatitis.

(Category B recommendation)

The insertion site should remain visible through the dressing (except if using gauze dressing).

(Category C Recommendation)

** **Note:** All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. View **MHRA alert**.

5.2 Recommendations for Maintenance of Central Venous Catheters

What administrative and clinical checks should be in place for maintenance of CVCs?

Ensure that the need for the CVC in situ is reviewed and recorded on a daily basis and during every access. This review should include a check to ensure that the CVC dressing is intact and does not require changing. The date and time of this check should be documented.

(Category C recommendation)

The insertion site should be inspected at least daily, and prior to each use, for signs of infection or complications, through an intact dressing. The frequency of assessment may be increased depending on patient factors such as age (neonates), clinical condition, type of therapy and healthcare setting.

(Category C recommendation)

For midlines, and PICCs, catheter insertion site should be monitored for signs of phlebitis using a standardised phlebitis scale such as the Visual Infusion Phlebitis (VIP) tool.

(Category C recommendation)

When should hand hygiene be performed when accessing/administering medication/throughout the process of maintenance?

Hand hygiene should be performed immediately before accessing the device and throughout the care and maintenance of CVCs, including dressing changes and removal.

(Category C recommendation)

How and when should hand hygiene be performed, what product should be used?

Hand hygiene should be performed before and after palpating the insertion site. The catheter insertion site should not be touched after the application of skin antisepsis unless aseptic technique is maintained.

(Category C recommendation)

As per the NICPM, hand hygiene should be performed with an alcohol-based hand rub (ABHR). Hands should be washed with soap and water if hands are visibly dirty, contaminated with blood and/or other body fluids or if patient is suspected or confirmed of having a known gastrointestinal infection (for example norovirus or a spore forming organism such as *Clostridioides difficile*)

(Category C recommendation)

What PPE should be worn and when?

Sterile gloves should be used to conduct dressing changes and any contact with key parts/critical sites.

(Category C recommendation)

Non-sterile gloves may be selected based on risk assessment for procedures that do not involve direct contact with the CVC insertion site, nearby wound area or key parts/critical sites of the device, during the ongoing care and maintenance of CVCs.

(Category C recommendation)

Single-use aprons should be worn during procedures or activities where there is a risk of exposure to blood and/or body fluids.

(Category C recommendation)

Note: Further precautions may be required for specific care activities or procedures. Recommendations for these can be found under 'How should the CVC access site be maintained?' and 'When should removal of CVCs be considered?'

How should the CVC access site be maintained?

Standard aseptic technique should be maintained for accessing or caring for CVCs, including dressing changes.

(Category C recommendation)

Ensure that a single-use antiseptic containing 2% chlorhexidine** in 70% isopropyl alcohol is used to clean the access hub prior to accessing – rub the access hub for at least 15 seconds ('scrub the hub'). The product should be allowed to dry fully in accordance with manufacturer's instructions. The compatibility of connectors/parts with disinfection agents should be checked via manufacturer's instructions.

(Category B recommendation)

Chlorhexidine** should be avoided in patients susceptible to skin irritation and an appropriate alternative antiseptic used (such as 70% isopropyl alcohol or 10% povidone-iodine).

(Category B recommendation)

Ensure that the CVC dressing is changed if it becomes damp, loose or visibly soiled, or if skin integrity becomes visibly compromised under the dressing.

(Category C recommendation)

Dressings should be changed on a regular basis according to the manufacturer's instructions. The following dressing change frequencies are recommended:

Where a sterile gauze dressing is indicated for use (such as for bleeding, oozing, perspiration), the dressing should by changed every 24 hours, or sooner. Gauze dressings prevent visual observation of the insertion site and should be replaced with a sterile, transparent semi-permeable dressing as soon as possible for example when bleeding/oozing has resolved.

(Category C recommendation)

For adults, ensure that the CVC dressing has been changed in the last seven days, including for both standard semi-permeable transparent dressings, and for chlorhexidine-based dressings.

(Category B recommendation)

For paediatric patients, ensure that CVC dressings have been changed in the last seven days.

(Category C recommendation)

For neonates, routine dressing changes can increase risk of skin barrier breakdown or damage and should not be performed if the dressing remains intact. Dressings should only be changed if clinically indicated and must be performed using a sterile technique with maximal barrier precautions.

(Category C recommendation)

Dressings may not be required for patients with well-healed implanted ports/tunnelled CVCs; clinical judgement should be used.

(No recommendation)

During dressing changes for adults, ensure that a single-use application of 2% chlorhexidine** in 70% isopropyl alcohol is used for cleaning the insertion site and allowed to dry according to the manufacturer's instructions.

(Category B recommendation)

Chlorhexidine** should be avoided in patients susceptible to skin irritation. An appropriate alternative antiseptic (such as 10% povidone-iodine) should be used to clean the insertion site and allowed to dry according to the manufacturer's instructions.

(Category B recommendation)

For paediatric patients, ensure that a single-use application of an appropriate antiseptic (based on individual patient clinical assessment) is used for cleaning the insertion site, and allowed to dry in accordance with manufacturer's instructions, during dressing changes.

(Category C recommendation)

For neonates, where dressing change is clinically indicated, ensure that a single-use, sterile application of an appropriate antiseptic (based on individual patient clinical assessment) is used for skin preparation of the insertion site, and allowed to dry in accordance with manufacturer's instructions.

(Category C recommendation)

Continued /follow-up patient/carer education should be provided throughout the care of CVCs

(Category C recommendation)

** Note: All medical and nursing staff involved in the use of all medical devices and medicinal products containing chlorhexidine should be aware of the risk of an anaphylactic reaction due to chlorhexidine allergy. View **MHRA alert**.

In patients of all ages, CVCs should be promptly removed when clinically indicated, or when no longer clinically required, to reduce the risk of catheter-related bloodstream infection.

(Category A recommendation)

In adults and paediatric patients, CVCs should not be replaced at scheduled intervals as a strategy to prevent risk of catheter-related infection.

(Category B recommendation)

In neonatal patients with an umbilical venous catheter in situ for 7-14 days who have an ongoing need for CVC access, a clinical risk assessment should be conducted to consider removal and replacement with a peripherally inserted central catheter (PICC).

(Category A recommendation)

After removal, the CVC insertion site wound should be covered with a sterile semi-transparent dressing and regularly assessed for adverse reactions until fully healed.

(Category C recommendation)

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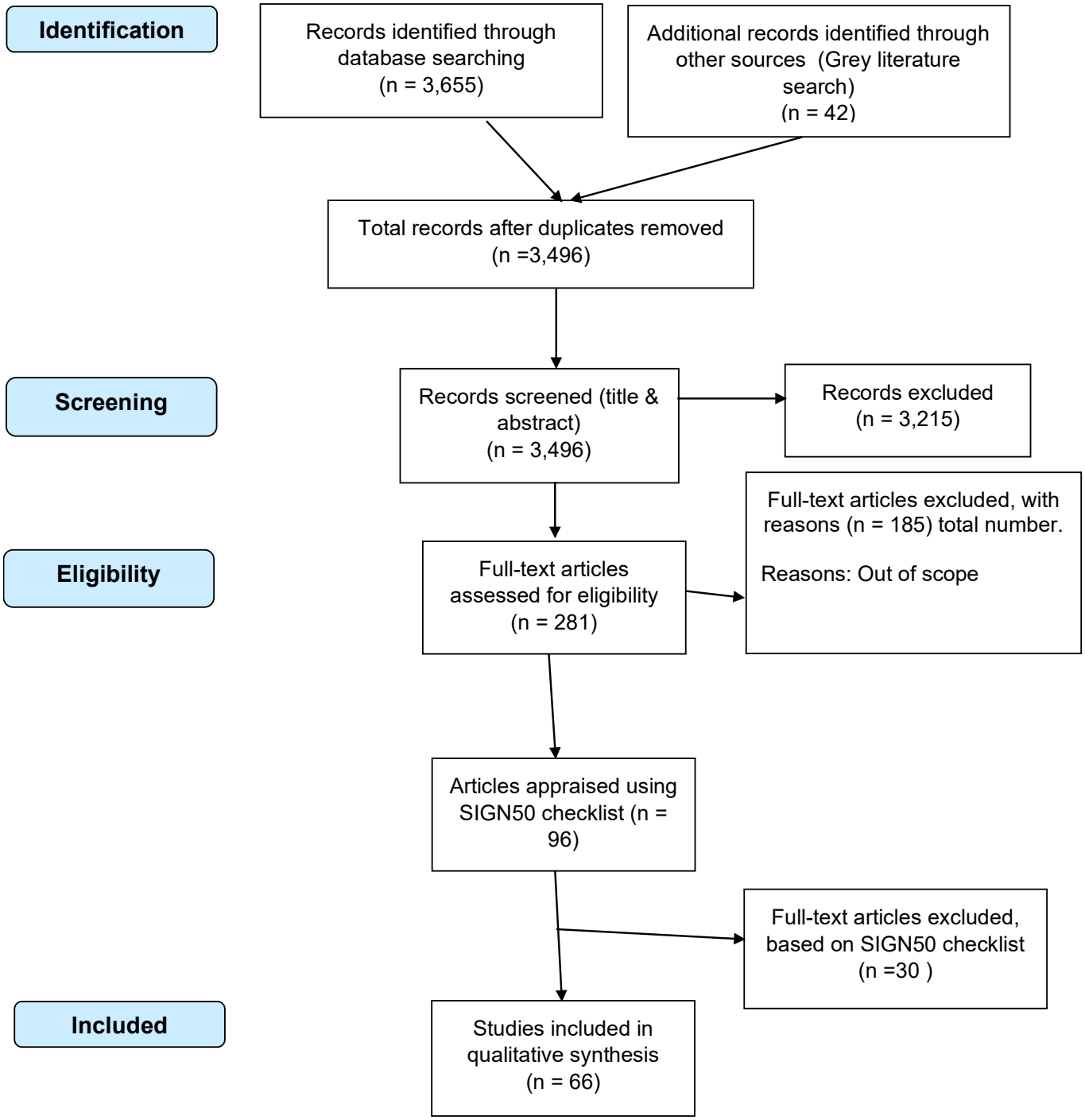
Appendices

Appendix 1: Grades of recommendation

Grade	Descriptor	Levels of evidence
Mandatory	'Recommendations' that are directives from government policy, regulations or legislation.	N/A
Category A	Based on high to moderate quality evidence.	SIGN level 1++, 1+, 2++, 2+, AGREE strongly recommend
Category B	Based on low to moderate quality of evidence which suggest net clinical benefits over harm.	SIGN level 2+, 3, 4, AGREE recommend
Category C	Expert opinion, these may be formed by the NIPC groups when there is no robust professional or scientific literature available to inform guidance.	SIGN level 4, or opinion of NIPC group
No recommendation	Insufficient evidence to recommend one way or another.	N/A

Appendix 2: PRISMA Flow Diagram[70]



Appendix 3: Definitions of CVCs

Table 1. Definitions of CVCs adapted from scientific literature[1, 2, 9, 10]

CVC	Definition
Non-tunnelled CVCs	Short-term CVC which can include single and multiple lumens (up to 5), and are percutaneously inserted into the subclavian, internal jugular or femoral veins. A short-term non-tunnelled CVC typically enters the vein from a skin puncture site over the vein. The uses of non-tunnelled CVCs include administration of fluids, blood and medication as well as access and blood draw. Typical duration is short - up to 7-10 days.
Tunnelled-CVC	Long-term CVCs, are image-guided or surgically implanted into the subclavian, internal jugular or femoral vein. These catheters have a cuff which is surgically implanted. The cuff embeds into the tissue of the patient providing additional protection against central line infection. Their uses include frequent, long-term access, for example parenteral nutrition, transfusion, haemodialysis, blood sampling. Typical duration is long-term (in months or years).
Peripherally inserted central catheters (PICCs)	Peripherally inserted CVCs, inserted into the basilic, cephalic or brachial veins and enter the superior vena cava. PICCs can be used for administration of fluids and medication including chemotherapy, parenteral nutrition, blood sampling. PICC duration is typically medium-term (for example 4 weeks to 6 months).
Totally implantable catheters	Also called implantable ports and are image-guided or surgically placed beneath skin and have a subcutaneous port that is accessed with a needle via a subcutaneous port or reservoir with a self-sealing septum that is accessible by needle puncture through intact skin. They are implanted into the subclavian or internal jugular vein. They can be single or double lumen and are typically used for infrequent access on a long-term basis; duration is long (months or years).
Umbilical catheter (neonates)	Inserted via the umbilical stump soon after birth, an umbilical venous catheter (UVC) is often used for vascular access in neonates. These permit both collection of blood samples and measurement of haemodynamic status. UVCs are used in the short-term.

Table 2. Other lines inserted and maintained as per CVC guidance[1, 2, 9, 10]

Line type	Definition
Midline catheters	Midline catheters are commonly placed in proximal basilic or cephalic veins via antecubital fossa; they do not enter central veins. Midline catheter uses include administration of fluids, blood and medication. Typical duration is between 1-4 weeks. They may be used where patients present with poor peripheral vascular access and when the use of a central venous catheter is contraindicated. The midline catheter provides venous accessibility along with an easy, less hazardous insertion at the antecubital fossa. For neonates and paediatric patients, basilic, cephalic, and brachial veins are used. Additional site selections include veins in the leg (eg saphenous, popliteal, femoral) with the tip below the inguinal crease and in the scalp with the tip in the neck, above the thorax. For neonates, in addition to arm veins, midline catheters may be inserted via a scalp vein with the distal tip located in the jugular vein above the clavicle or in the lower extremity with the distal tip located below the inguinal crease.