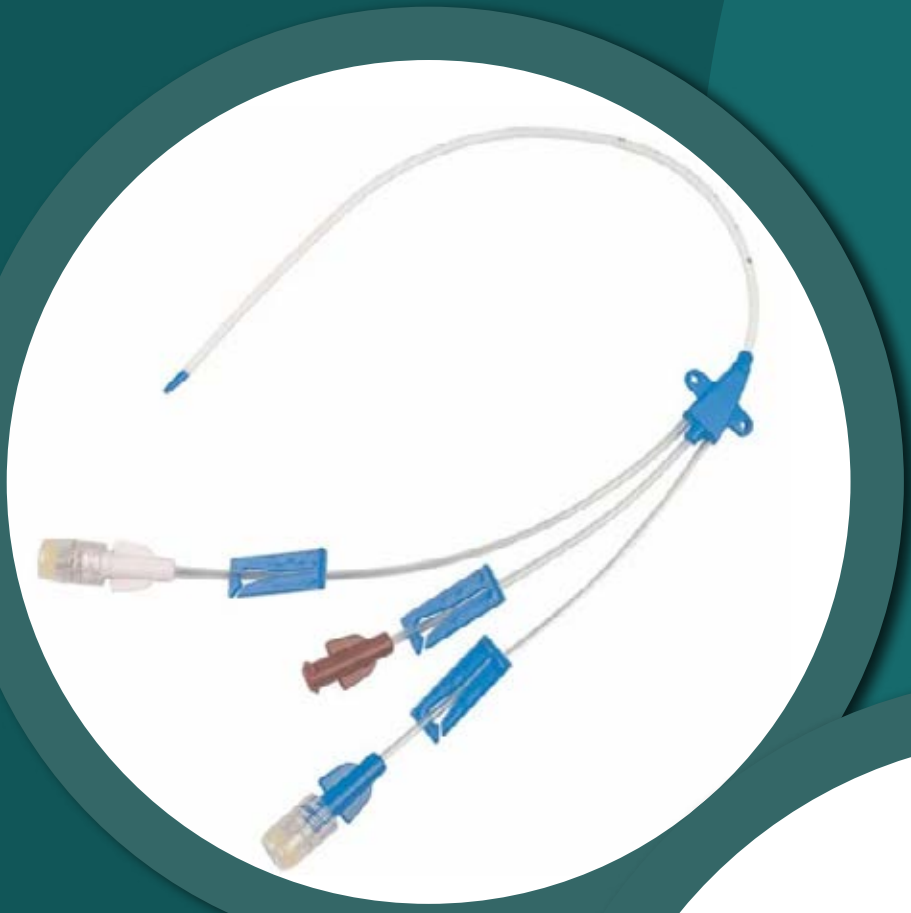
# Guidelines for the prevention of bloodstream infections and other infections associated with the use of intravascular catheters

## Part 2: central venous catheters



World Health Organization

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## Part 2: central venous catheters

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Guidelines for the prevention of bloodstream infections and other infections associated with the use of intravascular catheters. Part 2: central venous catheters

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Declarations of interest of external experts and participants are provided in Annex 1.

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# ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| AMR | antimicrobial resistance |
| BSI | bloodstream infection |
| ANTT | Aseptic non-touch technique |
| CDC | Centers for Disease Control and Prevention |
| COVID-19 | coronavirus disease 2019 |
| CRBSI | catheter-related bloodstream infection |
| CI | confidence interval |
| COE | certainty of evidence |
| CVC | central venous catheter |
| CVC-AIC | central venous catheter-associated infectious complications |
| CVC-BSI | central venous catheter-bloodstream infection |
| EDTA | ethylenediaminetetraacetic acid |
| EML | Essential Medicines List |
| GDG | Guideline Development Group |
| GPS | good practice statement(s) |
| GRADE | Grading of Recommendations, Assessment, Development and Evaluation |
| GRC | Guidelines Review Committee |
| HAI | health care-associated infection |
| HIC | high-income country |
| ICU | intensive care unit |
| IPC | infection prevention and control |
| IV | Intravenous |
| LMICs | low- and middle-income countries |
| MeSH | Medical Subject Headings |
| MMIS | multimodal improvement strategy |
| NHD-CVC | non-haemodialysis-central venous catheter |
| NRSI | non-randomized studies of interventions |
| OR | odds ratio |
| PAC | peripheral arterial catheter |
| PICC | peripherally-inserted central catheter |
| PICO | population (P), intervention (I), comparison /comparator (C), outcome (O) |
| PICU | paediatric intensive care unit |
| PIVC | peripheral intravenous catheter |
| PQ | PICO question |
| RCT | randomized controlled trial |
| REC | recommendation |
| RR | risk ratio |
| SDG | Sustainable Development Goals |
| USA | United States of America |
| WASH | Water, sanitation and hygiene |
| WHO | World Health Organization |

# GLOSSARY

**Age groups** were defined as follows: adults: ≥18 years of age; neonates: ≤1 month of age; children and adolescents: all other participants not framed in the above groups.

**Alcohol-based hand rub** is an alcohol-containing preparation (liquid, gel or foam) designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Such preparations may contain one or more types of alcohol, other active ingredients with excipients, and humectants *(1)*.

**Acute Physiology and Chronic Health Evaluation (APACHE)** score is the most widely used intensive care unit mortality prediction score. The APACHE II score is made up of 12 physiological and two disease-related variables collected within the first 24 hours of intensive care unit admission. Updated APACHE scoring systems have been developed, but APACHE II remains the most used.

**Aseptic technique** refers to the manner of handling, preparing and storing medications, injection equipment/supplies (for example, syringes, needles), catheters and other devices, which enter body cavities to prevent microbial contamination and infection. While an aseptic technique aims to reduce microbial contamination, a sterile technique (as defined separately) seeks to eliminate all microorganisms.

Definitions and protocols for aseptic technique may vary across countries and settings. Therefore, national and local guidelines should be followed to select the most appropriate approach based on the specific clinical context. Of note, the *Aseptic Non-Touch Technique* (ANTT®) *(2)* is a specific type of aseptic technique (with a unique theoretical and practice framework) that combines aseptic principles with non-touch techniques. It is designed to prevent contamination during clinical procedures by ensuring that key parts and key sites are not touched directly. If key parts and sites are required to be touched, sterile gloves should be used to carry out the procedure.

In these guidelines, we will use the term “aseptic technique” for simplicity. However, the Guideline Development members emphasized the critical importance of avoiding direct contact with key parts and sites when managing central venous catheters.

**Care bundles** are a set of evidence-based, patient-focused practices or interventions (generally three to five) that aim to improve patient outcomes when done collectively and reliably. They can also be a tool to guide the delivery of a specific aspect in patient care where the aim is to improve the care process and patient outcome in a structured manner or sequence, with the expectation that the impact will be greater than single interventions alone *(3)*.

**Central venous catheter** is an indwelling device inserted into a large, central vein (most commonly the internal jugular, subclavian or femoral) and advanced until the terminal lumen resides within the inferior vena cava, superior vena cava, or right atrium *(4)*.

Clinicians are defined as medical, nursing and allied health staff.

**Conditional recommendations** are made when a WHO Guideline Development Group is less certain about the balance between the benefits and harms or disadvantages of implementing a recommendation. Conditional recommendations generally include a description of the conditions under which the end-user should or should not implement the recommendation *(5)*.

**Strong recommendations** are made when the desirable effects of an intervention clearly outweigh the undesirable effects (or clearly do not, in case of a recommendation against a specific intervention) *(5)*.

**Formal training programme** is a structured programme that provides both theoretical and practical education, including demonstrable competency in clinical skills and adherence to appropriate clinical guidelines. Formal training programmes should include adequate specified time to undergo such training.

**Good practice statement** refers to a practice that is commonly accepted and unequivocally demonstrates a net benefit of the recommended action *(6)*.

**Grading of Recommendations Assessment, Development and Evaluation** (GRADE) is an approach used to assess the quality of a body of evidence and to develop and report recommendations.

**Hand hygiene** is a general term referring to any action of hand cleansing. Antiseptic hand rubbing refers to applying an antiseptic hand rub to reduce or inhibit the growth of microorganisms without the need for an exogenous source of water and requiring no rinsing or drying with towels or other devices. Hand washing refers to washing hands with plain or antimicrobial soap and water *(1)*.

**Health and care worker** is an individual who works in a community or health care facility setting and is mainly engaged in actions with the primary intent of enhancing health. This includes health service providers, such as doctors, nursing and midwifery professionals, public health professionals, technicians (laboratory, health, medical and non-medical), personal care workers, healers and practitioners of traditional medicine. It also includes health management and support workers, such as cleaners, drivers, hospital administrators, district health managers, social workers, and other occupational groups in health-related activities. This group includes those who work in acute care facilities and long-term care, public health, community-based care and other occupations in the health and social care sectors. Health and care workers may provide direct personal care services in the home, in health care and residential settings, while assisting with the routine tasks of daily life and performing a variety of other tasks of a simple and routine nature *(7)*.

**Health care-associated infection** is an infection occurring in a patient during the process of care in a hospital or other health care facility, which was not present or incubating at the time of admission. Health care-associated infections can also appear after discharge. They represent the most frequent adverse event associated with patient care.

**Low-, middle- and high-income countries:** WHO Member States are grouped into income groups (low, lower-middle, upper-middle and high) based on the World Bank list of analytical income classification of economies, calculated using the World Bank Atlas method. For the 2025 fiscal year, low-income economies are defined as those with a gross national income per capita of US$ 1145 or less in 2024; lower middle-income economies as those with a gross national income per capita between US$ 1146 and US$ 4515; upper-middle-income economies are those with a gross national income per capita between US$ 4516 and US$ 14 005; and high-income economies are those with a gross national income per capita of US$ 14 005 or more *(8)*.

**Maximal sterile barrier precautions** are defined as sterile barrier precautions that include the use of a cap, mask, sterile gown, sterile gloves and a sterile full body drape *(9)*.

**Multimodal improvement strategies** (MMIS) are a means of improving the implementation of interventions to achieve the required change of system, climate and behaviour to achieve a measurable outcome improvement from the intervention(s). MMIS comprise several components or elements (three or more, usually five) implemented in an integrated way with the aim of improving an outcome (prevention of health care-associated infections and antimicrobial resistance) and changing behaviour. They may include tools, such as bundles and checklists, developed by multidisciplinary teams that take into account local conditions. Multimodal thinking means that practitioners do not focus only on single strategies to change practices (for example, training and education), but consider a range of strategies that target different influencers of human behaviour. MMIS typically contain five key components: system change, that is, the availability of the appropriate infrastructure and supplies to enable good

practices in infection prevention and control ("*Build it*"); the education and training of health and care workers and key players ("*Teach it*"); monitoring infrastructures, practices, processes and outcomes and providing data feedback ("*Check it*"); reminders and communication ("*Sell it*"); and culture change within the establishment or the strengthening of a safety climate ("*Live it*"). All five elements are considered important and should be based on the local health context and situation, informed by periodic assessments *(10,11)*.

**Sterile technique** is defined as a set of specific practices and procedures performed to make equipment and areas free from all microorganisms and to maintain that sterility *(12)*.

**The strength of a recommendation** expresses the degree to which a WHO Guideline Development Group is confident in the balance between the desirable and undesirable consequences of implementing the recommendation. When a Guideline Development Group is very certain about this balance (that is, the desirable consequences clearly outweigh the undesirable consequences), it issues a **strong recommendation** in favour of an intervention. However, when it is uncertain about this balance, it issues a conditional (or "weak") recommendation *(5)*.

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* All references were accessed on 20 October 2025.

# Executive summary

# EXECUTIVE SUMMARY

Numerous reports from WHO and other organizations have clearly identified the increasing endemic burden of health care-associated infections (HAIs) and antimicrobial-resistant infections, which harm patients every day across health care systems in all countries, regardless of income status *(1)*. Among the most preventable are bloodstream infections (BSIs) and other infections associated with the use of central venous catheters (CVCs) *(2, 3)*, often defined as central line-associated BSI (CLABSI).

CLABSI is an important public health issue with a significant impact on patient morbidity and mortality, as well as contributing to increased health care costs and length of hospital stay *(4)*. Among all HAIs, the costs caused by a CLABSI can amount up to approximately US$ 46 000 per case, with most infections being preventable with proper aseptic techniques, surveillance and appropriate care bundles *(5)*. An estimated 250 000 BSIs occur annually in the United States of America (USA) and most are related to the presence of intravascular devices. In the USA, the CLABSI rate in intensive care units (ICUs) is estimated to be 0.8 per 1000 central line days. Although there is a paucity of data on the incidence of CLABSI in low- and middle-income countries (LMICs) due to the lack of mandatory reporting, a review of international studies from 50 different countries reported a much higher CLABSI rate of up to 44.6 per 1000 central line days *(6)*. In addition, higher incidences of line infections among coronavirus disease 2019 (COVID-19) patients were observed worldwide *(7)*, including Brazil *(8)* and some other LMICs *(9)*, highlighting the global extent of the problem.

The implementation of various strategies related to the insertion, maintenance, access and removal of CVCs can help reduce the incidence of CLABSI and related sepsis *(10)*. However, there is a paucity of international guidelines on the topic and practices may vary from country to country, and even within countries, potentially leading to confusion for health care providers and suboptimal patient care. By developing international guidelines based on a systematic review of the evidence, WHO aims to provide consistent recommendations for the prevention of CLABSI and other CVC-associated infections that can be applied across different health and care settings and countries.

## Purpose, scope and target audience

In the context of the prevention of infections associated with intravenous (IV) catheters, WHO has been developing a series of guidelines providing best practices for the prevention of BSI and other infections associated with the use of intravascular catheters, both peripherally- and centrally-inserted. Part 1 was published in 2024 *(11)* and covered peripherally-inserted intravascular catheters, including peripheral IV catheters (PIVCs), peripherally-inserted central catheters (PICCs) and peripheral arterial catheters (PACs), in three patient populations (adults, adolescents-children and neonates) during the provision of health care in any health care setting. These guidelines (Part 2) are focused instead on CVC-associated BSI and other infections in patients with short- and long-term IV catheters in the same populations, but with the exclusion of haemodialysis. Patients on haemodialysis are not included in the scope as specific guidance may be developed at a later stage (Part 3).

The intended audience for these guidelines is clinicians (that is, doctors, nurses, infection prevention and control [IPC] professionals, etc.) involved in the management of patients who require CVCs. However, to ensure appropriate support for clinicians for the practical, clinical adherence to the guidelines, hospital administrators and other professionals involved in health care need to understand their importance and the focus of the recommendations. Patients are also part of the audience of these guidelines as they need to be generally informed about practices performed for their care and, in some cases, understand the choice of the intervention(s).

## Guideline development methodology

The development of these recommendations was guided by standardized operating procedures in accordance with the process described in the *WHO handbook for guideline development*. The recommendations were developed and updated using the following steps:

1. establishing a WHO Guideline Steering Group and a Guideline Development Group (GDG);
2. identifying the primary critical outcomes and priority topics and formulation of a series of questions structured in a PICO (Population, Intervention, Comparison, Outcomes) format by the technical team leading the guideline development, supported by an independent methodologist, the WHO Guideline Steering Group, and the GDG;
3. producing an inventory of existing guidelines on the topic;
4. conducting systematic reviews for the retrieval of the evidence using a standardized methodology;
5. assessing and synthesizing the evidence;
6. developing recommendations by the GDG, using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach;
7. writing the guideline content;
8. applying a process of peer review by external experts;
9. planning for its dissemination and associated implementation strategies.

These guidelines are based on a systematic review of the published, scientific, quantitative evidence related to the effectiveness of preventive measures during the insertion, maintenance, access and removal of centrally-inserted catheters on CLABSI. The aim is to provide a practical template for the safe use of these devices and minimize the risk of CLABSI. The GRADE evidence-to-decision framework that considers desirable and undesirable effects, certainty of evidence, values, balance of effects, resources required, cost effectiveness, equity, acceptability and feasibility was used to develop these guidelines under the guidance of the independent methodologists. Additional scoping reviews were also performed on the cost-effectiveness of some of the interventions addressed in these guidelines.

The guidelines are structured into the following eight key sections related to the insertion and management of centrally-inserted intravascular catheters:

1. general statements regarding education and hand hygiene;
2. pre-insertion;
3. insertion;
4. maintenance;
5. access;
6. replacement and removal;
7. site and catheter selection;
8. other prevention measures (including line bundles).

Each section contains recommendations for both short- and long-term IV catheters unless specifically indicated.

## Recommendations and good practice statements

The GDG developed a total of 16 good practice statements and 25 recommendations. It also provided guidance regarding the importance of using a multimodal approach to implement all interventions.

For all "conditional" recommendations (based on the GRADE methodology), the GDG identified the conditions under which the recommendation would be considered as essential to adopt and implement for the prevention of CLABSI.

A summary of the good practice statements and recommendations is provided below in Table 1.

**Table 1: Good practice statements and recommendations for the prevention of BSI and other infections associated with the use of central venous catheters**

| Recommendations and good practice statements | Type of catheter | Population | Type of statement | Certainty of evidence |
|---|---|---|---|---|
| **1. General statements regarding education and hand hygiene** | | | | |
| **Education and training** | | | | |
| **GPS 1.** WHO recommends that clinicians be appropriately educated and formally trained about the indications for CVC insertion, maintenance, access, replacement and removal, the proper procedures for their use, and the appropriate infection control measures to prevent catheter-related infections in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **GPS 2.** WHO recommends that clinicians be regularly assessed for their knowledge of and adherence to guidelines for appropriately managing CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **GPS 3.** WHO recommends that clinicians be appropriately trained in an aseptic technique to prevent CVC-related infections in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **Hand hygiene** | | | | |
| **GPS 4.** WHO recommends that clinicians be appropriately trained in hand hygiene procedures in the context of the WHO multimodal improvement strategy for hand hygiene to prevent CVC-related infections in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **GPS 5.** WHO recommends that clinicians perform hand hygiene according to the "Five moments" during catheter insertion, maintenance, access, replacement and removal, preferably using the WHO hand rubbing technique with alcohol-based hand rub products or by handwashing with soap and water and using single-use or clean towels. | Short- and long-term catheters | All | Good practice statement | NA |
| **2. Pre-insertion** | | | | |
| **Chlorhexidine-containing body wash** | | | | |
| **REC1.** WHO suggests using a chlorhexidine-containing body wash (liquid or impregnated wipes) daily in critically-ill adults, adolescents and children. | Short- and long-term catheters | Adults, adolescents and children | Conditional recommendation | Low certainty of evidence |
| **3. Insertion** | | | | |
| **Insertion pack/kit** | | | | |
| **GPS 6.** WHO recommends that clinicians use a standardized insertion pack/kit when inserting a CVC in adults, adolescents, children and neonates | Short- and long-term catheters | All | Good practice statement | NA |
| **Sterile technique** | | | | |
| **GPS 7.** WHO recommends using a sterile technique for the insertion of all CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |

| Recommendations and good practice statements | Type of catheter | Population | Type of statement | Certainty of evidence |
|---|---|---|---|---|
| **GPS 8.** WHO recommends that clinicians use sterile single-use gloves compared to non-sterile gloves when inserting a CVC in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **REC2.** WHO suggests using a sterile technique involving maximal sterile barrier precautions over a sterile technique not involving maximal sterile barrier precautions at the time of CVC insertion in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **Skin disinfection** | | | | |
| **GPS 9.** WHO recommends that skin disinfection should always be used prior to insertion of all CVCs in adults, adolescents, children, and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **REC3.** WHO suggests using an alcohol-based formulation over an aqueous-based antiseptic formulation for skin disinfection before CVC insertion in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **REC4.** WHO suggests using an alcohol-chlorhexidine antiseptic (1% or 2%) over other antiseptics (alcohol-iodine or alcohol alone or aqueous formulations) for skin disinfection before CVC insertion in adults, adolescents and children. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **CVC dressing** | | | | |
| **REC5.** WHO suggests using either a transparent semi-permeable dressing or gauze dressing after CVC insertion in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **REC6.** WHO suggests using an antiseptic patch or dressing (for example, a chlorhexidine-gluconate- impregnated sponge or dressing or any other antiseptic) at the CVC insertion site in adults, adolescents and children. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **4. Maintenance** | | | | |
| **CVC dressing** | | | | |
| **GPS 10.** WHO recommends using a sterile dressing protocol at the insertion site of a CVC in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **REC7.** WHO suggests using a formal schedule of CVC dressing changes in adults, adolescents, children, and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **REC8.** If a formal schedule of CVC dressing changes is to be used, WHO suggests using dressing change intervals of 3 days or more in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **Catheter management with fluid infusion** | | | | |
| **REC9.** WHO suggests using either a continuous IV infusion or an intermittent infusion for the maintenance of CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **Sterile saline compared to anticoagulant solutions in "lock-off" flushing** | | | | |
| **REC101.** WHO suggests a system of "lock-off" flushing with normal sterile saline over "lock-off" flushing with heparinized saline for CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |

| Recommendations and good practice statements | Type of catheter | Population | Type of statement | Certainty of evidence |
|---|---|---|---|---|
| **Sterile flushing after product administration** | | | | |
| **GPS 11.** WHO recommends flushing a CVC with a compatible sterile fluid (saline or other) after product administration in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **Change of the CVC administration set (tubing/giving)** | | | | |
| **REC11.** WHO suggests using a schedule of regular changing of the CVC administration set (tubing/giving) every 7 days over other schedules (2, 3, 4 days) when administering routine IV fluids only in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **REC12.** WHO suggests regular changing of the CVC administration set (tubing/giving) after administering total parenteral nutrition or lipid products in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **5. Access** | | | | |
| **Aseptic technique** | | | | |
| **GPS 12.** WHO recommends using an aseptic technique to access CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Good practice statement | NA |
| **CVC access and use of a closed-access hub system** | | | | |
| **REC13.** WHO suggests using either a closed-access or an open-access CVC hub system in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **6. Replacement and removal** | | | | |
| **CVC replacement** | | | | |
| **GPS 13.** WHO recommends inspecting the insertion site of CVCs in adults, adolescents, children and neonates at least daily to assess for signs of inflammation and infection in order to guide whether the catheter should be removed. | Short- and long-term catheters | All | Good practice statement | NA |
| **GPS 14.** WHO recommends promptly removing any CVC no longer essential for patient care. | Short- and long-term catheters | All | Good practice statement | NA |
| **REC14.** WHO suggests against routinely replacing a CVC (unless clinically indicated) in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **7. Site and catheter selection** | | | | |
| **Site selection** | | | | |
| **REC15.** WHO suggests using the subclavian or jugular veins over the femoral vein for CVC insertion in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **REC16.** WHO suggests using the subclavian veins as the preferred site over jugular veins (if no contraindications) for CVC insertion in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **Antibiotic-impregnated and antiseptic-coated catheters** | | | | |
| **REC17.** WHO suggests using either antibiotic-impregnated or non-impregnated CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **REC18.** WHO suggests using antiseptic-coated CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |

| Recommendations and good practice statements | Type of catheter | Population | Type of statement | Certainty of evidence |
|---|---|---|---|---|
| **Catheter selection for long-term lines** | | | | |
| **REC19.** WHO suggests using a single lumen over a multi-lumen catheter (unless there is a specific reason that requires multiple lumens) in adults, adolescents, children and neonates requiring a long-term line. | Long-term catheters only | All | Conditional recommendation | Very low certainty of evidence |
| **REC20.** WHO suggests using either a Hickman CVC or a Port-a-Cath in adults, adolescents, children and neonates requiring a long-term line. | Long-term catheters only | All | Conditional recommendation | Low certainty of evidence |
| **8. Other prevention measures (including line bundles and surveillance)** | | | | |
| **Securement of CVC** | | | | |
| **REC21.** WHO suggests using either a suture-less or suture-based securement of CVCs in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **Antimicrobial lock solutions for short- and long-term catheters** | | | | |
| **REC22.** WHO suggests not using an antimicrobial lock solution in patients with short-term CVCs for the prevention of CVC infections in adults, adolescents, children and neonates. | Short-term catheters only | All | Conditional recommendation | Very low certainty of evidence |
| **Antiseptic line caps** | | | | |
| **REC23.** WHO suggests either using antiseptic-impregnated or non-impregnated line caps in adults, adolescents, children and neonates with short- and long-term catheters. | Short- and long-term catheters | All | Conditional recommendation | Low certainty of evidence |
| **Intravenous prophylactic antibiotics at the time of line insertion** | | | | |
| **REC24.** WHO suggests not using IV prophylactic antibiotics in adults, adolescents, children and neonates with short- and long-term catheters. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |
| **Surveillance** | | | | |
| **GPS 15.** WHO recommends that HAI surveillance (including CLABSI or related BSI and to detect AMR and outbreaks) should be performed to guide IPC interventions, combined with timely feedback of results to health care workers and stakeholders, including through national networks. | Short- and long-term catheters | All | Good practice statement | NA |
| **GPS 16.** WHO recommends that national HAI surveillance programmes and networks that include mechanisms for timely data feedback and with the potential to be used for benchmarking purposes should be established to reduce HAI and AMR. | Short- and long-term catheters | All | Good practice statement | NA |
| **Line care bundles** | | | | |
| **REC25.** WHO suggests using CVC practice bundles in adults, adolescents, children and neonates. | Short- and long-term catheters | All | Conditional recommendation | Very low certainty of evidence |

**Abbreviations:** WHO, World Health Organization; GPS, good practice statement; Rec, recommendation; CVC, central venous catheter; NA, not applicable; IV, intravenous; HAI, health care-associated infection; AMR, antimicrobial resistance; CLABSI, central line-associated bloodstream infection; IPC, infection prevention and control.

A local nurse prepares an IV drip for a patient at a local government funded hospital in the town of Menglong, Yunnan Province [China].
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# 1

# Introduction

# 1. Introduction

## 1.1 Background

Numerous reports from WHO and other organizations have clearly identified the increasing endemic burden of health care-associated infections (HAIs) and antimicrobial-resistant infections, which harm patients every day across health care systems in all countries, regardless of income status *(1)*. At any one time, around 7% of patients in high income countries (HICs) and 15% in low- and middle-income countries (LMICs) will acquire at least one HAI *(12)*. In intensive care units (ICUs), up to 30% of patients can be affected by HAIs, with an incidence that can be up to 20 times higher in LMICs compared to HICs, particularly among neonates. Approximately one in four (23.6%) of all hospital-treated sepsis cases are HAIs and almost one half (48.7%) of all cases of sepsis with organ dysfunction treated in adult ICUs are estimated to be acquired in the hospital *(1)*. Bloodstream infections (BSIs) and other infections that are associated with the use of central venous catheters (CVCs) are among the most preventable HAIs *(2, 3)*.

There are various parallel terms and definitions all over the world to define BSI associated with CVCs. In the United States of America (USA), a central line-associated BSI (CLABSI) is defined by the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network as the isolation of a pathogen from a blood culture in a patient who had an intravenous (IV) central line on the event day or one day before *(13)*. Another term used in some studies is 'catheter-associated' BSI (CABSI), based on the Infection in Critical Care Quality Improvement Programme definition in UK *(14)*. Finally, the recent WHO HAI case definitions for use in settings with limited resources use the term 'CVC-associated' BSI (CVC-BSI) *(15)*, defined as a confirmed BSI in a patient who had a central vascular catheter in place within the 2 days preceding the first confirmed diagnosis, together with a positive blood culture in accordance with the new WHO BSI definitions. This definition is similar to the one used by the European Centre for Disease Prevention and Control *(16)*. Some studies retrieved through the systematic review performed for these guidelines also reported on 'catheter-related' BSI (CRBSI) (based on the Infectious Diseases Society of America guidelines, currently being updated) *(17)*, which involves the identification of the same pathogen both in the bloodstream and on the catheter tip. For simplicity, the term 'CLABSI' will be used throughout this guideline to refer collectively to CLABSI, CRBSI, CABSI and CVC line infections, including in the evidence sections for each recommendation, unless specified otherwise.

CLABSI is an important public health issue with a significant impact on patient morbidity and mortality; it also increases health care costs and the length of hospital stay *(4)*. Costs caused by a CLABSI can amount up to approximately US$46 000 per case, with most infections being preventable with proper aseptic techniques, surveillance and appropriate care bundles *(5)*. An estimated 250 000 BSI occur annually in the USA, mostly are related to the presence of intravascular devices. In the USA, the CLABSI rate in ICUs is estimated to be 0.8 per 1000 central line days. Although there is a paucity of data on the incidence of CLABSI in LMICs due to the lack of mandatory reporting, a review of international studies from 50 different countries reported a CLABSI rate of up to 44.6 per 1000 central line days *(6)*. In addition, higher incidences of CLABSI among coronavirus disease 2019 (COVID-19) patients were observed all over the world *(7)*, including Brazil *(8)* and some other LMICs *(9)*, highlighting the global extent of the problem.

An analysis conducted by the CDC also revealed a prospective increase in HAIs (including CLABSI) in US hospitals during the COVID-19 pandemic *(18)*. This is also in line with reports from other countries, with a significant variation in the traditional epidemiology of BSIs identified during the COVID-19 pandemic, including higher rates of bacterial infections and diversity of microbial pathogens *(19, 20)*.

However, variations remain in some reports and the increase in CLABSI rates has not been consistent in all health care institutions, thus suggesting that other factors may have had an impact on the overall epidemiology, such as compliance with infection control measures or local line care policies.

Despite the importance of implementing effective infection prevention and control (IPC) measures, global compliance with the IPC core components and minimum requirements remains suboptimal. The results of a detailed global survey on the minimum requirements for national IPC programmes carried out by WHO in 2023–2024 showed that 71.3% (107/150) of countries had an active national IPC programme (that is, a functioning programme with an annual work plan and budget) *(21)*. However, only 6% (9/150) of participating countries met all WHO minimum requirements, although 14% (21/150) met 90% at the national level *(21)*. Of note, only 8.2% of HICs met all the minimum requirements. Significant discrepancies were observed across income levels, with HICs generally reporting more implementation, but gaps remained in budget allocation, training, as well as HAI surveillance and monitoring systems, especially in low-income countries.

Implementation of various strategies related to the insertion, maintenance, access and removal of CVCs can help reduce the incidence of CLABSI and related sepsis *(10)*. Nevertheless, there is a paucity of international guidelines on the topic and practices may vary from country to country, and even within countries, potentially resulting in confusion for health care providers and in suboptimal patient care. By developing these guidelines, WHO aims to provide consistent recommendations for the prevention of CLABSI and other CVC-associated infections that can be applied across different health and care settings and countries. Part 2 guidelines are based on a systematic review of the published scientific evidence, with a global scope based on the evidence-to-decision framework of the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology. They concern preventive measures to be adopted during the insertion, maintenance, access and removal of CVCs in order to provide a practical template for the safe use of these devices and thus minimize the risk of CLABSI and other infections.

## 1.2 Purpose

In the context of the prevention of infections associated with IV catheters, WHO has been developing a series of guidelines providing best practices for the prevention of BSI and other infections associated with the use of intravascular catheters, peripherally- and centrally-inserted. Part 1 was published in 2024 *(11)* and covered peripherally-inserted intravascular catheters, including peripheral IV catheters (PIVCs), peripherally-inserted central catheters (PICCs) and peripheral arterial catheters (PACs), in four patient populations (adults, adolescents, children and neonates) during the provision of health care in any health care setting. These guidelines (Part 2) cover BSI and other infections associated with CVCs in patients with short- and long-term IV catheters in the same populations, but with the exclusion of haemodialysis. Patients on haemodialysis are not included in the scope as specific guidance may be developed at a later stage (Part 3). Extracorporeal membrane oxygenation catheters were also excluded as beyond the scope of these guidelines.

The need for these guidelines is emphasized by the Sustainable Development Goal (SDG) targets 3.d ("*strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks*") and 3.d.2 (reduction of the "*percentage of bloodstream infections due to selected antimicrobial-resistant organisms*") *(22, 23)*.

Furthermore, the World Health Assembly resolution on sepsis *(24)* and both the global patient safety and IPC action plans *(25, 26)* identified the reduction of morbidity and mortality associated with HAIs as a core indicator to be targeted by countries. The proposed guidelines aim to support Member States to achieve these targets through improved practices.

## 1.3 Intended audience

The intended audience for these guidelines is clinicians (that is, doctors, nurses, IPC professionals, allied health staff) involved in the management of patients who require CVCs. However, to ensure an appropriate, practical, clinical adherence to the guidelines, hospital administrators and other professionals involved in health care need to understand their importance and the focus of the recommendations to ensure appropriate support for clinicians. This includes helping to provide the best possible organizational health care culture and context (including adequate staffing) and availability of the various required products to allow adherence to the guidelines. Patients are also part of the audience as they need to be informed about practices performed for their care. They may need to be informed about the choice of some interventions and to collaborate in safe practices (for example, hand hygiene or monitoring the status of the catheter dressing).

## 1.4 Scope

Part 2 of these guidelines focus on the prevention of CLABSI in four patient populations (adults, adolescents, children and neonates) during the provision of health care in any type of care setting, including acute and long-term health care facilities and primary care settings.

The catheter types covered in Part 2 of these guidelines include:

- Non-Tunneled CVCs – Inserted directly into a central vein, typically for short-term use in emergency or critical care settings.
- Tunneled CVCs – Placed under the skin before entering a vein.
- Totally Implantable Venous Access Devices (Port-a-Cath) – A small reservoir implanted under the skin, used for long-term medication administration, such as chemotherapy.

As mentioned, PICC lines were already included in Part 1 guidelines and haemodialysis catheters are not included in the scope as specific guidance may be developed at a later stage (Part 3). The priority research questions that guided the development of the recommendations are presented in Annex 2. These questions were structured in PICO format (population [P], intervention [I], comparison/ comparator [C], outcome [O]) and guided the evidence review and synthesis.

## 1.5 Desired impact

The primary outcomes considered for developing the recommendations of these guidelines were the occurrence of CLABSI and associated infection complications, including those due to antimicrobial-resistant pathogens, and the related all-cause and attributable mortality.

The desired impact of these guidelines is the improvement of practices targeted by the recommendations and good practice statements and the reduction of the occurrence of the above-mentioned primary outcomes.

# 2

# Methods for guideline development

# 2. Methods for guideline development

## 2.1 WHO guideline development process

The guidelines were developed in accordance with the approach recommended by the WHO Guidelines Review Committee (GRC) *(27)* and a planning proposal approved by the GRC) (GRC-24-01-1104). In summary, the development process included eight main stages:

1. Convening of a WHO Guideline Steering Group and a Guideline Development Group (GDG);
2. defining the primary critical outcomes and priority topics and formulation of PICO questions by the technical team leading the guideline development, supported by the methodologist(s), the WHO Guideline Steering Group and the GDG;
3. the conduct of an inventory of existing guidelines on this topic;
4. the conduct of a systematic review on evidence using a standardized methodology;
5. assessment and synthesis of the evidence;
6. development of recommendations by the GDG using the GRADE methodology;
7. writing of the guidelines and a process of peer review by external experts;
8. planning for the dissemination and implementation strategies.

The development process included the participation of four main groups that guided and contributed to the overall process: WHO Guideline Steering Group; GDG; Systematic Reviews Expert Group; and the External Peer Review Group.

Members of the GDG, observers and the External Peer Review Group who participated in the discussions completed a declaration of interest form and any potential conflict of interest was discussed with the Steering Committee Group and the Ethics Office if needed (Annex 1).

The roles and functions of these groups are described below.

### WHO Guideline Steering Group

The WHO Guideline Steering Group was chaired by the IPC unit head and technical lead for the IPC Taskforce and the Global IPC Network (Integrated Health Services, Universal Health Coverage/Life Course). Participating members were from the Antimicrobial Resistance Division, the Division of Access to Medicines and Health Products, the Chief Nursing Office at WHO headquarters, the Country Readiness Strengthening Department, the Integrated Health Services Department, the Department of Maternal and Perinatal Health, the Newborn Health Unit, the Water, Sanitation and Hygiene (WASH) Unit, and IPC focal points at the six WHO regional offices.

The Group contributed to the initial planning document for the development of the guidelines, identified the primary critical outcomes and topics, and formulated the research questions. It also identified the Systematic Reviews Expert Group, the guideline methodologists, the members of the GDG and the external peer reviewers. The GDG chair and the IPC Global Unit coordinator supervised the evidence retrieval, syntheses and analysis, organized the GDG meetings, prepared or reviewed the final guideline document, managed the external peer reviewers' comments, and the guideline publication and dissemination.

## WHO GDG

The WHO Guideline Steering Group identified 22 external experts, country delegates and stakeholders from the six WHO regions to constitute the GDG (also referred to as "the panel"). This was a diverse group representing various professional and stakeholder groups, such as IPC experts, clinical microbiologists, epidemiologists, intensivists, public health and infectious disease specialists and researchers, as well as affected communities, through the inclusion of a patient representative. Geographical representation and gender balance were also considerations when selecting GDG members. Members of this group appraised the evidence that was used to inform the recommendations, advised on the interpretation of the evidence, formulated the final recommendations, while taking into consideration the 2016 WHO guidelines on core components of IPC programmes at the national and acute health care facility level *(28)* and the Part 1 guidelines previously published *(11)*, and reviewed and approved the final guideline document.

When GDG members were unable to reach consensus, the disputed recommendation or decision was put to a vote, conducted electronically and anonymized. The recommendation was agreed only if more than two-thirds of participants voted in support of it, unless the disagreement involved a safety concern. In such cases, the WHO Secretariat reserved the right to delay or withhold the issuance of the recommendation.

## Systematic Reviews Expert Group

The Systematic Reviews Expert Group was selected by the WHO IPC Unit team through a bidding process that considered previous experience in the topic (or related fields), the availability to conduct the systematic reviews in due time, and value for money. This group reviewed the published evidence related to the effectiveness of preventive measures to be adopted during the insertion, maintenance, access and removal of CVCs and assessed its quality and features according to the GRADE criteria specified by the WHO GRC and presented the findings to the GDG.

## External Peer Review Group

The Group was composed of eight technical experts with high-level knowledge and experience in IPC, antimicrobial resistance (AMR), patient safety and health management, including field implementation, and a patient representative. The Group was geographically balanced to ensure views from both HICs and LMICs; no member declared a conflict of interest. The primary focus was to review the final guideline document, identify any inaccuracies or errors, and comment on technical content and evidence, clarity of language, contextual issues and implications for implementation. The Group ensured that the guideline decision-making processes incorporated the values and preferences of end-users, including health care professionals and policy-makers. Of note, it was not within the remit of this Group to change the recommendations formulated by the GDG. All reviewers agreed with each recommendation and some suggested selected editing changes.

These guidelines are based on the GRADE evidence-to-decision framework that considers desirable and undesirable effects, certainty of evidence, values, balance of effects, resources required, cost effectiveness, equity, acceptability and feasibility.

Based on the GRADE methodology, the GDG formulated "conditional" recommendations. The implications of "conditional" recommendations are that the majority of people to whom the recommendation applies would benefit from the suggested option and, in most contexts, the suggested option can be implemented as a policy. In contrast, a "strong" recommendation implies that most individuals should receive the intervention (as the desirable effects of an intervention clearly outweigh the undesirable effects, or clearly do not), and clinicians can be confident in its appropriateness

across settings *(29)*. For all "conditional" recommendations, the GDG aimed to provide the conditions under which the management strategy would be considered as essential to adopt and implement for preventing CLABSI.

The systematic reviews on the topic of prevention of CLABSI and its related subtopics (for example, "insertion", "maintenance", "access" and "removal", etc.) followed specific research questions in PICO format (Annex 2). More details on the systematic review methodology can be found in Annex 3.

Summaries of the systematic review findings and of the evidence-to-decision framework are included in each chapter of the guidelines. For each PICO question, the GDG agreed that there was no important uncertainty or variability in the values associated with the outcomes of interest. The full systematic review findings, as well as the evidence-to-decision tables for each recommendation, are available in the Web Annex. All documents were shared in advance with the GDG members and the Systematic Reviews Expert Group presented the main findings. Two independent methodologists facilitated the discussions and the completion of the evidence-to-decision tables.

The Web Annex is available on the WHO website: https://doi.org/10.2471/B09725

## 2.2. Good practice statements

In addition to recommendations, these guidelines also include "good practice statements" (also known as "best practice statements"). The term refers to a practice that is commonly accepted and unequivocally demonstrates a net benefit of the recommended action. Good practice statements are recommendations that guideline panels consider to be important, but are not appropriate for formal ratings of quality of evidence in the judgment of the GRADE working group *(30)*. The decision and appropriateness of developing good practice statements was discussed for each topic with the methodologists and agreed upon by the GDG. At the time of writing these guidelines, the WHO Secretariat, the methodologists, the Steering Group and the GDG were also aware of the current proposed changes to the way good practice statements are formulated *(31)* and advice was sought from the GRC at WHO headquarters. Whilst waiting for the final consensus on the definitions and nomenclature of good practice and similar statements, it was decided to continue with the traditional format and nomenclature, also for consistency with the Part 1 guidelines.

The use of CVCs is now a common component of good quality, clinical health care worldwide and many routine IPC good practices are equally applicable to these guidelines. Furthermore, the management of CVCs is also associated with specific risks that are similar to the use of other invasive devices and procedures where good practice statements are relevant. These good practice statements are included within this guideline in section 3.1 under "general statements", as well as in the following chapters where appropriate.

# 3

# Recommendations and Good Practice Statements

# 3. Recommendations and Good Practice Statements

## 3.1 General Statements regarding education and hand hygiene

### 3.1.1 Education and training

- **Good practice statement 1. WHO recommends that clinicians be appropriately educated and formally trained about the indications for CVC insertion, maintenance, access, replacement and removal, the proper procedures for their use, and the appropriate infection control measures to prevent catheter-related infections in adults, adolescents, children and neonates.**
  (Good practice statement)

- **Good practice statement 2. WHO recommends that clinicians be regularly assessed for their knowledge of and adherence to guidelines for appropriately managing CVCs in adults, adolescents, children and neonates.**
  (Good practice statement)

- **Good practice statement 3. WHO recommends that clinicians be appropriately trained in an aseptic technique to prevent CVC-related infections in adults, adolescents, children and neonates.**
  (Good practice statement)

### 3.1.2 Hand Hygiene

- **Good practice statement 4. WHO recommends that clinicians be appropriately trained in hand hygiene procedures in the context of the WHO multimodal improvement strategy for hand hygiene to prevent CVC-related infections in adults, adolescents, children and neonates.**
  (Good practice statement)

- **Good practice statement 5. WHO recommends that clinicians perform hand hygiene at any time indicated according to the "Five moments" during catheter insertion, maintenance, access, replacement and removal, preferably using the WHO hand rubbing technique with alcohol-based hand rub products or by handwashing with soap and water and using single-use or clean towels.**
  (Good practice statement)

## 3.2 Pre-insertion

### 3.2.1 Chlorhexidine-containing body wash

- **Recommendation 1. WHO suggests using a chlorhexidine-containing body wash (liquid or impregnated wipes) daily in critically-ill adults, adolescents and children.** (Conditional recommendation, low certainly of evidence)

#### Remarks

- The evidence did not differentiate between liquid and impregnated wipes and evaluated chlorhexidine concentrations ranging from 2% to 4%. It was noted that most of the studies provided evidence on the use of chlorhexidine, hence a decision was made to restrict the recommendation to chlorhexidine only and to adults, adolescents and children, but not neonates (due to the risk of chemical burns) *(32)*.
- The GDG noted that the use of this intervention would be particularly beneficial in settings with high baseline CLABSI rates. However, the GDG highlighted the need to prioritize resources at the local level based on other competing needs in the health care facility. The GDG also expressed concerns on the potential development of resistance to chlorhexidine and on waste generation when using wipes.
- Chlorhexidine products should be used with caution in patients with burns and according to the manufacturer's instructions in order to ensure they are safe for use .

#### Rationale for the recommendation

Overall, the GDG judged both the desirable and undesirable effects to be small, but with a balance of effects probably favouring the intervention, with a low certainty of evidence. Based on the evidence provided, the GDG opted for a conditional recommendation in favour of the intervention, in particular in the context of high CLABSI rates at baseline, where the overall benefit may be more noticeable.

#### Summary of the evidence

The Systematic Reviews Group identified 31 studies (10 randomized controlled trials [RCTs] *(33-42)* and 21 non-randomized studies of interventions [NRSIs]*(43-63)*) comparing daily antiseptic body washing with chlorhexidine to soap and water bathing in adults, adolescents and children.

- There was low certainty of evidence that daily antiseptic body washing may result in fewer CLABSI than no routine antiseptic body washing (risk ratio [RR]: 0.67; 95% confidence interval [CI]: 0.45 to 0.99; 10 RCTs *(33-42)*).
- There was low certainty of evidence that routine antiseptic body washing may result in lower catheter-related mortality than no routine antiseptic body washing (RR: 0.20; 95% CI: 0.01 to 4.13; one RCT *(41)*).
- There was low certainty of evidence that routine antiseptic body washing may result in little to no difference in all-cause mortality when compared with no routine antiseptic body washing (odds ratio [OR]: 0.90; 95% CI: 0.76 to 1.07; five RCTs *(33, 37-40)*).
- There was very low certainty of evidence that routine antiseptic body washing may result in little to no difference in sepsis when compared with no routine antiseptic body washing (RR: 1.92; 95% CI: 0.66 to 5.60; one RCT *(33)*).

- Subgroup analyses revealed no difference in the effect for CLABSI based on age (adults versus children) or setting (ICU versus general ward).

### Evidence-to-decision

A potentially reduced equity was noted due to the different availability of products around the world and their moderate costs, in particular when considering LMICs, but the intervention was considered probably cost-effective. No issues were identified in acceptability and feasibility.

### Implementation considerations

- The recommendation refers to using a chlorhexidine-containing body wash (liquid or impregnated wipes) daily and not immediately prior to line insertion. The GDG acknowledges that there are variations in the available protocols on body washing and directs health and care workers to follow their national and local policies.
- The recommendation refers to all critically-ill patients that require a CVC and not limited to the ICU.
- It is advisable to engage nursing and support staff as key stakeholders in the decision (that is, time required for bathing).
- It is also advisable to engage patients and their families, considering the potential adverse effects on the skin related to exposure to chlorhexidine, including asking for any known intolerance and rare allergic reactions to chlorhexidine.
- WASH services and standards *(64, 65)* are essential to enable critical IPC practices, including this recommendation on body wash.

### Research needs

- There is a significant variation in available protocols on how to perform patient bathing. The GDG identified this as an area of research interest to determine the most effective protocol and product to be used (that is, liquid wash versus wipes or other means, rinsing versus no rinsing, which solution to use).
- The GDG also identified the need for additional research on the use of antiseptic products other than chlorhexidine (that is, octenidine and others) using multicentre RCTs or other types of trials (that is, adaptive) and focusing on specific populations (such as haematology patients or the paediatric ICU).
- AMR and other wider implications (that is, impact on skin microbiome, cross-resistance to antibiotics and on the epidemiology of other infections caused by gram-positive and gram-negative bacteria) associated with the use of chlorhexidine and other body wash products were identified as important areas for research.
- Cost-benefit research studies including baseline surveillance data to define potential thresholds for universal use were also considered as other areas for further research.

## 3.3 Insertion

### 3.3.1 Insertion pack/kit

- **Good practice statement 6. WHO recommends that clinicians use a standardized insertion pack/kit when placing a CVC in adults, adolescents, children and neonates (Good practice statement)**

### 3.3.2 CVC insertion by an insertion team

- **WHO makes no recommendation regarding the use of a dedicated CVC insertion teams in adults, adolescents, children, or neonates, as the evidence remains inconclusive.**

#### Remarks

- A CVC insertion team is defined as consisting of individuals specifically trained and competent in CVC insertion who are dedicated to perform the insertion of CVCs.
- The search criteria used in the systematic review were inclusive as possible, including terms such as "*insertion team*", "*vascular access team*", *intravenous therapy team*".
- Establishing a dedicated CVC insertion team is an intervention that is different from ensuring specific training for all those tasked with CVC insertion, which is covered by good practice statements 1 to 3 in these guidelines.
- Consideration should also be given to specific populations (i.e., neonates, children, or patients with known difficult intravenous access) as the potential benefit in preventing CLABSI may be confined to these groups.
- The GDG members acknowledged the difficulties in designing a RCT to evaluate this topic and the very limited available evidence.

#### Rationale for the decision

Based on the evidence provided (two uncontrolled before-after studies and no RCTs), the GDG considered both the desirable and undesirable effects to be small. The GDG judged that the crucial factor was the adequate training of the clinician inserting the CVC, rather than having a dedicated team itself. For this reason, the GDG considered that the balance of effects did not favour either the intervention (a formal insertion team) or the comparison (insertion by a clinician who is not part of a formal insertion team), provided that the clinician has undergone appropriate training and demonstrated competency in CVC insertion. Another concern expressed by the GDG was the potential loss of knowledge and skills in CVC insertion among non-team members (doctors and nurses), such that their insertion competency could decline. This may be especially impactful in emergency situations where they are required to urgently insert a CVC without the assistance of a formal insertion team, with potential implications affecting the wider hospital capacity and patient care. Overall, given the very low certainty of the evidence, no recommendation could be made.

### Summary of the evidence

- The Systematic Reviews Expert Group did not identify any RCTs on the topic, but only two uncontrolled before-after studies *(66, 67)* evaluating the use of a dedicated CVC insertion (for non-haemodialysis) team compared with not using a dedicated CVC insertion team. The risk of bias in both studies was rated as high due to their uncontrolled design (no formal assessment).
- There was very low certainty of evidence from one study in children and adults reporting a 58% reduction in the number of CLABSIs after the introduction of a highly specialized vascular access team *(67)*. Similarly, there was very low certainty of evidence from another study in neonates reporting that overall CLABSI rates decreased by 65% after implementation of the line team *(66)*.
- There were no studies identified reporting on catheter-related mortality, all-cause mortality, sepsis pneumothorax, local site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.

### Evidence-to-decision

Increased moderate costs (due to the resources required to maintain a dedicated team), the probably reduced equity, variable acceptability by health care workers and patients (hospital management might not be in favour due to the additional costs, but patient satisfaction is likely to be improved) and low feasibility (as having a dedicated team is not always possible due to staff shortages) were all considered, resulting in a decision to make no recommendation.. The overall cost-effectiveness judgement did not favour either the intervention or the comparison.

### Research needs

- Further research is needed to compare the potential cost-benefit of using a formal CVC insertion team versus an educational/behavioural programme for clinicians inserting CVC, including both ICU and non-ICU settings.

## 3.3.3 Sterile technique

- **Good practice statement 7. WHO recommends using a sterile technique for the insertion of all CVCs in adults, adolescents, children and neonates.**
(Good practice statement)

- **Good practice statement 8. WHO recommends that clinicians use sterile single-use gloves compared to non-sterile gloves when inserting a CVC in adults, adolescents, children and neonates.**
(Good practice statement)

- **Recommendation 2. WHO suggests using a sterile technique involving maximal sterile barrier precautions over a sterile technique not involving maximal sterile barrier precautions at the time of CVC insertion in adults, adolescents, children and neonates.**
(Conditional recommendation, very low certainty of evidence)

### Remarks

- *Maximal sterile barrier precautions:* sterile barrier precautions that include the use of a cap, mask, sterile gown, sterile gloves and a sterile full body drape *(11)*.
- *Sterile technique* is defined as a set of specific practices and procedures performed to make equipment and areas free from all microorganisms and to maintain that sterility *(11)*.
- GDG members acknowledged that the above definition of sterile technique as comparator also seems to be generic and it may not provide enough practical details.

### Rationale for the recommendation

There was an extensive discussion during which a number of GDG members expressed the opinion that a strong recommendation would have been more suitable; others suggested a conversion into a good practice statement. However, it was decided to assess the available evidence and to proceed with the evidence-to-decision framework. Following the assessment, the GDG judged the desirable and undesirable effects to be small and trivial, respectively, but with a balance of effects probably favouring the intervention, despite the very low certainty of evidence. In view of the data presented, the GDG members opted for a conditional recommendation in favour of maximal sterile barrier precautions, but acknowledging that the current evidence is weak and more studies are needed to assess if less barriers may be sufficient.

### Summary of the evidence

The Systematic Reviews Expert Group identified eight studies (two RCTs *(68, 69)* and six NRSIs *(70-75)*) comparing maximal sterile barrier precautions in adults, children and adolescents, and neonates.

- There was very low certainty of evidence that maximal sterile barrier precautions may result in fewer CLABSIs than a lesser standard of precautions (RR: 0.47, 95% CI: 0.10 to 2.22; two RCTs *(68, 69)*).
- Two non-randomized studies also reported very low certainty of evidence that maximal sterile barrier precautions may result in fewer CLABSIs than a lesser standard of precautions (RR: 0.21; 95% CI: 0.05 to 0.94; two non-RCTs *(70, 71)*)
- There was very low certainty of evidence that maximal sterile barrier precautions may result in little to no difference in local insertion site infections when compared with a lesser standard of precautions (RR: 1.01; 95% CI: 0.06 to 16.03; one RCT *(68)*).
- There were no studies identified that reported on catheter-related mortality, all-cause mortality, sepsis and other complications.

### Evidence-to-decision

The intervention may increase costs due to the additional equipment required and it is probably accepted and feasible as it is already common practice. However, patients may have more discomfort with full body drapes. In addition, the GDG judged equity to be probably increased.

### Implementation considerations

- Ensure adequate training, understanding and competency in the application of maximal sterile barriers precautions.
- The GDG discussed the need for a dedicated procedure room for line insertion and noted that this is not practical for critically-ill patients and may be an issue in some health care facilities, particularly in LMICs. Furthermore, it is not part of the current definition of maximal sterile barrier precautions.

#### Research needs

- More research studies are needed to assess if lesser sterile precautions are needed, with a trial design and platform (for example, adaptive *(76, 77)*) that would allow to clearly distinguish the impact of the different components within maximal sterile barrier precautions (that is, cap, mask, full body drape, the environment where the line is placed) and allow to answer multiple questions simultaneously.

### 3.3.4 Skin disinfection

- **Good practice statement 9. WHO recommends that skin disinfection should always be used prior to the insertion of all CVCs in adults, adolescents, children and neonates.**
(Good practice statement)

- **Recommendation 3. WHO suggests using an alcohol-based formulation over an aqueous-based antiseptic formulation for skin disinfection before CVC insertion in adults, adolescents, children, and neonates.**
(Conditional recommendation, low certainty of evidence)

#### Remarks

- Alcohol-based antiseptics should be the preferred choice for skin disinfection before CVC insertion.
- It was acknowledged that alcohol-based formulations can cause skin irritation, dryness and a risk of pain in case of laceration and these potential side-effects should be taken into consideration when using these products. Some of these side-effects may be caused by either the alcohol or the antiseptic component.
- Alcohol-based antiseptics can cause skin lesions in preterm infants without intact skin.

#### Rationale for the recommendation

The GDG considered alcohol-based formulations as the preferred option for skin disinfection over aqueous formulations, with a conditional recommendation due to the low certainty of evidence. The GDG considered the desirable effects of alcohol-based formulations for skin disinfection to be moderate and the undesirable effects trivial, with a balance of effects probably favouring the intervention.

#### Summary of the evidence

The Systematic Reviews Expert Group found data from five RCTs *(78-82)*.

- There was low certainty of evidence that alcohol-based solutions may result in fewer CLABSIs than aqueous-based solutions for skin disinfection (RR: 0.59; 95% CI: 0.36 to 0.98; five RCTs *(78-82)*).
- There was very low certainty of evidence that alcohol-based solutions may result in less all-cause mortality than aqueous-based solutions for skin disinfection (RR: 0.79; 95% CI: 0.48 to 1.30; two RCTs *(78, 79)*).
- There was very low certainty of evidence that alcohol-based solutions may result in fewer sepsis episodes when compared with aqueous-based solutions for skin disinfection (RR: 0.68; 95% CI: 0.35 to 1.30; one RCT *(78)*).
- There were no studies identified that reported on catheter-related mortality, pneumothorax, local insertion site infections and other complications.

### Evidence-to-decision

The GDG considered that costs would be negligible, with the intervention probably being cost-effective. The GDG also judged that the intervention would probably increase equity, with no issues of acceptability and feasibility.

### Implementation considerations

- Alcohol-based formulations are widely available, with no need to use special applicators or devices or wipes.
- The GDG did not indicate a specific standardized technique for the application of the skin disinfectant before CVC insertion, but noted that a sufficient volume of product is needed.
- As per previous recommendation, all skin disinfectants should be allowed to dry for at least 30 seconds for a maximal effect.
- The development of a standard list of suitable skin disinfection products (including alcohol-chlorhexidine and alternative options) for CVC insertion may be of benefit, in particular in case of procurement problems and unavailability of products.

### Research needs

- Since several of the studies used different non-chlorhexidine-containing products as a comparator, the actual benefit (or not) of different disinfection products was difficult to assess accurately. Therefore, standardization of the comparator disinfection products in future research would be critical.

- **Recommendation 4. WHO suggests using an alcohol-chlorhexidine antiseptic (1% or 2%) over other antiseptics (alcohol-iodine or alcohol alone or aqueous formulations) for skin disinfection before CVC insertion in adults, adolescents and children.**
  (Conditional recommendation, low certainty of evidence)

### Remarks

- It was not possible to decide the precise chlorhexidine concentration to be used (with most studies using 0.5%, 1% or 2%), but the GDG preference (based on their expert opinion) is to use concentrations of chlorhexidine of at least 1%.
- The GDG also discussed that when inserting a CVC, a higher concentration of chlorhexidine might be necessary due to the prolonged presence of the device inside the body. However, it was noted that this may not be required for skin disinfection at other sites where a needle is inserted for only a short period.
- The recommendation applies to adults, adolescents and children, but not neonates (due to the risk of chemical burns with chlorhexidine) *(32)*.
- In the case of availability issues with alcohol-chlorhexidine, other alcohol-based antiseptics (that is, alcohol-iodine) provide an alternative option.

### Rationale for the recommendation

Overall, the GDG judged both the desirable and undesirable effects to be small and a balance of effects probably favouring the intervention, despite low certainty of evidence. Based on the evidence provided, the GDG decided on a conditional recommendation in favour of an alcohol-chlorhexidine antiseptic as first choice for skin disinfection prior to CVC insertion.

### Summary of the evidence

The Systematic Reviews Expert Group identified 13 studies (seven RCTs *(78-84)* and six NRSIs *(85-90)*) comparing alcohol-chlorhexidine to alcohol-iodine, alcohol alone or aqueous formulations for skin disinfection in adults, children and adolescents, and neonates.

- There was low certainty of evidence that alcohol-chlorhexidine may result in little to no difference in CLABSI than other antiseptics for skin disinfection (RR: 0.67; 95% CI: 0.41 to 1.10; five RCTs *(78, 80-82, 84)*).
- There was very low certainty of evidence that alcohol-chlorhexidine may result in less all-cause mortality than other antiseptics for skin disinfection (RR: 0.80; 95% CI: 0.48 to 1.34; one RCT *(78)*).
- There was low certainty of evidence that alcohol-chlorhexidine may result in little to no difference in sepsis when compared with other antiseptics for skin disinfection (RR: 0.50; 95% CI: 0.13 to 1.89; two RCTs *(78, 84)*).
- There were no studies identified that reported on catheter-related mortality, local insertion site infections and other complications.

### Evidence-to-decision

It was noted that some alcohol-chlorhexidine products may be more expensive depending on the specific applicator or device used, but this may vary by context, with a potential impact on equity, particularly in the case of access issues in LMICs. However, the intervention overall was considered as probably cost-effective and to be acceptable and feasible.

### Implementation considerations

- Consider local availability, context and the cost of suitable alternative skin disinfection preparations.
- Although some studies have referenced the use of 0.5% chlorhexidine, the GDG expresses a preference for concentrations of at least 1%. It is also acknowledged that alcohol–chlorhexidine preparations commonly used for skin disinfection prior to line insertion typically contain 2% chlorhexidine.
- Patients and/or families should be asked about previous chlorhexidine allergy before use.
- All skin antiseptics should be allowed to dry for at least 30 seconds for a maximal effect.

### Research needs

- To help select the most appropriate concentration of chlorhexidine in alcohol formulations, large RCTs comparing different concentrations (0.5% versus 1% versus 2%) would be valuable.
- To increase equity and potentially reduce costs, further research is needed to compare single-use applicators containing chlorhexidine versus a chlorhexidine solution without any specific device.

### 3.3.5 Ultrasound-guided assistance

- **WHO makes no recommendation regarding the use of ultrasound-guided assistance when inserting a CVC in adults, adolescents, children, and neonates to reduce infection risk, as the evidence remains inconclusive.**

#### Remarks

- The use of ultrasound-guided assistance for CVC insertion is recognized as being routine in most health care settings as it helps to ensure that the catheter tip is directed into the appropriate central vein and the number of insertion attempts are reduced; it also prevents mechanical complications.
- However, in the context of these guidelines, critical infectious outcomes were the main outcomes considered and influenced the decision not to make a recommendation.
- Regardless of the no recommendation, it is important to use sterile, single-use ultrasound gel if a local decision is made to perform ultrasonography for CVC insertion, as well as appropriately disinfected ultrasound probe to prevent contamination of the insertion site and infections.

#### Rationale for the decision

The GDG considered the very low certainty of evidence that using ultrasound-guided assistance can prevent CLABSI and other infection-related outcomes, judging both desirable and undesirable effects as trivial, with an overall balance of effects that does not favour either the intervention or the comparison. Therefore, the GDG decided that no recommendation could be made for the purpose of infection prevention. Furthermore, some GDG members expressed some theoretical concerns on the potential increased risk of CLABSI due to previous reports of contaminated ultrasound gel *(91)* or the use of inadequately decontaminated probes. The GDG noted that there is evidence on the effectiveness of ultrasound-guided assistance for the prevention of pneumothorax and that the use of ultrasound guidance for CVC insertion may be associated with a reduction in the number of insertion attempts. Overall, given the very low certainty of the evidence, no recommendation could be made.

#### Summary of the evidence

The Systematic Reviews Expert Group identified 17 studies (16 RCTs *(92-107)* and one NRSI *(108)*) comparing ultrasound-assisted catheter insertion with no ultrasound in adults, children and adolescents, and neonates, with 15 RCTs rated as having some concerns with risk of bias, one with high risk of bias, and one non-RCT with serious concerns regarding risk of bias.

- There was very low certainty of evidence that ultrasound-assisted insertion may result in fewer CLABSI than no ultrasound (RR: 0.45; 95% CI: 0.16 to 1.33; four RCTs *(93, 98, 99, 105)*).
- There was very low certainty of evidence that ultrasound-assisted insertion may result in less all-cause mortality than no ultrasound (RR: 0.58; 95% CI: 0.28 to 1.22; two RCTs *(102, 109)*).
- There was moderate certainty of evidence that ultrasound-assisted insertion probably results in fewer pneumothorax than no ultrasound (RR: 0.16; 95% CI: 0.04 to 0.16; 13 RCTs *(92-95, 97-100, 103-106, 110)*).
- There was very low certainty of evidence that ultrasound-assisted insertion may result in little to no difference in local insertion site infections than no ultrasound (RR: 1.20; 95% CI: 0.45 to 3.19; three RCTs *(96, 105, 106)*).

- There was very low certainty of evidence that ultrasound-assisted insertion may result in little to no difference in bleeding events that require action than no ultrasound (RR: 0.83; 95% CI: 0.36 to 1.93; three RCTs *(98, 102, 105)*).
- There was low certainty of evidence that ultrasound-assisted insertion may result in fewer deep vein thrombosis events than no ultrasound (RR: 0.16; 95% CI: 0.04 to 0.61; two RCTs *(101, 102)*).
- There was very low certainty of evidence that ultrasound-assisted insertion may result in little to no difference in cardiac tamponade than no ultrasound (RR: 0.33; 95% CI: 0.01 to 8.17; one RCT *(97)*).
- There was very low certainty of evidence that ultrasound-assisted insertion may result in less venous stenosis than no ultrasound (Mean Difference: 4.12; 95% CI: 1.18 to 7.06; one RCT *(105)*).
- There were no studies identified that reported on catheter-related mortality or sepsis following ultrasound-assisted CVC insertion.

#### Evidence-to-decision

The GDG noted that the use of ultrasound can increase costs (due to the cost of the machine, its maintenance and training) and probably reduces equity (as it may not be easily affordable in all health and care facilities), with an overall cost-effectiveness not favouring either the intervention or the comparison for the purpose of reducing infection risk, hence the decision not to make any recommendation. No issues were identified in acceptability and feasibility.

#### Research needs

- Research on optimal training requirements and teaching methods for ultrasound use (including standardized cleaning methods) is required.

### 3.3.6 CVC dressing

- **Recommendation 5. WHO suggests using either a transparent semi-permeable dressing or gauze dressing after CVC insertion in adults, adolescents, children and neonates. (Conditional recommendation, very low certainty of evidence)**

**Remarks**

- Transparent semi-permeable dressings offer several advantages, including enhanced visibility of the insertion site, which may allow earlier detection of local inflammation or infection. They also facilitate easier inspection, improve patient comfort, and reduce nursing workload due to their durability and reduced need for frequent changes.
- On the other hand, gauze dressings may offer the advantage of absorbing blood oozing and moisture, which transparent dressings do not. In such cases, a gauze dressing may be preferable.

#### Rationale for the recommendation

The GDG members considered the limited evidence provided (only one RCT *(111)*) and the old date of publication (potentially not taking into consideration modern types of dressings) and judged both desirable and undesirable effects as small, with an overall balance of effects not favouring either the intervention or the comparison. Therefore, the GDG decided on a conditional recommendation for either the intervention or the comparator.

### Summary of the evidence

- The Systematic Reviews Expert Group identified only one RCT *(111)* (published in 1996) comparing a transparent semi-permeable dressing with a gauze dressing in adults, children and adolescents, and neonates. The study had a small sample size and the results were characterized by large confidence intervals; it was rated as having some risk of bias.
- There was very low certainty of evidence that a transparent semi-permeable dressing may result in more CLABSIs than a gauze dressing (RR: 5.52; 95% CI: 0.67 to 45.59; one RCT *(111)*).
- There was very low certainty of evidence that a transparent semi-permeable dressing may result in more local insertion site infections than a gauze dressing (RR: 2.21; 95% CI: 0.42 to 11.52; one RCT *(111)*).
- No study reported on catheter-related mortality, all-cause mortality, sepsis and other complications.

### Evidence-to-decision

The GDG members judged moderate costs for the intervention (as semi-permeable dressing are more expensive than simple gauze) and probably reduced equity (as some GDG members reported recurrent procurement issues with semi-permeable dressing), with an overall cost-effectiveness not favouring either the intervention or the comparison. However, the intervention was considered as probably acceptable and feasible.

### Implementation considerations

- Ensuring the daily inspection of the CVC insertion site for signs of potential infection is critical. However, it is important to recognize that daily visual inspection might not be feasible if a gauze dressing is not being changed. In such situations, proper adherence to dressing maintenance protocols is essential for effective infection monitoring.
- From an implementation perspective, this should be supported by a clear SOP defining when each dressing type is used and by routine audit processes to ensure consistent practice.

### Research needs

- Given the limited evidence found and the date of publication, the impact of the use of gauze versus semi-permeable dressing would be worthy of further research studies, especially in countries with hot climates where a gauze dressing may be preferred in case of excessive skin sweating.
- Research on the optimal transparent semi-permeable dressing for use in all climates would be beneficial, especially for LMICs. Research into a standard, transparent, semi-permeable dressing product that can be mass produced at low cost would likely provide greater equity, especially for LMICs.

- **Recommendation 6. WHO suggests using an antiseptic patch or dressing (for example, chlorhexidine-gluconate-impregnated sponge or dressing or any other antiseptic) at the CVC insertion site in adults, adolescents and children.**
  (Conditional recommendation, low certainty of evidence)

### Remarks

- The GDG clearly noted that these products may not be easily available and affordable in LMICs and that other basic priority IPC measures should be in place before prioritizing this intervention.
- It is also worth mentioning that most of the studies were performed in ICU settings and HICs.
- It was noted that most of the evidence came from studies using chlorhexidine patches, but no difference was found when performing subgroup analyses for age, type of antiseptic and type of product used.
- The recommendation applies to adults, adolescents and children, but not neonates (due to the risk of chemical burns with chlorhexidine) *(32)*.

### Rationale for the recommendation

The desirable effects of the intervention (antiseptic patches or dressing) were considered moderate with small undesirable effects. The certainty of evidence was moderate for the CLABSI outcome, but low to very low for other outcomes, hence the overall low certainty of evidence for this recommendation. The GDG decided on a conditional recommendation in favour of the intervention, based on the number of studies available and the moderate certainty of evidence that an antiseptic patch or dressing probably results in fewer CLABSIs than a non-antiseptic dressing.

### Summary of the evidence

- The Systematic Reviews Expert Group identified 30 studies (19 RCTs *(112-129)* and 11 non-RCTs *(130-139)*) comparing an antiseptic patch or dressing with a non-antiseptic dressing in adults, children and adolescents, and neonates, with 17 RCTs rated as having some concerns with risk of bias and two *(127, 128)* with a low risk of bias. In most studies, chlorhexidine was the antiseptic used.
- There was moderate certainty of evidence that an antiseptic patch or dressing probably results in fewer CLABSI than a non-antiseptic dressing (RR: 0.66; 95% CI: 0.52 to 0.84; 17 RCTs *(112, 113, 115-120, 122-129, 140)*).
- There was low certainty of evidence that an antiseptic patch or dressing may result in little to no difference in catheter-related mortality than a non-antiseptic dressing (RR: 0.50; 95% CI: 0.05 to 5.47; two RCTs *(113, 122)*).
- There was very low certainty of evidence that an antiseptic patch or dressing may result in little to no difference in all-cause mortality than a non-antiseptic dressing (RR: 1.02; 95% CI: 0.89 to 1.17; six RCTs *(113, 114, 123, 127, 128, 140)*).
- There was low certainty of evidence that an antiseptic patch or dressing may result in little to no difference in sepsis than a non-antiseptic dressing (RR: 0.83; 95% CI: 0.26 to 2.69; one RCT *(113)*).
- There was very low certainty of evidence that an antiseptic patch or dressing may result in fewer local insertion site infections than a non-antiseptic dressing (RR: 0.79; 95% CI: 0.49 to 1.28; 11 RCTs *(113-117, 119, 120, 122-124, 140)*).
- There was very low certainty of evidence that an antiseptic patch or dressing may result in more deep vein thrombosis than a non-antiseptic dressing (RR: 3.72; 95% CI: 0.43 to 32.28; one RCT*(114)*).
- There were no studies identified that reported on other complications.

### Evidence-to-decision

Using an antiseptic patch or dressing would likely represent an additional cost compared with standard catheter dressings, which might be offset if it reduced the risk of CLABSI and so avoided the associated costs. Some cost-effectiveness analyses have been performed in HICs and demonstrated the cost-benefit of the intervention *(141-143)*. A reduced equity was also noted due to the additional costs mentioned. This intervention was considered generally acceptable and feasible to implement as procurement could be prioritized and the IPC teams could facilitate adoption of an antiseptic patch or dressing.

### Implementation considerations

- Antiseptic patches or dressings are only one element of infection prevention strategies and they should not be considered as a simple solution in facilities with higher CLABSI rates.
- It is also important to note that patches containing chlorhexidine are not licensed in neonates due to the risk of chemical burns *(32)*.
- There is no preferred option in terms of type of product (patches versus dressing) and this should be assessed based on local preferences, costs and availability.

### Research needs

- Further research is needed such as a randomized trial comparing chlorhexidine patches versus chlorhexidine dressings and their impact on infections and other outcomes (that is, impact on resistance, selection of specific bacteria and feasibility of the interventions in LMICs).
- The effectiveness of an antiseptic patch or dressing should also be assessed when it is used at the same time of other concomitant measures using the same antiseptic (that is, chlorhexidine bathing and/or alcohol-chlorhexidine for disinfection of the skin for line insertion and dressing changes).
- The impact on bacterial epidemiology and the potential emergence of chlorhexidine-resistant strains and cross-resistance to antibiotics were identified by the GDG as another important area for research.

## 3.4 Maintenance

### 3.4.1 CVC dressing

- **Good practice statement 10. WHO recommends using a sterile dressing protocol at the insertion site of a CVC in adults, adolescents, children and neonates.**
(Good practice statement)

- **Recommendation 7. WHO suggests using a formal schedule of CVC dressing changes in adults, adolescents, children and neonates.**
(Conditional recommendation based on expert opinion, very low certainty of evidence)

#### Remarks

- The GDG acknowledged that there may be some variability on the type of dressing used and the context, considering potential shortages of supplies in LMICs.

#### Rationale for the recommendation

According to the GDG judgement in the absence of evidence, both desirable and undesirable effects were considered as small, with an overall balance of effects probably favouring the intervention. The majority of GDG members (more than 70%) voted for a conditional recommendation in favour of a formal schedule of CVC dressing changes. This position was based on expert consensus and with the rationale that it would provide some benefit due to the regular checking of the CVC site (but not all GDG members agreed on this).

#### Summary of the evidence

No studies were identified for this PICO question.

#### Evidence-to-decision

Costs were perceived as moderate due to the potential impact on nursing time and procurement of supplies and the GDG considered that there should probably be no impact on equity. Overall cost-effectiveness was considered probably favouring the intervention and no issues of acceptability and feasibility were identified.

#### Implementation considerations

- Local guidelines and practices should be considered when deciding on a formal schedule of CVC dressing.

#### Research needs

- A randomized trial (or through an adaptive design) comparing the different approaches of CVC dressing schedules is needed , for example, comparing formal schedules to a clinically-indicated CVC dressing change.
- The impact on costs and the cost-effectiveness of different schedules and dressings used was also considered as a required area for future research.

- **Recommendation 8. If a formal schedule of CVC dressing changes is to be used, WHO suggests using dressing change intervals every 3 days or more in adults, adolescents, children and neonates.**
  (Conditional recommendation, very low certainty of evidence)

### Remarks

- This recommendation addresses CVC dressings that are not moistened or already disrupted.
- The GDG noted that all the evidence related to this recommendation pertained to transparent semi-permeable dressings.
- Because dressing disruption has been determined to be a major factor in the development of CLABSI *(144)*, it is important to ensure the integrity and adherence of the dressing and to reduce dressing disruption in post-insertion care bundles.

### Rationale for the recommendation

The GDG members considered both desirable and undesirable effects as trivial, with an overall balance of effects that does not favour either the intervention (using shorter intervals in a formal schedule of CVC dressing changes) or the comparison. GDG members endorsed a conditional recommendation against using shorter intervals, considering the very low certainty of evidence and the date of the studies retrieved in the systematic review (more than 20-years-old). There was inconsistency and very low certainty in the evidence presented, with little or no effect or benefit in the prevention of CLABSI with shorter intervals. In addition, the GDG noted that this could also cause increased local insertion site infections. Based on their expert opinion, GDG members were also concerned about the consequence of frequent dressing changes (also in terms of health care staff time) and the risk of additional line manipulation. Finally, it was noted that all the evidence was related to transparent semi-permeable dressing where it is still possible to inspect the CVC site, hence a shorter interval to replace the line dressing may not be necessary.

### Summary of the evidence

- The Systematic Reviews Expert Group identified six RCTs *(128, 145-149)* comparing a shorter interval between dressing changes with a longer interval between dressing changes in adults, children and adolescents, and neonates.
- Four RCTs were rated as having some concerns with risk of bias, one with high risk of bias *(149)* and one with low risk of bias *(128)*.
- There was very low certainty of evidence that a shorter interval between dressing changes may result in little to no difference in CLABSI than a longer interval (RR: 0.69; 95% CI: 0.32 to 1.49; three RCTs *(128, 145, 149)*).
- There was low certainty of evidence that a shorter interval between dressing changes may result in less all-cause mortality than a longer interval (RR: 0.95; 95% CI: 0.84 to 1.07; one RCT *(128)*).
- There was very low certainty of evidence that a shorter interval between dressing changes may result in more local insertion site infections than a longer interval (RR: 1.08; 95% CI: 0.77 to 1.53; three RCTs *(145, 146, 150)*).
- There were no studies identified that reported on catheter-related mortality, sepsis, pneumothorax, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis following a shorter interval between dressing changes.

### Evidence-to-decision

Moderate costs and probably reduced equity and issues of acceptability and feasibility related to more frequent (and thus higher staff time) dressing changes were considered in the final decision against the intervention.

### Implementation considerations

- Despite this current recommendation, GDG members agreed that dressings should be changed regardless of the schedule if there is a clinical indication. This could also include clinical situations when there is serous or bloody exudate or when the edges of the dressing are lifting, requiring a replacement prior to the scheduled date.

### Research needs

- There is a need for studies assessing if dressing changes could be prolonged, particularly with the concomitant use of antimicrobial patches or different dressings, including the use of liquid adhesives.

## 3.4.2 Catheter management with fluid infusion

- **Recommendation 9. WHO suggests using either a continuous IV infusion or an intermittent infusion for the maintenance of CVCs in adults, adolescents, children and neonates.**
  (Conditional recommendation, very low certainty of evidence)

### Remarks

- The GDG defined a "*continuous infusion*" as an uninterrupted IV administration over an extended period during the day, whereas an "*intermittent infusion*" involves breaks and interruptions in the flow.
- The choice of continuous versus intermittent infusion will often depend on the clinical settings (that is, ICU versus non-ICU), the requirements of the treatment regimen being administered, and the patient's clinical conditions (that is, mobile versus bedbound patient; critically ill versus non-critically ill patient).
- GDG members noted that neither continuous infusion nor intermittent infusion schedules have been associated with the prevention of CLABSI. Continuous infusion may reduce the risk of non-infection-related phlebitis, occlusion and thrombosis, depending on the drugs administered via the catheter. However, it may also increase the risk of fluid overload and incur additional costs. Other GDG members pointed out that intermittent infusion requires more frequent manipulation of the catheter, potentially increasing the risk of infection. These factors should be considered when choosing the type of infusion.
- Regardless of the infusion type used, it is crucial to train health care personnel on aseptic techniques when accessing the CVC line.

### Rationale for the recommendation

Based on the limited evidence found (only one NRSI), the GDG considered both the desirable and undesirable effects as small, with an overall balance of effects not favouring either the intervention or the comparison. The certainty of evidence provided was judged very low.

### Summary of the evidence

- The Systematic Reviews Expert Group identified only one NRSI *(151)* evaluating the maintenance of a CVC using a continuous IV infusion versus maintenance of a non-haemodialysis (NHD)-CVC using intermittent infusion. The risk of bias was assessed as moderate.
- There was very low certainty of evidence that intermittent IV infusion may result in little to no difference in CLABSI than continuous IV infusion (RR: 0.79; 95% CI: 0.28 to 2.23; one NRSI *(151)*).
- There were no studies reporting on catheter-related mortality, all-cause mortality, sepsis, pneumothorax, local insertion site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.

### Evidence-to-decision

The GDG noted that the resources required for continuous infusion were negligible in terms of costs and savings, but the panel was split on this topic with contrasting opinions. Continuous infusion often requires an electric pump and additional IV fluids, both potentially resulting in added costs. On the other hand, continuous infusion may also result in decreased nursing time compared to intermittent infusion, hence leading to potential savings. The overall cost-effectiveness considerations were not in favour of either type of infusion. The GDG also judged a variable impact on equity as equipment for continuous infusion may not be always available in low-resource settings. However, in general, either type of infusion was considered both acceptable and feasible, depending on the clinical settings (ICU versus non-ICU). It was noted that continuous infusion may limit patient mobility and it may also be associated with an increased risk of patient falls and injury due to entanglement in IV tubing associated with the infusion. Hence, it may be an inconvenient choice for mobile and non-critically-ill patients.

### Implementation considerations

- If the catheter is to be maintained using a continuous infusion, it should be administered according to a clearly-defined protocol. However, caution should be used when adopting a protocol of continuous fluid infusion for catheter maintenance to avoid excessive fluid being administered and resulting in potential fluid overload of the patient.
- Where feasible, the patient's preferences should also be considered when deciding the type of infusion to be administered.

### Research needs

- Further research is needed such as a randomized trial or an adaptive design trial comparing continuous IV infusion versus intermittent infusion and considering multiple outcome measures, that is, infectious and non-infectious complications, nursing time, costs and patient preferences.

## 3.4.3 Sterile Saline compared to anticoagulant solutions in "lock-off" flushing

- **Recommendations 10. WHO suggests a system of "lock-off" flushing with normal sterile saline over "lock-off" flushing with heparinized saline for CVCs in adults, adolescents, children and neonates.**
  (Conditional recommendation, very low certainty of evidence)

### Remarks

- The GDG expressed concerns regarding the potential risk of heparin-induced thrombocytopenia, bleeding and allergic reactions with the use of heparinised saline for "lock-off" flushing.
- However, the GDG also acknowledged that heparinized saline may have a favourable effect in decreasing the risk of deep vein thrombosis.

### Rationale for the recommendation

The GDG considered that the use of sterile saline for "lock-off" flushing of CVCs is associated with moderate desirable effects, especially considering the avoidance of heparin-induced thrombocytopenia, despite some studies suggesting that a system of "lock-off" flushing of a CVC with normal saline may result in more CLABSI. Undesirable effects were judged as trivial, with an overall balance of effects probably favouring the use of sterile saline over heparinized saline for the "lock-off" flushing of catheters. The GDG considered the very low certainty of evidence and the risk of adverse events as major determining factors when deciding on the final recommendation. The GDG also noted that among the published studies, there was significant heterogeneity in the results and wide CIs, with little assessment of the potential side-effects when using heparin.

### Summary of the evidence

- The Systematic Reviews Expert Group identified seven studies (four RCTs *(152-155)*, and three NRSIs *(156-158)*) comparing a system of "lock-off" flushing of a CVC with normal saline versus "lock-off" flushing of a CVC with heparinized saline in adults, children and adolescents, and neonates. Three RCTs *(152-154)* were rated as having some concerns and one RCT *(155)* as having a low risk of bias.
- There was very low certainty of evidence that a system of "lock-off" flushing of a CVC with normal saline may result in more CLABSI than "lock-off" flushing of a CVC with heparinized saline (RR: 2.52; 95% CI: 0.65 to 9.73; four RCTs *(152-155)*). There was no significant subgroup difference between adults and children.
- There was very low certainty of evidence that a system of "lock-off" flushing of a CVC with normal saline may result in little to no difference in local insertion site infections than "lock-off" flushing of a CVC with heparinized saline (RR: 5.00; 95% CI: 0.26 to 95.61; one RCT *(154)*).
- There was very low certainty of evidence that a system of "lock-off" flushing of a CVC with normal saline may result in fewer deep vein thromboses compared with "lock-off" flushing of a CVC with heparinized saline (RR: 0.81; 95% CI: 0.44 to 1.52; one RCT *(153)*).
- There were no studies identified that reported on catheter-related mortality, all-cause mortality, sepsis, pneumothorax, bleeding events that require action, cardiac tamponade or venous stenosis following "lock-off" flushing with normal saline.

### Evidence-to-decision

The GDG considered that in terms of resources, there were moderate savings associated with using sterile saline for "lock off" flushing of CVCs and that cost-effectiveness considerations probably favour its use over heparinized saline. Equity and acceptability are probably increased with saline use and feasibility is also increased given that sterile saline is generally more readily available and likely to be cheaper than heparinized saline.

### Implementation considerations

- Use of multi-use vials of sterile saline and heparinized saline should be avoided due to the risk of potential contamination.

### Research needs

- Further research on the rate of heparin-induced thrombocytopenia linked to heparinized saline use in "lock-off" flushing would help to quantify the clinical risk of using this product more accurately.
- Further research may also be needed to investigate the comparative impact on mortality between saline and anticoagulant solutions, considering all potential adverse effects, including heparin-induced thrombocytopenia.

## 3.4.4 Sterile flushing after product administration

- **Good practice statement 11. WHO recommends flushing a CVC with a compatible sterile fluid (saline or crystalloid) after product administration in adults, adolescents, children and neonates.**
  (Good practice statement)

## 3.4.5 Changing of the CVC administration set (tubing/giving)

- **Recommendation 11. WHO suggests using a schedule of regular changing of the CVC administration set (tubing/giving) every 7 days over other schedules (2, 3, 4 days) when administering routine IV fluids in adults, adolescents, children and neonates.**
  (Conditional recommendation, low certainty of evidence)

### Remarks

- The GDG noted that the purpose of the intervention was to evaluate whether extending the duration between changes leads to a higher incidence of infections.
- Some GDG members stated that regular changing of the CVC administration set every 7 days is the standard in many health care facilities, especially in HICs. Other GDG members reported that changing every 2-3 days is still common practice in LMICs.

### Rationale for the recommendation

The GDG members judged both desirable and undesirable effects as small, noting that the intervention (changing of the CVC administration set every 7 days) had no effect on CLABSI reduction, but it may result in less all-cause mortality. The overall balance of effects was considered not favouring either the intervention or the comparison. Based on the evidence provided, the GDG members opted for a conditional recommendation in favour of the intervention. It was acknowledged that the evidence supporting the prevention of CLABSI is not significant, but the effect (low certainty of evidence) in preventing all-cause mortality was taken into consideration to support the recommendation. Contextual factors (see below) were also considered when reaching the final recommendation.

### Summary of the evidence

- The Systematic Reviews Expert Group identified three RCTs *(159-161)* comparing a schedule of 7 days regular changing of the NHD-CVC administration (tubing/giving) set with other schedules (2, 3 and 4 days) in adults, children and adolescents, and neonates. Two RCTs *(159, 160)* were judged as having some concerns with risk of bias, with one having a low risk of bias *(161)*.
- There was low certainty evidence that a 7-day schedule of changing the CVC administration set may result in little to no difference in CLABSI than a 2-4 day schedule (RR: 1.28; 95% CI: 0.90 to 1.83; three RCTs *(159-161)*).
- There was low certainty of evidence that a 7-day schedule of changing the CVC administration set may result in less all-cause mortality than a 2-4 day schedule (RR: 0.73; 95% CI: 0.49 to 1.08; one RCT *(161)*).
- There were no studies identified that reported on catheter-related mortality, sepsis, pneumothorax, local insertion site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis following a 7-day schedule of changing the CVC administration set.

### Evidence-to-decision

Moderate savings and probably increased equity (with an overall cost-effectiveness probably favouring the intervention), with no concerns in acceptability and feasibility, were considered when reaching the final recommendation.

### Implementation considerations

- A sterile technique should be ensured when changing the administration (tubing/giving) set for a CVC.

### Research needs

- Further research to assess the effect of a schedule of regular changing of the CVC administration set (tubing/giving) every 7 days (versus other durations) to reduce CLABSI is required.
- Research (ideally in the form of an RCT comparing 7 days versus clinically-indicated administration set changing) to identify the optimal time of regular changing of administration (tubing/giving) sets when using a CVC is needed.

- **Recommendation 12. WHO suggests changing of the CVC administration set (tubing/giving) after administering total parenteral nutrition or lipid products in adults, adolescents, children and neonates.**
  (Conditional recommendation based on expert opinion, very low certainty of evidence)

### Remarks

- Some GDG members highlighted that there is indirect evidence about outbreak occurrence when using these products, with total parenteral nutrition and lipid formulations considered as a risk factor for catheter colonization and CLABSI *(162-165)*. Sepsis that can occur in between 20% and 30% of patients receiving parenteral nutrition *(162)* and microbiological studies suggest microbial growth in lipid formulations *(166)*.
- The GDG did not reach a definitive consensus on recommending a specific schedule based on the evidence provided. However, they noted that a reasonable interval could be within 24 hours of administering lipid products.

### Rationale for the recommendation

In the initial discussion on the optimal schedule for changing the NHD-CVC administration (tubing/giving) set and the most common clinical practices, some GDG members initially proposed a good practice statement, but it was decided instead to formulate a PICO question on this topic to be included in the systematic review undertaken for these guidelines. However, no evidence was found.

In the absence of evidence, the GDG members considered the desirable and undesirable effects of the intervention as moderate and trivial, respectively, with a balance of effects probably in favour of the intervention. Despite the absence of evidence, most GDG members opted for a conditional recommendation in favour of changing the CVC administration set (tubing/giving) after administering total parenteral nutrition or lipid products based on their expert opinion and the above-mentioned indirect evidence. The majority of GDG members (67%) were in favour of a strong recommendation, but it was decided to make it conditional due to the lack of direct evidence and lack of achievement of the established threshold for GDG consensus to formulate a strong recommendation (at least 70%).

### Summary of the evidence

The GDG noted that the studies initially identified by the Systematic Reviews Expert Group only tested the duration of tubing change. They did not specifically address the PICO question, which compared regular schedules for changing the CVC administration set (tubing/giving) after administering total parenteral nutrition or lipid products versus not having a scheduled change. Therefore, these studies were deemed unsuitable and no studies were identified to respond to this PICO question.

### Evidence-to-decision

Despite the moderate costs, the intervention was considered as probably cost-effective, with no impact on equity, acceptability and feasibility.

### Implementation considerations

- Although the GDG did not recommend a specific schedule, the GDG remarked that regular changing should be done frequently (for example, within 24 hours from administration of lipid products, according to manufacturers' instructions).
- A sterile technique should be ensured when changing the administration (tubing/giving) set for a CVC.
- It is also acknowledged that multiple factors probably influence the increased risk of sepsis in patients receiving parenteral nutrition and this recommendation should be considered as one of multiple measures to be implemented.

### Research needs

- There was debate among GDG members if more studies on this topic should be encouraged or not, considering the available indirect evidence and the potential ethical issues when designing any trial on this topic.

## 3.5 Access

### 3.5.1 Aseptic technique

- **Good practice statement 12. WHO recommends using an aseptic technique to access CVCs in adults, adolescents, children and neonates.**
(Good practice statement)

### 3.5.2 CVC access and use of a closed-access hub system

- **Recommendation 13. WHO suggests using either a closed-access CVC hub system or an open-access CVC hub system in adults, adolescents, children and neonates.**
(Conditional recommendation, very low certainty of evidence)

#### Remarks

- *Closed-access hub systems* are those that allow intravascular access using a needleless device and are designed to prevent blood leakage and air entry and to reduce the risk of pathogen entry into the device access site *(11)*.
- *Open-access hub systems* are those that are directly accessible using a routine syringe *(11)*. When accessed, the device is potentially open to the environment and may be associated with blood leakage or an increased risk of pathogen entry if aseptic access protocols are not strictly followed.
- The choice between a closed- or open-access CVC hub system will depend on the availability of local resources as closed-access systems have a higher cost.
- It was acknowledged that a closed-access system provides additional benefits such as a reduction in needlestick injuries.
- The GDG recognizes that disinfecting the CVC hub before accessing it is a good practice in many healthcare facilities, regardless of whether the hub is open or closed. However, no comprehensive systematic review has been conducted to evaluate the impact of this practice on reducing CLABSI.

#### Rationale for the recommendation

The GDG members considered the very low certainty of evidence on the effectiveness of using closed-access hub systems to reduce the risk of CLABSI and discussed the balance between the small desirable effect and additional costs (with economic implications for LMICs). The GDG finally opted for a conditional recommendation for either a closed-access or open-access CVC hub. The desirable effects were considered small and with trivial undesirable effects, with an overall balance of effects probably favouring the intervention (due to potential other benefits, such as the reduction in needlestick injuries).

### Summary of the evidence

- The Systematic Reviews Expert Group identified 12 studies (five RCTs *(167-171)* and seven NSRIs *(172-178)*) comparing a closed-access with an open-access CVC hub system in adults, children and adolescents, and neonates. One RCT *(167)* was discussed by the GDG and thought to have a very high risk of bias and unclear definition of CLABSI. All RCTs were rated as having some concerns with risk of bias.
- There was low certainty of evidence that a closed-access CVC hub system may result in fewer CLABSIs than an open-access CVC hub system (RR: 0.53; 95% CI: 0.27 to 1.06; five RCTs *(167-171)*). The sensitivity analysis omitting one RCT *(167)* of concern resulted in a very low certainty of evidence of fewer CLABSIs with a closed-access CVC hub system (RR: 0.75; 95% CI: 0.39 to 1.44).
- There was very low certainty of evidence that a closed-access CVC hub system may result in lower all-cause mortality than an open-access CVC hub system (RR: 0.64; 95% CI: 0.39 to 1.04; two RCTs *(167, 169)*). The sensitivity analysis omitting one RCT *(167)* of concern resulted in similar results (RR: 0.62; 95% CI: 0.36 to 1.06).
- There were no studies identified reporting on catheter-related mortality, sepsis, pneumothorax, local insertion site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis with a closed-access CVC hub system.

### Evidence-to-decision

Needleless (closed-access) devices come with considerable costs and this would probably reduce equity, but with no issues in acceptability and feasibility. The GDG judgment on cost-effectiveness did not favour either the intervention or the comparison.

### Implementation considerations

- All IV medications should be prepared in a sterile manner to avoid the risk of contamination.
- Open-access systems require the access caps to be replaced reliably and using a sterile technique.
- GDG members agreed that the aseptic technique would be considered adequate to access the CVC for the routine administration of medications using a closed-access system.

### Research needs

- Further research is needed to identify the most cost-effective design of closed-access hub systems that could help reduce the cost and health care staff time using the catheter, especially in LMICs.
- Research on the potential for low-cost, self-disinfecting, closed-access systems is required.
- Additionally, good-quality RCTs on closed-access versus open-access CVC hub systems are needed.

## 3.6 Replacement and removal

### 3.6.1 CVC replacement

- **Good practice statement 13. WHO recommends inspecting the insertion site of CVCs in adults, adolescents, children and neonates at least daily to assess for signs of inflammation and infection to guide whether the catheter should be removed.**
(Good practice statement)

#### Remarks

- Signs of inflammation and infection at the catheter insertion site include cutaneous redness, swelling, tenderness and discharge (purulent or non-purulent).

- **Good practice statement 14. WHO recommends promptly removing any CVC no longer essential for patient care.**
(Good practice statement)

- **Recommendation 14. WHO suggests against routinely replacing a CVC (unless clinically indicated) in adults, adolescents, children and neonates.**
(Conditional recommendation, very low certainty of evidence)

#### Remarks

- The GDG members acknowledged that this recommendation does not apply in situations where it is clinically indicated to replace a CVC (for example, catheter failure due to blockage or other complications).

#### Rationale for the recommendation

The GDG considered the desirable effects as small, but the undesirable effects as moderate (due to the mechanical complications associated with catheter insertion), with an overall balance of effects probably favouring the comparison. Therefore, the GDG decided to make a conditional recommendation against routinely replacing a CVC, considering the small impact on the prevention of CLABSI, but the increased risk of potential mechanical complications associated with new catheter insertion.

#### Summary of the evidence

- The Systematic Reviews Expert Group identified four studies (two RCTs *(179, 180)* and two NSRIs *(181, 182)*) comparing routine CVC replacement with no routine CVC replacement in adults, adolescents, children and neonates and rated both RCTs as having some concerns with risk of bias.
- There was very low certainty of evidence that routine CVC replacement may result in more CLABSI than no routine CVC replacement (RR: 1.38; 95% CI: 0.58 to 3.29; two RCTs *(179, 180)*).
- There was very low certainty of evidence that routine CVC replacement may result in more pneumothorax than no routine CVC replacement (RR: 2.27; 95% CI: 0.43 to 12.03; one RCT*(179)*).

- There was very low certainty of evidence that routine CVC replacement may result in little to no difference in local insertion site infections than no routine CVC replacement (RR: 0.38; 95% CI: 0.02 to 9.12; one RCT*(179)*).
- There was very low certainty of evidence that routine CVC replacement may result in more deep vein thrombosis than no routine CVC replacement (RR: 2.27; 95% CI: 0.21 to 24.50; one RCT*(179)*).
- There were no studies identified that reported on catheter-related mortality, all-cause mortality, sepsis, bleeding events that require action, cardiac tamponade or venous stenosis after routine CVC replacement.

### Evidence-to-decision

Increased moderate costs (due to the additional supplies required), the reduced equity, low acceptability from patients (due to potential pain and inconvenience) and low feasibility (due to additional clinicians' time required for line insertion) were all considered when voting against the intervention. The overall cost-effectiveness judgement was probably in favour of the comparison.

### Implementation considerations

- Some studies have shown that infectious complications gradually increase with the dwell time of the catheter, in particular after 10 days *(181)* and if left in situ for more than 2 weeks *(183)*.
- Routine replacement may also carry a theoretical risk of increased sharps injuries as performing more procedures inherently raises the likelihood of exposure.

### Research needs

- The optimal time after which a CVC should be removed remains an open and unanswered question. The GDG members highlighted the need for studies (ideally RCTs) to address the research question if CVC replacement should be done at certain time intervals, such as 10 days.

## 3.7 Site and catheter selection

### 3.7.1 Site selection

- **Recommendation 15. WHO suggests using the subclavian or jugular veins over the femoral vein for CVC insertion in adults, adolescents, children and neonates.**
(Conditional recommendation, low certainty of evidence)

#### Remarks

- The GDG acknowledged that the risk and benefit of different insertion sites should be considered on an individual basis regarding infectious (that is, CLABSI) and non-infectious complications (in particular, pneumothorax).
- It is important to ensure that clinicians are appropriately trained in CVC insertion to reduce the risk of complications.
- In some emergency situations, the need to prioritize and rapidly establish an IV access may also determine the choice of access site.

#### Rationale for the recommendation

The GDG judged both the desirable and undesirable effects as small, with low certainty of evidence and an overall balance of effects not favouring either the intervention or the comparison. GDG members also acknowledged the existing controversy regarding the use of the femoral site *(184, 185)*, but it was considered that the proximity of the femoral vein to the skin of the groin area can contribute to increased bacterial contamination during insertion and a greater likelihood of developing an infection, compared to other access points like the internal jugular or subclavian veins. The GDG noted that in general, avoiding the femoral insertion site is widely accepted practice for the purpose of reducing infection risk. The potential risk of mechanical complications (in particular, pneumothorax) using other sites was also acknowledged, but reducible with appropriate training and the use of ultrasound.

#### Summary of the evidence

- The Systematic Reviews Expert Group identified a total of 13 RCTs *(106, 186-197)* comparing CVC insertion into the subclavian veins, jugular veins, or femoral veins. In addition, three NRSIs *(198-200)* also compared subclavian/jugular insertion versus femoral veins.
- Three RCTs *(191, 196, 197)* were included that specifically compared CVC insertion into the subclavian or jugular vein with CVC insertion in the femoral vein. All studies were rated as having some concerns with risk of bias, apart from one RCT that was assessed as having a low risk of bias *(191)*.
- There was very low certainty of evidence that there may be little to no difference in CLABSI between a CVC inserted into the subclavian or jugular veins compared with a CVC inserted in the femoral vein (RR: 0.77; 95% CI: 0.36 to 1.62; two RCTs *(191, 196)*).
- There was low certainty of evidence that CVC insertion in the subclavian or jugular veins may result in more all-cause mortality than CVC insertion in the femoral vein (RR: 1.22; 95% CI: 1.02 to 1.46; two RCTs *(191, 197)*).
- There was very low certainty of evidence that there may be fewer cases of sepsis with NHD-CVC insertion in the subclavian or jugular veins compared with a CVC inserted in the femoral vein (RR: 0.26; 95% CI: 0.03 to 2.33; one RCT *(196)*).

- There was very low certainty of evidence that there may be little to no difference in deep vein thrombosis with NHD-CVC insertion in the subclavian or jugular veins compared with a CVC inserted in the femoral vein (RR: 0.19; 95% CI; 0.04 to 0.86; three RCTs *(191, 196, 197)*).
- There were no studies identified reporting on catheter-related mortality, local insertion site infections, bleeding events that require action, cardiac tamponade or venous stenosis.

### Evidence-to-decision

The GDG considered that the use of subclavian or jugular sites would bring negligible costs and savings, with no impact on equity and overall cost-effectiveness, thus not favouring either the intervention or the comparison. The upper sites would be probably considered acceptable and feasible by clinicians and patients.

### Implementation considerations

- Insertion into the subclavian site is technically more difficult and requires additional and appropriate training.
- The subclavian site should be avoided in patients currently receiving or likely to require haemodialysis due to the risk of subclavian vein stenosis *(201, 202)*.
- Subclavian vein access carries a risk of pneumothorax, particularly in mechanically-ventilated patients. Additionally, achieving haemostasis can be difficult in individuals with thrombocytopenia or an elevated bleeding risk, further increasing the likelihood of adverse outcomes. Given these concerns, caution should be exercised when considering subclavian access in these scenarios.

### Research needs

- Further research and epidemiological data are needed on the advantages and disadvantages comparing the different insertion sites and the preferred selection.
- Further research may also be needed to define the impact of ultrasound guidelines and insertions into the subclavian vein.

- **Recommendation 16. WHO suggests using the subclavian veins as preferred site over jugular veins (if no contraindications) when inserting a CVC for the purpose of reducing infection risk, in adults, adolescents, children and neonates.**
  (Conditional recommendation, low certainty of evidence)

### Remarks

- The GDG acknowledged the potential increased risk of mechanical complications (particularly pneumothorax) when using the subclavian veins, but reducible with appropriate training and the use of ultrasound. The expected dwell time of the CVC was judged as an important factor to be taken into consideration. In the case of shorter dwell times and the smaller likelihood of developing an infection, the jugular site may be considered more appropriate, despite the overall recommendation.

### Rationale for the recommendation

The GDG judged the desirable effect as moderate and the undesirable effects as small, with low certainty of evidence and an overall balance of effects favouring the intervention. The potential risk of mechanical complications (particularly pneumothorax) using the subclavian site was also acknowledged, but reducible with appropriate training and the use of ultrasound.

### Summary of the evidence

- The Systematic Reviews Expert Group identified a total of 13 RCTs *(106, 186-197)* comparing CVC insertion into the subclavian, jugular or femoral veins. In addition, nine NRSIs *(200, 203-210)* also compared subclavian versus jugular sites.
- Eleven RCTs *(106, 186-195)* were included, specifically comparing CVC insertion into the subclavian versus the jugular vein. All studies were rated as having some concerns with risk of bias, apart from three RCTs that were assessed as having a low risk of bias *(191, 194, 195)*.
- There was low certainty of evidence that CVC insertion in the subclavian vein may result in fewer CLABSI compared to CVC insertion in the jugular vein (RR: 0.49; 95% CI: 0.24 to 1.00; four RCTs *(187, 189, 191, 193)*).
- There were no cases of catheter-related mortality in either group in one RCT *(186)*.
- There was a moderate certainty of evidence that CVC insertion in the subclavian vein probably results in lower all-cause mortality than CVC insertion in the jugular vein (RR: 0.84; 95% CI: 0.70 to 1.00; three RCTs *(106, 186, 191)*).
- There was low certainty of evidence that CVC insertion in the subclavian vein may result in little to no difference in pneumothorax compared to CVC insertion in the jugular vein (RR: 2.37; 95% CI: 1.06 to 5.33; nine RCTs *(106, 186-191, 194, 195)*).
- There was low certainty of evidence that CVC insertion in the subclavian vein may result in little to no difference in local insertion site infections compared to CVC insertion in the jugular vein (RR: 1.47; 95% CI: 0.25 to 8.71; three RCTs *(106, 189, 193)*).
- There was low certainty of evidence that CVC insertion in the subclavian vein may result in fewer deep vein thrombosis events compared to CVC insertion in the jugular vein (RR: 0.38; 95% CI: 0.21 to 0.68; three RCTs *(186, 191, 192)*).
- There were no cases of venous stenosis in either group in one RCT*(192)*.

### Evidence-to-decision

The GDG considered that the use of the subclavian site would bring negligible costs and savings, with no impact on equity, and an overall cost-effectiveness favouring the intervention. The use of the subclavian site would be probably considered acceptable and feasible by clinicians and patients.

### Implementation considerations

- Insertion into the subclavian site is technically more difficult and requires additional and appropriate training.
- The subclavian site should be avoided in patients currently receiving or likely to require haemodialysis due to the risk of subclavian vein stenosis *(201, 202)*.
- The subclavian vein should be avoided in patients with coagulopathy as it carries a higher risk of bleeding.

### Research needs

Although the use of ultrasound guidance for CVC insertion is recognized as being common practice in most health care settings, the procedure itself may jeopardize the strict observation of sterile technique. Hence, a re-evaluation of the balance between benefit and harm associated with its use in different insertion sites should be conducted, given the rapid increase in the number of practitioners familiar with the use of ultrasound and the rapid decrease regarding the experience of clinicians in introducing subclavian catheters.

### 3.7.2 Antibiotic-Impregnated and antiseptic-coated catheters

- **Recommendation 17. WHO suggests using either antibiotic-impregnated or non-impregnated CVCs in adults, adolescents, children and neonates.**
  (Conditional recommendation, low certainty of evidence)

#### Remarks

- The GDG noted that the use of antibiotic-impregnated CVCs should be reserved for specific indications, for example, in high-risk patients (such as immunosuppressed individuals).
- However, some GDG members raised strong concerns about the use of antibiotic-impregnated CVCs and the theoretical and potential development of antimicrobial resistance (including in *Mycobacterium tuberculosis* when using rifampicin as coating agent).
- The GDG also specifically requested the performance of a systematic review on the cost-effectiveness of using antibiotic-impregnated CVCs. Upon evaluation of the results, the GDG acknowledged that all the cost-effectiveness studies were performed in HICs and the affordability and clinical impact of these catheters in LMICs have yet to be assessed.
- Many studies evaluating antibiotic-impregnated central venous catheters (CVCs) were conducted prior to the widespread implementation of infection prevention bundles, making it unclear whether these catheters have a measurable impact on CLABSI rates in current practice. It was also noted that the majority of these studies date back several years.
- Moreover, most studies were performed in settings with high baseline CLABSI rates, and their findings may not be generalisable to clinical environments where catheter-related infections are already infrequent.
- The recommendation applies to adults, adolescents and children, but not neonates, because only antibiotic-impregnated PICC lines are available for this age group.

#### Rationale for the recommendation

The GDG members judged the desirable and undesirable effects as moderate and small, with an overall balance of effects probably favouring the intervention. The certainty of evidence was moderate for the CLABSI outcome, but low to very low for other outcomes. Hence, the GDG judged the overall certainty of evidence as low. However, concerns about the potential development of antibiotic resistance and the greater costs required, which would have a significant impact on LMICs, were two major considerations that influenced the final recommendation.

#### Summary of the evidence

- The Systematic Reviews Expert Group identified 17 studies (eight RCTs *(211-219)* and nine NRSIs *(220-228)*) evaluating the use of antibiotic-impregnated CVCs compared with the use of non-impregnated CVCs. All studies were conducted many years ago and had some concerns of risk of bias, apart from one RCT that was assessed as low risk *(214)*.
- There was moderate certainty of evidence that using antibiotic-impregnated CVCs probably results in fewer CLABSI than non-impregnated CVCs (RR: 0.35; 95% CI: 0.20 to 0.62; eight RCTs *(211-219)*).
- There were no cases of catheter-related mortality in either group in one RCT *(215)*.
- There was very low certainty of evidence that using antibiotic-impregnated CVCs may result in more all-cause mortality than non-impregnated CVCs (RR: 1.10; 95% CI: 0.52 to 2.33; two RCTs *(214, 216)*).

- There was very low certainty of evidence that using antibiotic-impregnated CVCs may result in fewer local insertion site infections than non-impregnated CVCs (RR: 0.62; 95% CI: 0.23 to 1.66; four RCTs *(214-216, 219)*).
- There were no studies reporting on sepsis, pneumothorax, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.
- No specific evidence regarding the impact on AMR and/or on allergic reactions were found in the studies considered or in the literature *(229)*.

### Additional assessment on cost-effectiveness

After consultation with the guideline methodologists and upon request of the GDG members, further additional cost-effectiveness searches were also performed. The results retrieved an additional five studies *(230-234)* that compared the cost-effectiveness of antibiotic-impregnated CVCs with the use of non-impregnated CVCs. As meta-analysis was not appropriate due to heterogeneity, results are summarized narratively.

- All studies were conducted in ICU/paediatric ICU (PICU) settings. Two were from the USA and one each from Australia, United Kingdom of Great Britain and Northern Ireland and Spain *(230-234)*. Four studies compared antibiotic-coated catheters to standard uncoated catheters *(230, 231, 233, 234)*, of which two studies additionally compared antibiotic-coated catheters (that is, minocycline/rifampicin) to antiseptic-coated catheters (that is, chlorhexidine/silver sulfadiazine) *(230, 234)*. One study only compared antibiotic-impregnated catheters (minocycline/rifampicin) to antiseptic-coated catheters (chlorhexidine/silver sulfadiazine) *(232)*.
- All studies employed the analytical perspective of the hospital or health care payer. Health outcomes evaluated were CLABSI in three studies *(231, 233, 234)*, while two studies used quality-adjusted life years gained *(230, 232)*.
- Compared to uncoated CVC controls, three of the four included studies *(230, 231, 234)* found antibiotic-coated CVCs to be more effective and less costly. The fourth study evaluation *(233)* calculated an incremental cost-effectiveness ratio of £ 54 057 per BSI avoided, based on 2013 price values. However, there is uncertainty regarding its cost-effectiveness. The likelihood of rifampicin/minocycline CVCs being cost-effective was estimated as 38% at a threshold of £ 10 000, 49% at £ 50 000, and 62% at £ 100 000, respectively, per BSI avoided.
- Overall, antibiotic-coated CVCs appear likely to be cost-effective when compared to uncoated catheters.

### Evidence-to-decision

Antibiotic-impregnated catheters are more expensive compared to standard catheters. Hence, these greater costs would have an impact on equity and their acceptability, as well as varied feasibility. Despite the results of the additional cost-effectiveness analysis, the GDG members judged the overall cost-effectiveness as variable, depending on the setting (HICs versus LMICs) and the baseline CLABSI rates.

### Implementation considerations

- Health care facilities with high CLABSI rates should first consider the implementation and compliance with the other recommendations present in these guidelines before considering the adoption of antibiotic-impregnated catheters.
- Patients should be monitored for allergic reactions, including anaphylaxis.

### Research needs

- Further research is needed such as aa RCT comparing antibiotic-impregnated, antiseptic-coated and standard CVCs in adults and children, as well as in different clinical and socioeconomic settings (HICs versus LMICs).
- The impact on bacterial epidemiology and the potential emergence of antibiotic-resistant strains and cross-resistance to antibiotics were identified by the GDG as another important area for research.
- Further studies are also needed to evaluate whether their impact remains consistent under modern clinical practices.
- As the coating of some  catheters elutes within 1 to 2 days, research should focus on assessing their effectiveness in relation to risk per day, while meticulously tracking the duration of catheterization.

## Recommendation 18. WHO suggests using antiseptic-coated CVCs in adults, adolescents, children and neonates.

(Conditional recommendation, low certainty of evidence)

### Remarks

- The GDG noted that antiseptic-coated CVCs should be preferably used in specific patient populations, such as immunocompromised, obese, burn and transplant patients, patients with limited venous access and a history of recurrent CLABSI, and patients at risk of severe sequelae from a CLABSI, (for example, patients with recently implanted intravascular devices such as a prosthetic heart valve or aortic graft).
- The impact on AMR was judged less problematic than for antibiotic-impregnated catheters, hence the difference in recommendations between antibiotic- and antiseptic-coated catheters.
- The GDG also noted that most of these catheters last a maximum of 21 days and therefore they should not be used when there is a need for a long-term catheter.
- As for the previous recommendation, the GDG specifically requested the performance of a systematic review on the cost-effectiveness of using antiseptic-coated catheters. Upon evaluation of the results, the GDG acknowledged that most of the cost-effectiveness studies were performed in HICs (apart one study *(235)*) and the affordability and clinical impact of these catheters in LMICs have yet to be fully assessed.
- It was also noted that many studies were performed in settings with high CLABSI rates. Thus, antiseptic-coated catheters may not provide any additional benefit in clinical settings that have already demonstrated a low incidence of catheter infections. Additionally, most studies were conducted several years ago.

### Rationale for the recommendation

The GDG members judged both the desirable and undesirable effects as small, with an overall balance of effects probably favouring the intervention. The certainty of evidence was moderate for the CLABSI outcome, but low to very low for other outcomes. Hence, the overall certainty of evidence was judged as low. The GDG had less concerns about the potential development of AMR and the cost implications on LMICs, hence the recommendation of using antiseptic-coated catheters, depending on resources available and patient needs.

### Summary of the evidence

- The Systematic Reviews Expert Group identified 50 studies (35 RCTs *(112, 236-249) (235, 250-263) (264-268)* and 15 NRSIs *(215, 220-222, 224, 228, 269-271)*) evaluating the use of antiseptic-coated CVCs compared with the use of non-coated CVCs.
- The risk of bias was assessed as low in one RCT *(268)* and high in seven RCTs *(237, 243, 247, 249, 250, 258, 266)*, whereas the remaining RCTs were considered to have some concerns regarding risk of bias.
- There was moderate certainty of evidence that antiseptic-coated CVCs probably result in fewer CLABSI than non-impregnated CVCs (RR: 0.76; 95% CI: 0.61 to 0.95; 35 RCTs).
- There was low certainty of evidence that antiseptic-coated CVCs may result in little to no difference in catheter-related mortality compared with non-coated CVCs (RR: 0. 22; 95% CI: 0.01 to 4.45, five RCTs *(244, 245, 247, 261, 264)*).
- There was very low certainty of evidence that antiseptic-coated CVCs may result in less all-cause mortality than non-impregnated CVCs (RR: 0.94; 95% CI: 0.79 to 1.12; seven RCTs *(236, 238, 245, 260, 262, 263, 268)*).
- There was low certainty of evidence that antiseptic-coated CVCs may result in more sepsis than non-impregnated CVCs (RR: 1.18; 95% CI: 0.62 to 2.27; one RCT *(268)*).
- There was very low certainty of evidence that antiseptic-coated CVCs may result in little to no difference in pneumothorax than non-coated CVCs (RR: 2.75; 95% CI: 0.11 to 67.07; one RCT *(240)*).
- There was low certainty of evidence that antiseptic-coated CVCs may result in little to no difference in local insertion site infections than non-coated CVCs (RR: 0.74; 95% CI: 0.52 to 1.03; seven RCTs *(235, 247, 259, 261, 262, 264, 267)*).
- There was very low certainty of evidence that antiseptic-coated CVCs may result in little to no difference in deep vein thrombosis than non-coated CVCs (RR: 0.31; 95% CI: 0.03 to 2.97; one RCT *(247)*).
- There were no studies reporting on bleeding events that require action, cardiac tamponade or venous stenosis.
- No evidence on the impact of AMR and/or adverse reactions were found in the studies considered or in the literature *(229)*.

### Additional assessment on cost-effectiveness

After consultation with the guideline methodologists and upon request of the GDG members, further additional cost-effectiveness searches were performed. The results retrieved an additional 11 studies *(230, 232, 234, 235, 256, 271-276)* that compared the cost-effectiveness of antiseptic-coated CVCs with non-coated CVCs. As meta-analysis was not appropriate due to heterogeneity, results are summarized narratively below.

- All studies were performed in ICU/PICU patients, apart from one study that included both ICU and non-ICU patients *(275)*. Six studies were from the USA, two from Spain and one each from Australia, Argentina and Germany *(230, 232, 234, 235, 256, 271-276)*. All studies compared antiseptic-coated catheters to standard uncoated catheters, apart from one study that only compared antibiotic- coated catheters (minocycline/rifampicin) to antiseptic-coated catheters directly *(232)*. The antiseptic agents used in the studies were chlorhexidine-silver sulfadiazine, but one study assessed silver-coated attachable cuffs for CVCs *(275)*.
- All studies employed the analytical perspective of the hospital or health care payer. Health outcomes evaluated were mainly CRBSI. One study evaluated death attributable to the combination of CRBSI and/or a hypersensitivity reaction *(276)*, while two studies used quality-adjusted life years gained *(230, 232)*.

- Compared to uncoated CVC controls, 90% of evaluations found antiseptic-coated CVCs to be dominant, that is, more effective and less costly. However, they were considered not cost-effective in the study from Argentina *(235)*.
- Antiseptic-coated CVCs appear likely to be cost-effective in most contexts compared to uncoated catheters.

#### Evidence-to-decision

Antiseptic-coated catheters are moderately more expensive when compared to standard catheters, hence the reduced equity, but with an overall cost-effectiveness favouring the intervention. There were no issues identified in terms of acceptability and feasibility.

#### Implementation considerations

- Similar to antibiotic-impregnated catheters, many studies were performed before infection preventive bundles were routine. Whether antiseptic-coated catheters have an impact on CLABSI in such settings remains unknown.
- Health care facilities with high CLABSI rates should first consider the implementation and compliance with the other recommendations present in these guidelines before considering the adoption of antiseptic-coated catheters.
- Patients should be monitored for adverse events and potential allergic reactions, including anaphylaxis.

#### Research needs

- The benefit of antiseptic-coated catheters should be re-evaluated in settings where the risk of infection and the overall CLABSI rates are low.
- Research studies should also assess if these catheters lose their effectiveness after a certain number of days, in particular when considering long-term catheters.
- The impact on bacterial epidemiology and the potential emergence of AMR and cross-resistance to antibiotics were identified by the GDG as another important area for research

### 3.7.3 Catheter selection for long-term central lines

- **Recommendation 19. WHO suggests using a single lumen over a multi-lumen catheter (unless there is a specific reason that requires multiple lumens) in adults, adolescents and children requiring a long-term central line.**
  (Conditional recommendation, very low certainty of evidence)

#### Remarks

- The decision about whether to use a single lumen over a multi-lumen CVC should be made solely on the clinical need for multiple catheter lumens.
- GDG members acknowledged that this recommendation would be more suitable for non-critically ill patients and outside of the ICU settings (where the clinical need often dictates the demand for a multiple-lumen catheter).
- The GDG also commented on the age of the evidence published (from years 1987 to 1995) and that such evidence may not be relevant any longer when considering current clinical practices and additional IPC measures available (including bundles) to prevent CLABSI.

- The recommendation applies to adults, adolescents and children, but not neonates as no multi-lumen long-term catheters other than PICC lines are available for this age group.

### Rationale for the recommendation

Based on the evidence provided, the GDG considered that the use of a single lumen CVC is associated with small desirable and trivial undesirable effects, and an overall balance probably not favouring either the intervention or the comparison. The overall certainty of evidence was judged as very low. However, it was acknowledged that this recommendation is more relevant for non-critically ill patients outside of the ICU settings and in those with a long-term line where the use of a single lumen may reduce the risk of contamination and the risk of CLABSI. Each lumen in a catheter represents a potential pathway for bacteria to enter the bloodstream, especially during use or maintenance. By limiting the number of lumens, single lumen CVCs minimize these pathways, thereby lowering the likelihood of CLABSI. Additionally, single lumen CVCs are often used in situations where fewer infusions are required, reducing the frequency of handling and manipulation, which further decreases the infection risk.

### Summary of the evidence

- The Systematic Review Expert Group identified six RCTs *(277-282)* and 17 NRSIs *(203, 283-298)* that compared the use of a single lumen catheter (both CVC and Hickman) with the use of a multi-lumen catheter. All RCTs were rated as having some concerns with risk of bias.
- There was very low certainty of evidence that the use of a single lumen catheter may result in fewer CLABSI than the use of a multi-lumen catheter (RR: 0.58; 95% CI: 0.18 to 1.90; six RCTs *(277-282)*).
- There was very low certainty of evidence that the use of a single lumen catheter may result in lower all-cause mortality than the use of a multi-lumen catheter (RR: 0.82; 95% CI: 0.51 to 1.32; one RCT *(278)*).
- There was very low certainty of evidence that the use of a single lumen catheter may result in fewer cases of pneumothorax than the use of a multi-lumen catheter (RR: 0.22; 95% CI: 0.01 to 4.36; one RCT *(281)*).
- There was very low certainty of evidence that the use of a single lumen catheter may result in fewer local insertion site infections than the use of a multi-lumen catheter (RR: 0.75; 95% CI: 0.17 to 3.32; three RCTs *(279, 281, 282)*).
- There was very low certainty of evidence that the use of a single lumen catheter may result in little to no difference in deep venous thrombosis compared to the use of a multi-lumen catheter (RR: 3.00; 95% CI: 0.13 to 69.87; one RCT *(282)*).
- There were no studies identified that reported on catheter related mortality, sepsis, bleeding events that require action, cardiac tamponade and venous stenosis.

### Evidence-to-decision

The GDG considered that the resources required for the use of a single lumen CVC over a multi-lumen CVC are associated with moderate savings and cost-effectiveness considerations probably favour the use of single lumen CVCs. Equity is not affected, patient acceptability is probably increased, and feasibility is likely to be increased with the use of single lumen CVCs.

### Implementation considerations

- As for all CVCs, clinicians should have received training in the appropriate sterile/aseptic protocols to maintain and access an intravascular catheter, including those with multiple lumens.

### Research needs

- Research on the respective advantages of multi-lumen CVCs would be helpful.

## Recommendation 20. WHO suggests using either a Hickman CVC or a Port-a-Cath in adults, adolescents and children requiring a long-term central line.

(Conditional recommendation, low certainty of evidence)

### Remarks

- PICCs were not included in the comparison as they were considered in previous guidelines *(11)*.
- The decision on which type of long-term line to be inserted should be based on clinical needs and patient preferences. Please see also under implementation considerations below.
- The recommendation applies to adults, adolescents and children, but not neonates as Hickman CVC and Port-a-Cath are not applicable for this age group.

### Rationale for the recommendation

The GDG considered both the desirable and undesirable effects of using a Hickman CVC compared to a Port-a-Cath as small, with an overall balance of effects not favouring either the intervention or the comparison. The certainty of evidence provided was considered to be low.

### Summary of the evidence

- The Systematic Reviews Expert Group identified four RCTs *(299-302)* and 21 NRSIs (*303-318*) (*319-323*) comparing the insertion/use of a Hickman CVC versus insertion/use of a Port-a-Cath. One RCT was rated as at high risk of bias *(301)*, whilst the others were considered at low risk.
- There was low certainty of evidence that the insertion/use of a Hickman CVC resulted in fewer CLABSI than the insertion/use of a Port-a-Cath (RR: 0.69; 95% CI: 0.40 to 1.18; two RCTs *(299, 301)*), but the GDG highlighted the limited sample size and the dated nature of one study *(301)*.
- There were no reported events of pneumothorax in either group in one RCT (very low certainty of evidence of little to no difference; one RCT *(299)*).
- There was low certainty of evidence that the insertion/use of a Hickman CVC may result in little to no difference in local insertion site infections than the insertion/use of a Port-a-Cath (RR: 2.09; 95% CI: 1.16 to 3.78; four RCTs *(299-302)*).
- There was very low certainty of evidence of little to no difference in bleeding events that require action with the insertion/use of a Hickman CVC compared to the insertion/use of a Port-a-Cath(RR: 2.63; 95% CI: 0.11 to 61.05; two RCTs *(300, 302)*).
- There was very low certainty of evidence of little to no difference in venous thrombosis with the insertion/use of a Hickman CVC compared to the insertion/use of a Port-a-Cath(RR: 1.24; 95% CI: 0.51 to 3.02; four RCTs *(299-302)*).
- The studies that assessed the effect on all-cause mortality were deemed unreliable due to the specific patient populations (haematology and oncology patients) and the follow-up period of up to 12 months. Consequently, the mortality outcome was excluded from consideration for this PICO question.
- There were no studies identified that reported on catheter related mortality, sepsis, cardiac tamponade or venous stenosis.

### Evidence-to-decision

The additional resources required were considered as negligible costs, with an overall cost-effectiveness not favouring either the intervention or the comparison. Equity was considered as probably increased as GDG members considered the insertion of a Hickman catheter easier in terms of personnel required. However, acceptability would probably be reduced as patients would find a Port-a-Cath more comfortable. No issues were identified in terms of feasibility.

### Implementation considerations

The decision on which long-term central line to be inserted should be based on the clinical need and patient preferences. The choice between a Hickman line versus a Port-a-Cath depends on factors such as the type and duration of treatment, the patient's lifestyle, maintenance requirement, and the risk of infection, as summarized below.

- **Hickman line**

  *When it is used:* often chosen for patients who need continuous or frequent IV access over a long period, such as for chemotherapy, total parenteral nutrition or long-term antibiotics.

  *Advantages:* it has external lumens that allow for easy access without the need for repeated venipunctures. It can also accommodate multiple infusions simultaneously if it has multiple lumens. Generally easier to insert and requires fewer specialized resources than a Port-a-Cath.

- **Port-a-Cath (or totally implantable venous access devices)**

  *When it is used:* typically recommended for patients who require long-term, intermittent treatments such as chemotherapy, long-term antibiotics, or regular infusions. It is also used when frequent blood sampling is needed.

  *Advantages:* the device is implanted entirely under the skin, making it less prone to infection and more discreet and convenient for patients (allowing greater mobility). It can remain in place for months or even years.

### Research needs

- More research comparing Hickman CVC or Port-a-Cath versus PICC lines is needed to investigate their impact on clinical needs, infectious and non-infectious complications, and patient preferences.

## 3.8 Other preventive measures (including surveillance and bundles)

### 3.8.1 Securement of CVC

- **Recommendation 21. WHO suggests using either a suture-less or suture-based securement of CVCs in adults, adolescents, children and neonates.**
  (Conditional recommendation, very low certainty of evidence)

#### Remarks

- Clinicians may be concerned about the accidental removal of the CVC whilst using a suture-less securement.
- Please note that PICC lines were not assessed in this comparison.

#### Rationale for the recommendation

Considering the very low certainty of evidence in the literature and the great heterogeneity of the findings, the GDG judged the desirable and undesirable effects as trivial and small, respectively. Despite a perceived belief that skin sutures may increase the risk of infections, no evidence was found supporting this claim. The GDG also discussed the potential risk of the accidental removal of the CVC, with one study *(324)* citing an unplanned line removal in 2% of cases (2/86 patients) in the suture group versus 6% (5/85 patients) in the suture-free group. However, the study was not powered to detect statistically significant differences in the two parameters. Overall, the GDG considered the balance of effects not favouring either the intervention or the comparison and this is reflected in the current recommendation.

#### Summary of the evidence

- The Systematic Reviews Expert Group identified four RCTs *(324-327)* evaluating the use of suture-less securement of a CVC versus use of suture-based securement. The risk of bias was assessed as low in one RCT *(326)* and some concerns in the remaining three RCTs *(325, 327)*.
- There was very low certainty of evidence that suture-less securement of a CVC may result in more CLABSI than suture-based securement (RR: 1.26; 95% CI: 0.46 to 3.46; two RCTs *(326, 327)*).
- There was very low certainty of evidence that suture-less securement of a CVC may result in more all-cause mortality than suture-based securement (RR: 1.38; 95% CI: 0.34 to 5.63; two RCTs *(326, 327)*).
- There was very low certainty of evidence that suture-less securement of a CVC may result in little to no difference in local insertion site infections than suture-based securement (RR: 1.24; 95% CI: 0.87 to 1.76; four RCTs *(324-327)*).
- There were no studies reporting on catheter-related mortality, sepsis, pneumothorax, bleeding events that require action, cardiac tamponade or venous stenosis.

#### Evidence-to-decision

Suture-less devices are more expensive compared to standard sutures, with moderate additional costs involved and reduced equity, when taking into consideration LMICs. Overall, the GDG considered the cost-effectiveness in favour of the suture-based securement of a CVC due to the lack of convincing evidence that suture-less devices could reduce the number of infectious complications. Acceptability

and feasibility of suture-less devices may also be variable, depending on the clinician's and patient's preferences.

#### Implementation considerations

- The GDG considered that additional training was needed for the securement, maintenance and removal of suture-less devices.

#### Research needs

- As data on suture-less devices for CVC are scarce, further RCTs are required to evaluate their clinical utility and benefits in preventing infectious and non-infectious complications, including the use of new materials, such as liquid adhesives.
- More research on their cost-effectiveness is also needed.

### 3.8.2 Antimicrobial lock solutions for short- and long-term catheters

- **Recommendation 22. WHO suggests not using an antimicrobial lock solution in patients with short-term CVCs for the prevention of CVC infections in adults, adolescents, children and neonates.**
  (Conditional recommendation, very low certainty of evidence)

#### Remarks

- Concerns regarding ethanol as a lock solution were expressed by some GDG members and included the risk of causing catheter occlusion, increased risk of thrombosis, damage to the catheter material, and a potential for systemic toxicity if leaked into the bloodstream *(328-330)*.
- Some GDG members expressed concerns about the potential development of AMR following the use of prophylactic antimicrobial lock therapy and the wider impact on bacterial epidemiology.
- For comparison among different agents, ethylenediaminetetraacetic acid (EDTA) was considered among the antimicrobials due to previous evidence suggesting antibacterial properties *(331, 332)*.
- It should be noted that this recommendation is only relevant for short-term catheters.

#### Rationale for the recommendation

Given the varied nature of the interventions, antimicrobials and populations studied, the GDG found it challenging to make a definitive judgment on the positive effects of antimicrobial lock solutions in patients with short-term CVCs. Although the systematic review indicated a trend towards a beneficial effect, drawing a strong conclusion was not feasible due to the very low certainty of evidence. Although some GDG members noted that the results of the identified studies are consistent, the GDG finally judged the desirable effects of using an antimicrobial lock solution as small. The GDG highlighted the toxicity of chlorhexidine and ethanol, noting that the only alternative antimicrobials would be taurolidine and fusidic acid. Based on this, the GDG judged undesirable effects as moderate, with a balance of effects probably favouring the comparison (no use of antimicrobial lock solutions) and a final decision against the intervention.

### Summary of the evidence

- The Systematic Reviews Expert Group identified seven studies (all RCTs *(333-339)*) in adults, children and neonates comparing the use of an antimicrobial lock solution with the use of a non-antimicrobial solution, all rated as having some concerns with risk of bias.
- There was low certainty of evidence that the use of an antimicrobial lock solution resulted in fewer CLABSI than the use of non-antimicrobial lock solutions (RR: 0.28; 95% CI: 0.15 to 0.54; seven RCTs *(333-339)*). There were no significant subgroup differences between adults, children and neonates.
- There was very low certainty of evidence that use of an antimicrobial lock solution resulted in lower catheter-related mortality than the use of non-antimicrobial lock solutions (RR: 0.36; 95% CI: 0.04 to 3.20; two RCTs *(335, 337)*).
- There was very low certainty of evidence that use of an antimicrobial lock solution resulted in lower all-cause mortality than the use of non-antimicrobial lock solutions (RR: 0.93; 95% CI: 0.60 to 1.44; four RCTs *(334, 335, 338, 339)*).
- There was very low certainty of evidence that the use of an antimicrobial lock solution resulted in little to no difference in local insertion site infections compared to the use of non-antimicrobial lock solutions (RR: 3.21; 95% CI: 0.13 to 77.22; one RCT *(334)*).
- There was very low certainty of evidence that use of an antimicrobial lock solution resulted in little to no difference in deep venous thrombosis compared to the use of non-antimicrobial lock solutions (RR: 1.02; 95% CI: 0.07 to 15.86; one RCT *(337)*).
- There were no studies identified that reported on sepsis, pneumothorax, bleeding events that require action, cardiac tamponade or venous stenosis following use of an antimicrobial lock solution.

### Evidence-to-decision

Implementing antimicrobial lock solutions would incur moderate additional costs and might reduce equity, especially in LMICs. However, overall cost-effectiveness was considered probably in favour of the comparison. The GDG highlighted that there could be challenges related to acceptability and feasibility due to potential supply and procurement issues, depending on the specific context.

### Implementation considerations

- An additional comment from GDG members was that it may be difficult to instil an antimicrobial lock solution in ICU settings where short-time CVCs are often in continuous use.

### Research needs

- There is a need for RCTs to evaluate the efficacy of antimicrobial lock solutions in patients with short-term CVCs and their cost-effectiveness.

- **WHO makes no recommendation regarding the routine use of prophylactic antimicrobial lock therapy (for example, vancomycin, ethanol, taurolidine, or minocycline) in preventing catheter-related infections in adults, adolescents, children, and neonates with long-term central venous catheters, as the evidence remains inconclusive.**

  This guidance specifically excludes dialysis patients, whose catheter management follows distinct protocols.

### Remarks

- It should be noted that patients undergoing haemodialysis were not included in the current scope as specific guidance for this group may be developed at a later stage (Part 3).
- Many of the studies focused on taurolidine and ethanol for prophylactic antimicrobial lock therapy, with the evidence predominantly supporting the use of taurolidine. However, the studies had small sample sizes and a low certainty of evidence.
- Concerns regarding ethanol as a lock solution were expressed by some GDG members and included the risk of causing catheter occlusion, increased risk of thrombosis, damage to the catheter material, potential for systemic toxicity if leaked into the bloodstream, and a lack of consistent data on its efficacy and safety across different studies, especially regarding long-term use *(328-330)*.
- Some GDG members expressed concerns about the potential development of AMR following the use of prophylactic antimicrobial lock therapy and the wider impact on bacterial epidemiology.
- For comparison among different agents, EDTA was considered among the antimicrobials due to previous evidence suggesting antibacterial properties *(331, 332)*.

### Rationale for the decision

The GDG members judged both the desirable and undesirable effects as small, with an overall balance of effects probably favouring the intervention. However, the GDG was initially divided between a conditional recommendation for the intervention and a conditional recommendation for either option. After intense discussion and considering the low certainty of evidence and the limited availability in LMICs, consensus was reached that no recommendation could be made.

### Summary of the evidence

- The Systematic Reviews Expert Group identified 70 studies (18 RCTs *(308, 340-356)* and 52 NRSI *(357-363) (364-388) (389-399)*) reporting on the use of prophylactic antimicrobial lock therapy (for example, vancomycin, ethanol, taurolidine, minocycline) compared with no use. Most studies were rated as having some concerns regarding risk of bias *(308, 340-343, 346, 349, 350, 353, 355)*, two studies with a high risk of bias *(344, 354)* and six with a low risk of bias *(345, 347, 348, 351, 352, 356)*.
- There was low certainty of evidence that the use of prophylactic antimicrobial lock therapy may result in fewer CLABSI than no prophylactic antimicrobial lock therapy (RR: 0.54; 95% CI: 0.37 to 0.78; 17 RCTs *(308, 340-353, 355, 356)*).
- There were no catheter-related deaths reported in either group in four RCTs *(346, 349, 350, 353)*.
- There was low certainty of evidence of little to no difference in all-cause mortality with prophylactic antimicrobial lock therapy compared to no prophylactic antimicrobial lock therapy (RR: 1.24; 95% CI; 0.49 to 3.11; five RCTs *(345, 346, 349, 351, 352)*).
- There was moderate certainty of evidence that prophylactic antimicrobial lock therapy probably results in little to no difference in local insertion site infections compared to no prophylactic antimicrobial lock therapy (RR: 0.74; 95% CI: 0.40 to 1.39; six RCTs *(308, 342, 349, 352, 353, 355)*).
- There was moderate certainty of evidence that prophylactic antimicrobial lock therapy probably results in little to no difference in deep vein thrombosis compared to no prophylactic antimicrobial lock therapy (RR: 0.63; 95% CI: 0.38 to 1.05; five RCTs *(342, 350, 351, 353, 355)*).
- There were no studies identified that reported on sepsis, pneumothorax, bleeding events that require action, cardiac tamponade or venous stenosis.

- Subgroup analyses based on the age of participants revealed no difference in effect for CLABSI.
- Subgroup analysis based on the type of lock indicated that the use of taurolidine lock therapy (RR: 0.43; 95% CI: 0.27 to 0.68; 12 RCTs *(308, 340, 341, 343-347, 350, 352, 353)*) may result in fewer CLABSI than trisodium citrate (RR: 1.12; 95% CI: 0.76 to 1.65; one RCT*(342)*).

#### Evidence-to-decision

Implementing antimicrobial lock solutions would incur moderate additional costs and might reduce equity, especially in LMICs and in settings where patients may have to pay out of pocket. The overall cost-effectiveness was considered to likely favour the intervention for long-term catheters and the intervention was judged to be probably acceptable and feasible. However, some objections from clinicians may arise due to the time required to prepare the solution. Overall, no recommendation could be made.

#### Implementation considerations (regardless of the no recommendation)

- Despite no recommendation, antimicrobial lock therapy could still be considered for the most vulnerable patients at high risk of developing CLABSI. This includes immunocompromised and transplant patients, those on parenteral nutrition, obese or burn patients, individuals with limited venous access and a history of recurrent CLABSI, and those at risk of severe complications from CLABSI, such as patients with recently implanted intravascular devices like prosthetic heart valves or aortic grafts.
- In case a local decision is made to administer antimicrobial lock therapy, clear protocols should be established for its administration, including dwell times, concentrations and removal of the lock solution rather than flushing into the circulation, including training based on these protocols should be provided to health care professionals.
- If prepared at the facility level, all antimicrobial lock solutions should be formulated in strict adherence to good manufacturing practice guidelines and sterility standards.

#### Research needs

- The GDG considered it worthwhile to conduct randomized trials comparing different prophylactic lock solutions and evaluating their cost-effectiveness.
- Future research should also focus on determining the optimal concentrations of antibiotics or antimicrobials used in various protocols for lock solutions. Additionally, studies should evaluate the potential side-effects associated with these concentrations to ensure both efficacy and safety in clinical practice.

### 3.8.3 Antiseptic line caps

- **Recommendation 23. WHO suggests either using antiseptic-impregnated or non-impregnated line caps in adults, adolescents, children and neonates with short- and long-term catheters.**
  (Conditional recommendation, low certainty of evidence)

#### Remarks

- Patients undergoing haemodialysis were not included in the scope of the current guidelines as specific guidance for this group may be developed at a later stage (Part 3).

- The GDG acknowledged the low quality of the evidence, noting that the before-and-after design of most of the studies was likely to introduce bias.

### Rationale for the recommendation

The GDG determined that the desirable effects of using antiseptic-impregnated line caps were small and the undesirable effects were trivial, with the overall balance likely favouring the intervention. However, the low certainty of evidence and other contextual factors were considered, such as additional moderate costs and reduced equity due to availability and affordability in LMICs. Consequently, the final recommendation suggested the use of either antiseptic-impregnated or non-impregnated line caps.

### Summary of the evidence

- The Systematic Reviews Expert Group identified 14 studies (two RCTs *(400, 401)* and 12 NRSIs *(402-413)*) evaluating the use of antiseptic-impregnated line caps compared with non-impregnated line caps. One RCT was rated as having some concerns with risk of bias *(400)* and one as at high risk of bias *(401)*.
- There was low certainty of evidence of little to no difference in CLABSI with the use of antiseptic-impregnated line caps compared with non-impregnated line caps (RR: 0.35; 95% CI: 0.04 to 2.93; two RCTs *(400, 401)*.
- There were no studies identified that reported on catheter-related mortality, all-cause mortality, sepsis, pneumothorax, local site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.

### Evidence-to-decision

The GDG considered that the cost of antiseptic-impregnated line caps was not particularly high compared to other preventive interventions. However, they were significantly higher than non-impregnated caps and this would have an impact on equity, with an overall cost-effectiveness not favouring either the intervention or the comparison. However, GDG members did not foresee any issues with acceptability and feasibility.

### Implementation considerations

- Antiseptic line caps are typically single-use devices. As there is a potential risk of re-use when the line is accessed, it is important to provide regular staff training to help preventing any misuse.

### Research needs

- More evidence is needed to explore the potential clinical benefits of antiseptic line caps, also when used as part of a comprehensive care bundle to prevent infections. This further research could help determine their cost-effectiveness in various clinical settings (including LMICs) and provide insights into their role within a holistic infection prevention strategy.
- Further research should investigate whether antiseptic-impregnated caps have a specific role in long-term compared to short-term CVCs, or within distinct patient groups. Particular attention should be given to patients undergoing chemotherapy for haematological malignancies as they may receive specific benefits.

### 3.8.4 Intravenous Prophylactic antibiotics at the time of line insertion

- **Recommendation 24. WHO suggests not using IV prophylactic antibiotics in adults, adolescents, children and neonates with short- and long-term catheters. (Conditional recommendation, very low certainty of evidence)**

#### Remarks

- The GDG members discussed short- and long-term catheters separately. However, the final recommendation and the decision-making process arrived at the same conclusions for both types of catheters.
- GDG members also voiced their concerns about the inappropriate use of antibiotics and its impact on AMR. They also highlighted the increased risk of *Clostridium difficile* infections and the potential for adverse events related to antibiotic use.

#### Rationale for the recommendation

The GDG deemed the desirable effects to be trivial for both short- and long-term catheters. The undesirable effects (as listed in the remarks) were considered small for long-term lines, but moderate for short-term lines due to the higher number of patients using CVCs for shorter periods. Overall, the balance of effects favoured the comparison (no antibiotic) for both types of catheters. The evidence was rated to be of very low certainty.

#### Summary of the evidence

- The Systematic Reviews Expert Group identified 13 studies (five RCTs and eight NRSIs *(414-421)*) reporting on IV prophylactic antibiotic administration versus no use. All five RCTs were rated as having some concerns with risk of bias *(422-426)*.
- Short-term catheters
- For short-term catheters, there was very low certainty of evidence that there may be fewer CLABSI with IV prophylactic antibiotic administration versus no use (RR: 0.13; 95% CI 0.01 to 2.38; one RCT *(422)*).
- For short-term catheters, there were no studies identified that reported on catheter-related mortality, all-cause mortality, sepsis, pneumothorax, local site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.
- Long-term catheters
- For long-term catheters, there was very low certainty of evidence of little to no difference in catheter- related BSI between IV prophylactic antibiotic administration and no use (RR: 0.48; 95% CI: 0.05 to 5.09; two RCTs*(423, 425)*).
- There was very low certainty of evidence of little to no difference in sepsis between IV prophylactic antibiotic administration versus no use (RR: 0.92; 95% CI: 0.60 to 1.42; two RCTs *(423, 426)*).
- There was low certainty of evidence that IV prophylactic antibiotic administration may result in fewer local insertion site infections compared to no use (RR: 0.80; 95% CI: 0.51 to 1.26; three RCTs *(423-425)*).
- For long-term catheters, there were no studies identified reporting on catheter-related mortality, all-cause mortality, pneumothorax, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.

#### Evidence-to-decision

The use of IV antibiotics would incur additional moderate costs and reduce equity. Overall, the cost-effectiveness was considered to favour not administering antibiotics at the time of CVC insertion. While this approach may face acceptability issues among key stakeholders, it does not present major feasibility challenges.

#### Implementation considerations

- The GDG recognized that there may be rare instances where IV antibiotics are used in current practice and might occasionally be considered, such as during the exchange of tunnelled lines in renal dialysis patients. However, no systematic reviews were conducted to support this claim.

#### Research needs

Further research is required to determine whether antibiotic prophylaxis would be beneficial for any specific population or type of line.

### 3.8.5 Surveillance

- **Good practice statement 15. WHO recommends that HAI surveillance (including CLABSI or related BSI and to detect AMR and outbreaks) should be performed to guide IPC interventions, combined with timely feedback of results to health care workers and stakeholders, including through national networks.**
(Good practice statement)

- **Good practice statement 16. WHO recommends that national HAI surveillance programmes and networks that include mechanisms for timely data feedback and with the potential to be used for benchmarking purposes should be established to reduce HAI and AMR.**
(Good practice statement)

### 3.8.6 Line care bundles

- **Recommendation 25. WHO suggests using CVC practice bundles in adults, adolescents, children and neonates.**
(Conditional recommendation very low certainty of evidence)

#### Remarks

- *Care or practice bundles* are a set of evidence-based, patient-focused practices or interventions (generally three to five) that aim to improve patient outcomes when done collectively and reliably. They can also be a tool to guide the delivery of a specific aspect of a patient care where the aim is to improve the care process and patient outcomes in a structured manner or sequence, with the expectation that the impact will be larger than single interventions alone *(427)*.

- The GDG members acknowledged that there is no current consensus on which core interventions are essential for a CVC practice bundle and more data are needed to determine which components of the bundle are essential in reducing CLABSI.

### Rationale for the recommendation

Based on the evidence provided by the Systematic Reviews Expert Group, the GDG considered both the desirable and undesirable effects as small, with an overall balance of effects favouring the intervention. The certainty of the evidence provided was judged very low, but the GDG also acknowledged the heterogeneity of studies and the variety of study designs, which complicated the comparison of different interventions or bundles with varying components.

### Summary of the evidence

- The Systematic Reviews Expert Group identified 14 studies (four RCTs *(428-431)* and 14 NRSIs *(432-445)*) evaluating the use of CVC practice bundles compared with no use. Three NRSIs were controlled before-after studies (with a parallel control group) *(434, 442, 443)* and 11 were interrupted time series *(432, 433, 435-441, 444, 446)* (with appropriate analysis) reporting on the use of CVC practice bundles. One study was rated as having a low risk of bias *(428)*, one as having some concerns with risk of bias *(431)* and two studies as having a high risk of bias *(429, 430)*. The NRSIs were all rated with at least a moderate risk of bias *(432-445)*.
- There was a low to very low certainty of evidence from three RCTs *(429-431)*, two non-RCTs *(442, 443)*, and 11 interrupted time series *(432, 433, 435-441, 444, 446)* that the use of CVC bundles reduce CLABSI compared to no use.
- Rate ratios reported in the three RCTs were 0.38 (95% CI: 0.27 to 0.52) *(430)*, 0.97 (95% CI: 0.57 to 1.66) *(431)* and 0.19 (95% CI: 0.06 to 0.57) *(429)*. Data from the three RCTs were not meta-analysed because of heterogeneity in the care bundles.
- The two non-RCTs reported lower rates of CLABSI in the intervention compared to the control groups. One reported a RR of 0.85 (95% CI 0.73 to 0.99) *(443)* and the other a rate ratio of 0.32 (95% CI: 0.08 to 0.99) *(442)*.
- There was very low certainty of evidence from 11 interrupted time series studies *(432, 433, 435-441, 444, 445)* showing a decrease in CLABSI rates following care bundle interventions.
- There was very low certainty of evidence that CVC care bundles may result in more cases of sepsis compared to no care bundle use (RR: 1.08; 95% CI: 0.75 to 1.58; one RCT *(447)*).
- There was very low certainty of evidence that CVC care bundles may result in fewer cases of sepsis compared to no care bundle use (RR: 0.47; 95% CI: 0.20 to 1.08; one NRSI *(434)*).
- There were no studies identified reporting on catheter-related mortality, all-cause mortality, pneumothorax, local insertion site infections, bleeding events that require action, cardiac tamponade, deep vein thrombosis or venous stenosis.

### Evidence-to-decision

Overall, CVC practice bundles have a negligible impact on costs as most of the interventions should be part of routine clinical practice and are already considered as cost-effective, with no impact on equity and no issues of acceptability and feasibility.

### Implementation considerations

- Bundles are most effective when implemented in an environment with an established patient safety culture and their success depends on adherence to each specific measure.
- The GDG emphasized the importance of prioritizing resources and tasks at the local level, considering other competing needs within the health care facility. This prioritization can help determine which components should be included in the CVC care bundle.
- The GDG also observed that having a bundle in place may not be enough on its own. Additional factors should also be considered, such as ensuring sufficient personnel for its implementation.

### Research needs

- Randomized or adaptive trials design are needed to determine which bundle elements are essential to reduce risk. An alternative option would be to emulate a target trial using observational data *(448)* from high-quality cohort studies and this approach could be an effective way to address multiple research questions without conducting new RCTs.

# 4

# WHO Multimodal improvement strategy

# WHO Multimodal improvement strategy

## 4.1 Introduction

Multimodal improvement strategies (MMIS) are a means of improving the implementation of interventions to achieve the required system, institutional climate and behavioural changes for measurable outcome improvement from the intervention(s). In general, MMIS include tools, such as bundles and checklists, developed by multidisciplinary teams that consider local conditions. Multimodal thinking means that practitioners do not focus only on single strategies to change practices (for example, training and education), but consider a range of strategies that target different influencers of human behaviour. MMIS typically contains five key components: system change ("*Build it*"); training and education ("*Teach it*"); monitoring and feedback ("*Check it*"); reminders and communication ("*Sell it*"); and culture change ("*Live it*") *(427, 449)*. All five elements are considered important and should be based on the local health context and situation, informed by periodic assessments.

A recent systematic review *(450)* on MMIS for the implementation of IPC interventions using at least three WHO multimodality elements demonstrated a significant effect on HAI prevention and hand hygiene improvement, confirming the findings by previous reviews of the WHO core components *(451)*. However, the quality of evidence remains limited and only a minority of studies were from low- or middle-income countries. Future research should focus therefore on higher quality studies in resource-limited settings.

## 4.2 Evidence on MMIS and CLABSI

The Systematic Reviews Expert Group identified 11 studies (three cluster RCTs *(452-454)*, one non-randomized study *(455)* and seven interrupted time series studies *(446, 456-461)* [with appropriate analysis]) evaluating MMIS for CVC management interventions and/or practice bundles. All three cluster RCTs *(452-454)* were rated as having some concerns, the non-randomized study *(455)* as having a moderate risk of bias, and the seven interrupted times series studies *(446, 456-461)* with at least some unclear items of risk of bias. There was very low certainty of evidence from the three RCTs *(452-454)* on MMIS reporting on BSI. Data from the three RCTs were not meta-analysed because of heterogeneity in the interventions.

- O'Neil et al (2016) *(452)* reported a 2.5% monthly decrease in the CLABSI incidence density on intervention floors, but this was not statistically significant (95% CI: −5.3% to 0.4%). On control floors, there was a smaller, but marginally significant decrease in CLABSI incidence during the study (change in monthly rate, −1.1%; 95% CI: −2.1% to −0.1%). The rate ratio was 1.23 (95% CI: 0.62–2.45).
- Reynolds et al (2021) *(453)* also reported that overall rates of CLABSI decreased 27.4% (from 2.59 to 1.88) on average from baseline to post-intervention. The intervention effect was found to be non-significant (b=1.22; p=0.56).
- Speroff et al (2011) *(454)* reported that the CLABSI rate was 2.42/1000 catheter days at baseline and 2.73/1000 catheter days at 18 months (p=0.59). Neither group improved outcomes over time and there was no difference between the two groups in respect of CLABSI rates (p=0.71)

Additionally, there was very low certainty of evidence from one non-randomized study *(455)* that MMIS may result in no difference in CLABSI (RR: 1.04; 95% CI: 0.48 to 2.33).

All seven interrupted time series studies *(446, 456-461)* reported a decrease in CLABSI following implementation.

- Salm et al (2016) *(457)* reported a significant change in the slope for the frequency of BSI from the start to the end of the intervention (change in slope incidence rate ratio, 0.97; p=0.001). The CLABSI effect RR was 0.75 (95% CI: 0.6 to 0.93).
- Apisarnthanarak et al (2010) *(458)* reported in period 1 a total of 88 episodes of CABSI (14/1000 catheter-days). During period 2, the CABSI rate decreased by 54.1% (6.4/1000 catheter-days). The CABSI rate was further decreased by 78% (1.4/1000 catheter-days) during period 3.
- Costello et al (2008) *(446)* reported a significant reduction in CLABSI rates from pre-intervention (=7.8 [5.6-10.5]), partial intervention (=4.7 [3.4-6.3]; p=0.029 compared to pre-intervention) to full intervention (=2.3 [1.2-3.8];p=0.0002 compared to pre-intervention).
- Harris et al (2024) *(461)* reported that the CLABSI bundle was associated with a significant immediate effect in reducing the CLABSI rate in the surgical ICU compared with control ICUs.
- Ben-David et al (2023) *(459)* reported an incidence rate ratio of 0.63 (95% CI: 0.51–0.79) between phases I and II, and 0.78 (95% CI: 0.59–1.02) between phases II and III.
- Hansen et al (2014) *(460)* reported that compared with baseline, the relative risk for CLABSI was 0.88 (95% CI: 0.70-1.11) for the intervention period and 0.72 (95% CI: 0.58-0.88) for the follow-up period. No changes were observed in either control group.
- Pronovost et al (2010) *(456)*reported that multilevel regression analysis showed that the incidence rate ratios decreased from 0.68 (95% CI: 0.53 to 0.88) at 0-3 months to 0.38 (95% CI: 0.26 to 0.56) at 16-18 months and 0.34 (95% CI: 0.24-0.48) at 34-36 months' post-implementation.

## 4.3 WHO recommendations on MMIS

WHO considers the use of MMIS as the most effective way to implement IPC interventions. This is based on the initial development of the WHO hand hygiene MMIS, which was shown to be highly effective in several studies *(462-466)*. This concept was extended to any intervention aimed at improving IPC practices when WHO developed the guidelines on core components for IPC programmes *(28)*, among which MMIS is core component 5 *(451)*. Within these evidence-based guidelines, two strong recommendations are included (Table 2), for which the evidence represented the highest number of studies of the entire guideline.

**Table 2: WHO evidence-based recommendations on MMIS for IPC interventions**

| CORE COMPONENT 5: | NATIONAL LEVEL | FACILITY LEVEL |
|---|---|---|
| CORE COMPONENT RECOMMENDATION | The panel recommends that national IPC programmes should coordinate and facilitate the implementation of IPC activities though multimodal strategies on a nationwide or sub-national level. | The panel recommends that IPC activities using multimodal strategies should be implemented to improve practices and reduce HAI and AMR. |

Core component 5: Both at national and facility levels, IPC activities should be implemented using multimodal strategies.
Abbreviations: IPC, infection prevention and control; HAI, health care-associated infection; AMR, antimicrobial resistance.

In 2019, WHO further issued guidance on the minimum requirements for IPC programmes at the national and facility level *(65)*, which were derived from the core components' recommendations, including the minimum requirements for core component 5 (Table 3).

**Table 3: Minimum requirements for IPC programmes at the national and facility level related to the implementation of MMIS**

| Level | Minimum requirement |
|---|---|
| National | ***Use of multimodal strategies*** to implement IPC interventions under the coordination of the national IPC team. |
| Primary care facilities | ***Use of multimodal strategies*** – **at the very least** to implement interventions to improve **hand hygiene, safe injection practices, decontamination** of medical instruments and devices and **environmental cleaning.** |
| Secondary care facilities | ***Use of multimodal strategies*** – ***at the very least*** to implement interventions to improve **standard and transmission-based precautions and triage.** |
| Tertiary care facilities | ***Use of multimodal strategies*** to implement interventions to improve **standard and transmission-based precautions, triage**, and those targeted at the **reduction of specific infections in high-risk areas/patient** groups, in line with local priorities. |

*Abbreviation:* IPC, infection prevention and control.
*Source*: WHO minimum requirements *(65)*

Implementation of the IPC interventions should always be tackled using a stepwise approach, including a careful assessment of the status of the IPC practices and local activities related to the intervention to be improved. To undertake this process, WHO proposes a five-step cycle of implementation to support the management and planning of any IPC improvement intervention or programme, based on implementation and quality improvement science *(427, 449)*. Each step is relevant to the process of improvement and the cycle should be continuously used and refreshed for several years for each IPC intervention in order to ensure maximum impact and sustainability.

The GDG advises that the MMIS approach and five-step cycle could be used also for the implementation of this guideline. In particular, a country or a health care facility should evaluate local guidelines and/or standard operating procedures for the prevention of BSI and other infections associated with central line catheters and determine whether any update is needed by exploring their alignment with this WHO guideline. Furthermore, local practices should be assessed to identify the most common gaps and thus enable the development of improvement plans including interventions, based upon the relevant recommendations and/or good practice statements of this guideline.

# 5

# Research needs

# Research needs

Although CVCs are widely used in health care globally, their safe usage still requires substantial clarification and research due to their link to both infectious and non-infectious complications. Consequently, it is essential to conduct further studies on the insertion, maintenance, access and removal of these intravascular devices across diverse health care settings. Ideally, due to the several knowledge gaps and low evidence recommendations, it would be interesting to set up an international adaptive trial platform to test different CLABSI prevention measures in different settings.

GDG members identified several critical research areas to enhance the practical application and safety of CVCs worldwide. Each guideline recommendation includes specific considerations on the research gaps and needs, which are summarized in Table 4 for convenient reference.

**Table 4: List of research needs and related domains for the prevention of CLABSI**

| Domain and research gaps |
|---|
| **Pre-insertion** |
| • Patient bathing protocols: there is a significant variation in existing protocols and research is needed to determine the most effective methods and products (for example, liquid wash versus wipes, rinsing versus no rinsing, and which solutions to use).<br>• Antiseptic products: additional research is required on antiseptic products other than chlorhexidine (for example, octenidine) using multicentre RCTs or adaptive trials, particularly for specific populations/settings such as haematology patients or paediatric ICUs.<br>• AMR and other implications: the impact of chlorhexidine and other body washes on the skin microbiome, cross-resistance to antibiotics, and the epidemiology of infections caused by gram-positive and gram-negative bacteria are important research areas.<br>• Cost-benefit analysis: studies including baseline surveillance data are needed to define potential thresholds for the universal use of these products. |
| **Insertion** |
| • Cost-benefit of CVC insertion teams: investigate the potential cost-benefit of using a formal CVC insertion team versus an educational/behavioural programme for clinicians in both ICU and non-ICU settings.<br>• Sterile precautions: assess if lesser sterile precautions are safe using adaptive trial designs to distinguish the impact of different components within maximal sterile barrier precautions (for example, cap, mask, full body drape, environment).<br>• Disinfection products: standardize comparator disinfection products in future research to accurately assess the benefits of different non-chlorhexidine-containing products.<br>• Chlorhexidine concentrations: conduct large RCTs comparing different concentrations of chlorhexidine (0.5% versus 1% versus 2%) to select the most appropriate concentration.<br>• Single-use applicators versus solutions: compare single-use applicators containing chlorhexidine versus chlorhexidine solutions without specific devices to increase equity and potentially reduce costs.<br>• Ultrasound training: research optimal training requirements and teaching methods for ultrasound use, including standardized cleaning methods.<br>• Gauze versus semi-permeable dressings: investigate the impact of gauze versus semi-permeable dressings, especially in hot climates where gauze may be preferred due to excessive skin sweating.<br>• Transparent semi-permeable dressing: research the optimal transparent semi-permeable dressing for use in all climates, particularly for LMICs.<br>• Low-cost dressing products: develop a standard, transparent, semi-permeable dressing product that can be mass-produced at low cost to provide greater equity, especially for LMICs.<br>• Chlorhexidine patches versus dressings: conduct randomized trials comparing chlorhexidine patches versus chlorhexidine dressings and their impact on infections, resistance, bacterial selection and feasibility in LMICs.<br>• Antiseptic patch/dressing effectiveness: assess the effectiveness of antiseptic patches or dressings when used alongside other measures using the same antiseptic (for example, chlorhexidine bathing, alcohol-chlorhexidine for skin disinfection).<br>• Bacterial epidemiology and resistance: investigate the impact on bacterial epidemiology and the potential emergence of chlorhexidine-resistant strains and cross-resistance to antibiotics. |

| Domain and research gaps |
|---|
| **Maintenance** |
| • Prolonging dressing change: assess if dressing change intervals can be extended, particularly with the use of antimicrobial patches, different dressings and liquid adhesives.<br>• Regular changing of CVC administration sets: investigate the effect of regularly changing the CVC administration set (tubing/giving) every 7 days versus other durations to reduce CLABSI.<br>• Optimal time for administration set changes: conduct RCTs comparing 7-day intervals versus clinically-indicated changes to determine the optimal schedule for changing administration sets when using a CVC.<br>• Continuous versus intermittent infusion: conduct a randomized trial comparing continuous IV infusion versus intermittent infusion, considering multiple outcome measures (for example, infectious and non-infectious complications, nursing time, costs, patient preferences).<br>• Heparin-induced thrombocytopenia: further research on the rate of heparin-induced thrombocytopenia linked to heparinized saline use in "lock-off" flushing to quantify the clinical risk more accurately.<br>• Saline versus anticoagulant solutions: investigate the comparative impact on mortality between saline and anticoagulant solutions, considering all potential adverse effects, including heparin-induced thrombocytopenia. |
| **Access** |
| • Cost-effective closed-access hub systems: determine the most cost-effective design to reduce costs and health care staff time, especially in LMICs.<br>• Low-cost, self-disinfecting systems: explore the potential for low-cost, self-disinfecting closed-access systems.<br>• Closed-access versus open-access systems: conduct high-quality RCTs comparing closed-access and open-access CVC hub systems. |
| **Replacement and removal** |
| • CVC replacement: the GDG has identified the need for further research to determine the optimal time for CVC replacement. Specifically, studies (ideally RCTs) are needed to address whether CVC replacement should be performed at specific time intervals, such as every 10 days. |
| **Site and catheter section** |
| • Insertion sites: investigate the advantages and disadvantages of different CVC insertion sites and preferred selections.<br>• Ultrasound guidance: assess the impact of ultrasound guidelines and insertions into the subclavian vein, balancing the benefits and harms associated with its use in different insertion sites.<br>• Antibiotic-impregnated versus antiseptic-coated CVCs: conduct RCTs comparing antibiotic-impregnated, antiseptic-coated and standard CVCs in various clinical and socioeconomic settings.<br>• Effectiveness of antibiotic catheters: focus on assessing the effectiveness of antibiotic catheters in relation to risk per day, considering the duration of catheterization. Also, evaluate whether the impact of these catheters remains consistent under modern clinical practices.<br>• Antiseptic-coated catheters: re-evaluate the benefit of antiseptic-coated catheters in settings with low infection risk and overall CLABSI rates.<br>• Bacterial epidemiology and resistance: study the impact on bacterial epidemiology and the emergence of antibiotic-resistant strains and cross-resistance to antibiotics.<br>• Multi-lumen CVCs: research the advantages of multi-lumen CVCs.<br>• Hickman CVC vs Port-a-Cath vs PICC Lines: Compare Hickman CVC, Port-a-Cath, and PICC lines regarding clinical needs, complications and patient preferences. |
| **Other preventive measures** |
| • Suture-less devices for CVC: further RCTs are needed to evaluate their clinical utility and benefits in preventing infectious and non-infectious complications, including the use of new materials like liquid adhesives. Research on their cost-effectiveness is also needed.<br>• Antimicrobial lock solutions: RCTs are required to evaluate the efficacy and cost-effectiveness of antimicrobial lock solutions in patients with short-term CVCs. Trials comparing different prophylactic lock solutions and their cost-effectiveness are also worthwhile.<br>• Optimal concentrations for lock solutions: future research should determine the optimal concentrations of antibiotics or antimicrobials used in lock solutions and evaluate potential side-effects to ensure efficacy and safety.<br>• Antiseptic line caps: more evidence is needed to explore the clinical benefits and cost-effectiveness of antiseptic line caps, especially when used as part of a comprehensive care bundle to prevent infections. Research should also investigate their role in long-term versus short-term CVCs and in specific patient groups, such as those undergoing chemotherapy for haematological malignancies.<br>• Essential bundle elements: randomized or adaptive trial designs are needed to determine which bundle elements are essential to reduce risk. An alternative approach could be to emulate a target trial using observational data from high-quality cohort studies to address multiple research questions without conducting new RCTs. |

*Abbreviations:* RCT, randomized controlled trials; ICU, intensive care unit; AMR, antimicrobial resistance; CVC, central venous catheter; LMICs, low- and middle-income countries; CLABSI, central line-associated bloodstream infection; IV, intravenous; GDG, Guideline Development Group; PICC, peripherally-inserted central catheter.


Epidemiologist B. Gnoevoi cleans his hands using alcohol-based handrub in the Diagnostic Laboratory at “Dnipropetrovsk Regional Clinical Hospital Named After I.I. Mechnikov.”[Ukraine].

# 6

# Monitoring and evaluating the impact of guidelines

# Monitoring and evaluating the impact of guidelines

Since centrally-inserted intravascular catheters are one of the frequent invasive health care devices used worldwide, any complications potentially linked to their use should ideally be routinely monitored, recorded and the results fed back to clinicians to improve the safety of their use. Monitoring, evaluation and feedback are key elements for the success of the WHO MMIS (see chapter 4). Furthermore, WHO recommends using a stepwise cycle to implement any IPC intervention or project as assessment steps at the baseline are critical for evaluating impact and planning sustainability Therefore, interventions aimed at improving practices related to the use of centrally-inserted intravascular catheters should include steps focusing on this critical element *(467)*.

Monitoring of the impact of these guidelines should be considered using the following approaches.

1. Measure clinician education, training and competencies in CVC management (insertion, maintenance, access and removal) using an ongoing system of regular assessment.
2. Monitor clinician adherence to the practices recommended in the guidelines' good practice statements and recommendations.
3. Assess any complications associated with CVC and correlate these data with adherence to the guidelines in clinical practices.

Investigate all health care-associated BSI to determine the source of these infections and whether they are associated with intravascular catheters or other health care interventions. Such an approach should allow clinicians to determine the proportion of BSIs that are catheter-associated and thereby provide an indicator for the impact of these guidelines. Ideally, such data should then be correlated with a valid measure of clinical activity (for example, infections per 1000 catheter days or per 1000 inpatient bed days).

# 7

# Update and dissemination of the guidelines

# Update and dissemination of the guidelines

These guidelines are available as a printed document and a web-based product for dissemination. They include all evidence as presented to the GDG (within the text and in Annex 2, Annex 3 and the Web Annex).

The recommendations issued in the guidelines will remain valid for 5 years. The WHO Secretariat will monitor scientific evidence as they become available, as well as users' needs, to decide on the need to update the recommendations during that period. The Steering Group will continue to follow research developments in the prevention of BSI and other infections associated with CVCs, particularly for the questions in which the systematic reviews showed that: (1) no evidence was found; (2) low-certainty evidence was identified; or (3) where additional new recommendations or further changes in published recommendations would be needed.

Following publication and dissemination of the guidelines, any concern about the validity of any recommendation will be promptly communicated to the guidelines' implementers and revisions will be made.

We plan to disseminate the guidelines on the WHO website, specifically on the IPC webpage, through the regional offices' focal points, dissemination lists, and through the Global Infection Prevention and Control Network, a collaborative mechanism between more than 20 organizations in the field of IPC and WHO.

The Steering Group will invite relevant WHO departments to contribute to a wider dissemination plan, as appropriate. Technical meetings will be held within WHO departments to share the products with the teams responsible for policy and programme implementation. We will also liaise with the WHO Press close to the time of publication of the guideline to agree on a publication plan. We will publish the full report and a summary report, including full details of the methodology and results of the evidence appraisal on the website at the same time as the release these guidelines.

## 7.1 Derivative products

Evidence briefs will be produced to target policy-makers and programme managers. This is important to enhance interpretation and uptake of the guideline, particularly in areas where the technical expertise to fully understand the current guideline format may be limited. The evidence briefs will highlight the recommendations and related contextual issues for implementation. In addition, to increase awareness of the guideline, the recommendations will be published as a commentary in peer-reviewed scientific journals.

Finally, implementation tools to reflect the WHO multimodal strategies for the implementation of IPC interventions will be developed in collaboration with regional offices, key stakeholders and field implementers.

## 7.2 Essential medicines list

The recommendations issued in the guidelines will not affect a priori modifications in the Essential Medicines List. If case changes are required, the Essential Medicines List Secretariat will be contacted to discuss the inclusion of new products.

## 7.3 Adaptation

All WHO regional offices have been invited to be observers at the GDG meetings. Immediately after the GDG meetings, we will meet with the regional offices to make detailed plans for local adaptation and implementation guidance. WHO departments and other partners will support national and subnational groups to adapt the guideline. This process may include the development or revision of existing national guidelines or protocols based on the WHO guidelines.

## 7.4 Implementation

Implementation guidance will be developed in partnership with the regional offices. WHO departments and other partners will support national and subnational groups to implement the recommendations. In addition, in collaboration with other WHO departments, the WHO IPC team will develop a plan for research on effective implementation strategies.

A local nurse prepares an IV drip for a patient at a local government funded hospital in the town of Menglong, Yunnan Province [China].
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# 8

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Trecia Simone Stewart, 41, a certified emergency nurse assists Dr Nashoni Mitchell with a patient who is in distress at the Spanish Town Hospital [Jamaica].

# 9

# Annexes

# Annex 1. Guideline development group contributors and participants, with their declarations of interests

**Table 5: Declarations of interest[1] for the Guideline Development Group**

| Name (alphabetical order) | 1.Consulting and technical advisory boards | 2. Research support | 3. Investments and business interests | 4. Intellectual property | 5. Public statements and positions | 6. Additional information | 7.Tobacco products | Conflicts management plan |
|---|---|---|---|---|---|---|---|---|
| Based on the Declaration of interests (WHO Experts) form, available from http://intranet.who.int/homes/cre/ethics1/doiexperts/ | | | | | | | | |
| **Abdelwahed Ismail, Ghada –** Supreme High Council of University Hospitals, Egypt | None | None | None | None | None | None | none | Full participation |
| **Abu Sin**, **Muna** – Robert Koch Institute, Germany | None | Research grants from the German Ministry of Health and WHO | None | None | None | None | none | Full participation |
| **Adusei, Alex** – Women's Hope Foundation and Patient for Patients Safety Network, Ghana | None | None | None | None | None | None | none | Full participation |
| **Ahmed, Altaf** – Pakistan Kidney and Liver Institute & Research Center, Pakistan | None | None | None | None | None | None | none | Full participation |
| **Al Bahrani, Maher –** Royal Hospital, Muscat, Oman | None | None | None | None | None | None | None | Full participation |
| **Azrag**, **Hiba** – Federal Ministry of Health, Sudan | None | None | None | None | None | None | None | Full participation |
| **Buetti**, **Niccolò** – Geneva University Hospitals and Faculty of Medicine, WHO Collaborating Centre, Switzerland | None | None | None | None | None | None | None | Full participation |
| **Cruickshank**, **Marilyn** – Faculty of Health, University of Technology Sydney, Australia | None | None | None | None | None | None | None | Full participation |
| **Desai**, **Anita** – National Institute of Mental Health and Neurosciences, India | None | None | None | None | None | None | None | Full participation |



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| Name (alphabetical order) | 1. Consulting and technical advisory boards | 2. Research support | 3. Investments and business interests | 4. Intellectual property | 5. Public statements and positions | 6. Additional information | 7.Tobacco products | Conflicts management plan |
|---|---|---|---|---|---|---|---|---|
| Based on the Declaration of interests (WHO Experts) form, available from http://intranet.who.int/homes/cre/ethics1/doiexperts/ | | | | | | | | |
| **Gao, Bin –** Tianjin 4th Central Hospital, Tianjin Medical University, China | None | None | None | None | None | None | None | Full participation |
| **Hopkins**, **Susan** – United Kingdom Health Security Agency, United Kingdom of Great Britain and Northern Ireland | None | None | None | None | None | None | None | Full participation |
| **Jacob**, **Shevin** – Liverpool School of Tropical Medicine & African Sepsis Alliance, Uganda | None | Director of Global Health Research Group on Adult Sepsis<br>Chief Scientist Officer and Principal Investigator of Research Consortium | None | None | Board of Directors and Executive Committee for the Global Sepsis Alliance<br>Co-Founder, Secretary General and Executive Committee Member of the African Sepsis Alliance | None | None | Full participation |
| **Jayatilleke**, **Kushlani** – Sri Jayewardenepura General Hospital, Sri Lanka | Employed as consultant microbiologist by Sri Jayewareden-pura General Hospital | None | None | None | None | None | None | Full participation |
| **Machado Ribeiro, Flavia** – Escola Paulista de Medicina, Universidade Federal de São Paulo | None | None | None | None | None | Co-author of manuscript on coated devices, part of research project with industry support (not direct, but to hospital) | None | Full participation |
| **Marimuthu, Kalisvar** – National Centre for Infectious Diseases and Tan Tock Seng Hospital, Singapore | None | None | None | None | None | None | None | Full participation |
| **Mermel, Leonard –** Brown University, USA | Advisory board (Citius Pharma, antibiotic lock treatment)<br>Consultant CorMedix (catheter lock solutions) and Pristine Access Technologies (haemodialysis catheters) | None | Stock options (Citius Pharma and Pristine Access Technologies) | None | None | Honoraria for speaking publicly | None | General full participation, but excluded from decision process on antiseptic- and antibiotic-impregnated catheters |

| Name (alphabetical order) | 1.Consulting and technical advisory boards | 2. Research support | 3. Investments and business interests | 4. Intellectual property | 5. Public statements and positions | 6. Additional information | 7.Tobacco products | Conflicts management plan |
|---|---|---|---|---|---|---|---|---|
| Based on the Declaration of interests (WHO Experts) form, available from http://intranet.who.int/homes/cre/ethics1/doiexperts/ | | | | | | | | |
| **Orsini, Mauro** – National Infection Prevention Control Programme, Department of Quality and Patient Safety, Ministry of Health, Santiago, Chile | None | None | None | None | As part of the Chile Ministry of Health, review and development of policies related to the topic | None | None | Full participation |
| **Roberts, Sally** – Health New Zealand, Te Whatu Ora, Te Toka Tumai Auckland, New Zealand | None | None | None | None | None | None | None | Full participation |
| **Timsit**, **Jean-François** – Bichat Hospital and Université Paris Cité, France | Advisory board (Becton, Dickinson and Company, BD, to discuss positioning of BD in French market) | None | None | None | None | None | None | General full participation, but excluded from decision process on antiseptic-patches or dressings |
| **Walter Zingg**, Zurich University Hospital, Switzerland | None | None | None | None | None | None | none | Full participation |

**Table 6: Declaration of Interest for external reviewers, methodologists, systematic review team, and other technical support members**

| Name | 1.Consulting and technical advisory boards | 2.Research support | 3. Investments and business interests | 4. Intellectual property | 5. Public statements and positions | 6. Additional information | 7.Tobacco products | Conflicts management plan/notes |
|---|---|---|---|---|---|---|---|---|
| **Ling Moi Lin** – Singapore General Hospital, Singapore | None | None | None | None | None | None | None | External reviewer |
| **Rima Moghnieh** – Lebanese American University and Medical Center, Beirut, Lebanon) | None | None | None | None | None | None | None | External reviewer |
| **Jordi Riello** – Universitat Autònoma de Barcelona and Vall d'Hebron University Hospital, Barcelona, Spain) | None | None | None | None | None | None | None | External reviewer |
| **Thomas Talbot** – Vanderbilt University Medical Center, Nashville, United States of America | None | None | None | None | None | None | None | External reviewer |
| **Miliya Thyl** – Angkor Hospital for Children, Siem Reap, Cambodia | None | None | None | None | None | None | None | External reviewer |

| Name | 1. Consulting and technical advisory boards | 2. Research support | 3. Investments and business interests | 4. Intellectual property | 5. Public statements and positions | 6. Additional information | 7. Tobacco products | Conflicts management plan/notes |
|---|---|---|---|---|---|---|---|---|
| **Alimuddin Zumla** – University College London and University College London Hospitals NHS Foundation Trust, United Kingdom of Great Britain and Northern Ireland | None | None | None | None | None | None | None | External reviewer |
| **Elie Akl** – American University of Beirut, Beirut, Lebanon | None | None | None | None | None | None | None | Methodologist |
| **Sally Yaacoub** – Centre for Research in Epidemiology and Statistics, Cochrane France, Paris, France | None | None | None | None | None | None | None | Methodologist |
| **Nicholas Henschke** – Cochrane Response, London, United Kingdom of Great Britain and Northern Ireland | None | None | None | None | None | None | None | Part of the systematic review team |
| **Katrin Probyn** – Cochrane Response, London, United Kingdom of Great Britain and Northern Ireland | None | None | None | None | None | None | None | Part of the systematic review team |
| **Gemma Villanueva** – Cochrane Response, London, United Kingdom of Great Britain and Northern Ireland | None | None | None | None | None | None | None | Part of the systematic review team |
| **Lindsay Grayson** – Austin Health, Heidelberg, Australia | None | None | None | None | None | None | None | Expert technical input for the initial selection of the PICO questions, but no participation in the guideline decision process |
| **Catho, Gaud** – Geneva University Hospitals and Faculty of Medicine, WHO Collaborating Centre, Switzerland | None | None | None | None | None | None | None | Ad hoc participation as rapporteur during one GDG meeting |

# Annex 2. PICO questions

All PICO questions (PQ) are listed below. The populations included in the searches comprised adults, adolescents, children and neonates, with dialysis patients being excluded. Unless otherwise specified, all searches encompassed both short- and long-term types of CVCs.

### Pre-insertion patient preparation

**PQ1:** Should antiseptic body washing (liquid or impregnated wipes with chlorhexidine or octenidine) be routinely used versus not routinely used prior to CVC insertion to reduce the rates of CVC-BSI and CVC-AIC?[1]

### Insertion

**PQ2:** Should alcohol-chlorhexidine (CHG) antiseptic (0.5%, 1% or 2%) versus alcohol-iodine versus alcohol alone versus aqueous formulations (CHG or iodine) be used for skin disinfection at the insertion site prior to CVC insertion to reduce the rates of CVC-BSI and CVC-AIC?

**PQ3:** Should sterile technique involving "maximal sterile barrier precautions"[2] versus "sterile technique"[3] (a lesser standard of precautions) be used at the time of CVC insertion to reduce the rates of CVC-BSI/CVC-AIC?

**PQ4:** In patients in whom ultrasound is being considered to reduce mechanical complications, should ultrasound be used versus not used to reduce CLABSI?

**PQ5:** Should a transparent semi-permeable dressing versus gauze dressing be used after CVC insertion to reduce the rates of CVC-BSI/CVC-AIC?

**PQ6:** Should an antiseptic patch or dressing (for example, CHG-impregnated sponge or dressing or any other antiseptic) be used versus not used (no antiseptic) to reduce the rates of CVC-BSI/CVC-AIC?

**PQ7:** Should a formal schedule of CVC dressing changes versus a clinically-indicated CVC dressing change be used to reduce the rates of CVC-BSI/CVC-AIC?

**PQ8:** If a formal schedule of CVC dressing changes is to be used, what is the optimal schedule to reduce the rates of CVC-BSI/CVC-AIC?

**PQ9:** Should a schedule of 7 days regular changing of the NHD-CVC administration (tubing/giving) set be used versus other schedules (2, 3 and 4 days) when administering routine IV fluids only (not blood products or parenteral feed) to reduce the rates of CVC-BSI/CVC-AIC?

**PQ 9a:** Should a schedule of regular changing of the NHD-CVC administration (tubing/giving) set be used versus not used when administering total parenteral nutrition or lipid products to reduce the rates of CVC-BSI/CVC-AIC?

### Access

**PQ10:** Should a closed-access CVC hub system versus an open-access CVC hub system be used to reduce the rates of CVC-BSI/CVC-AIC?

### Replacement

**PQ11:** When a CVC needs replacement, should reinsertion using the existing insertion site (for example, using guidewire replacement) versus CVC insertion in a new site be used to reduce the rates of CVC-BSI/CVC-AIC?

*A decision was made to drop this PICO question (95% of GDG members in favour). GDG members agreed that using the guidewire is no longer considered common practice and may increase the risk of catheter colonization.*

**PQ12:** Should a CVC be routinely replaced versus not routinely replaced to prevent infection and reduce the rates of CVC-BSI/CVC-AIC?

### Practice bundles and the use of MMIS

**PQ13:** Should CVC practice bundles be used versus not used to reduce the rates of CVC-BSI/CVC-AIC?

**PQ14:** Should a MMIS for CVC management interventions and/or practice bundles be used versus not used to reduce the rates of CVC-BSI/CVC-AIC?

*No recommendation was made; some GDG members requested a good practice statement, but the final decision was for a specific chapter on MMIS as per Part 1 guidelines.*

### Training in CVC insertion

**PQ15:** Does the use of a specific NHD-CVC insertion team versus not using a specific NHD-CVC insertion team reduce the rates of CVC-BSI/CVC-AIC or other insertion-related complications?

### CVC insertion site

**PQ16:** Is an NHD-CVC inserted into the jugular veins versus an NHD-CVC inserted in the subclavian veins associated with reduced rates of CVC-BSI/CVC-AIC?

**PQ17:** Does an NHD-CVC inserted into the jugular or subclavian veins versus a NHD-CVC inserted in the femoral veins reduce the rates of CVC-BSI/CVC-AIC?

### Tunnelled versus non-tunnelled CVC

**PQ18:** Does the insertion of a tunnelled NHD-CVC versus insertion of a non-tunnelled CVC reduce the rates of CVC-BSI/CVC-AIC or other insertion-related complications?

*A decision was made to drop this PICO question (94% of GDG members in favour). GDG members agreed that tunnelling a short-term catheter is no longer a common practice.*

### Composition of the CVC

**PQ19:** Does the use of antibiotic-impregnated NHD-CVCs versus use of non-impregnated NHD-CVCs reduce the rates of CVC-BSI/CVC-AICs and other NHD-CVC complications (for example, allergy, emergence of antibiotic-resistant CVC infections)?

**PQ20:** Does the use of antiseptic-coated catheters (for example, with chlorhexidine, silver sulfadiazine and other antiseptic) versus the use of non-coated catheters reduce the rates of CVC-BSI/CVC-AICs and other NHD-CVC complications (including the emergence of antibiotic-resistant CVC infections)?

### Cutaneous securing of a CVC

**PQ21:** Does the use of suture-less securement of an NHD-CVC versus use of suture-based securement of a NHD-CVC reduce the rates of CVC-BSI/CVC-AICs?

### Maintenance

**PQ22:** Does maintenance of an NHD-CVC using a continuous IV infusion versus maintenance of a NHD-CVC using intermittent infusion reduce the rates of CVC-BSI/CVC-AIC or other complications?

**PQ23:** Does regular flushing of an NHD-CVC with normal saline versus no regular flushing of a NHD-CVC reduce the rates of CVC-BSI/CVC-AIC or other complications?

As no evidence from randomized controlled trials was found, GDG members agreed (100%) to remove this PICO question and its conversion into a good practice statement.

**PQ24:** Does a system of "lock-off" flushing of an NHD-CVC with normal saline versus "lock-off" flushing of a NHD-CVC with heparinized saline reduce the rates of CVC-BSI/CVC-AIC or other complications (including heparin allergy)?

**PQ25:** Does the use of an antimicrobial lock solution versus the use of a non-antimicrobial solution (that is, EDTA or none) reduce the risk of CVC-BSI/CVC-ACIs in patients with short-term catheters (NHD-CVC)?

### Longer-term CVCs (that is, Hickman line, Port-a-Cath)

**PQ26:** Does the insertion/use of a Hickman's CVC versus insertion/use of a Port-a-Cath reduce the rates of CVC-BSI/CVC-AIC or other insertion-related complications?

**PQ27:** Regarding a Hickman's CVC where the insertion site is well-healed, does a dressing versus no dressing over the insertion site reduce the rates of CVC-BSI/CVC-AIC?

As no evidence was found, a decision was made to drop this PICO question (93% of GDG members in favour).

### Other preventive measures

**PQ28:** Does the use of a single lumen (both NHD-CVC and Hickman's) versus use of a multi-lumen reduce the rates of CVC-BSI/CVC-AICs?

**PQ29:** Does the use of prophylactic antimicrobial lock therapy (for example, vancomycin, ethanol, taurolidine, minocycline) versus no use reduce the risk of CVC-BSI/CVC-AICs in patients with long-term catheters?

**PQ30:** Does the use of antimicrobial-impregnated line caps versus non-impregnated line caps reduce the risk of CVC-BSI/CVC-AICs patients with short- and long-term catheters?

**PQ31:** Does the use of IV prophylactic antibiotic administration versus no use reduce the risk of CVC-BSI/CVC-AICs in patients with short- and long-term catheters?

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[1] *Abbreviations:* CVC, central venous catheter; NHD-CVC, non-haemodialysis-CVC; BSI, bloodstream infection; CVC-AIC, CVC-associated infectious complications; IV, intravenous; MMIS, multimodal implementation strategy.

[2] *Maximal sterile barrier precautions:* sterile barrier precautions that include the use of a cap, mask, sterile gown, sterile gloves and a sterile full body drape.

[3] *Sterile technique:* set of specific practices and procedures performed to make equipment and areas free from all microorganisms and to maintain that sterility.

# Annex 3. Methods

This systematic review was conducted to assess the effectiveness and safety of different methods for preventing BSIs and other infectious complications associated with the use of CVCs. The review followed the guidance outlined in the Cochrane Handbook, including the search, screening and selection of studies, data extraction and management, assessment of risk of bias, and data analysis. The GRADE Handbook was used to assess the certainty of evidence for each outcome. All stages of the process were documented. Distiller software was used for screening and data extraction, while Stata and RevMan Web were utilized for data analysis.

The review adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement. The systematic review was registered in PROSPERO.

Population, intervention, comparators, outcomes, and study design (PICOS)

The inclusion criteria for the review were based on the following PICOS elements.

*Population*

Studies involving adults (>19 years old), children (1 month – 18 years) and neonates (<4 weeks old) were included.

*Interventions*

Only NHD-CVCs were included, which were analysed under two categories:

- shorter-term NHD-CVCs – temporary CVCs (jugular, subclavian, other);
- longer-term NHD-CVCs – specifically Hickman's catheters and Port-a-Cath.

Studies that included a mix of haemodialysis and NHD-CVCs were excluded unless outcomes were reported separately for NHD-CVCs.

**Table 7: Inclusion and exclusion criteria for the systematic reviews**

| Inclusion | Exclusion |
|---|---|
| Catheters inserted through a large vein of the body:<br>• internal jugular vein;<br>• subclavian vein;<br>• axillary vein;<br>• saphenous vein;<br>• femoral vein. | Catheters inserted through a peripheral vein of the extremities (arms and legs):<br>• basilica;<br>• brachial;<br>• cephalic;<br>• medial cubital vein;<br>• any vein (not specified) of the extremities (arms and leg). |
| Hickman line | Catheters inserted through scalp |
| Port-a-Cath | Midline catheters |
| Broviac catheter | Peripheral arterial catheters (including open or per-cutaneous brachial and radial access) |
| | Urinary catheters |
| | Haemodialysis catheters |
| | Peripherally-inserted central catheters |

*Comparators*

All comparators were included, including no intervention, placebo and other interventions.

*Outcomes*

The primary outcomes assessed were catheter-associated or catheter-related BSIs (CLABSI/CABSI/CRBSI), catheter-related mortality, all-cause mortality, sepsis, pneumothorax, local insertion site infection, bleeding events requiring action, cardiac tamponade, deep venous thrombosis, venous stenosis, and other relevant outcomes. Outcome prioritization was informed by an outcome prioritization survey sent to the GDG members.

### Outcome prioritization survey

The outcomes used in this systematic review were informed by an outcome prioritization survey sent to GDG members, as summarized in the Table below.

**Table 8: Outcome prioritization result**

| Outcome | Average score |
|---|---|
| Sepsis | 8.4 |
| Catheter (CLABSI/CABSI/CRBSI)-related mortality | 8.4 |
| CLABSI/CABSI/CRBSI rate or incidence | 8 |
| All-cause mortality | 7.65 |
| Pneumothorax | 6.75 |
| Local insertion site infection | 6.55 |
| Bleeding events requiring action | 6.55 |
| Cardiac tamponade | 6.5 |
| Deep venous thrombosis | 6.25 |
| Venous stenosis | 5.6 |
| Arrhythmia | 5.55 |
| Nerve injury | 5.45 |
| Arteriovenous fistula | 5.4 |
| Arterial puncture | 5.4 |
| Arterial cannulation | 5.1 |
| Haematoma | 4.9 |
| Improper position | 4.85 |

*Abbreviations:* CLABSI, central line-associated bloodstream infection; CABSI, catheter-associated bloodstream infection; CRBSI, catheter-related bloodstream infection.

*Study designs*

The review included RCTs, non-RCTs, controlled observational studies, controlled before-after studies, and interrupted time series and repeated measures studies. Case series, case reports, systematic and non-systematic reviews, studies without a comparison group, and pooled data analyses were excluded.

### Search strategies

Comprehensive searches were performed to identify all relevant studies, regardless of language or publication status (published, unpublished, in press, and in progress). Searches covered the period from 1 January 1980 to the 31 August 2024 and were conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (PubMed) and Embase (OVID). Additional searches were performed in the WHO International Clinical Trials Registry Platform, ISRCTN registry, and clinicaltrials.gov for ongoing studies. Reference lists of relevant systematic reviews published within the search dates were also reviewed.

### Selection of studies

Two review authors independently screened all citations and abstracts identified in the search. Full reports of potentially eligible studies were obtained and independently screened by two review authors, with any disagreements resolved by a third reviewer to obtain consensus.

### Data extraction and management

Data were extracted by one reviewer using pre-tested data extraction forms and cross-checked by a second reviewer. Disagreements about data extraction were resolved by referring to the study report and through discussion. Study authors were contacted if data were insufficient or missing.

### Assessment of risk of bias

The risk of bias of each included study was assessed independently by one reviewer and cross-checked by a second reviewer. Disagreements were resolved through discussion with a content expert. For RCTs or quasi-RCTs, the Cochrane Risk of Bias tool for RCTs was used. For observational cohort studies with a comparison, the Cochrane Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used.

### Measures of treatment effect

For dichotomous outcomes, RR with 95% CIs were calculated. For continuous data, mean differences or standardized mean differences were used. Cluster-RCT data adjusted for clustering were pooled with data from individual RCTs using the generic inverse variance method. When cluster-RCT results had not been adjusted for clustering, adjustments for the design effect were made prior to meta-analysis following recommended methods.

### Summarizing and interpreting results

The GRADE approach was used to interpret findings and to create 'Summary of findings' tables for each PICO question following the GRADE handbook. These tables provided effect estimates and the associated certainty of evidence for each outcome of interest. Certainty of evidence from RCTs and observational studies assessed with ROBINS-I started at high certainty and was downgraded to moderate, low or very low, based on limitations in study design or execution (risk of bias), inconsistency of results, indirectness of evidence, imprecision or publication bias. Publication bias was assessed using funnel plot asymmetry if at least 10 studies were included in a meta-analysis.

### Evidence-to-decision framework

The review focused on the benefits and harms of different interventions to prevent BSI and other infections related to CVC. Contextual factors for the evidence-to-decision framework were collected to assist the guideline methodologists in the decision-making process. These factors included outcome importance, resource use, equity, acceptability and feasibility of the interventions.

## Searches: Bloodstream Infections and CVC – Ovid MEDLINE(R) ALL <1980to June 10, 2024>

1 exp Catheterization, Central Venous/

2 Central Venous Catheters/

3 (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp.

4 (central adj (catheter* or line*)).mp.

5 cvad.ti,ab,kf.

6 Hickman.tw.

7 1 or 2 or 3 or 4 or 5 or 6

8 (dialysis or h?emodialysis).ti.

9 exp *Renal Dialysis/

10 8 or 9

11 7 not 10

12 (complication* or infection* or Bacteraemia).tw.

13 ((exp Catheterization, Central Venous/ or Central Venous Catheters/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or exp *Renal Dialysis/)) adj3 (complication* or infection* or Bacteraemia).tw.

14 (Phlebitis or Thrombophlebitis).mp.

15 ((exp Catheterization, Central Venous/ or Central Venous Catheters/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or exp *Renal Dialysis/)) adj3 (Phlebitis or Thrombophlebitis).mp.

16 Catheter-Related Infections/

17 Catheter-related bloodstream infection*.mp.

18 Central Line Associated Bloodstream Infection*.mp.

19 CLABSI.tw.

20 (CRBSI or CABSI).tw.

21 ((bacterial or microbial or Staphylococcal or cutaneous or microorganism*) adj2 colonization).mp.

22 MRSA.mp. or Methicillin-Resistant Staphylococcus aureus/

23 21 or 22

24 ((exp Catheterization, Central Venous/ or Central Venous Catheters/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or exp *Renal Dialysis/)) adj2 (((bacterial or microbial or Staphylococcal or cutaneous or microorganism*) adj2 colonization).mp. or (MRSA.mp. or Methicillin-Resistant Staphylococcus aureus/))

25 13 or 15 or 16 or 17 or 18 or 19 or 20 or 24

26 antimicrobial*.mp.

27 Anti-Infective Agents, Local/ or Anti-Bacterial Agents/ or antiseptic*.mp. or Chlorhexidine/

28 Antibiotic Prophylaxis/

29 Decolonization.mp.

30 decolonisation.mp.

31 mupirocin.mp. or Mupirocin/

32 (infection adj3 prevent*).mp.

33 bundle.mp.

34 (lock adj3 (therapy or solution*)).tw.

35 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36 25 and 35

37 limit 36 to (clinical study or clinical trial, all or comparative study or controlled clinical trial or meta analysis or multicenter study or practice guideline or pragmatic clinical trial or randomized controlled trial)

38 exp randomized controlled trial/

39 controlled clinical trial.pt.

40 randomized.ab.

41 placebo.ab.

42 drug therapy.fs.

43 randomly.ab.

44 trial.ab.

45 groups.ab.

46 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45

47 exp animals/ not humans/

48 46 not 47

49 36 and 48

50 exp cohort studies/

51 cohort*.tw.

52 *epidemiologic methods/

53 longitudinal studies/ or controlled before-after studies/

54 50 or 51 or 52 or 53

55 36 and 54

56 37 or 49 or 55

57 Meta-Analysis as Topic/

58 meta analy*.tw.

59 metaanaly*.tw.

60 Meta-Analysis/

61 (systematic adj (review*1 or overview*1)).tw.

62 exp Review Literature as Topic/

63 “systematic review”/

64 57 or 58 or 59 or 60 or 61 or 62 or 63

65 36 and 64 231

66 limit 65 to yr=”2019 - 2024” 75

**Embase 1947-Present, updated daily**

1 intravascular catheter/ or peripheral venous catheter/ or catheter/ or intravenous catheter/

2 peripherally inserted central venous catheter/

3 (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp.

4 (central adj (catheter* or line*)).mp.

5 cvad.ti,ab,kf.

6 Hickman.tw.

7 1 or 2 or 3 or 4 or 5 or 6

8 (dialysis or h?emodialysis).ti.

9 hemodialysis/

10 8 or 9

11 7 not 10

12 (complication* or infection*).tw. or Bacteraemia/

13 ((intravascular catheter/ or peripheral venous catheter/ or catheter/ or intravenous catheter/ or peripherally inserted central venous catheter/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or hemodialysis/)) adj2 ((complication* or infection*).tw. or Bacteraemia/)

14 Phlebitis/ or Thrombophlebitis.mp.

15 ((intravascular catheter/ or peripheral venous catheter/ or catheter/ or intravenous catheter/ or peripherally inserted central venous catheter/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or hemodialysis/)) adj2 (Phlebitis/ or Thrombophlebitis.mp.)

16 catheter infection/

17 catheter related bloodstream infection/

18 Central Line Associated Bloodstream Infection*.mp.

19 CLABSI.tw.

20 (CRBSI or CABSI).tw.

21 ((bacterial or microbial or Staphylococcal or cutaneous or microorganism*) adj2 colonization).mp.

22 MRSA.mp. or methicillin resistant Staphylococcus aureus/

23 21 or 22

24 ((intravascular catheter/ or peripheral venous catheter/ or catheter/ or intravenous catheter/ or peripherally inserted central venous catheter/ or (central adj (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp. or (central adj (catheter* or line*)).mp. or cvad.ti,ab,kf. or Hickman.tw.) not ((dialysis or h?emodialysis).ti. or hemodialysis/)) adj2 (((bacterial or microbial or Staphylococcal or cutaneous or microorganism*) adj2 colonization).mp. or (MRSA.mp. or methicillin resistant Staphylococcus aureus/))

25 13 or 15 or 16 or 17 or 18 or 19 or 20 or 24

26 antibiotic agent/

27 antiinfective agent/ or antiseptic*.mp. or Chlorhexidine/

28 Antibiotic Prophylaxis.tw.

29 Decolonization.mp.

30 decolonisation.mp.

31 mupirocin.mp. or Mupirocin/

32 (infection adj3 prevent*).mp.

33 bundle.mp.

34 (lock adj3 (therapy or solution*)).tw.

35 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34

36 25 and 35

37 exp Meta Analysis/

38 ((meta adj analy*) or metaanalys*).tw.

39 (systematic adj (review*1 or overview*1)).tw.

40 37 or 38 or 39

41 36 and 40 444

42 ‘randomized controlled trial’/

43 controlled clinical trial/

44 Clinical Trial/

45 multicenter study/

46 Phase 3 clinical trial/

47 phase 4 clinical trial/

48 exp RANDOMIZATION/

49 Single Blind Procedure/

50 Double Blind Procedure/

51 Crossover Procedure/

52 placebo/

53 randomi?ed controlled trial*.tw.

54 rct.tw.

55 (random* adj2 allocat*).tw.

56 single blind*.tw.

57 double blind*.tw.

58 ((treble or triple) adj blind*).tw.

59 placebo*.tw.

60 Prospective Study/

61 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60

62 Case Study/ or case report.tw. or abstract report/ or letter/ or Conference proceeding.pt. or Conference abstract.pt.

63 (Editorial or Letter or Note).pt.

64 62 or 63

65 61 not 64

66 exp ANIMAL/ or exp NONHUMAN/ or exp ANIMAL EXPERIMENT/ or exp ANIMAL MODEL/

67 exp human/

68 66 not 67

69 65 not 68

70 36 and 69

71 cohort study.mp. or cohort analysis/

72 longitudinal study/

73 (before and after study).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

74 71 or 72 or 73

75 36 and 74

76 75 not 70

### Cochrane Central Register of Controlled Trials

Issue 5 of 12, May 2024

### Cochrane Database of Systematic Reviews

Issue 6 of 12, June 2024

ID Search Hits

#1 MeSH descriptor: [Catheterization, Central Venous] explode all trees

#2 MeSH descriptor: [Central Venous Catheters] explode all trees

#3 (central and (venous or intravenous or intravascular or vascular) and (catheter* or access* or line* or device*)):ti,ab,kw

#4 (central and (catheter* or line*)):ti,ab,kw

#5 (cvad):ti,ab,kw

#6 ("Hickman catheter"):ti,ab,kw

#7 #1 or #2 or #3 or #4 or #5 or #6

#8 ((dialysis or hemodialysis or haemodialysis)):ti

#9 MeSH descriptor: [Renal Dialysis] explode all trees

#10 #8 or #9

#11 #7 not #10

#12 ((complication* or infection* or Bacteraemia)):ti,ab,kw

#13 #11 and #12

#14 ((Phlebitis or Thrombophlebitis)):ti,ab,kw

#15 #11 and #14

#16 MeSH descriptor: [Catheter-Related Infections] explode all trees

#17 (Catheter-related bloodstream infection*):ti,ab,kw

#18 (Central Line Associated Bloodstream Infection*):ti,ab,kw

#19 (CLABSI or CRBSI or CABSI):ti,ab,kw

#20 ((bacterial or microbial or Staphylococcal or cutaneous or microorganism*) and colonization):ti,ab,kw

#21 (MRSA):ti,ab,kw

#22 MeSH descriptor: [Methicillin-Resistant Staphylococcus aureus] explode all trees

#23 #20 or #21 or #22

#24 #11 and #22

#25 #13 or #15 or #16 or #17 or #18 or #19 or #24

#26 (antimicrobial*):ti,ab,kw

#27 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees

#28 MeSH descriptor: [Anti-Bacterial Agents] explode all trees

#29 (antiseptic*):ti,ab,kw

#30 MeSH descriptor: [Chlorhexidine] explode all trees

#31 MeSH descriptor: [Antibiotic Prophylaxis] explode all trees

#32 (Decolonization or decolonisation):ti,ab,kw

#33 MeSH descriptor: [Mupirocin] explode all trees

#34 ((infection near/3 prevent*)):ti,ab,kw

#35 (bundle):ti,ab,kw

#36 (lock and (therapy or solution*)):ti,ab,kw

#37 #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36

#38 #37 and #25

**searches: Bloodstream Infections & CVCs – MEDLINE (Revised Sept. 23, 2024)**

1. exp Catheterization, Central Venous/
2. Central Venous Catheters/
3. (central* adj2 (venous or intravenous or intravascular or vascular) adj3 (catheter* or access* or line* or device*)).mp.
4. (central* adj2 (catheter* or line* or port$1)).mp.
5. ((cvc or cvad) and (catheter* or line* or port$1)).mp.
6. (CVC or CVAD or TIVAD or TIVAP).ti,kf.
7. ((implanted or implantable) adj3 (port$1 or catheter*)).mp.
8. (port$1 adj3 (cath$1 or catheter*)).mp.
9. (Hickman* or portacath$1).mp.
10. Catheter-Related Infections/
11. (CLABSI or CRBSI or CABSI).mp.
12. or/1-11

13. (dialy* or h?emodialy* or peripheral* or PICC or urinary or urethra* or shunt*).ti.
14. 12 not 13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. randomized.ab.
18. placebo.ab.
19. drug therapy.fs.
20. randomly.ab.
21. trial.ab.
22. groups.ab.
23. or/15-22
24. exp animals/ not humans.sh.
25. 23 not 24
26. exp epidemiologic studies/ or exp clinical trial/ or comparative study/
27. ((control and study) or program).mp.
28. or/26-27
29. (animals/ not humans/) or comment/ or editorial/ or exp review/ or meta analysis/ or consensus/ or exp guideline/
30. hi.fs. or case report.mp.
31. or/29-30
32. 28 not 31
33. 25 or 32
34. 14 and 33
35. Catheter-Related Infections/ or bacterial infections/ or cross infection/ or exp sepsis/ or exp bacteremia/ or wound infection/ or mycoses/ or exp invasive fungal infections/ or exp fungemia/
36. (infection* or sepsis or septic or CLABSI or CRBSI or CABSI or bacter?emi* or fung?emi*).ti,ab,kf.
37. (complication* or adverse or harm* or safe* or allerg* or anaphyla*).ti,ab,kf.
38. risk.ti.
39. (Ae or Co).fs.
40. (DVT or vein thromb* or venous thromb*).mp.
41. Venous Thromboembolism/ or Venous Thrombosis/ or upper extremity deep vein thrombosis/
42. exp Mortality/

43. pneumothorax/
44. Hemorrhage/
45. Cardiac Tamponade/
46. (mortality or death* or pneumothorax or bleed* or h?emorrhage or cardiac tamponade* or pericardial tamponade* or venous stenosis).mp.
47. or/35-46
48. 34 and 47
49. exp Anti-Infective Agents, Local/ or exp Anti-Bacterial Agents/ or Antibiotic Prophylaxis/
50. (antiseptic* or anti septic* or chlorhexidine or octenidine or iodine or silver sulfadiazine or mupirocin or skin disinfect*).mp.
51. ((antimicrobial* or anti microbial* or antibiotic*) adj6 (prophyla* or impregnated or solution* or wash* or bath* or wipe* or patch* or dressing* or sponge*)).mp.
52. infection control/ or exp antisepsis/ or asepsis/ or disinfection/
53. ((sterile or aseptic) adj6 (technique* or precaution* or method* or barrier* or practice* or procedure*)).mp.
54. ultrasonography/ or ultrasonography, interventional/
55. (ultrasound or ultrasonograph*).mp.
56. (dressing* adj6 (insertion or type* or composition* or material* or occlusive or nonocclusive or gauze or permeable or semipermeable)).mp.
57. (dressing* adj6 (chang* or schedule* or evaluat*)).mp.
58. ((tubing* or administration set$1 or giving* set$1 or cvc set$1 or cvad set$1 or catheter* set$1 or line set$1 or port set$1) adj6 (chang* or schedul* or timing* or time* or days or frequen*)).mp.
59. ((closed or open) adj6 (access or hub$1 or system$1)).mp.
60. ((replace* or replacing) adj6 (reinsert* or re-insert* or site$1 or guidewire* or guide wire* or routine* or strateg* or technique* or method* or practice* or procedure*)).mp.
61. ((bundle* or multimodal* or multi-modal*) adj6 (implement* or manage* or intervention* or routine* or strateg* or technique* or method* or practice* or procedure*)).mp.
62. (insert* adj6 (team* or speciali* or train*)).mp.
63. (insert* adj6 (jugular or subclavian or femoral)).mp.
64. tunnel?ed.ti,ab,kf.
65. (suture* or securing or securement).mp.
66. ((continuous or intermittent) adj6 (infusion* or intravenous or IV)).mp.
67. ((lock* or saline or regular* or routine*) adj6 flush*).mp.
68. ((single or multi) adj6 lumen*).mp.
69. Hickman*.mp.

70. ((longterm or long* term) and dressing*).mp.

71. ((lock* or cap or caps) adj6 (therap* or solution* or antimicrobial* or anti microbial* or antibiotic* or vancomycin or ethanol or alcohol or taurolidine or minocycline)).mp.

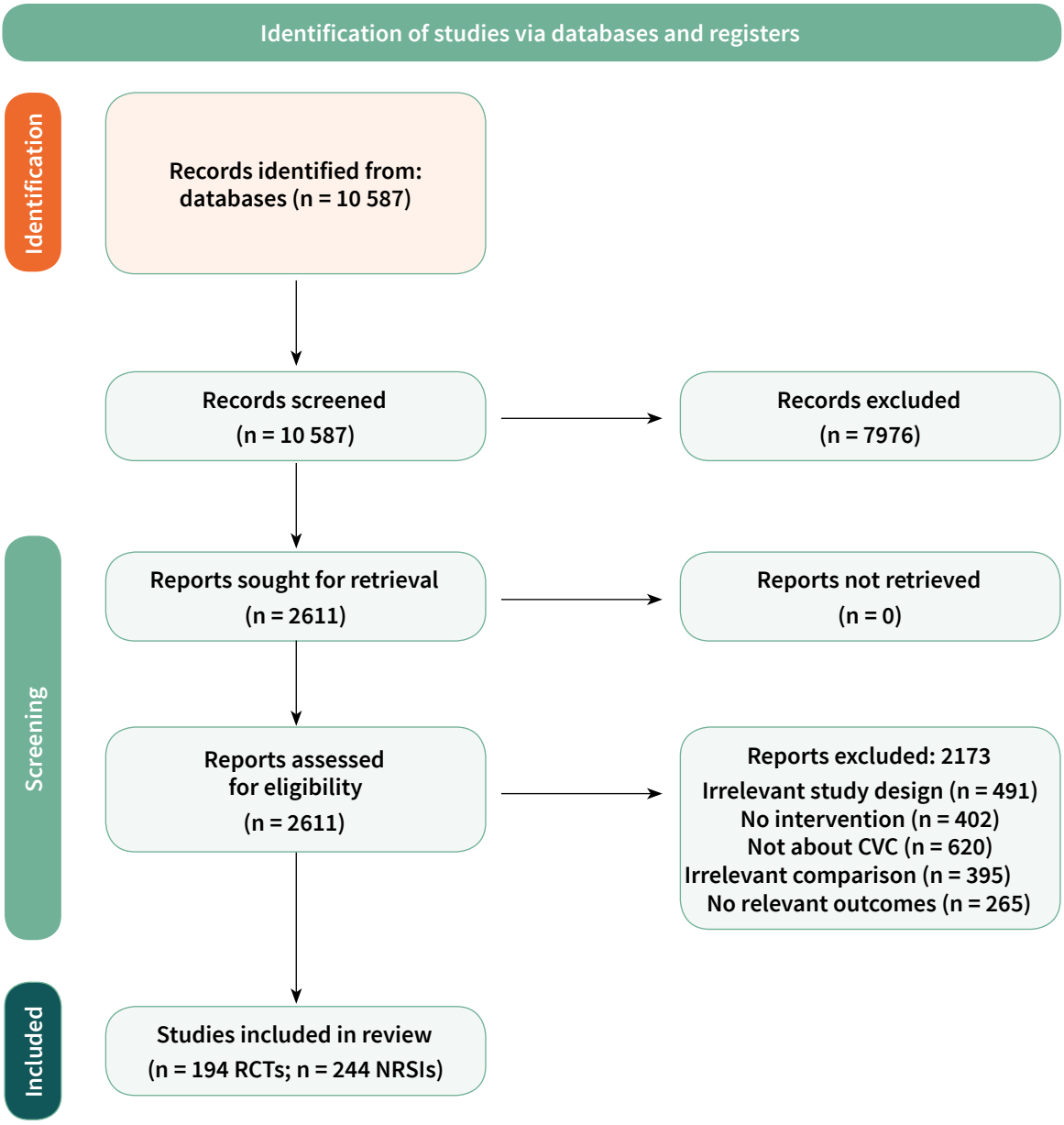
72. or/49-71

73. 48 and 72

74. (editorial or comment or news or newspaper article).pt.

75. 73 not 74

**Figure 1: PRISMA flow diagram**




*Abbreviations:* RCT, randomized controlled trial; NRSI, non-randomized studies of interventions.

## Web Annex. Summary of evidence findings and evidence-to-decision tables by population, intervention, comparison, outcome (PICO) question

The summary of evidence findings and evidence-to-decision tables by PICO question are available on the WHO website: https://doi.org/10.2471/B09725

# 10

# List of tables

# List of tables

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