

Consistency between guidelines and reported practice for reducing the risk of catheter-related infection in British paediatric intensive care units

Katie Harron¹, Geethanjali Ramachandra², Quen Mok², Ruth Gilbert¹ on behalf of the CATCH team*

1 MRC Centre of Epidemiology and Child Health. UCL Institute of Child Health, London, UK

2 Paediatric Intensive Care Unit, Great Ormond Street Hospital, London, UK

Correspondence to: Dr Quen Mok, Paediatric Intensive Care Unit. Great Ormond Street Hospital UK. Telephone +442074059200, Facsimile: +442077626830 Email: mokq@gosh.nhs.uk

ABSTRACT

Purpose: Optimal strategies for reducing catheter-related blood stream infection (CR-BSI) differ for adults and children. National guidelines do not make child-specific recommendations. We determined whether evidence explained inconsistencies between guidelines and reported practice in Paediatric Intensive Care Units (PICUs).

Methods: We conducted a survey of eight interventions for reducing CR-BSI in all 25 British PICUs, 2009. Interventions were categorised as requiring child-specific evidence, generalisable to adults and children, or organisational recommendations.

Results: 24/25 PICUs responded.

For child-specific interventions, practice diverged from guidelines for “Insert into subclavian/jugular veins” (18 PICUs frequently used femoral veins, supported by observational evidence for increased safety in children). Practice reflected guidelines for: “Use standard but consider antimicrobial-impregnated CVCs for high-risk patients” (14 used standard only, 3 used standard and antimicrobial-impregnated despite no RCT evidence for antimicrobial-impregnated CVCs in children, 7 used heparin-bonded for some or all children); “Use 2% chlorhexidine for skin preparation” (20 PICUs); “Avoid routine CVC replacement” (20 PICUs).

For generalisable interventions, practice was consistent with guidelines for “Administration set replacement” (21 PICUs) but deviated for “Maintenance of CVC asepsis” (11 PICUs used alcohol due to inconclusive evidence for chlorhexidine). Practice diverged from guidelines for organisational interventions: “Train healthcare workers in CVC-care” (9 PICUs); “Monitor BSI rates” (8 PICUs).

Conclusions: Guidelines should explicitly address paediatric practice and report quality of evidence and strength of recommendations. Organisations should ensure doctors are trained in CVC-insertion and invest in BSI monitoring, especially in PICU. Type of CVC and insertion site are important gaps in evidence for children.

Key Words: Central venous catheter (CVC), infection, guidelines, paediatric

Central venous catheters (CVCs) are widely used in the NHS with an estimated 238,000 inserted each year [1]. CVCs are associated with an increased risk of nosocomial blood stream infection (BSI), an important cause of mortality, morbidity, increased length of stay and substantial extra cost for paediatric patients [2-6]. An estimated 70% of nosocomial BSI in Paediatric Intensive Care Units (PICU) is caused by CVCs, with PICUs having the second highest rate of nosocomial BSI of all specialties (7.9 BSI per 1000 patient-days) [7].

Evidence from cohort studies and time series analyses shows that improving multiple elements of CVC insertion, access and maintenance can successfully reduce the rates of catheter-related BSI (CR-BSI) in PICU [8-11]. Maintenance care bundles have been found to be even more important than insertion care bundles for reducing CR-BSI in the paediatric setting [12]. Since 2005, campaigns to reduce CR-BSI rate across all specialties have been launched in the UK, including the Department of Health's (DoH) *Saving Lives* care bundle based on the epic2 guidelines (National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England), and the Matching Michigan scheme (<http://www.nrls.npsa.nhs.uk/matchingmichigan/>), based on a successful evidence-based intervention in Michigan ICUs [13-15].

The DoH guidelines apply to all patients, whereas US guidelines recognise the specific considerations needed for the prevention of CR-BSI in children [16, 17]. For example, CVCs are more difficult to insert in children compared with adults due to smaller veins and they are often left in for longer periods of time due to difficulties in venous access [11]. In addition, the femoral vein is considered to be safer in children for emergency CVC insertion.

We hypothesised that divergence between national guidelines and reported practice in the UK might be explained by evidence specific to the paediatric setting. We selected eight interventions to reduce CR-BSI, and grouped interventions into those requiring paediatric specific evidence, those where recommendations could be generalised across adult and paediatric populations, and non-clinical recommendations that require implementation at an organisational level.

Methods:

We developed a 20-question survey about interventions to reduce CR-BSI and current CVC practice, including four open questions on factors impacting on infection control in PICUs and estimated rates of bacteraemia (available from the authors). The questionnaire was piloted on four clinicians prior to sending by email or post to a designated consultant at each of the 25

PICUs in the Paediatric Intensive Care Audit Network (PICANet) in Great Britain. Repeated requests were made to non-responders and responders with missing data. Responses were collected between January and October 2009.

We defined interventions that required child-specific evidence, according to the principles of the Cochrane Applicability and Recommendations Methods Group (<http://armg.cochrane.org>), as those where physiological or technical reasons cause different benefits or harms, where different and identifiable factors may cause effect modification, or where clinically important differences in absolute risk exist, in children compared with adults. We classified four of the eight interventions as requiring child specific evidence, two as being generalisable to children and adults, and two as organisational interventions requiring evidence comparing teams or hospitals (see Table 1). Categorisation was implemented post data collection.

Table 1: Guidelines and categorisation for eight interventions

Intervention	Guideline [13, 14]	Categorisation
1) Insertion site	Use subclavian or internal jugular veins – avoid femoral.	Child-specific
2) Type of CVC	Use standard CVC but consider antimicrobial impregnated catheter if duration 1 to 3 weeks or risk of CR-BSI high.	Child-specific
3) Skin preparation	Use 2% chlorhexidine gluconate in 70% isopropyl alcohol and allow to dry.	Child-specific
4) Avoid routine catheter replacement	Check if still required daily.	Child-specific
5) Administration set replacement	Replace administration set following total parenteral nutrition – after 24 hours (72 hours if no lipid). With other fluid sets – replace after a maximum of 72 hours.	Generalisable
6) Maintenance of CVC asepsis	Use aseptic technique and swab ports or hub with 2% chlorhexidine gluconate in 70% isopropyl alcohol prior to accessing the line for administering fluids or injections.	Generalisable
7) Training in CVC care	Healthcare workers caring for a patient with a central venous access device should be trained and assessed.	Organisational
8) Monitor BSI rates	Monitor BSI rates to identify lapses in infection-control practices.	Organisational

For child-specific interventions, guidelines were classified as consistent with evidence if the guideline followed the best available evidence for children. All other guidelines were classified as consistent with evidence if the guideline followed the best available evidence. Consistency between reported practice and guidelines was categorised as a) majority of PICUs reporting practice consistent with guidelines, b) majority of PICUs reporting practice diverging from guidelines, or c) majority of PICUs reporting practice diverging from guidelines but consistent with best available evidence. For intervention 2) Type of CVC, we determined that practice was consistent with guidelines if PICUs followed the primary recommendation (use standard) or both the primary and secondary recommendations (use standard / consider antimicrobial-impregnated).

The guidelines evaluated were those from the DoH *Saving Lives* care bundle and the epic2 guidelines. Guidelines were appraised by a search of all evidence referenced within their documentation [13, 14]. For child-specific interventions, we updated the reported searches by searching PubMed using search terms and synonyms for child, paediatric, intensive care and individual interventions. To evaluate the best available evidence underpinning guidelines, we classified studies into randomised controlled trials (RCTs) and observational studies. For the organisational interventions “Training in CVC care” and “Monitor BSI rates”, RCTs may not be available and so we accepted observational evidence for these interventions. We evaluated the quality of all evidence using standard criteria for internal validity [18].

Results: Responses were received from 24 of the 25 PICUs (96%). The majority of units estimated that 51-75% of emergency and 76-100% of post-operative admissions required a polyurethane CVC during their admission to PICU. Further results relating to each intervention are shown in Tables 2, 3 and 4.

TABLES 2-4 HERE

Thirteen PICUs reported a decline in nosocomial bacteraemia over the preceding two years. In response to being asked for any aspects of infection control considered to have had a significant impact on BSI in patients with a CVC, PICUs stated that factors contributing to declining infection rates included strict adherence to insertion asepsis, the introduction of CVC care bundles, use of 2% chlorhexidine, use of heparin-bonded or antibiotic-impregnated CVCs, nurse training, early removal of CVCs when not required, and auditing of hand-hygiene.

Table 2: Evidence, reported practice and guidelines requiring child-specific evidence for clinical interventions

✓ = Reported practice consistent with guidelines, X = Reported practice diverged from guidelines, † = Reported practice diverged from guidelines but consistent with best available evidence.

	Reported Practice	Evidence	Consistency	
1. Insertion site	In emergency patients, the femoral site was used more than 50% of the time in 18/21 PICUs. In post-operative patients, the internal jugular site was used more than 50% of the time in 12/20 PICUs	<p>Systematic reviews found no RCTs comparing subclavian, jugular and femoral sites for CR-BSI or venous thrombosis in children (one RCT favoured the subclavian site compared with the femoral for adults) [19-21].</p> <p>In children, observational studies suggest a similar risk of infection with femoral and non-femoral catheters, increased safety with femoral insertion sites compared with subclavian or jugular sites and greater ease of insertion in emergency situations [22-24].</p>	<p>Evidence: RCT evidence of benefit for adults, weak observational evidence of harm for children.</p> <p>Guideline: Does not follow best available evidence for children.</p> <p>Practice: Majority (18/21) of PICUs were consistent with best available evidence but inconsistent with guidelines.</p>	†
2. Type of CVC	<p>Standard CVCs were used for all patients in 14/24 PICUs. A further 3/24 PICUs used standard and antibiotic-impregnated CVCs.</p> <p>Heparin-bonded CVCs were used for all patients in 3/24 PICUs. A further 4/24 PICUs used standard and heparin-bonded CVCs.</p>	<p>Systematic reviews of RCTs show antibiotic-impregnated CVCs significantly reduce CR-BSI in adults, but there are no RCTs of antibiotic-impregnated CVCs in children [25].</p> <p>RCTs and cost-effectiveness studies have shown large benefits of heparin-bonded CVCs regardless of risk status [25].</p>	<p>Evidence: Strong RCT evidence of benefit for antibiotic-impregnated CVCs in adults but a lack of evidence for children. Strong RCT evidence of benefit for heparin-bonded CVCs in children.</p> <p>Guideline: Does not follow best evidence for children.</p> <p>Practice: Majority of PICUs (17/24) were consistent with guidelines. 3/24 PICUs consistent with best available evidence contrary to the guidelines.</p>	✓

<p style="text-align: center;">3. Skin preparation</p>	<p>19 and 20/24 responders in emergency and postoperative admissions respectively used 2% chlorhexidine to clean the skin prior to CVC insertion.</p> <p>Practice for neonates was not separately recorded.</p>	<p>A meta-analysis of RCTs indicated that use of chlorhexidine reduced the risk of CR-BSI by an estimated 49% for short-term catheterisation compared with povidone-iodine [26, 27].</p> <p>Evidence for paediatric patients is lacking [28]. One RCT in neonates found chlorhexidine gluconate more effective than povidone-iodine in reducing CVC tip colonization in NICU, and an observational study found chlorhexidine to be more effective than povidone-iodine in children on long-term haemodialysis [29, 30]. Cases of skin irritation have been reported with 2% chlorhexidine for preterm and very low birth weight neonates [31, 32].</p>	<p>Evidence: Strong RCT evidence of benefit for adults, weak RCT evidence of benefit for children and observational evidence of harm for preterm and very low birth weight babies.</p> <p>Guideline: Follows best evidence for adults and children, but does not address harms for neonates.</p> <p>Practice: Majority of PICUs (20/24) were consistent with guidelines and best available evidence. Consistency with evidence is unknown for neonates.</p>	✓
<p style="text-align: center;">4. Avoid routine replacement</p>	<p>CVCs were not routinely replaced after seven days by 20/24 PICUs unless under special circumstances. CVCs were routinely replaced after seven days in 4/24 PICUs. Only 12/24 responders reported a system for daily recording of the need for CVC.</p>	<p>Systematic reviews of RCTs show no benefit of routine replacement of CVCs to reduce infection in children or adults [33, 34].</p>	<p>Evidence: Strong RCT evidence of no benefit of routine replacement for adults or children.</p> <p>Guideline: Follows best evidence for adults and children.</p> <p>Practice: Majority of PICUs (20/24) were consistent with evidence and guidelines.</p>	✓

Table 3: Evidence, reported practice and guidelines generalisable to adults and children for clinical interventions

✓ = Reported practice consistent with guidelines, X = Reported practice diverged from guidelines, † = Reported practice diverged from guidelines but consistent with best available evidence.

	Reported Practice	Evidence	Consistency	
5. Administration set replacement	Administration sets for total parenteral nutrition were reported to be changed every 24 hours by almost all (21/24) responders, every 48 hours by 1/24, every 72 hours by 1/24, and routinely less often than 72 hours by 1/24. Administration sets for fluids and medications were reported to be changed every 24 hours by 20/24 responders, every 48 hours by 1/24 and every 72 hours by 3/24.	A Cochrane review found that administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours, and administration sets which contain lipids should be changed every 24 hours, with no differences between children and adults [35].	<p>Evidence: Strong RCT evidence of benefit.</p> <p>Guideline: Follows best available evidence.</p> <p>Practice: Majority of PICUs (21/24) were consistent with evidence and guidelines.</p>	✓
6. Maintenance of CVC asepsis	12/24 PICUs used 2% chlorhexidine in alcohol to clean hubs prior to CVC access; 1 PICU used 0.5% chlorhexidine; 11 used alcohol.	Guidelines are based on one RCT in adults that found needle-less connectors disinfected with alcohol had significantly higher rates of contamination compared with those disinfected with chlorhexidine/alcohol or povidone-iodine (69.2%, 30.8% and 41.6% respectively) [36].	<p>Evidence: Inconclusive evidence of benefit.</p> <p>Guideline: Based on inconclusive evidence.</p> <p>Practice: Half (12/24) of the PICUs were consistent with guidelines.</p>	X

Table 4: Evidence, reported practice and guidelines for organisational interventions

✓ = Reported practice consistent with guidelines, X = Reported practice diverged from guidelines, † = Reported practice diverged from guidelines but consistent with best available evidence.

	Reported Practice	Evidence	Consistency	
7. Training in CVC care	A small proportion of responders held specific training sessions on CVC insertion for doctors (9 and 7/24 responders for emergency and post-operative admissions respectively), whilst 22/23 responders had dedicated training sessions on CVC care for nurses.	The effectiveness of training in insertion and maintenance of CVCs for reducing complications relating to CVCs has been well documented through observational studies. Before-after studies have shown systematic interventions of education in combination with care bundles reduced infection rates by 23-37% in paediatric settings [9, 37].	<p>Evidence: Strong observational evidence for benefit.</p> <p>Guideline: Follows best available evidence.</p> <p>Practice: Less than half (9/24) of the PICUs were consistent with available evidence and guidelines for doctors; the majority (22/24) were consistent for nurses.</p>	X
8. Monitoring BSI	Six PICUs monitored BSI rates by catheter-day (ranging from 0-6.3 per 1000 catheter-days) and a further 2 PICUs monitored BSI per patient (0.5-11.8% of patients). There was no routine recording of BSI rates in the remaining 16/24 PICUs. Nine responders stated that rates had remained the same over the past two years; 13 thought rates had decreased; the remaining 2 did not know.	Guidelines are based on the National Nosocomial Infections Surveillance (NNIS) at the Centers for Disease Control and Prevention (CDC) [38]. This system has shown substantial improvements in infection control within NNIS hospitals. Surveillance systems have been shown to improve quality of care and to be critical for assessing effectiveness of interventions, although they have also been associated with higher rates of BSI in PICU [39-42].	<p>Evidence: Inconclusive observational evidence for benefit.</p> <p>Guideline: Follows best available evidence.</p> <p>Practice: Majority (16/24) of PICUs were inconsistent with best available evidence and guidelines.</p>	X

Discussion

National guidelines for reducing the risk of BSI are not child-specific, yet for certain recommendations, physiological or technical reasons mean that benefits or harms might differ in children compared with adults. For the four clinical interventions that required child-specific evidence, guidelines were supported by evidence of effectiveness, including safety in children, for only two of the interventions. Reported practice was consistent with guidelines for these two interventions. In contrast, lack of child-specific evidence on which to base guidelines explains why many PICUs choose to follow best available evidence contrary to guidelines for site of CVC insertion and type of CVC inserted. Without high quality evidence supporting these guidelines, potential benefits or harms to children are uncertain. Reported practice also deviated from guidelines for one clinical intervention that did not require child-specific evidence but for which the evidence base was poor (swab hub with 2% chlorhexidine alcohol prior to access).

Evidence from clinicians and research is needed to assess whether physiological or technical factors could lead to different benefits or harms, whether there is any evidence of effect modification of the interventions in children, and whether there are clinically important differences in the absolute risks of beneficial and/or harmful outcomes [43, 44]. Interventions based on high quality evidence in adults should not automatically be recommended for children and guidelines should be clear about areas of uncertainty and very careful when extrapolating evidence from adults to children [45].

Our findings emphasised the challenge in implementing evidence-based interventions at an organisational level, even where strong evidence already exists, such as for monitoring of BSI and staff training in CVC care [41]. Discrepancies between evidence and practice for these interventions may reflect the greater difficulties of overcoming system and organisational barriers to achieve evidence-based, institutional interventions compared with individual clinician or team-based decisions. Adoption of organisational interventions can be promoted by PICU clinicians but requires commitment from the top of the organisation and infrastructure. For example, establishing BSI surveillance could require considerable investment of staff time but measures of BSI both within and between units over time could be achieved through improving the feedback from the existing national surveillance system of BSI operated by the Health Protection Agency. This would overcome difficulties in obtaining consistent and meaningful measures for BSI rates across NHS PICUs [46].

This is the first survey conducted in the UK to assess variations in practice and adherence to multiple guidelines for reducing the risk of catheter-related infection in PICUs. The survey is limited in revealing only reported practice, although the Matching Michigan initiative may give a clearer picture of actual versus recommended practice in the future.

Our survey identified important areas of uncertainty and inconclusive evidence. Guidelines and reported practice in some PICUs diverged from best available evidence regarding the safety and effectiveness of heparin-bonded CVCs for reducing BSI. This question is currently being addressed by a large multi-centre RCT to determine the effectiveness of antibiotic-impregnated and heparin-bonded compared with standard CVCs (CATCH – CATHeter infections in CHildren <http://www.hta.ac.uk/1867>). Research is needed to compare the risk of infection with CVC insertion at femoral, subclavian or internal jugular insertion sites, to investigate safety of chlorhexidine in neonates, and to assess the optimal time for catheter replacement. Hospitals should provide infrastructure to ensure training in optimal CVC care and monitoring of infection rates in PICU as these require implementation at an organisational level or a change in hospital culture.

Acknowledgements

The authors wish to thank Roger Parslow and other members of the PICANet team for their support and the following intensivists for completing the survey form: James Fraser, Helen Fardy, Akash Deep, Duncan Macrae, Samir Latiff, Oliver Bagshaw, Iain MacIntosh, Martin Gray, Julie Freeman, Raghu Ramaiah, Mehrengise Cooper, Iain Johnstone, Ann Karimova, Samantha Jukes, Shane Tibby, Robert Yates, Andrew Magnay, John Roche, Andrew McIntyre, Steve Kerr, Josep Panisello, Jane Cassidy

*CATCH trial team: Centre PIs: Quen Mok, John Roche, Anne Karimova, P Ramnarayan, Shane Tibby, Duncan Macrae, Mehrengise Cooper, Iain Macintosh, Michelle White, Steve Kerr, Oliver Bagshaw, N Moore, Raghon Ramajah, Barbara Fulton, Jane Cassidy; Trial Steering Group: Robert Tasker, Jim Gray, Andy Vail, Derek Roebuck, Hazel Greig-Midline, Oliver Bagshaw, Shane Tibby, P Ramnarayan; Trial Management Group: Ruth Gilbert, Tracy Ball, Rachel Breen, Quen Mok, Mike Millar, Paula Williamson, Carrol Gamble, Kerry Dwan, Dyfrig Hughes, Elizabeth Draper; Statistical analyses: Carrol Gamble, Kerry Dwan, Katie Harron, Angie Wade; Independent Data Safety Monitoring Committee: Paul Ewing, Mike Sharland, Neena Modi.

Funding: This project was funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme (project number 08/13/47). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health.

References

1. Hockenhull J, Dwan K, Boland A, Smith G, Bagust A, DüNDAR Y, Gamble C, McLeod C, Walley T, Dickson R (2008) The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation. *Health Technol Assess Rep* 12(12):1-154.
2. Yogaraj J, Elward A, Fraser V (2002) Rate, risk factors, and outcomes of nosocomial primary bloodstream infection in pediatric intensive care unit patients. *Pediatrics* 110(3):481.
3. Appelgren P, Hellström I, Weitzberg E, Söderlund V, Bindslev L, Ransjö U (2001) Risk factors for nosocomial intensive care infection: a long-term prospective analysis. *Acta Anaesthesiol Scand* 45(6):710-719.
4. Urrea M, Pons M, Serra M, Latorre C, Palomeque A (2003) Prospective incidence study of nosocomial infections in a pediatric intensive care unit. *Pediatr Infect Dis J* 22(6):490.
5. Elward A, Hollenbeak C, Warren D, Fraser V (2005) Attributable cost of nosocomial primary bloodstream infection in pediatric intensive care unit patients. *Pediatrics* 115(4):868.
6. Brown R, Stechenberg B, Sands M, Hosmer D, Ryczak M (1987) Infections in a pediatric intensive care unit. *Arch Pediatr Adolesc Med* 141(3):267.
7. Nosocomial Infection National Surveillance Service (2007) Surveillance of Hospital-acquired Bacteraemia in English Hospitals, 1997-2002. Public Health Laboratory Service.
8. Bhutta A, Gilliam C, Honeycutt M, Schexnayder S, Green J, Moss M, Anand K (2007) Reduction of bloodstream infections associated with catheters in paediatric intensive care unit: stepwise approach. *BMJ* 334(7589):362-365.
9. Costello J, Morrow D, Graham D, Potter-Bynoe G, Sandora T, Laussen P (2008) Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. *Pediatrics* 121(5):915.
10. Jeffries H, Mason W, Brewer M, Oakes K, Muñoz E, Gornick W, Flowers L, Mullen J, Gilliam C, Fustar S (2009) Prevention of central venous catheter-associated bloodstream infections in pediatric intensive care units: a performance improvement collaborative. *Infect Control Hosp Epidemiol* 30(7):645-651.
11. McKee C, Berkowitz I, Cosgrove S, Bradley K, Beers C, Perl T, Winner L, Pronovost P, Miller M (2008) Reduction of catheter-associated bloodstream infections in pediatric patients: Experimentation and reality*. *Pediatr Crit Care Med* 9(1):40.

12. Miller MR, Griswold M, Harris JM, II, Yenokyan G, Huskins WC, Moss M, Rice TB, Ridling D, Campbell D, Margolis P, Muething S, Brill R (2010) Decreasing PICU Catheter-Associated Bloodstream Infections: NACHRI's Quality Transformation Efforts. *Pediatrics* 125(2):206-213.
13. Department of Health (2005) Saving Lives: a delivery programme to reduce healthcare associated infections including MRSA. Department of Health: London.
14. Pratt R, Pellowe C, Wilson J, Loveday H, Harper P, Jones S, McDougall C, Wilcox M (2007) epic2: National evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *J Hosp Infect* 65:S1-S59.
15. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C (2006) An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. *N Engl J Med* 355(26):2725-2732.
16. Harris J (1997) Pediatric nosocomial infections: Children are not little adults. *Infect Control Hosp Epidemiol* 18(11):739-742.
17. O'Grady N, Alexander M, Dellinger E, Gerberding J, Heard S, Maki D, Masur H, McCormick R, Mermel L, Pearson M (2002) Guidelines for the prevention of intravascular catheter-related infections. *Am Acad Pediatr Policy* 110(5):e51-e74.
18. Straus SE, Richardson WS, Glasziou P, Haynes RB (2005) Evidence-based medicine: how to practice and teach EBM.
19. Hamilton HC, Foxcroft D (2007) Central venous access sites for the prevention of venous thrombosis, stenosis and infection in patients requiring long-term intravenous therapy. *Cochrane Database Syst Rev*. CD 004084 DOI: 10.1002/14651858.CD004084.pub2.
20. Ruesch S, Walder B, Tramèr M (2002) Complications of central venous catheters: internal jugular versus subclavian access-a systematic review. *Crit Care Med* 30(2):454-460.
21. Merrer J, De Jonghe B, Golliot F, Lefrant J, Raffy B, Barre E, Rigaud J, Casciani D, Misset B, Bosquet C (2001) Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *Jama* 286(6):700-707.
22. Casado-Flores J, Barja J, Martino R, Serrano A, Valdivielso A (2001) Complications of central venous catheterization in critically ill children. *Pediatr Crit Care Med* 2(1):57.
23. Rey C, Álvarez F, De La Rúa V, Medina A, Concha A, Díaz J, Menendez S, Arcos M, Mayordomo-Colunga J (2009) Mechanical complications during central venous cannulations in pediatric patients. *Intensive Care Med* 35(8):1438-1443.

24. Venkataraman S, Thompson A, Orr R (1997) Femoral vascular catheterization in critically ill infants and children. *Clin Pediatr* 36(6):311-319.
25. Gilbert R, Harden M (2008) Effectiveness of impregnated central venous catheters for catheter related blood stream infection: a systematic review. *Curr Opin Infect Dis* 21(3):235-245.
26. Wang H, Huang T, Jing J, Jin J, Wang P, Yang M, Cui W, Zheng Y, Shen H (2010) Effectiveness of different central venous catheters for catheter-related infections: a network meta-analysis. *J Hosp Infect* 76(1):1-11.
27. Chaiyakunapruk N, Veenstra D, Lipsky B, Saint S (2002) Chlorhexidine Compared with Povidone-Iodine Solution for Vascular Catheter–Site Care. *Ann Intern Med* 136(11):792-801.
28. Carson S (2004) Chlorhexidine versus povidone-iodine for central venous catheter site care in children. *J Pediatr Nurs* 19(1):74-80.
29. Garland J, Alex C, Mueller C, Otten D, Shivpuri C, Harris M, Naples M, Pellegrini J, Buck R, McAuliffe T (2001) A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics* 107(6):1431.
30. Onder A, Chandar J, Billings A, Diaz R, Francoeur D, Abitbol C, Zilleruelo G (2009) Chlorhexidine-based antiseptic solutions effectively reduce catheter-related bacteremia. *Pediatr Nephrol* 24(9):1741-1747.
31. Tamma P, Aucott S, Milstone A (2010) Chlorhexidine Use in the Neonatal Intensive Care Unit: Results from a National Survey. *Infect Control Hosp Epidemiol* 31(8):846-849.
32. Mermel LA (2007) Prevention of central venous catheter-related infections: what works other than impregnated or coated catheters? *J Hosp Infect* 65(Supplement 2):30-33.
33. Mermel L (2000) Prevention of intravascular catheter–related infections. *Ann Intern Med* 132(5):391-402.
34. Cook D, Randolph A, Kernerman P, Cupido C, King D, Soukup C, Brun-Buisson C (1997) Central venous catheter replacement strategies: a systematic review of the literature. *Crit Care Med* 25(8):1417-1424.
35. Gillies D, Wallen Margaret M, Morrison Anne L, Rankin K, Nagy Sue A, O’Riordan E (2005) Optimal timing for intravenous administration set replacement. *Cochrane Database Syst Rev*. DOI: 10.1002/14651858.CD003588.pub2.
36. Casey A, Worthington T, Lambert P, Quinn D, Faroqui M, Elliott T (2003) A randomized, prospective clinical trial to assess the potential infection risk associated with the PosiFlow® needleless connector. *J Hosp Infect* 54(4):288-293.

37. East D, Jacoby K (2005) The effect of a nursing staff education program on compliance with central line care policy in the cardiac intensive care unit. *Pediatr Nurs* 31(3):182-194.
38. Centers for Disease Control (2000) Monitoring hospital-acquired infections to promote patient safety-United States, 1990-1999. *MMWR Morb Mortal Wkly Rep* 49:149-153.
39. Gaynes R, Richards C, Edwards J, Emori T, Horan T, Alonso-Echanove J, Fridkin S, Lawton R, Peavy G, Tolson J (2001) Feeding back surveillance data to prevent hospital-acquired infections. *Emerg Infect Dis* 7(2):295.
40. Zuschneid I, Schwab F, Geffers C, Rüden H, Gastmeier P (2003) Reducing central venous catheter-associated primary bloodstream infections in intensive care units is possible: data from the German nosocomial infection surveillance system. *Infect Control Hosp Epidemiol* 24(7):501-505.
41. Weber D, Sickbert-Bennett E, Brown V, Rutala W (2007) Comparison of hospitalwide surveillance and targeted intensive care unit surveillance of healthcare-associated infections. *Infect Control Hosp Epidemiol* 28(12):1361-1366.
42. Niedner MF (2010) The harder you look, the more you find: Catheter-associated bloodstream infection surveillance variability. *Am J Infect Control* 38(8):585-595.
43. Lachman P, Yuen S (2009) Using care bundles to prevent infection in neonatal and paediatric ICUs. *Curr Opin Infect Dis* 22(3):224.
44. Lee O, Johnston L (2005) A systematic review for effective management of central venous catheters and catheter sites in acute care paediatric patients. *Worldviews Evid Based Nurs* 2(1):4-13.
45. Guyatt G, Oxman A, Vist G, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann H (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336(7650):924-926.
46. Davies EG, Sharland M, Nicoll A (2003) Health protection and a new strategy for combating infection in children. *Arch Dis Child* 88(1):1-3.