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ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Venous access

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1. Methods

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Type of publications: randomized trials, observational studies (case-controls, prospective cohort studies, time series, retrospective data), meta-analyses, and systematic reviews

Key words: catheterization, central venous catheters, central line, central catheter, central venous access, parenteral nutrition, intravenous nutrition, Broviac, Hickman, ultrasound, placement, catheter related thrombus, catheter blockage, catheter related infection, skin hygiene, skin site, topical treatment, dressing type & change, catheter submersion, swimming, bathing, care standardization, multimodal preventive strategies, bundles

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Search: Searches were performed in three stages. First, all the titles on the relevant key words were retrieved by the Cochrane Collaboration Department from Budapest/Hungary, who also performed the first reduction. Members of the Working Group subsequently read all the titles and abstracts, and selected potentially relevant ones. These were retrieved and full articles were assessed.

Table: List of recommendations on venous access

R 10.1	In newborns and children, PICC and tunneled CVC should be used for administration of prolonged PN during hospitalization (GPP, strong recommendation for)
R 10.2	In children requiring long-term PN and home PN a tunneled CVC is recommended (GPP, strong recommendation for)
R 10.3	Where possible a CVC should be used only for giving PN (LOE 2−, RG B, strong recommendation for)
R 10.4	A catheter with the minimal number of ports or lumens may be used (LOE 2−, RG 0, strong recommendation for)
R 10.5	If a multi-lumen CVC is in place, dedicate one lumen to PN; blood sampling, transfusion and central venous pressure monitoring from the CVC should be avoided (Extrapolated evidence from adult studies rated as LOE 1−, RG B, strong recommendation for)
R 10.6	To improve quality of life for patients on long term PN, blood sampling via CVC for routine monitoring is recommended providing full aseptic protocol is followed (GPP, strong recommendation)
R 10.7	Catheters used for long-term PN made of silicone or polyurethane may be preferred (LOE 2−, RG 0, strong recommendation for)
R 10.8	Antimicrobial coated CVC should not be used for children on long-term PN (Extrapolated evidence from adult studies rated as LOE 1+, RG B, conditional recommendation against)
R 10.9	In infants and children in whom CVC cannot be placed in superior vena cava, an option of femoral vein catheter insertion can be recommended as a higher incidence of mechanical and infectious complications has not been shown in comparison with jugular and subclavian sites (LOE 2−, RG 0, conditional recommendation for)
R 10.10	In children, an option of subclavian venous access can be recommended as the risk of mechanical complications does not exceed the rate of complications with other insertion sites under appropriate conditions of insertion (LOE 2−, RG 0, conditional recommendation for)
R 10.11	Subclavian insertion can be recommended for long-term use (GPP, conditional recommendation for)
R 10.12	In newborns, umbilical vessels can be used for short term PN (GPP, conditional recommendation for)
R 10.13	The CVC tip should lie outside the pericardial sac to avoid the risk of pericardial effusion/tamponade (GPP, strong recommendation for)
R 10.14	In small infants (body length 47–57 cm) the catheter tip of a jugular or subclavian CVC should lie at least 0.5 cm above the carina on a chest x-ray, while in older/larger infants (body length 58–108 cm) that distance should be at least 1.0 cm (GPP, strong recommendation for)
R 10.15	In children, as in adults, we recommend that positioning the CVC tip above the carina means it is likely to be in the superior vena cava and therefore outside the pericardial sac (LOE 3, RG 0, strong recommendation for)
R 10.16	The catheter tip of a femoral catheter should lie above the renal veins (first lumbar vertebra) (GPP, strong recommendation for)
R 10.17	A percutaneous, radiologically or ultrasound guided insertion method may be used since this is equally effective as a surgical cut-down, and carries less risk of complications (LOE 2−, RG 0, strong recommendation for)
R 10.18	Ultrasound guidance may be used in order to reduce complications during venous catheterization (LOE 2−, RG 0, strong recommendation for)
R 10.19	CVC shall not be changed routinely in order to reduce the risk of sepsis (Extrapolated evidence from adult studies rated as LoE 1+, RG A, strong recommendation against)
R 10.20	If a CVC requires removal, replacement rather than exchange over a guidewire decreases the risk of infection. CVC exchange may be reserved for those patients with difficult venous access (Extrapolated evidence from adult studies rated as LoE 3, RG 0, conditional recommendation for)
R 10.21	Prophylactic antibiotics do not reduce the risk of CRBSI, therefore they should not be administered (LoE 2+, RG B, conditional recommendation against)
R 10.22	Antibiotic line locks should not be used alone for treating catheter related blood stream infection (CRBSI) as these have not been shown to be effective (LoE 1−, RG B, conditional recommendation against)
R 10.23	Antibiotic line locks can be used in conjunction with systemic antibiotics to assist in the eradication of CRBSI in some patients (LoE 3, RG 0, conditional recommendation for)
R 10.24	Ethanol line locks may be considered for preventing CRBSI (LoE 3, RG 0, conditional recommendation for)
R 10.25	Taurolidine is effective in preventing CRBSI and should be used during long term catheter use (Extrapolated evidence from adult studies rated as LoE 1+, RG B, strong recommendation for)
R 10.26	Routine use of heparin flush for the prevention of thrombotic occlusion in CVC being used on a daily basis cannot be recommended over use of saline flush due to lack of proven benefit in children (LoE 2−, RG 0, conditional recommendation against)
R 10.27	For CVC that are being accessed intermittently, flushing with 5–10 U/mL heparinized saline 1–2 × weekly helped maintain patency and therefore can be recommended (Extrapolated evidence from adult studies rated as LoE 2−, RG 0, conditional recommendation for)
R 10.28	Routine use of heparin has been shown to be effective in prevention of PICC occlusion in newborns, but since the potential risks have not been defined, its routine use cannot be recommended (LoE 3, RG 0, recommendation for research)
R 10.29	In infants and children recombinant tissue plasminogen activator or urokinase shall be used to unblock a catheter (LoE 1+, RG A, strong recommendation for)
R 10.30	There is insufficient evidence to advocate the prophylactic use of anticoagulants in children receiving home parenteral nutrition to reduce catheter related thrombosis, occlusion and infection (LoE 3, RG 0, strong recommendation against)
R 10.31	Appropriate hand hygiene procedures should be followed before accessing the intravascular device or the insertion site (Extrapolated evidence from adult studies rated as LoE 1+, RG B, strong recommendation for)
R 10.32	Before insertion of an intravascular device and for post-insertion site care, clean skin should be disinfected with 2% chlorhexidine solution in 70% isopropyl alcohol (Extrapolated evidence from adult studies rated as LoE 1, RG B, strong recommendation for)
R 10.33	Antiseptic solution should remain on the insertion site and be allowed to air dry before catheter insertion or dressing application (GPP, strong recommendation for)
R 10.34	Due to potential side effects, skin antisepsis with chlorhexidine in infants younger than two months cannot be recommended (LOE 2−, RG 0, conditional recommendation against)
R 10.35	Catheter connectors, ports and hubs should be disinfected before accessing, preferably with 2% chlorhexidine solution in 70% isopropyl alcohol (LoE 2+, RG B, strong recommendation for)
R 10.36	Both sterile gauze with tape and transparent semi-permeable polyurethane dressing can be used to cover the catheter insertion site (LoE 3, RG 0, conditional recommendation for)
R 10.37	Sterile gauze dressing is preferable if the catheter site is bleeding or oozing (GPP, conditional recommendation for)
R 10.38	For short term CVC, site dressings may be replaced every 2 days for gauze dressing, and every seven days for transparent dressing. (LoE 2−, RG 0, conditional recommendation for)
R 10.39	A dressing should be changed sooner if it becomes damp, loosened or soiled (GPP, strong recommendation for)
R 10.40	A tunneled CVC with a well-healed exit site does not require dressing to prevent dislodgement, however, in children it is useful to have them looped and covered (GPP, conditional recommendation for)
R 10.41	Chlorhexidine-impregnated sponge dressing should be considered in patients older than two months with short-term catheters who are at high risk for infection (LoE 2+, RG B, strong recommendation for)
R 10.42	

(*continued*)

	Topical antimicrobial treatment at the insertion site cannot be routinely used as it may promote fungal infection, antimicrobial resistance and damage the surface of the catheter (LoE 3, RG 0, strong recommendation against)
R 10.43	Children with well-healed tunneled catheters may be allowed to swim, provided that a water resistant dressing is used to cover the whole catheter. Immediately after swimming the catheter exit site should be cleaned and disinfected, and the dressing changed (GPP, conditional recommendation for)
R 10.44	Regular training and education of healthcare staff with respect to catheter insertion and maintenance should be recommended (LoE 2+, RG B, strong recommendation for)
R 10.45	Multimodal protocols for health care providers, aiming to standardize clinical practice on insertion and maintenance of the intravascular devices, should be developed and regularly audited (LoE 2+, RG B, strong recommendation for)

2. Introduction

Securing reliable venous access is of paramount importance when considering parenteral nutrition (PN). However, the presence of a central venous catheter (CVC) is the principal risk factor for major, potentially lethal complications, such as nosocomial bloodstream infection [1] and venous thrombosis [2]. Moreover, the most important risks associated with complications arising from the use of CVC are administration of PN, young age and extended use (long indwelling time) [3–5]. CVC related complications in children on long-term PN contribute significantly to patient morbidity, mortality, and health care costs [6]. Notably, a large proportion of complications are preventable by means of appropriate catheter choice, selection of site and method of insertion, nursing care, handling and hygiene of venous access, all of which are addressed in this chapter.

In the following discussion it is necessary to differentiate between peripheral and central venous access, and between non-tunneled CVC (i.e. inserted via a peripheral vein - PICC) and tunneled CVC inserted subcutaneously.

3. Intravascular catheters: choice and insertion

3.1. Types of catheter

R 10.1	**In newborns and children, PICC and tunneled CVC should be used for administration of prolonged PN during hospitalization (GPP, strong recommendation for, strong consensus)**
R 10.2	**In children requiring long-term PN and home PN a tunneled CVC is recommended (GPP, strong recommendation for, strong consensus)**

High osmolality solutions are more likely to induce phlebitis and a CVC is generally required to maintain long term venous access (i.e. more than a few weeks). Although peripheral venous access can be used in preterm infants, extravasation injuries may be severe and frequent loss of venous access can compromise effective nutritional support. Central venous access is obtained by advancing a catheter into one of the central veins, either directly via a deep vein (subclavian, internal jugular or femoral), peripherally through a subcutaneous vein, or through the umbilical vein. CVC are usually selected according to the anticipated duration of use: short and medium term non-tunneled PICC and long-term use cuffed, tunneled CVC or implantable ports [7]. Any type of CVC can be used for providing short term PN in hospitalized patients, however, the advantages of a PICC are that it can often be inserted without general anesthesia, does not require manipulation of the vein, and has proven to be safe and effective for PN in newborns and children [3,8–11] (LoE 2−), although complications were more frequent in younger patients [12]. There is, however, limited and weak evidence showing that prolonged use (>14–21 days) of a PICC increases the risk for catheter-related bloodstream infection (CRBSI) [3,8,13] (LoE 2−).

For long term PN and home PN, cuffed tunneled CVC (e.g. Broviac, Hickman catheter) are recommended [7,14]. These devices have several advantages: the subcutaneous cuff attached to the catheter provides better fixation, and the longer distance between the insertion site and the entry into the vein decreases migration of microorganisms from skin to bloodstream [15,16] (LoE 1−). Implantable ports are useful for long-term intermittent use, but because port access requires insertion of a specially designed transdermal needle, their value for long-term PN in children is limited [7,14].

3.2. Catheter dedicated only to PN

R 10.3	**Where possible a CVC should be used only for giving PN (LOE 2−, RG B, strong recommendation for, strong consensus).**
R 10.4	**A catheter with the minimal number of ports or lumens may be used (LOE 2−, RG 0, strong recommendation for, strong consensus).**
R 10.5	**If a multi-lumen CVC is in place, dedicate one lumen to PN; blood sampling, transfusion and central venous pressure monitoring from the CVC should be avoided (Extrapolated evidence from adult studies rated as LOE 1−, RG B, strong recommendation for, strong consensus).**
R 10.6	**To improve quality of life for patients on long term PN, blood sampling via CVC for routine monitoring is recommended providing full aseptic protocol is followed (GPP, strong recommendation, strong consensus).**

To reduce the risk of infection it is recommended that the CVC should be used exclusively for administration of PN and not for blood sampling or giving other fluids and drugs [17] (LoE 2−). However, in critically ill children with poor venous access multi-lumen catheters may be used, with one lumen dedicated to PN. Double and triple lumen catheters appear to be associated with an increased risk of bacteremia compared to single lumen ones [18–21] (LoE 2−). They may be more at risk of becoming infected, possibly because of more frequent catheter manipulations [17,22,23] (LoE 2−) with rates of sepsis as high as 10–20% compared to 0–5% with single lumen catheters [17,23,24] (LoE 1−). In some adult studies, catheter sepsis does not appear to have been increased with multi-lumen devices [25–30] (LoE 1−). The authors of these studies suggested that PN can be given safely through multi-lumen catheters only when the following conditions are implemented:

- one lumen reserved exclusively for PN;
- only compatible medications and solutions to be given;
- not to be used for blood sampling, blood transfusion or central venous pressure measurement.

3.3. Catheter material

R 10.7	**Catheters used for long-term PN made of silicone or polyurethane may be preferred (LOE 2−, RG 0, strong recommendation for, strong consensus)**
R 10.8	**Antimicrobial coated CVC should not be used for children on long-term PN (Extrapolated evidence from adult studies rated as LOE 1+, RG B, conditional recommendation against, strong consensus)**

More flexible catheters made of silicone or polyurethane are less thrombogenic and less traumatic than CVC made of stiffer material [14] (LoE 2−). Because of this, in clinical practice, more flexible materials such as silicone or polyurethane have gradually replaced stiffer ones.

For short-term use, non-tunneled CVC impregnated with mini cycline/rifampicine or chlorhexidine/silver sulfadiazine in adults reduce infection rates more effectively than conventional catheters [31]. Similarly, RCT in critically ill children show that antibiotic-impregnated CVC significantly reduced the risk of bloodstream infection compared with standard catheters [32]. However, meta-analysis for adult patients showed that impregnated (coated) CVC do not prevent infection during prolonged PN [33] (LoE 1+; adult studies). There are no studies in children receiving long term PN.

3.4. Insertion sites

R 10.9	**In infants and children in whom CVC cannot be placed in superior vena cava, an option of femoral vein catheter insertion can be recommended as a higher incidence of mechanical and infectious complications has not been shown in comparison with jugular and subclavian sites (LOE 2−, RG 0, conditional recommendation for, consensus)**
R 10.10	**In children, an option of subclavian venous access can be recommended as the risk of mechanical complications does not exceed the rate of complications with other insertion sites under appropriate conditions of insertion (LOE 2−, RG 0, conditional recommendation for, strong consensus)**
R 10.11	**Subclavian insertion can be recommended for long-term use (GPP, conditional recommendation for, strong consensus)**
R 10.12	**In newborns, umbilical vessels can be used for short term PN (GPP, conditional recommendation for, strong consensus)**

CVC are commonly inserted via the internal jugular, subclavian, or femoral veins. The choice of vein is affected by several factors including venipuncture technique, the risk of related mechanical complications, the feasibility of appropriate nursing of the catheter site, the risk of thrombotic and infective complications, duration of anticipated central venous access, and operator experience [7,34]. Overall, there are no randomized controlled trials (RCT) comparing all three sites for CVC placement. Meta-analysis performed in adult studies [35] found that subclavian and internal jugular routes had similar risks for catheter-related complications in long-term catheterization in cancer patients (LoE 1+; adult studies). Subclavian was preferable to femoral insertion for short-term catheterization because femoral insertion was associated with higher risks of catheter colonization and thrombotic complications [35] (LoE 1+; adult studies). No significant differences were found between femoral and internal jugular CVC in catheter colonization, CRBSI and thrombotic complications, but fewer mechanical complications occurred in femoral CVC [35] (LoE 1+; adult studies). According to a recent meta-analysis which included RCT and cohort studies in adults, there were no differences in the incidence of CRBSI between those three sites of vascular access [36] (LOE 1+; adult studies). In children data are more scarce; there is a suggestion that the cannulation of the subclavian vein is more often associated with haemothorax, and that cannulation of the internal jugular vein is associated with a lower risk of pneumothorax, and is more easily compressible if bleeding occurs [37] (LoE 2−). A prospective, multicenter cohort study in children showed an increased incidence of venous thromboembolism with femoral and subclavian compared to jugular CVC [38] (LoE 2−). With regard to infection, a large case−control study of critically ill children found no association between femoral insertion and sepsis [39]. Similarly, in a cohort study of 4512 children, no association was found between femoral CVC placement and greater occurrence of infection, regardless of whether the catheter was placed in the emergency department, PICU or operating room [40] (LoE 2−). Moreover, a retrospective analysis of all the tunneled CVC placed in newborns found that total complication and catheter infection rates were significantly higher in neck lines [41] (LoE 3). For PICC in newborns no significant difference in complications was found between upper versus lower extremity [42] (LoE 2−). However, femoral access is uncomfortable for the child and the consequences of inferior vena cava thrombosis may be severe [14]. Moreover, subclavian insertion means there is a tunneled section of the CVC, and the site can be easily maintained so that it is preferred when longer use is anticipated [43,44].

In neonates umbilical vessel catheterization is often used for short term vascular access [45]. The incidences of catheter colonization and infections are similar for umbilical vein catheters and umbilical artery catheters [45]. Umbilical artery catheters placed above the diaphragm are associated with a lower incidence of vascular complications (LoE 2−) [14]. A recent randomized trial found that long-term umbilical venous catheterization (up to 28 days) resulted in a higher incidence of CRBSI compared with short term catheterization (7−10 days), but the result was not significant and the study was underpowered [46] (LoE 1−). However, there are studies indicating a similar infection rate at day 14 for umbilical venous catheter and PICC lines [47] (LoE 2−). Because there is a lack of quality data (and head to head comparisons) it was decided not to change the previous recommendation on the duration of umbilical catheter use [14].

3.5. Positioning of the catheter tip

R 10.13	**The CVC tip should lie outside the pericardial sac to avoid the risk of pericardial effusion/tamponade (GPP, strong recommendation for, strong consensus)**
R 10.14	**In small infants (body length 47−57 cm) the catheter tip of a jugular or subclavian CVC should lie at least 0.5 cm above the carina on a chest x-ray, while in older/larger infants (body length 58−108 cm) that distance should be at least 1.0 cm (GPP, strong recommendation for, strong consensus)**
R 10.15	**In children, as in adults, we recommend that positioning the CVC tip above the carina means it is likely to be in the superior vena cava and therefore outside the pericardial sac (LOE 3, RG 0, strong recommendation for, strong consensus)**
R 10.16	**The catheter tip of a femoral catheter should lie above the renal veins (first lumbar vertebra) (GPP, strong recommendation for, strong consensus)**

There is continuing debate regarding the optimal position of the catheter tip: the lower third of the superior vena cava, atrio-caval junction or the upper portion of the right atrium [7,48]. Case reports of cardiac tamponade associated with a catheter tip within the right atrium led to the recommendation that the CVC tip should lie outside the pericardial sac [14]. However, in adults erosive perforation has almost exclusively been described for CVC made of more rigid materials and these materials have gradually been replaced by more flexible ones [48]. There are unequivocal data in adults indicating that tip positioning peripherally to the right atrium increases the risk for symptomatic venous thrombosis [49−51]. Taking this into account, adult guidelines recommend that high osmolarity PN should be delivered through a catheter with the tip sited in the lower third of the superior vena cava, at the atrio-caval junction, or in the upper portion of the right atrium [7].

In children, there are reports of cardiac tamponade caused by the CVC eroding into the pericardial sac [52]. The risk is especially increased in preterm neonates where a tamponade incidence of 1.8% was reported even with CVC made of new polyurethane

material [53,54] (LoE 3). Weil et al. reported a pericardial effusion causing pericardial tamponade due to CVC in 1.3% of all children who experienced tamponade and all of these children were newborns [55] (LoE 3). Although rare, cardiac tamponade associated with a CVC is a life threatening complication, and it is therefore advisable that the CVC tip lies outside the pericardial sac and is repositioned whenever necessary.

In adults, the level of the carina can be used as a landmark for CVC tip positioning because the pericardial boundaries are below the tracheal bifurcation [56]. Radiological confirmation that the CVC tip is above the level of the carina reduces the risk of pericardial perforation in adults and older children [14]. In newborns it has been found that the pericardial reflection is located at a distance of 4 mm above to 5 mm below the carina [57] (LoE 3). Therefore, the carina is not a good landmark for newborns and infants; it has been shown that the catheter tip should be localized at least 0.5 cm for smaller infants (body length: 47–57 cm) and 1 cm for older infants (body length: 58–108 cm) above the carina to ensure that it is outside the pericardial sac [58] (LoE 3). Similarly, it has been shown that the mean distance from the carina to the atriocaval junction was 22.0 ± 9.98 mm [59]. In children beyond infancy the carina can be used as a landmark. Optimal catheter tip positioning following femoral vein insertion has not been elucidated, but for long-term use, the catheter tip should be positioned above the entry points of the renal veins (mainly above 1st lumbar vertebra) [14,60] (LoE 3).

3.6. Methods of insertion

R 10.17	**A percutaneous, radiologically or ultrasound guided insertion method may be used since this is equally effective as a surgical cut-down, and carries less risk of complications (LOE 2–, RG 0, strong recommendation for, strong consensus)**
R 10.18	**Ultrasound guidance may be used in order to reduce complications during venous catheterization (LOE 2–, RG 0, strong recommendation for, strong consensus)**

Meta-analyses and randomized controlled trials in adults [61–65] indicate that real-time ultrasound guided venipuncture compared with the anatomic landmark approach has a higher first insertion attempt success rate, reduced access time and higher overall successful cannulation rate. Based on this finding, guidelines for adults recommend real time ultrasound support for all CVC insertions [7]. A meta-analysis of five pediatric randomized trials found that ultrasound guidance decreased the number of punctures required and tended to decrease the time spent accessing the internal jugular vein, however, there was no significant difference in the rate of access failure, arterial puncture or other complications [66] (LoE 1+). Retrospective studies have indicated that ultrasound guided placement and tip position confirmation of lower-extremity CVC at the bedside in critically ill newborns and infants has similar complications and catheter outcomes when compared with fluoroscopic guidance [67] (LoE 2–). Similarly, results of RCTs for PICC placement also show shorter insertion time and fewer manipulations and radiographs when compared with conventional placement [68,69] (LoE 1–).

Methods of CVC insertion (including tunneled catheters) are by percutaneous placement and by surgical cut-down technique. The percutaneous insertion method under radiological surveillance is as effective as the surgical cut-down [70] (LoE 2–). While evidence suggests that tunneled CVC can be successfully placed percutaneously using ultrasound guidance [71–73], in order to minimize complications an experienced team is required [74] (LoE 2–).

3.7. Alternative sites

CVC complications following multiple catheterizations can cause depletion of commonly used venous access sites especially in children requiring long-term PN. Alternative sites for CVC placement include azygous, transhepatic, translumbar, intercostal veins, together with direct right atrial insertion and arteriovenous fistula [75–78] (LoE 3).

4. Interventions to reduce CVC infection

4.1. Antibiotics prior to CVC insertion, and routine catheter exchange

R 10.19	**CVC shall not be changed routinely in order to reduce the risk of sepsis (Extrapolated evidence from adult studies rated as LoE 1+, RG A, strong recommendation against)**
R 10.20	**If a CVC requires removal, replacement rather than exchange over a guidewire decreases the risk of infection. CVC exchange may be reserved for those patients with difficult venous access (Extrapolated evidence from adult studies rated as LoE 3, RG 0, conditional recommendation for, strong consensus)**
R 10.21	**Prophylactic antibiotics do not reduce the risk of CRBSI, therefore they should not be administered (LoE 2+, RG B, conditional recommendation against, strong consensus)**

A systematic review by Lee and Johnston [79] concluded that there was no evidence on which to base recommendations for the degree of barrier precautions or the type of aseptic technique used at the time of catheter insertion. Moreover, there is insufficient evidence to support the use of antibiotic flushes, and a lack of evidence with regard to use of in line filters and frequency of administration set changes with regard to prevention of CRBSI [79]. In line filtration is used to trap particulate contaminants of PN fluids, as well as to retain bacteria in the unlikely event the feed product is contaminated. There is no data relating to an effect of filters on CRBSI or blockage. Some centres have advocated routine changes of CVC after a specified period of time. A meta-analysis of 12 trials failed to demonstrate any reduction in risk of infection [80] (LoE 1+; adult studies); there is no evidence to support this practice in children.

It is possible for a malfunctioning CVC to be taken out and a new catheter inserted via a different site, or removed over a guidewire and replaced by a new device (catheter exchange). In a retrospective review of adult patients, those in the catheter exchange group had 3.2 greater odds of infection compared with the catheter replacement group [81] (LoE 3). The authors suggested reserving catheter exchange for those patients with very limited venous access.

Use of antibiotic prophylaxis prior to CVC insertion is controversial. In adult cancer patients, a systematic review or prophylactic antibiotics for preventing early Gram-positive infection indicated no benefit from vancomycin/teicoplanin prior to catheter insertion, but a possible role for flushing with heparin and vancomycin [82] (LoE 2++). One case control study in children suggested that peri-operative administration of antibiotics reduced the risk of early CVC infection [83] (LoE 2–). A systematic review by Huang et al. concluded however that there is no benefit from systemic prophylactic antibiotics at the time of catheter insertion [84] (LoE 2++).

4.2. CVC locks and flushes

R 10.22	**Antibiotic line locks should not be used for treating catheter related blood stream infection (CRBSI) as these have not been shown to be effective (LoE 1−, RG B, conditional recommendation against, strong consensus)**
R 10.23	**Antibiotic line locks can be used in conjunction with systemic antibiotics to assist in the eradication of CRBSI in some patients (LoE 3, RG 0, conditional recommendation for, strong consensus)**
R 10.24	**Ethanol line locks may be considered for preventing CRBSI (LoE 3, RG 0, conditional recommendation for, strong consensus)**
R 10.25	**Taurolidine is effective in preventing CRBSI and should be used during long term catheter use (Extrapolated evidence from adult studies rated as LoE 1+, RG B, strong recommendation for, strong consensus)**

Rather than removing an infected CVC, attempts have been made to fill the catheter with a high concentration of antibiotic and leave for a specified period of time with the intention of sterilizing the internal lumen. In a systematic review (largely of adult patients) the authors concluded that antibiotic locks could not be endorsed because the antibiotics tested were heterogeneous, outcome measures were non-specific, and the estimated effect of marginal significance [85] (LoE 1−).

In a randomized double blind study in very low birth weight critically ill infants, PICC were locked 2−3 times daily for 20 or 60 min with either heparinized normal saline or heparinized saline containing vancomycin [86]. There was a significant reduction in CRBSI in the vancomycin lock group (2.3 v 17.8/1000 catheter days) but asymptomatic hypoglycemia was noted in 26/85 patients at the end of the lock period (LoE 1+). A Cochrane review found only 3 studies in neonates (including ref 86) and suggested antibiotic lock might decrease infection risk by 18.5% without increasing risk of hypoglycemia (LoE 1−) [87].

A recent meta-analysis of anti-microbial line lock solutions mostly in adult patients suggested a potential 67% reduction in CRBSI [88]; line locks under investigation included a variety of different antibiotics, taurolidine and ethanol (LoE 1−).

Ethanol is an antiseptic and commonly used to sterilize catheter hubs. Studies of ethanol line locks to prevent CRBSI are mostly small and retrospective, but do suggest a positive effect [89,90] (LoE 3). A meta-analysis of studies comparing heparin and ethanol locks suggested that use of ethanol reduced CRBSI by 81% and need for CVC replacement by 72% [91]. Ethanol and heparin together may cause a precipitate, and ethanol can be damaging to catheters. In a group of seven children with intestinal failure, a retrospective study suggested that 70% ethanol used as a line lock on a daily basis compared with heparin saline decreased CRBSI rates from 10.3 to 1.4/1000 catheter days [92] (LoE 3); there was, however, an increasing trend in CVC thrombosis and need for catheter repair (LoE 3). In a randomized trial involving 307 paediatric oncology patients with CVC, 2 h ethanol lock was compared with heparin at a maximum frequency of once a week; infection rate was 10% in the ethanol and 19% in the heparin groups (LoE 1+) [93].

Taurolidine is a potent anti-septic agent derived from the amino acid taurine, and is active against a wide range of micro-organisms, both Gram negative and positive bacteria, and fungi. It is used as a line lock to prevent CVC sepsis, together with citrate to prevent catheter blockage. A systematic review of the literature (largely observational studies) concluded that it deserved further investigation before use could be recommended [94]. In a retrospective review of children on home PN, CRBSI rate was examined before and after the introduction of taurolidine; catheter sepsis rate fell from 8.6/1000 catheter days with heparin as line lock to 1.1/1000 with taurolidine [95] (LoE 3). Similarly, in high risk adult home PN patients, a retrospective study of taurolidine suggested a reduction from 5.71 to 0.99 episodes of CRBSI per 1000 patient PN days [96] (LoE 3). Bisseling et al. conducted a prospective randomized trial of adult home PN patients who had previously suffered an episode of CRBSI; patients were given either taurolidine or heparin (controls) [97]. Re-infections occurred in 10/14 heparin controls, while there was only one episode of sepsis in a patient randomized to taurolidine during a total of 5370 days of home PN (LoE 1+). In a trial of taurolidine versus heparin in children with cancer, 129 tunneled CVC were randomized [98]. The rate of CRBSI was 0.4/1000 catheter days in the taurolidine group and 1.4/1000 in the controls (LoE 1+). The authors concluded that taurolidine significantly reduced the risk of CRBSI. In a retrospective study of adult home PN patients over an 11 year period during which use of taurolidine became standard, CRBSI occurred 1.1 times/1 year of PN with heparin line lock and 0.2 times with taurolidine [99]; CVC occlusion was halved with taurolidine. In patients using taurolidine who still get recurrent infections, no evidence of adaptation of organisms (i.e. resistance to taurolidine) has been found [100]. A number of different taurolidine products are available including 2% solution, 1.34% with citrate, and 1.34% with citrate and heparin. An investigation into their relative efficacy [101] showed equal effectiveness in killing *Escherichia coli, Staphylococcus aureus* and *Candida glabrata*, with no difference in their effects on the catheter biofilm [101]. In a study of pediatric patients with cancer, Handrup et al. found use of taurolidine was associated with reduced risk of CRBSI compared with heparin, but electron microscopy of removed CVC found no difference in intraluminal biofilm formation or catheter colonization [102]. Some free fatty acids have antithrombotic and antimicrobial properties. Luther et al. [103] conducted an in vitro investigation of different line locks including a novel free fatty acid emulsion ML8-X10. This demonstrated activity against biofilm-forming *Staphylococci* similar to or greater than that of vancomycin. Taurolidine was the most active lock solution at 8 and 24 h, but all three demonstrated high activity at 72 h.

5. Interventions to decrease thrombotic complications and CVC occlusion

R 10.26	**Routine use of heparin for the prevention of thrombotic occlusion in CVC being used regularly in children cannot be recommended over use of saline flush due to lack of proven benefit (LoE 2−, RG 0, conditional recommendation against)**
R 10.27	**For CVC that are being accessed intermittently, flushing with 5−10 U/mL heparinized saline 1−2 × weekly helped maintain patency and therefore can be recommended (Extrapolated evidence from adult studies rated as LoE 2−, RG 0, conditional recommendation for, strong consensus)**
R 10.28	**Routine use of heparin has been shown to be effective in prevention of PICC occlusion in newborns, but since the potential risks have not been defined, its routine use cannot be recommended (LoE 3, RG 0, recommendation for research, strong consensus)**
R 10.29	**Recombinant tissue plasminogen activator or urokinase shall be used to unblock a catheter (LoE 1+, RG A, strong recommendation for, consensus)**
R 10.30	**There is insufficient evidence to advocate the prophylactic use of anticoagulants in children receiving home parenteral nutrition to reduce catheter related thrombosis, occlusion and infection (LoE 3, RG 0, strong recommendation against, strong consensus)**

Catheter-related thrombus occurs at the CVC tip and where the CVC enters the vein wall. Thrombus can lead to catheter blockage or

thromboembolism. The pediatric and adult literature reports a wide range of catheter-related thrombus formation (often subclinical), from 0.4% to 61% [104] (LoE 2−). Risk factors include length of catheter, low ratio of catheter and vessel diameter, and long indwelling time. Valved and tunneled catheters (i.e. Groshong) were expected to prevent thrombus formation at the tip by preventing backflow of blood into the lumen; this was not confirmed in clinical practice [105,106] (LoE 1−). CVC are the most frequent cause of venous thromboembolism and are responsible for over 80% of thromboembolism in newborns and 40% in other children [107]. CVC thrombosis is one of the most clinically significant complications of PN [107,108] (LoE 2+). Risk factors for thrombosis include endothelial damage during catheter placement, blood vessel occlusion, low flow states, blood stasis, turbulent flow, hyperviscosity or hypercoagulability, catheter composition, and characteristics of patients and infusates [109,110] (LoE 3). Adult oncology patients are known to be at high risk of CVC related thrombosis. In a large trial involving 1590 such patients, randomization was to no warfarin, warfarin at fixed dose, or warfarin to maintain an international normalized ratio between 1.5 and 2.0 [111]. There was no demonstrable reduction in symptomatic catheter related or other thromboses in patients given warfarin (LoE 1+). Schoot et al. [112] reviewed three randomized controlled trials and three controlled clinical trials of systemic treatment (low molecular weight heparin, antithrombin supplementation or low dose warfarin) and found no significant effects compared with no intervention in preventing venous thromboembolic events in pediatric cancer patients with tunneled CVC, and no differences in adverse events. In an investigation of the role of prophylactic anticoagulation in children receiving home PN, Vegting et al. [113] compared outcomes with retrospective data from a time when their patients did not receive this treatment. Sixteen children received low molecular weight heparin (nadoparin) and two vitamin K antagonists. CVC related thrombosis developed in 9 (33%) of patients with no prophylaxis, and 1 (6%) of patient with prophylaxis. Cumulative five-year thrombosis free survival was 48% and 93% respectively. Per 1000 PN days, CVC occlusion for non-prophylaxis and prophylaxis patients were 2.6 and 0.1, and for CRBSI 4.6 and 2.1. No complications (including bleeding) were observed with anticoagulation.

Heparinisation has been suggested as a way of prolonging CVC patency as well as reducing the risk of thrombosis and embolism [114,115] (LoE 2+); there is little new evidence since the first edition of these PN guidelines. Heparin is a glycosaminoglycan with anticoagulant effects mediated through its interaction with antithrombin III, accelerating its ability to inactivate coagulation enzymes (thrombin, factor Xa and factor IXa) [116]. Giving heparin during PN has the following theoretical advantages:

1. Anticoagulant action − besides reducing CVC fibronectin deposition, heparin makes the catheter hydrophobic, giving it a negative charge, both effects potentially influencing catheter thrombogenicity [109,117,118].
2. Prevention of infection − a thrombus or the biofilm in the internal lumen of the catheter may serve as a nidus for microbial colonization [119,120]. Heparin bonded catheters are reported to decrease bacterial adherence [121] as well as lowering the incidence of positive blood cultures, possibly by lowering the incidence of thrombus [109], or reducing the number of organisms attached to the surface of the catheter [117].
3. Activation of lipoprotein lipase − given in infusion, heparin also activates lipoprotein lipase and increases lipolysis and re-esterification of infused triglycerides, but has no effect on lipid oxidation and net energy gain [122–125].

There are, however, potential disadvantages:

1. Bleeding, thrombocytopenia, allergic reactions, osteoporosis, all of which may result in harm [116,126–128] (LoE 2+); in premature newborns who are unique in their resistance and sensitivity to heparin [129], there may be an increased risk of intraventricular hemorrhage [130] (LoE 2+). Both low molecular weight heparin and heparin when used as a catheter coating are associated with these complications, and the risk is even higher if unfractionated heparin is given [127,131,132] (LoE 1−).
2. Destabilization of lipid emulsions − calcium and heparin can destabilize lipid emulsions so that coalescence of fat droplet occurs with lipid emboli [133]. This is unlikely to be a problem if low heparin concentrations are used (0.5–1.0 U/mL) (LoE 2−) and is reduced if mixing of lipid emulsion and PN solution occur as close to the CVC as possible, and by co-administration of vitamin preparations [134] (LoE 2−).

Unresolved questions in relation to heparin include whether to use or not; if yes − how much, and whether to give as a flush or infusion? In practice there is considerable variation [135–141] with, for example, flushes given from twice a day to once every three weeks. Boluses in children often contain 200–300 U of heparin, and for infants weighing <10 kg, a dose of 10 U/kg is frequently used [131]. In a meta-analysis evaluating the benefits of heparin prophylaxis (3 U/mL in PN solution; 5000 U every 6–12 h flush or 2500 U of low molecular weight heparin subcutaneously) the risk of CVC thrombosis was significantly reduced. Although bacterial colonization was also reduced, no reduction in the rate of catheter related infection was seen [142] (LoE 1−; adult studies). Only one of these 11 studies involved children; in this randomized cross-over study, there were no difference in the incidence of blocked catheters or other complications comparing twice daily flushes with heparin with once weekly saline [136] (LoE 2−). Another randomized double-blind study in children compared saline infusion with or without 1 U/mL heparin and found no significant effect on catheter patency [143] (LOE 2−), although there was a trend to fewer blockages in the heparin group. Neither study was sufficiently powered to draw firm conclusions. In a study of implantable venous access devices in adult cancer patients, randomization was to saline flush or heparin saline (100 U/mL) [144]. The device was flushed before and after blood sampling, at the end of IV therapy, after blood transfusion or PN, or every eight weeks if not in use. No differences were found in frequency of port malfunction or sepsis (LoE 1−). Conway et al. performed a systematic review of CVC flushing in pediatric oncology patients [145]. Once daily flushing of Broviac/Hickman catheters (when not in use for infusing fluids) with 10 U/mL heparin was widely used but with little evidence to support. A Cochrane review in adult patients comparing heparin with normal saline flushes found no convincing difference in maintaining CVC patency [146]. After a change in practice, Rosenbluth et al. [147] explored the effect of using 100 U/mL v 10 U/mL heparin solution for flushing implantable vascular ports in pediatric oncology patients, and found no difference in complication rates.

A systematic review on the prophylactic use of heparin for prevention of complications in PICC for newborns by Shah et al. [148] indicated that use of heparin decreased the frequency of CVC occlusion but studies were not adequately powered to assess the potential risks (LoE 1−). Subsequently a trial was performed showing that use of 1 U/mL heparin was not associated with any differences with respect to blocked or infected catheters, hypertriglyceridaemia, hyperbilirubinaemia, coagulopathy or intraventricular hemorrhage [149] (LoE 2+). It seems unlikely that use of heparin (with the aim of maintaining catheter patency in newborns

and infants) has any impact on risk of thrombosis [150,151] (LoE 4). In a recent Cochrane review comparing heparin-bonded and non-heparin bonded CVC [152], two eligible studies were included. The mean duration of CVC use was only one week, and there was no difference in catheter related thrombosis. One study showed a significant reduction in CVC occlusion, CRBSI and CVC colonization.

Baskin et al. reviewed the management of catheter occlusion or thrombosis [153]. For blocked central venous infusion devices, a double blind randomized trial demonstrated the superiority of urokinase (5000 U/mL) via the catheter lumen over placebo with patency restored in 54% and 30% of catheters [154] (LoE 1+). Other than this study there is little data to support evidence−based recommendations for unblocking CVC. Van Miert and colleagues found seven studies that investigated different strengths of thrombolytic and anticoagulant drug interventions for treating catheter occlusion thought to be caused by thrombus [155]. The quality of evidence was low but urokinase appears to be more effective than placebo in restoring patency. Following a review of the adult and paediatric literature on management of CVC occlusion and CVC related thrombosis, Giordano et al. recommended that either tissue plasminogen activator or urokinase be used for unblocking thrombosed CVC. (LoE 2++) [156].

6. Hygiene and antisepsis on CVC insertion and during subsequent care

R 10.31	**Appropriate hand hygiene procedures should be followed before accessing the intravascular device or the insertion site (Extrapolated evidence from adult studies rated as LoE 1+, RG B, strong recommendation for, strong consensus)**
R 10.32	**Before insertion of an intravascular device and for post-insertion site care, clean skin should be disinfected with 2% chlorhexidine solution in 70% isopropyl alcohol (Extrapolated evidence from adult studies rated as LoE 1, RG B, strong recommendation for, strong consensus)**
R 10.33	**Antiseptic solution should remain on the insertion site and be allowed to air dry before catheter insertion or dressing application (GPP, strong recommendation for, strong consensus)**
R 10.34	**Due to potential side effects, skin antisepsis with chlorhexidine in infants younger than two months cannot be recommended (LOE 2−, RG 0, conditional recommendation against)**
R 10.35	**Catheter connectors, ports and hubs should be disinfected before accessing, preferably with 2% chlorhexidine solution in 70% isopropyl alcohol (LoE 2+, RG B, strong recommendation for, strong consensus)**

Migration of microbes from the skin surrounding the insertion site is the commonest route for catheter colonization and subsequent infection in short-term CVC [157]. In tunneled CVC the most important source are direct contacts with contaminated hands of health care providers, contaminated devices and fluids [158]. Therefore, appropriate hand, skin and catheter hygiene on insertion and on all subsequent contacts before, during and after CVC manipulations, cleansing, setting up the PN infusion and dressing exchange are crucial for prevention of infectious complications. How to perform hand hygiene, regarded as the most scientifically sound and cost-effective method for infection prevention, is described elsewhere [7,45,159] (LoE 1+).

Chlorhexidine-based antiseptic solutions, particularly as 2% chlorhexidine gluconate in 70% isopropyl alcohol, have been confirmed in adult patients as the most effective way of removing micro-organisms from the skin surface before catheter insertion and during subsequent catheter care [84,160,161] (LoE 1+). Pediatric studies have considered the possible side effects of systemic chlorhexidine absorption and skin irritation in preterm babies and critically ill newborns. In their pilot trial, Garland et al. did not identify contact dermatitis as an important problem. However, chlorhexidine was present in the blood of five out of ten treated infants after the first application and in seven of ten patients at some time during the study [162]. Visscher et al. reported that skin erythema and dryness occurred in their NICU patients most frequently when chlorhexidine was used in conjunction with an adhesive dressing [163], and Andersen et al. found erythema present only in preterm infants with BW less than 1000 g (4/36 study neonates − 11%) [164]. Therefore, the use of chlorhexidine in infants younger than two months of age is not recommended on the basis of the present evidence, and awaits further studies (LoE 2−). With the aim to prevent the skin damage, aqueous solution of octenidin has been used and recommended in some European countries for children younger than 2 months [165]. However, it is well documented that water based solutions are less efficacious than alcohol-based products [166], and the evidence to support the aqueous solution of octenidin in preterm neonates for successful skin antisepsis is almost non-existent [167]. Moreover, a recent survey on the use of octenidin in German NICU has documented that skin complications were also frequent (reported in 27% of patients), and that their prevalence did not differ with respect to the type of octenidin solution used (aqueous *vs.* octenidin + phenoxyethanol *vs.* alcohol-based octenidin product) [168].

Catheter connectors, ports and hubs are important entry sites for intraluminal contamination, and should therefore be accessed in a sterile way and disinfected prior to access. Besides studies in adult patients, two recent pediatric trials showed that addition of 2% chlorhexidine to 70% isopropanol resulted in significantly decreased number of positive blood cultures compared to disinfection with 70% alcohol only [169,170] (LoE 2+).

7. Dressing methods

R 10.36	**Both sterile gauze with tape and transparent semi-permeable polyurethane dressing can be used to cover the catheter insertion site (LoE 3, RG 0, conditional recommendation for, strong consensus)**
R 10.37	**Sterile gauze dressing is preferable if the catheter site is bleeding or oozing (GPP, conditional recommendation for, strong consensus).**
R 10.38	**For short term CVC, site dressings should be replaced every 2 days for gauze dressing, and every seven days for transparent dressing (LoE 2−, RG 0, conditional recommendation for, strong consensus)**
R 10.39	**A dressing should be changed sooner if it becomes damp, loosened or soiled (GPP, strong recommendation for, strong consensus)**
R 10.40	**A tunneled CVC with a well-healed exit site does not require dressing to prevent dislodgement, however, in children it is useful to have them looped and covered (GPP, conditional recommendation for, strong consensus)**
R 10.41	**Chlorhexidine-impregnated dressing should be considered in patients older than two months with short-term catheters who are at high risk for infection (LoE 2+, RG B, strong recommendation for, strong consensus)**
R 10.42	**Topical antimicrobial treatment at the insertion site cannot be routinely used as it may promote fungal infection, antimicrobial resistance and damage the surface of the catheter (LoE 3, RG 0, strong recommendation against, strong consensus)**
R 10.43	**Children with well-healed tunneled catheters may be allowed to swim, provided that a water resistant dressing is used to cover the whole catheter. Immediately after swimming the catheter exit site should be cleaned and disinfected, and the dressing changed (GPP, conditional recommendation for, strong consensus)**

The purposes of a dressing are to secure the CVC, protect it from external contamination, and prevent trauma and dislodgement. Traditionally, the CVC insertion site was dressed with dry sterile gauze and tape. This method gave way to a transparent dressing

composed of a thin polyurethane membrane coated with a layer of acrylic adhesive. Potential advantages include improved security, visibility of the insertion site, provision of a barrier to colonization, and therefore, less frequent need for dressing changing. However, studies have indicated that transparent polyurethane dressing may increase skin surface humidity resulting in increased colonization of the insertion site and of the catheter. To enable better evaporation, highly permeable polyurethane dressings have been developed. Numerous studies have examined the differences between dressing regimens. A recently updated Cochrane Systematic Review by Webster J et al. [161], summarized the results of RCT in hospitalized children and adults that evaluated the effect of the dressing type on CVC-related infection, catheter security, tolerance and dressing condition. Six studies were included, four of which compared gauze and tape to transparent polyurethane dressings, while two compared different types of polyurethane dressings. With respect to CRBSI and other outcomes there were no differences between the highly and less permeable transparent polyurethane dressings. However, when compared with sterile gauze and tape, a four-fold increase in CRBSI was found with use of polyurethane dressing (OR 4.19). Despite this apparently large difference in favor of gauze and tape, the authors commented that the trials were small and of poor quality, with a high risk of bias and wide confidence intervals (95% CI 1.02–17.23) such that better quality research would be required to confirm this finding [171] (LoE 1−).

Optimum frequency of dressing changes for short-term CVC is another unresolved issue. Based on the evidence summarized elsewhere, it has been suggested that gauze dressings are exchanged every 2 days and transparent dressings at least every 7 days [45] (LoE 2−). However, a recent Cochrane review suggested that evidence on the frequency of dressing changes is inconclusive with respect to the frequency of catheter-related infection, mortality or pain [172].

Recently published evidence-based recommendations, reviews and meta-analyses summarized the evidence for the use of chlorhexidine-impregnated dressings both in adult [7,45] and pediatric patients [45,84,173], concluding that they are effective in reducing contamination of the catheter insertion site and the tip (LoE 1+). Moreover, subsequent randomized trials in adult patients have shown that chlorhexidine impregnated sponge dressings also decrease the incidence of CRBSI [174,175]. With respect to pediatric patients, a substantial risk of contact dermatitis at the dressing site limits their use in very low birth weight infants, as has already been addressed in the previous edition of this guideline [176] (LoE 1+). Since the chlorhexidine impregnated sponge is designed to release the antiseptic material onto the skin maximally in the first three days, followed by a slower release within the next week, this dressing type is recommended for use with short term CVC [7,45].

Children on long-term home PN and their families are restricted in many ways. They should be encouraged to undertake normal daily activities whenever possible as long as this does not pose an increased risk. Recreational swimming including submerging the well healed tunneled CVC in water would be a welcome activity, however, according to a recent review which aimed to evaluate the risk of catheter-related infections after swimming, the existing evidence is of low quality and cannot support a recommendation that swimming with tunneled CVC is safe [177] (LoE 3). In the same article, the authors investigated the current practice of home PN programs in the United States. Only 3/16 home PN programs that responded to the survey did not allow swimming of any sort. The others differed with respect to allowing swimming in the ocean and private pools only, or including hot tubs, etc. Instructions on the procedures to be followed before and after swimming were also inconsistent; most recommended the use of a transparent dressing to cover the whole catheter during swimming, and immediately after swimming to clean the site and to change the dressing [177] (LoE 3).

8. Multimodal strategies for prevention of CVC-related complications

R 10.44	**Regular training and education of healthcare staff with respect to catheter insertion and maintenance should be recommended (LoE 2+, RG B, strong recommendation for, strong consensus)**
R 10.45	**Multimodal protocols for health care providers, aiming to standardize clinical practice on insertion and maintenance of the intravascular devices, should be developed and regularly audited (LoE 2+, RG B, strong recommendation for, strong consensus)**

Most of the guidelines identify and address scientific evidence on single topics. Recently, multimodal protocols (“bundles”) have been developed within hospitals in which different strategies are applied together to improve clinical performance and compliance with the guidelines. Such “bundles” provide instructions on who should have access to intravascular devices, methods of staff education and training, procedures on insertion and catheter maintenance, etc. There is good evidence in adults [178–180] and in children [181,182] although coming mostly from “before and after” studies, that standardization of catheter related care results in clinically relevant and persistent reduction in the incidence of complications (LoE 2+).

Conflict of interest

None declared.

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