European recommendations on the proper indication and use of peripheral venous access devices (the ERPIUP consensus): A WoCoVA project

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Abstract
Since several innovations have recently changed the criteria of choice and management of peripheral venous access (new devices, new techniques of insertion, new recommendations for maintenance), the WoCoVA Foundation (WoCoVA = World Conference on Vascular Access) has developed an international Consensus with the following objectives: to propose a clear and useful classification of the currently available peripheral venous access devices; to clarify the proper indication of central versus peripheral venous access; to discuss the indications of the different peripheral venous access devices (short peripheral cannulas vs long peripheral cannulas vs midline catheters); to define the proper techniques of insertion and maintenance that should be recommended today. To achieve these purposes, WoCoVA have decided to adopt a European point of view, considering some relevant differences of terminology between North America and Europe in this area of venous access and the need for a common basis of understanding among the experts recruited for this project. The ERPIUP Consensus (ERPIUP = European Recommendations for Proper Indication and Use of Peripheral venous access) was designed to offer systematic recommendations for clinical practice, covering every aspect of management of peripheral venous access devices in the adult patient: indication, insertion, maintenance, prevention and treatment of complications, removal. Also, our purpose was to improve the standardization of the terminology, bringing clarity of definition, and classification.

Keywords
Peripheral venous access devices, short peripheral catheters, long peripheral catheters, midline catheters, mini-midlines, short midlines, peripheral intravenous cannulas

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Introduction

Peripheral venous access devices (PVADs) represent the most widely used venous access devices (VADs) in clinical practice, but they have also been neglected for many decades, as the attention of the medical literature has been mainly focused on central VADs, commonly recognized as potentially associated with severe complications. In the last decade, it has become evident that though PVADs – and in particular short peripheral catheters (SPCs) – by large the most widely used – may be somehow inexpensive, easy to insert and easy to remove, they are nonetheless associated with a high incidence of minor local complications, which all concur eventually to the same outcome, “catheter failure”, that is, forced, unscheduled removal of the VAD. Catheter failure has been estimated to occur in approximately half of the cases: 43%–59%1–6 and its pathogenesis is often difficult to define.7,8 The reasons for catheter failure include: “phlebitis” (i.e. “thrombophlebitis”) of superficial veins, secondary to bacterial contamination and/or chemical injury and/or mechanical injury and/or local obstruction of the blood flow; partial dislodgment of the catheter with associated infiltration/extravasation of the infusate in the surrounding tissues; occlusion of the catheter lumen. Furthermore, more recently, peripheral VADs have also been related to more severe systemic complications such as bloodstream infections.

During the last decade, PVADs have reappeared in clinical guidelines and in the scientific literature, starting an era of new “awareness” of their relevance. The current aptitude, universally accepted, is that clinicians should make every effort to optimize their use, minimizing the rate of complications, as much as it has been done for central VADs.

The world of PVADs have changed dramatically in the last ten years:

1. The most important guidelines have released new recommendations about the insertion and management of peripheral VADs. Both the EPIC guidelines (EPIC = Evidence-based Prevention and Infection Control)19 and the Standards of Practice of INS (Infusion Nursing Society)20 recommend skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol before insertion of any PVAD, as well as securement and protection of the exit site with transparent semipermeable membranes whenever possible. Also – and this may be regarded as the most relevant, habit-changing innovation – both EPIC and INS recommend that peripheral venous catheters should be re-sited only when clinically indicated (i.e. if complications occur) and not routinely, as previously recommended.11,12

2. Clinicians have become more conscious of the different indications between peripheral versus central VADs, particularly in terms of the chemical characteristics of the infusate and its potential damage to the endothelium. Both INS13 and GAVeCeLT14 have released tables that specify which intravenous infusions can be delivered safely by the peripheral route, and which infusions preferably require a central line.

3. The category of SPC has become more complex, with the introduction in clinical practice of new, “integrated” SPC, characterized by new material (polyurethane rather than polytetrafluoroethylene), new design (large wing; pre-assembled extension; preassembled needle-free connector) and new strategies of protection of the operator (“no-stick” and “blood-stop” mechanisms). This new type of “integrated” SPC is meant to be associated with less risk of phlebitis, easier securement, increased safety, and longer duration (up to 1 week and more), compared to old-fashioned SPCs.

4. A new type of peripheral VAD has become available, the long peripheral catheter (LPC), leading most authors to modify the classification of PVADs. Today, current guidelines10 differentiate between short peripheral cannulas (SPC), long peripheral cannulas (LPC) (6–15 cm long) and midline catheters (MC) or “midclavicular” (>15 cm). There has been a lot of uncertainty about the appropriate term for LPC, since many different terms have been utilized in different clinical studies for referring to the same device (mini-midline, short midline, etc.).15 The term “PIVC” (peripheral intravenous catheter) – or simply “PIV” – has become somehow ambiguous since it apparently defines any peripheral VAD, without distinction between SPC, LPC, and MC.

5. Also, new technologies for insertion of peripheral VADs have been developed. The INS Standards of Practice10 recommend considering the use of Near-Infrared technology (NIR) for insertion of peripheral VADs in superficial veins and the use of ultrasound (US) guidance for their insertion in deep veins. A vast scientific literature has recently been published on this subject, addressing the technical aspects, the indications, the advantages, and the limits of such imaging techniques.

6. Last but not least, new algorithms for the proper choice of the VAD have been released, which now take into consideration a wider range of peripheral VADs, and have also adopted new terminology, such as the term DIVA (Difficult Intra-Venous Access) that identifies the patient whose superficial veins of the upper arm are not visible and/or palpable.16–18 Examples of this kind are the “MAGIC”19 and the “VAD Expert” developed by GAVeCeLT,20 quite different but both conceived with the goal of optimizing the choice of the VAD. With regards to peripheral VADs, the MAGIC has
some limits since still adopts ambiguous terms such as “PIV” and “Midline”, which today require a stricter definition.\textsuperscript{21}

The almost simultaneous occurrence of so many innovations in a range of few years supports the need for an international consensus on peripheral VADs, which was developed by the WoCoVA Foundation (WoCoVA=World Conference on Vascular Access) with the following objectives:

- to propose a clear and useful classification of the currently available peripheral VADs;
- to clarify the indication of the different VADs (central vs peripheral) and of the different peripheral VADs (SPC vs LPC vs MC);
- to define the proper techniques of insertion and maintenance.

To achieve these purposes, WoCoVA have decided to adopt a European point of view, considering some relevant differences of terminology between North America and Europe in this area of venous access and the need for a common basis of understanding among the experts recruited for this project.

This WoCoVA consensus – nicknamed ERPIUP (European Recommendations for Proper Indication and Use of Peripheral venous access) – was designed to offer systematic recommendations for clinical practice, covering every aspect of management of peripheral VADs (SPC, LPC, MC) in the adult patient: indication, insertion, maintenance, prevention and treatment of complications, and removal. Also, our purpose was to improve the standardization of the terminology, bringing clarity of definition, and classification.

After a description of our methodology, this document will present the results of the consensus in five parts, each one related to a specific issue.

\section*{Methods}

The coordinators of the project – the President of WoCoVA (TVB) and the Chairman of the Scientific Committee of WoCoVA (MP) – selected a panel of eleven well known experts in venous access from different European Countries, representative of different National vascular access associations affiliated to WoCoVA: Italy (SB, GS, ML, FP), UK (SI, JN, LS), France (CD), Greece (EK), Spain (GOM), Ireland (PC), and Belgium (GAG).

A bibliography search was carried out (GP), according to the following criteria:

- search was initially limited to 6 years (from Jan 2013 to Dec 2018), considering that many interesting studies had already been incorporated in some very good guidelines and evidence-based consensus documents published in 2013–2014;\textsuperscript{9,22} an update of the literature from Jan 2019 till Jan 2021 was added later, due to the long time required by development of the project;
- search was limited to papers in English or with English abstract;
- search was focused on peripheral VAD, that is, all kinds of peripheral venous access devices (short cannulas, long peripheral cannulas or “short midline” or “mini-midline”, midline catheters), both in the intra-hospital and in the extra-hospital (community) setting, but considering exclusively adult patients;
- search included both retrospective and prospective clinical studies, published in this time period; studies published only as abstracts or as letters to the editor were not considered; some 2013–2016 reviews of clinical studies have also been collected, as additional material; the most important guidelines and evidence-based documents of this same span of time (2013–2021) have also been included as additional material;
- search was articulated into five topics: (1) classification and indication of peripheral VADs; (2) indication to peripheral vs central VADs; (3) insertion: techniques, complications, training; (4) management: strategies for complication prevention; (5) removal: indication, technique, complications.

The bibliography was forwarded to all panelists, and five working groups of 2–3 experts were defined, one for each topic: 1 – classification and definition (MP – SI), 2 – indications (GAG – EK), 3 – insertion (PC-ML-TVB), 4 – maintenance (LS – GS); 5 – removal (GOM – CD). Each working group had the task of reviewing the literature on the assigned topic and produce a few statements answering specific questions, previously developed by the whole panel:

Group 1: What is the most appropriate definition of a peripheral VAD? What is the most appropriate classification to describe the different types of peripheral VADs?

Group 2: What are the different indications for peripheral versus central VAD, taking into account clinical performance and the risk of complications? What are the most appropriate indications for the different types of peripheral VADs in the adult patient, taking into account clinical performance and the risk of complications?

Group 3: What is the role of site selection in reducing insertion-related complications? What is the most appropriate insertion strategy for reducing the risk of infection? What is the most appropriate strategy for securing the peripheral VAD? What is the role of ultrasound guidance when inserting a peripheral VAD? What is the role of NIR technology when inserting a peripheral VAD?

Group 4: What is the most appropriate method of teaching peripheral VAD insertion?
Group 4: What is the most appropriate maintenance strategy to reduce the risk of infection? What is the most appropriate maintenance strategy to reduce the risk of occlusion? What is the most appropriate maintenance strategy to reduce the risk of phlebitis/thrombosis?

Group 5: When is the removal of a PVAD indicated? Are there any complications related to removal? What strategies can minimize such complications?

Each group prepared a preliminary report on their topic, consisting of a short discussion of the literature and in a series of statements answering the specific questions. All five reports were merged in one single document that was peer-reviewed by all the other members of the panel, including three experts not directly included in the working groups (JN, SB, FP). After proper adjustments, the consensus on all final statements was achieved and the panel approved a final document, that we hereby present in five sections, corresponding to the five different topics.

Results

Section 1 – Definition and classification

Venous access devices (VADs) are defined as peripheral or central based on the position of the tip of the catheter. Any VAD with the tip located in the superior vena cava (SVC) or in the inferior vena cava (IVC) or in the right atrium (RA) should be considered as a central venous access device (CVAD). This definition is arbitrary, but it is based on clinical practice, since the presence of the tip in SVC, IVC or RA – that is, in a location with blood flow equal or superior to 2 L/min in the adult patient – will guarantee the possibility of infusing any type of solutions, even if potentially detrimental to the endothelium, and of withdrawing blood samples easily.

A peripheral VAD (PVAD) can be defined as any VAD with the tip not located in SVC or RA or IVC. This definition includes not only VADs that – due to their length and to the venous approach – are meant to be peripheral, but also VADs that are meant to be used as CVAD but whose tip is not in a central vein because of primary or secondary malposition (for example: a PICC that after accidental partial dislodgement has become “too short” and its tip is now in the brachiocephalic vein; or, a central VAD whose tip has migrated into the ipsilateral internal jugular vein).

The most widely used PVAD is the short cannula, or SPC, made either of polyurethane (PUR) or polytetrafluoroethylene (PTFE), with a gauge ranging between 26 and 14G and a length usually not exceeding 5.4 cm. Short cannulas were the first plastic cannulas introduced in clinical practice, more than 40 years ago, replacing steel needles. Steel needles – either as simple needles or “butterfly” needles – are not acceptable any more for prolonged infusions, due to the prohibitive risk of local complications; they can still be used for episodic blood drawing or for bolus infusions. SPCs have been the only available PVAD for decades.

Approximately 25 years ago, longer plastic catheters – made of silicon or PUR – were introduced in the clinical practice and they were named “midline catheters” (MC), to indicate that their length was somehow in between the “short” catheters (SPC) and the “long” catheters (PICC). Originally, these catheters were 15–25 cm long; since they were meant to be inserted in superficial veins of the antecubital fossa, considering that in adults the distance between the elbow and the axilla ranges from 21 to 28 cm, the tip of an MC was expected to be in a deep vein of the upper arm, typically in the brachial tract of the axillary vein. At the beginning of the 21st century, when ultrasound guidance gained popularity in the field of venous access, clinicians started to insert MCs in deep veins of the upper arm. Without trimming, the tip of these catheters was now located in the thoracic tract of the axillary vein or in the subclavian vein (hence the name “midclavicular” catheters). This tip location has the disadvantage that in case of inappropriate infusion of peripherally incompatible solutions, the resulting venous thrombosis is more severe and more dangerous than a thrombosis in the veins of the arm.23 However, in Europe MC are still widely used, both in hospitalized patients24,25 and in palliative care.26,27

In the last decade, a new PVAD has appeared, longer than SPC but shorter than MC: it has been named “long peripheral catheter” (LPC) or “mini-midline” or “short midline”. It is a plastic cannula, made of PUR or polyether-bloc-amide (PEBA), 6–15 cm long (typically, 8 or 10 cm), with a gauge ranging from 22 to 18 G. It is meant to be inserted in superficial veins of the forearm or of the upper arm (in palpable/visible veins or by NIR visualization) or in deep veins of the upper arm (by US guidance). The tip is always located in the veins of the arm. Due to its shorter length, the expected dwell time is less if compared to an MC. Though, LPCs have many advantages over MCs: they are less expensive, less invasive and associated with less morbidity in case of venous thrombosis.28 Different types or designs exist: some LPC are designed similarly to SPC and must be inserted with a “catheter over needle” technique; some other types of LPC are inserted by direct Seldinger technique (“catheter over guide-wire”); some others are designed as an all-in-one coaxial device, still using the direct Seldinger technique. Unfortunately, these new 6–15 cm PVADs (LPCs) have brought some misunderstanding into the classification and terminology of VADs: they have been called “midline” in North America, generating some confusion between LPC and MC in clinical studies, in guidelines and sometimes in evidence-based recommendations.15,29,30

In fact, LPC and MC are different devices: they differ in terms of material (PUR or PEBA, vs PUR or silicon), of...
technique of insertion (catheter-over-needle or simple Seldinger technique, versus modified Seldinger technique), of expected duration (2–4 weeks for LPC vs months for MC), of clinical performance (longer and better for MC), and of cost (lower for LPC).

In the last decade a new generation of SPC has appeared, different in terms of design (presence of a large wing w/o preassembled extension and preassembled needle-free connector), of material (PUR, less thrombogenic than PTFE) and equipped with mechanisms for full protection of the clinician (“no stick” and “blood stop” safety mechanisms). Thus, two different kinds of SPC can be now described, with different design complexity, different clinical performance, and different cost: so-called “simple” SPCs (absent or minimal wing, catheter usually made of PTFE, no extension, sometimes called “open system”) and so-called “integrated” SPCs (large wing, catheter usually made of PUR, preassembled extension, sometimes called “closed system”). These different features imply different clinical performances, in terms of risk of catheter failure and probability of duration (24–48 h for SPC vs 2–7 days for “integrated” SPC).

Of course, all these PVADs (SPC, LPC, MC) are none-theless peripheral catheters. This implies that they should be used exclusively for peripherally compatible infusions. The feasibility of blood sampling may vary, since it depends on the position of the tip and the caliber of the cannula: it may be minimal for SPC (where blood can be withdrawn only at the time of insertion) but maximal for 5 Fr single lumen MC. Also, the feasibility of apheresic procedures may vary, being minimal for short cannulas <18 G and maximal for short cannulas >16 G and for 5 Fr single lumen Midlines.

Panel’s recommendations:
Peripheral VADs are defined as catheters whose tip is located in the venous system but outside the superior vena cava, the right atrium and the inferior vena cava.

On the basis of their length, they can be classified as follows:

(a) short peripheral catheters (SPC) (<6 cm): SPC may be further classified as “simple” or “integrated”, based on their design and material;
(b) long peripheral catheters (LPC) (6–15 cm);
(c) midline catheters or “midclavicular” (MC) (>15 cm).

Section 2 – Indications
Peripheral versus central venous access devices. CVADs are more invasive and more expensive than PVADs and are associated with a higher risk of insertion-related complications and catheter-related bloodstream infections (CRBSI).33,114,115 Though, CVADs may tolerate the infusion of any type of solutions without risk of endothelial damage. In this regard, there is a wide consensus in the recent literature that vesicant drugs, solutions with low (<5) or high (>9) pH or very high osmolarity (>600 mOsm/L), as well as any other solution with potential irritant effects on the vein wall by other mechanisms not involving pH or osmolarity, should be preferably delivered by a CVAD.10,33,34

The infusion of irritant or vesicant solutions in a low-flow system as a peripheral vein will be associated with injury to the endothelial layer of the intima (leading to thrombus formation) and with inflammation of the tunica media of the vein (leading to edema, infiltration, and possibly rupture of the integrity of the wall): these phenomena are the pathological correlates of clinical entities variously described as “phlebitis”, “phlebo-thrombosis” or “thrombophlebitis”.35 Though, there is also a time effect to take into consideration. Solutions with osmolarity as high as 800–850 mOsm/L might be well tolerated by the endothelium, if they are delivered very slowly, for instance with a 24-h infusion, as it happens with parenteral nutrition. When a vesicant drug is infused via a PVAD, if the infusion lasts less than 30–60 min the risk of endothelial damage is minimized. Dilution also might have a role in reducing the risk of vein damage, but only for solutions with high osmolarity: dilution cannot significantly modify the pH of a solution.

The other risk of any irritant or vesicant solution is related to the potential dislocation of the PVAD and the subsequent tissue damage, which may range in gravity from absence of symptoms to severe tissue necrosis, depending on the detrimental effect of the drug: “infiltration” and “extravasation” are the terms used respectively for the damage secondary to irritant and vesicant drugs.36

Many associations and institutions have provided lists of drugs potentially associated with endothelial damage, or – to use a popular term – “peripherally incompatible” drugs. These lists include vesicant antiblastic drugs, high-osmolality parenteral nutrition, but also antibiotics, antiviral drugs, vasoactive amines, and many other drugs commonly used in hospitalized patients. It is highly recommended that any clinical unit should have a list of peripherally incompatible drugs (possibly coherent with the hospital policies) and should use it as a guide when choosing between a CVAD and a PVAD. In the setting of the emergency department,37 it is considered acceptable to deliver vasopressors/inotropes or potassium enriched solutions by the peripheral route, at least for a limited time.13 Also, in the setting of chemotherapy, when the clinical conditions indicate a temporary contraindication to a CVAD or when the patient refuses a CVAD, it is acceptable that some vesicant drugs might be delivered peripherally, if some specific conditions are met (the PVAD should be inserted ex novo; the infusion must be delivered for a short period time and under strict control of the clinicians; the PVAD must be removed soon after the infusion), the highest risk of vesicant administration being an undetected extravasation or an extravasation detected too late.38 LPC
and MC might be theoretically less at risk than SPC in terms of dislodgment and subsequent extravasation.

Of course, even when using the PVADs exclusively for peripherally compatible solutions, there will still be a risk of other types of phlebitis, due to bacterial contamination (bacterial phlebitis) or due to mechanical friction of the cannula on the vein wall typically when PVAD is not properly stabilized or when the cannula is too large if compared to the caliber of the vein (mechanical phlebitis).39–41

Apheretic procedures might be also carried out using PVADs of appropriate flow, so that the choice of a CVAD in these situations is mainly based on logistic considerations and/or on the unavailability of superficial veins of proper caliber.42 Repeated daily blood samples usually require a CVAD, though some PVADs may allow blood sampling for a long period time.

Simultaneous continuous infusion of two different drugs does not necessarily imply use of a CVAD, if both drugs are compatible with the peripheral route: a 5 Fr double-lumen MC may be used, or two separate PVADs.

Finally, though some MC may stay in place for months, long-term intravenous access (>3–4 months) is a recognized indication for a central VAD.

**Short peripheral catheters versus long peripheral catheters versus midline catheters.** As already mentioned above, a SPC should be considered as the first option in the patient who needs intravenous infusion for less than 1 week, if only peripherally compatible infusions are to be delivered. Current guidelines recommend removing the cannula only peripherally compatible infusions are to be delivered. Current guidelines recommend removing the cannula only when the intravenous treatment is over or when a complication leading to “catheter failure” occurs.10 Though, most SPC are expected to last just a few days, the actual duration depending on several factors (the technique of insertion, the site of insertion, the ratio between caliber of the catheter and diameter of the vein, the design and the material of the catheter, the technique of stabilization, and dressing). A “simple” SPC in PTFE inserted on a vein of the arm in an emergency will probably last less than 24 h, while an “integrated” SPC inserted on a vein of the forearm with a proper aseptic technique, covered with transparent dressing, may last more than 5–6 days. A SPC inserted by ultrasound (US) guidance will probably last 48 h or even less, particularly if inserted in a deep vein of the arm (see below). The length of a PVAD may also affect its expected duration: shorter catheters will be more rapidly wrapped by the fibroblastic sleeve that inevitably forms around any vascular device, and this is a possible cause of malfunction. Malfunction will more rapidly occur when the tip of the catheter is in a vein of small caliber. These considerations explain why a SPC will rarely last more than 1 week and why a LPC will typically last no more than 4 weeks. On the other hand, MC may stay in place even for a few months. The length of stay of a LPC or of a MC will also be strongly influenced by the training of the staff performing the insertion and the maintenance of the VAD.43,44

The choice of the PVAD depends also on the availability of the superficial veins. When the superficial veins of the arm are difficult to visualize and palpate (so-called “DIVA”), SPC can be inserted only accessing deep veins of the arm by US guidance; though, US-guided short cannulas usually have a limited duration, due to the fact most of the cannula stays outside of the vein, with high risk of dislocation. In this condition, unless the line is required only for <24 h, the recommendation is to place a LPC in a deep vein of the arm, by US guidance.42,45

Nonetheless, considering the longer duration of LPC if compared to SPC, the insertion of a LPC (with or without ultrasound guidance) may be indicated also in patients with visible/palpable superficial veins of the arm, if the intravenous treatment is expected to last more than 1 week.46,47 MC have a higher cost than SPC or LPC, but their use becomes cost-effective when the PVAD must stay in place for more than 1 month, as sometimes happens in palliative care patients who receive intravenous treatment at home or in a hospice.

The location of the tip of the PVAD will also have an impact on the feasibility of blood sampling. Blood withdrawal through a SPC will be possible only at the time of insertion; blood withdrawal will be easier via an MC than via an LPC.

While PVADs have a lower incidence of CRBSI if compared to CVADs,48 LPC, and MC are reported to have a lower risk of bacterial phlebitis, mechanical phlebitis, thrombophlebitis, and infiltration/extravasation, if compared to SPC.49,50 These features explain the increasing success of LPC in clinical practice: they are less expensive than MC, and they have a clinical performance superior to SPC, both in terms of risk of complications and of in terms of duration. Though the evidence is still limited, LPC, reducing the number of punctures needed for repeated placements of SPC, may be also favorable in terms of patients’ satisfaction. LPCs are also a good alternative option in critically ill patients with sepsis, if a central line is not specifically indicated.51 Considering that they can be inserted by US guidance, the presence of a DIVA patient is not a limit to their use.52

Significantly, an important limit to the use of LPC is any evidence of chronic renal failure stage 3b, 4 or 5, which implies a contraindication to the use of any superficial or deep vein of the forearm or of the upper arm; in this condition, the only acceptable PVADs are SPC in veins of the hand, or in the superficial tract of the external jugular vein or in veins of the lower limbs; though, it is recommended that such cannulas should be removed as soon as possible, within 24 h, considering the high risk of extravasation and phlebitis.

Other contraindications to the placement of a PVAD include any condition leading to difficult access to both
superficial and deep veins of the arm (previous severe thrombosis or extravasation, obesity, etc.) or any clinical situation which requires a central VAD (infusion of peripherally incompatible solutions, hemodynamic monitoring, repeated blood sampling).

Panel’s recommendations:

PVADs are indicated in the following circumstances:

1. short to medium term infusion of peripherally compatible solutions
   - solutions with pH 5–9
   - drugs with osmolarity <600 mOsm/L
   - parenteral nutrition with osmolarity <800–850 mOsm/L
   - any drug or solution not associated with potential endothelial damage
2. apheresis/ultrafiltration, but only in specific situations and using specific devices.

PVADs are contraindicated in the following circumstances:

- infusion of vesicant drugs or prolonged infusion (>30 min) of peripherally incompatible solutions
- repeated daily blood sampling
- hemodialysis
- need for hemodynamic monitoring
- need for long term intravenous access (>3–4 months).

The indications for specific PVADs are mainly based on the expected duration of treatment:

- SPCs are appropriate for emergency and/or short duration access (24–48 h)
- “integrated” SPCs are appropriate for non-emergency access, when expected duration is 2–7 days
- LPCs are appropriate in DIVA patients, or when expected duration is 1–4 weeks
- MCs are appropriate when expected duration >4 weeks.

Section 3 – Insertion

Site selection. Site selection plays a major role during the insertion of PVAD. In the adult patient, SPCs should be preferably inserted in veins of the forearm or of the upper arm and not in flexion area such as the hand or the wrist or the antecubital fossa, since the placement of a SPC in these locations is associated with a very high risk of dislodgement. Insertion of a SPC in the superficial tract of the external jugular vein at mid-neck should be preferably avoided for the same reason. The use of a vein of the lower limb (such as the saphenous vein at the medial part of the ankle) is also to be avoided, due to the high risk of thrombophlebitis (and subsequent risk of pulmonary embolism). SPCs inserted in emergency situations in these locations – flexion areas of the upper limb, external jugular vein or lower limb – should be removed as soon as possible and always within 24 h. Insertion of a SPC in a vein in the ventral part of the wrist must always be avoided, because of the high risk of arterial injury.

Infection prevention. Though PVADs are less prone to CRBSI if compared to CVADs, still infection is a remarkable risk if proper precautions are not considered. A phlebitis that occurs 2–3 days after the insertion of an SPC (particularly in emergency) is usually a bacterial phlebitis. SPCs should be inserted after proper hand hygiene, skin cleansing with a proper antiseptic (2% chlorhexidine in 70% isopropyl alcohol), clean gloves and aseptic technique (the glove must not touch the site of puncture after skin disinfection). If such recommendations have not been adopted – for example in emergency – the SPC should be removed (or replaced if needed) as soon as possible, within 24–48 h.

All PVADs should be inserted adopting a proper aseptic technique, as defined by ANTT (Aseptic No Touch Technique). When inserting an LPC or an MC, apart from the adoption of proper hand hygiene and skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol, the use of maximal barrier precautions (mask, cap, sterile gown, sterile gloves, long sterile cover for the ultrasound probe, wide sterile field) is also recommended. If these precautions have not been adopted – such as it may occur with a LPC inserted as an emergency procedure in a DIVA patient – the line should be preferably removed (or replaced, if needed) within 24–48 h.

All PVADs should have the exit site covered and protected with semipermeable transparent dressings. Cyanoacrylate glue, if applied in minimal quantity (0.2 ml) around the exit site, may reduce the risk of local bleeding and of bacterial contamination by the extra-luminal route, by sealing the breech. Cyanoacrylate is especially indicated in patients at high risk of bleeding (cirrhosis, chronic renal failure, hematologic diseases, patients on anticoagulants,
etc.) and/or when a modified Seldinger technique has been used (typically, for MC).

For reducing the risk of infection, the use of multilumen MC should be limited as much as possible.

Recent additional strategies proposed for reducing the risk of MC-related infection are the “extended subcutaneous route” (or “pseudo-tunneling”) and tunneling; both strategies may be effective in reducing bacterial contamination by the extraluminal route.

**Securement.** Coverage with transparent dressing is also important for the securement. Bordered transparent dressing is a simple and reliable securement and should be the first choice when the SPC must stay in place for several days. Cyanacrylate glue may also play an important additional role in this regard. The PVADs meant to stay in place for longer periods of time (LPC and MC) should be secured either with a bordered transparent dressing with an integrated securement device, or by using simultaneously a transparent dressing and a skin-adhesive sutureless device. Subcutaneously anchored securement devices have usually no indication in PVADs, though they might be considered for MCs.

Proper securement of a PVAD will not only reduce the risk of dislodgement but will also affect favorably the incidence of infection and thrombosis. For a long-lasting securement, it is important to connect an extension to the PVAD, so that the connection remains below the transparent dressing and the infusion line can be changed by maneuvering the extension only. A PVAD provided with a preassembled extension (such as an “integrated” SPC, or some LPCs and MCs) will be even a better option.

**Ultrasound guidance.** Short cannulas are typically inserted by direct puncture and cannulation of palpable and/or visible superficial veins (<7 mm from the skin surface). When superficial veins of the arm are not easily palpated or visualized (DIVA), a possible option is to puncture and cannulate deep veins (>7 mm from the skin surface) of the forearm or of the upper arm, using US. US-guided SPCs are characterized by an expected success of cannulation close to 100%, but unfortunately the line often lasts only 24–48 h, particularly if the vein accessed by US is quite deep (>1 cm) and if the cannula is particularly short. Thus, in DIVA patients, if the device must stay in place for several days, it is preferable to insert an US-guided LPC rather than US-guided SPC. Although LPCs can also be inserted without US, they seem to have a better clinical performance when inserted using US-guidance. On the other hand, MCs should always be inserted by US-guidance and modified Seldinger technique.

**Near-Infra-Red technology.** In the last decade, many devices using Near-Infra-Red (NIR) technology have become available. They enhance the visualization of superficial veins, using a specific wavelength in the near-infrared spectrum (760 nm), which is specifically absorbed by the desaturated hemoglobin. This technology has been used with some success in the insertion of SPCs in pediatric patients, while the experience in adults is less convincing. There are several limits to this technology: first, due to the limited penetration of the infrared rays, it can visualize only superficial veins (<7 mm deep), so that it may be more appropriate in neonates and children than in adults. Second, there is good evidence that NIR devices enhance the visualization of the veins, but limited evidence that they facilitate the puncture and the cannulation. Cost-effectiveness is also still uncertain. Finally, no proper model of training has been developed yet.

Nonetheless, it is most likely that soon NIR guidance will prove to be useful in specific categories of DIVA patients, particularly in those patients where the main obstacle to the visualization of the vein is the pigmentation of the skin.

**Training.** The literature on training in insertion of PVADs is quite limited if compared to CVADs. As any other clinical procedure, insertion of PVADs needs specific training. In alignment with the educational pathway proposed years ago by the WoCoVA consensus on training on insertion of central VADs, the training in PVAD insertion should include theory, lab practice, proctored learning curve, independent learning curve and a final audit with a consideration for a revalidation option. Of course, the characteristics of this training will be quite different depending on the complexity of the maneuver. Direct insertion of a SPC will require a relatively short training. The training will become longer adding specific techniques (US guidance; NIR guidance) and/or using devices of increased complexity (Seldinger technique; coaxial Seldinger technique; modified Seldinger technique). In all trainings, during the phase of lab practice, the use of simulators is recommended. It must be kept in mind that the development of specific “insertion bundles” for each type of device is a simple and powerful tool for teaching, learning, and performing the maneuver effectively.

**Panel’s recommendations:**

- Insert PVADs at the forearm or upper arm, avoiding areas of flexion
- If insertion in the hand, in the external jugular vein, or at the lower limb is unavoidable (as in emergency), remove the PVAD within 24–48 h
- Prepare the skin with 2% chlorhexidine in 70% isopropyl alcohol using 30 s friction and allowing 30 s to dry
- In DIVA patients, consider the use of NIR guidance for access to the superficial veins of the arm and/or US guidance for access to the deep veins of the arm
- Cover the exit site with sterile semipermeable transparent dressing
• apply cyanoacrylate glue in patients with bleeding risk
• secure with sutureless devices if peripheral access is expected to last >48 h
• train inserters to adopt “insertion bundles”.

Section 4 – Maintenance

Risk of infection. PVADs are characterized by an incidence of CRBSI which is very low if compared to CVADs, probably ranging between below 0.5 episodes per 1000 catheter days. Still, CRBSI due to PVADs may occur and the incidence is probably underestimated.8,92–96 The actual incidence of local infections is also difficult to define, since the differential diagnosis between bacterial phlebitis versus other causes of “catheter failure” (dislodgment, mechanical phlebitis, chemical phlebitis, occlusion, infiltration) is often difficult or impossible. It is estimated that bacterial infection may be involved in a high percentage of cases of “catheter failure”.

As regards the risk of infection, there is lots of evidence-based literature.8,10,93 The main recommendations for infection prevention during management of PVADs can be classified into three groups.

(1) General recommendations for the management of the device:10
• Use quality improvement interventions to support the appropriate use and management of PVAD (protocols for choice, insertion, and management; reminder to review the removal; continuing professional education).9
• Train the healthcare workers and assess periodically their competence in using practices for the prevention of VAD related infections.9
• Consider establishing an infusion team for insertion, care, and removal of the PVADs.9
• Enforce the adoption of a strict policy for hand hygiene with an alcohol-based hand rub (or by using soap and water, when indicated) before and after any contact with the catheter or with the exit site.8,9
• Use the proper standard aseptic technique, as defined by ANTT, for the management of the exit site and when administering intravenous solutions and medications.9
• Consider adopting a “bundle” approach (i.e. definition of a specific “maintenance bundle” for PVADs) and using a checklist to ensure adherence of the health operators to the bundle.8,9
• Evaluate all adverse events (infiltration, phlebitis, bloodstream infections, obstruction, etc.) and monitor their incidence rates.
• Remove the VAD (either SPC, LPC or MC) when it is no longer required or when complications occur. The practice of changing the site of SPCs on a scheduled basis is not supported by evidence.

(2) Recommendations for minimizing bacterial contamination by the extra-luminal route10:
• Assess the exit site of short PVADs at least every shift, and at least daily for LPCs and MCs, and evaluate possible local abnormalities using a visual exit score.
• Cover the exit site with a sterile semipermeable transparent dressing and change it at least every 5–7 days or sooner if no longer intact.8,9,22,98
• For long dwell PVADs such as MC, consider using a chlorhexidine-impregnated sponge dressing (to be changed weekly, simultaneously with the dressing change).
• At the time of dressing change, clean the exit site with a single application of 2% chlorhexidine in 70% isopropyl alcohol (use povidone-iodine in alcohol only for patients with sensitivity to chlorhexidine).9
• Allow any skin antiseptic to fully dry (at least 30 s) when it is no longer required or when complications occur.
• If the PVADs is secured with a sutureless device, replace it periodically according to manufacturer’s instructions.

(3) Recommendations for minimizing bacterial contamination by the intraluminal route10:
• Disinfect needle-free connectors or catheter hub with vigorous mechanical scrub with 70% isopropyl alcohol, or with povidone-iodine or 2% chlorhexidine in alcohol solution. The optimal scrub time is not yet defined (at least 15 s). When the PVAD is closed with a needle-free connector, consider the use of passive disinfection caps (so-called “port protectors”).9
• Use a closed rather than an open system PVAD.
• Change continuous administration sets (used for other than lipid solutions or blood or blood products) not more frequently than every 96 h.9
• Change intermittent administration sets every 24 h.
• Change administration sets for PN at least every 24 h.
• Change administration sets for blood products at the end of every unit or every 4 h.9
• Change needle-free connectors with the administration sets or when blood is not completely cleared.

Risk of occlusion. Lumen occlusion may be secondary to blood clots or drug precipitates.99,100 The basic recommendations for minimizing the risk of lumen occlusion are:

• Adopt a proper flushing technique: every PVAD should be flushed with saline only, before each infusion and after each infusion;9,117 considering that the
flush must be more than twice the priming volume of the PVAD (catheter + extension), a 5 ml flush will be appropriate for most PVAD in adult patients.

- If the VAD is used intermittently, after the final flush, lock the device with saline only; while locking, consider using positive pressure techniques (pulsatile flushing) to minimize blood reflux.9
- For flushing and locking the device, use single-dose vials of saline or prefilled syringes.8,10,93,101,102
- When flushing and locking a PVAD that is not power injectable, use a syringe with low injection pressure (i.e. 10 ml syringe). Power injectable VADs can be flushed and locked with 5 ml syringes.
- The most appropriate frequency of flushing and locking a PVAD that is used intermittently is not well defined; in the intra-hospital setting, consider flushing and locking every 24 h.
- Always check for incompatibility when two or more drugs are infused together, as precipitation of incompatible drugs is a recognized cause of lumen obstruction. Always flush between two incompatible drugs to create a barrier between two drugs.33
- Work in collaboration with the pharmacy department to assess the best practices surrounding the proper use of drugs (dilution, stability, compatibility).
- Consider the use of active infusion systems (volumetric pumps for example) to prevent lumen occlusion.

Risk of dislodgment. All PVADs should be appropriately covered and secured: stabilization is a key factor in ensuring the duration of the VAD.103 Poor stabilization is not just associated with risk of dislocation and subsequent infiltration or extravasation, but also with risk of infection and thrombosis. The risk may increase with “micro-motion” of the catheter at the exit site. Risk of dislodgment can be reduced by a stable puncture site (PVADs inserted at the forearm or at the upper arm have a longer duration than devices inserted in flexion areas such as hand, wrist or antecubital fossa). Assessment of the exit site at every shift will play a role not only in early detection of local inflammation, but also in ensuring the appropriate securing of the device.

Several securement strategies are available, and the most appropriate one should be determined on the basis of the expected duration of the line.104 “Minimal” securement of a SPC can be ensured by sterile semipermeable transparent dressing only, preferably bordered.105 A more effective securement for “integrated” SPC and for LPC will be achieved by using a bordered transparent dressing inclusive of a securement system, or by using a standard bordered transparent dressing after application of cyanoacrylate glue at the exit site.106,107 Recent evidence shows that both strategies are superior to transparent dressing only. LPC may also be secured with a skin-adhesive sutureless device. MCs are usually secured by skin-adhesive sutureless devices: there is no experience with the use of subcutaneously anchored securement device for MC, though this new kind of securement might be appropriate for MCs with expected long duration or when a high risk of dislodgment is anticipated.

Risk of phlebitis/thrombosis. Different types of injuries may cause an inflammation of the vein wall and a disruptive damage of the endothelial integrity, which is followed by the local formation of a thrombus.108 These pathophysiological events are variously described as “phlebitis” or “thrombophlebitis” or “thrombosis”, though there is little pathological evidence to differentiate the prevalence of the inflammation of the vein from the local venous thrombosis. Furthermore, the same phenomena may be elicited by a mechanical injury, by bacteria or by chemical substances contained in the infused solution. The local changes may be self-limiting, or they may be associated with a loss of the integrity of the vein wall, with resulting infiltration or extravasation.109

Prevention of bacterial phlebitis has been discussed above.

Prevention of mechanical and chemical phlebitis is based on the following recommendations:

(1) General measures
- Ensure adequate training and education for those who insert and maintain PVADs including structured education in the identification of phlebitis.110
- Consider a dedicated vascular access team for the insertion of LPC and MC.
- Monitor the phlebitis rates using surveillance methods and definitions that are consistent and permit comparison to benchmark data.
- When possible, educate the patient to inform staff if pain or other unexpected comfort develops at the site of the PVAD.

(2) Specific measures:
- Avoid insertion of PVADs on the hand, in the external jugular vein and in veins of the lower limb, if not necessarily required by an emergency; remove the cannulas inserted in such sites within 24–48 h.
- Preferably avoid flexion areas (such as the wrist and the antecubital fossa) and ideally prefer insertion at the forearm or in the upper arm.
- Do not reinsert a PVAD that has inadvertently become partially dislodged.
- Use the smallest practical size of PVAD, still compatible with the infusion required; in most adult patients 20–22G short cannulas will be appropriate; use larger size (18–16G) for short cannulas inserted in an emergency room or in an operating room;8,10 use preferably 3–4Fr LPC and MC. Also, LPC and MC should be chosen respecting the 1:3 catheter/vein ratio.
Use appropriate stabilization (see above) to avoid micro-motion of the catheter, which is known to be associated with the risk of mechanical phlebitis.

Assess the exit site for signs of phlebitis/thrombosis periodically (at least every shift for SPC and every time the device is accessed).\textsuperscript{111}

Do not use a PVAD (SPC, LPC or MC) for repeated or prolonged administration of solutions that are not peripherally compatible (chemical irritants, vesicant drugs, parenteral nutrition with osmolality >850 mOsm/L, etc.).

Remove the device when signs of phlebitis/thrombosis appear.\textsuperscript{112}

Use LPC or MC rather than SPC in patients likely to require non-irritating intravenous therapy for >7 days.

Panel’s recommendations:

Minimize the risk of infection using the following strategies:

- use 2\% chlorhexidine in alcohol to disinfect needle-free connectors and to clean the exit site if dressing change is required
- use semipermeable transparent dressings
- use needle-free connectors and disinfecting caps
- adopt a policy of visual inspection on each shift and every time the device is accessed.

Minimize the risk of occlusion using the following strategies:

- use normal saline for flushing and locking the device
- consider possible drug incompatibilities.

Minimize the risk of dislodgment using the following strategies:

- place PVADs in the forearm or upper arm, avoiding areas of flexion
- if insertion is in the hand, the external jugular vein, or the lower limb is unavoidable, remove within 24–48 h
- use a sutureless device to secure the PVAD
- use a semipermeable transparent dressing
- consider the use of cyanoacrylate glue.

Minimize the risk of phlebitis/thrombosis using the following strategies:

- avoid micro-movements of the device
- use the PVAD only for peripherally compatible infusions
- adopt a policy of visual inspection on each shift and every time the device is accessed.

Section 5 – Removal

Which are the proper indications for removing a PVAD? As with any other device, there are five main indications for removal of a PVAD:\textsuperscript{113}

1. \textit{End of treatment}. The device is no longer needed, as the patient stops the intravenous therapy. The inappropriate persistence of a device without clinical reason is a well-recognized source of complications and a waste of resources.

2. \textit{The device is not appropriate anymore}. The type of intravenous treatment has changed (for example, the patient has to shift to the infusion of peripherally incompatible solutions), or the expected duration of the treatment has been prolonged (which might indicate the replacement of a SPC with a LPC or MC), or the patient moves to a different setting of care that requires a different device (for example, from hospitalization to home care, this being a setting inappropriate for a SPC), or the clinical conditions of the patient require a CV AD for hemodynamic monitoring or repeated daily blood samples.

3. \textit{The device has been inserted in emergency}. The standard recommendations for infection prevention (in terms of site selection, aseptic technique, skin antisepsis, coverage and securement) have not been fully adopted. As already stated above, any PVAD or CV AD inserted in emergency with low attention to asepsis should be removed within 24–48 h. Emergency insertion carries a very high risk of complications (in particular, bacterial phlebitis or CRBSI) if the VAD is left in place for a longer period of time.

4. \textit{A VAD-related complication has occurred, which requires the removal of the device}. For PVADs, virtually any complication (dislodgment, phlebitis, thrombosis, occlusion, infection, infiltration, extravasation, etc.) is associated with “catheter failure” and implies the removal of the device. The currently used visual exit scores help in this decision: the simple presence of redness of the exit site (without local tenderness or other abnormalities) or of local tenderness (in absence of any other local alterations) is the only situation that requires further surveillance but not removal. All other local abnormalities of the exit site, in different combinations, require prompt removal of the CV AD. SPC should also be promptly removed if fever starts during short infusion (1 h) or soon after (30 min) end of the infusion: the VAD might be infected, and since blood cultures cannot be performed from a SPC, the risk-benefit ratio indicates a rapid removal of the device. The presence of signs and symptoms suggesting extravasation,
occlusion, infection, thrombosis and dislocation are usually an indication for removal also for LPC and for MC, but with some exceptions. For example, in the presence of very limited venous access with a malfunctioning, but not infected MC, a replacement over guidewire may be considered. Also, an accidental dislodgement of the external tract of an MC, if minimal (<2 cm), does not require intervention, while a more significant dislodgement may be treated by guidewire replacement, in the absence of infection. Venous thrombosis of an MC at the site of venipuncture of the arm should be treated with anticoagulants leaving the catheter in place, as long as the catheter is still in use and works properly.

(5) The patient refuses to maintain the device. As much as the patient must give his informed consent to the insertion of the VAD, he/she can waive his/her consent at any time.

The routine removal/replacement of a PVAD, in absence of complications, but only based on a scheduled repositioning (for example every 4 days) is not considered appropriate any more by the recent international guidelines, which have shown that such strategy is not cost-effective and does not increase the safety or comfort of the patient.9–12,22,33,55 The scheduled periodic replacement is associated (a) with the risk of failing to insert the new device, (b) with a progressive undesirable exploitation of all the veins of the arm, (c) with a reduced comfort, as the patient must face further unnecessary venipunctures, (d) with an increased risk of needle stick injuries for the caregivers, and (e) with an increased cost of health care for every single patient. The currently recommended strategy of removing the PVAD only in case of complications requires a proper surveillance of the performance of the line and of the visual aspect of the exit site; this can be achieved (a) adopting a proper terminology in the definition of the local signs and symptoms, (b) using semipermeable transparent dressings (that permits the inspection of the exit site) and (c) standardizing the findings through validated visual exit scores. Any SPC used in a hospitalized patient should be examined at each shift of the nursing staff. LPC and MC should be examined at least daily, both in the intra-hospital and in the extra-hospital setting.

Are there any complications potentially related to removal? The removal of SPC or of LPC is usually not associated with relevant complications.

The most likely undesirable event is bleeding from the exit site, with or without local hematoma: this most commonly happens in patients with large-caliber catheters and/or coagulation abnormalities (anticoagulant treatment, chronic renal failure, hepatic failure or hematological disorders).

If there is inflammation at the exit site, local skin antiseptics during VAD removal may be associated with burning sensation and discomfort of the patient.

Removal of the transparent dressing and/or of the skin adhesive sutureless device may be associated with skin injury in aged patients with fragile skin.

Though never described in the literature, the removal of a MC with a severe catheter-related venous thrombosis located in the thoracic tract of the axillary vein or in the subclavian vein may be associated with a potential risk of pulmonary embolism, particularly if the thrombosis is of recent onset (<72 h) and if anticoagulant treatment has not been started.

On the other hand, the occurrence of air embolism at removal of a PVAD (either SPC, or LPC, or MC) is technically impossible.

Is there any special strategy to minimize such complications? After the removal of the device, the exit site should be manually compressed with sterile dry gauzes. If the risk of local bleeding is anticipated, after compression, a minimal amount of cyanoacrylate glue (0.15–0.30 ml) should be applied to the exit site, to stop any oozing or bleeding.

If signs of MARS (Medical Adhesive Related Skin Injury) are evident at the exit site, the dressing and the securement must be removed very slowly, so not to amplify the local injury and pain; alcohol-based antiseptics should be preferably avoided; the use of adhesive remover wipes should be considered. After removal, local treatment of the MARS by a specifically competent vascular access specialist is warranted.

Before removing an LPC or an MC with signs and symptoms suggesting a venous thrombosis, it is recommended to perform an ultrasound exam of the whole venous tract where the catheter lies, so to rule out the presence of thrombosis at the puncture site or along the catheter or at the distal tip and/or detect the presence of other phenomena (such as a fibroblastic sleeve). Recent studies suggest performing a pre-removal ultrasound examination in patients at high risk of venous thrombosis, such as those with hematologic malignancies, COVID-19 or chronic renal failure. Pre-removal ultrasound scan may be omitted in patients on anticoagulant treatment. The presence of a thrombus at the tip is an indication for postponing the removal and starting an anticoagulant treatment with low-molecular-weight heparin. The presence of a thrombus in the brachial tract of the catheter is not an absolute contraindication to removal, though removal should be performed slowly and – preferably – under ultrasound control.

All SPC and LPC are usually removed with ease. On the other hand, in some instances, resistance may be felt during the extraction of a MC (as sometimes happens during PICC extraction). If this occurs, an ultrasound exam should be performed to exclude thrombosis. In most of these cases, the ultrasound scan reveals the presence of a fibroblastic sleeve strictly adherent to the catheter; removal will be easy by inserting a micro-guidewire inside the
catheter and extracting guidewire and catheter simultaneously, with a gentle rotating movement.

As not all peripheral VADs are power injectable, rupture of a catheter could happen (especially SPC), so that a fast check of length of the catheter after removal is recommended.

Panel’s recommendations:

Removal of PVADs is indicated in the following circumstances:

- device no longer required
- device no longer appropriate
- device failure
- device inserted in emergency conditions (to be removed within 24–48)
- request of the patient.

Potential complications at removal include:

- local bleeding (to be prevented by compression and glue)
- skin injury
- mobilization of thrombus (rare – only for MC).
Conclusions

In the decade 2011–2021, peripheral venous access has dramatically evolved, as an effect of the implementation in the clinical practice of new devices (long peripheral catheters, “integrated” short peripheral cannulas, etc.), new technologies (skin antisepsis with 2% chlorhexidine, semi-permeable transparent dressing, ultrasound guidance, near-infra-red guidance, cyanoacrylate glue, sutureless securement, port protectors, etc.), and new behavioral strategies (ANNT, hand hygiene with alcohol-based rub, vascular access teams, etc.).

This consensus documents offers an overview of the current recommendations about indication, insertion, management, and removal of the peripheral venous access devices, as developed by a panel of European experts in this area. A summary of the results of thus consensus is reported in Table 1. As new evidence is continuously being produced in this area, it is inevitable that some of these recommendations may change in the next decade. Still, this is an effort to define which are the currently most appropriate strategies to optimize patients’ safety, clinical efficacy, and cost-effectiveness in this field in 2021.

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