The road to zero nosocomial infections in neonates: a narrative review

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REVIEW ARTICLE

The road to zero nosocomial infections in neonates—a narrative review

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Abstract

Aim: Nosocomial infections (NI) in neonates are associated with prolonged hospitalisation, adverse neurodevelopmental outcome and high mortality. Over the past decade, numerous prevention strategies have resulted in significant reductions in NI rates. In this review, we aim to provide an overview of current NI rates from large, geographically defined cohorts.

Methods: PubMed, Web of Science, EMBASE and Cochrane Library were searched for evidence regarding epidemiology and prevention of NI in neonates. Extracted studies were synthesised in a narrative form with experiential reflection.

Results: Despite the abundance of geographically defined incidence proportions, an epidemiological overview of NI is difficult to provide, given the lack of consensus definition for neonatal NI and different baseline populations being compared. Successful prevention efforts have focused on implementing evidence-based practices while eliminating outdated strategies. The most promising model for reduction in infection rates is based on quality improvement (QI) collaboratives and benchmarking, involving identification and implementation of best practices, selection of measurable outcomes and fostering a sense of community and transparency.

Conclusion: The preventative rather than curative approach forms the new paradigm for reducing the burden of neonatal infections. Despite progress achieved, continued work towards improved prevention practices is required in the strive towards zero NIs.

KEYWORDS
neonates, nosocomial infections, quality improvement

Abbreviations: ASP, antibiotic stewardship programme; BW, birth weight; CLABSI, central line–associated bloodstream infection; GA, gestational age; HH, hand hygiene; NHSN, The National Healthcare Safety Network; NI, nosocomial infections; NICHD, National Institute for Child Health and Human Development; NICU, neonatal intensive care units; OBU, open-bay unit; PQCNC, Perinatal Quality Collaborative of North Carolina; QI, quality improvement; SRU, single-room unit; VLBW, very-low-birth-weight.

1 | INTRODUCTION

Preterm infants admitted to the neonatal intensive care unit (NICU) are highly susceptible to hospital-acquired, or nosocomial infections (NI), due to impaired host-defence mechanisms, systematic and long-lasting use of invasive medical devices, prolonged hospitalisation, and concomitant medical conditions.[1] Compared to uninfected counterparts, those who experience one or more NIs during hospitalisation are significantly more likely to die. In addition, numerous studies have found late-onset sepsis to be independently associated with increased risk of moderate to severe motor impairments,[2] and lower IQ.[3,4] As such, the prognostic importance of neonatal infections relative to other comorbidities on neurocognitive outcomes are to be carefully considered in the overall infection burden. Risk adjusted costs of NICU care and duration of stay associated with bloodstream infections among very–low-birth-weight (VLBW, <1500 grams) infants have been estimated to be up to $16800[5] and 24 days per infant, respectively.[6]

Central lines, especially umbilical venous, umbilical arterial and peripherally inserted central lines are commonly used in preterm infants for nutritional support, medication administration, blood pressure monitoring and blood sampling, thereby constituting an integral component of care to infants in the NICU.[7] While essential, central lines pose a risk of central line–associated bloodstream infections (CLABSI) which are among the most common NIs encountered in the NICU.[1,7]

Because NIs are considered a preventable healthcare-associated condition, they have been subject to a great deal of attention given their high rate of short-term and long-term morbidity and mortality. Over the last decade, several successful initiatives aimed at reducing NIs, in particular CLABSIs, in NICUs have been reported including hygiene measures, central line management policies, human milk feeding, curtailment of unnecessary antibiotic use and prophylactic pharmacological interventions.[8-10] These efforts have led to substantial global reductions in CLABSI and overall NI rates across all birth weight and gestational age categories. Despite these accomplishments, further reductions or even complete elimination of NIs remain a challenge for many institutions.

We provide an overview of current NI rates from large geographically defined cohorts and show that improved neonatal outcomes are largely steered by a preventative rather than curative approach. We also discuss key successful principles and strategies used in collaborative infection prevention efforts, with a particular focus on CLABSI specific initiatives. Finally, we highlight some of the vexing and unanswered issues that remain to be solved in the 'quest for zero tolerance against nosocomial infections'.

1.1 | Epidemiological aspects of NI

Table 1 lists the incidence rates of general NIs as reported by several large, geographically defined neonatal surveillance networks over the last 15 years. Among infants born at <32 weeks gestational age (GA) and/or with a birth weight (BW) <1500 g, NI proportions range from 5.6% to 34.4% in the first 120 days of life, and are inversely related to BW and GA.[11,12] According to Boghossian et al.[13], who described the incidence of NIs in infants admitted to clinical centres of the NICHD Neonatal Research Network, 65.5% of neonates with BW of 401–500 g had at least one episode of infection compared to 32.5% neonates with BW of 751–1000 g. Aside from prematurity and low BW, other well-known risk factors for NI include high burden of invasive procedures, delayed enteral feeding, empiric antimicrobial exposure, surgery and underlying pulmonary and cardiac disease.[14-16] Moreover, given the presumed interindividual variation in risk of and response to therapy, polymorphisms in immunity-related genes may also play a role in infection risk.[13]

Key Notes

- Surveillance data from large neonatal networks have demonstrated that progress in tackling neonatal nosocomial infections has been made, although study comparability is complicated by variability in definitions and baseline populations being compared.
- Over the last decade, several successful initiatives have demonstrated that improvement in neonatal outcomes is largely steered by a preventative rather than curative approach.
- The most promising model for lasting improvement has been demonstrated through quality improvement collaboratives and benchmarking.

While essential to provision of high-quality care in neonatal units, the use of central lines has been identified as an important independent risk factor for NIs.[17] Analysis and evaluation of NICU surveillance data have yielded essential information regarding the incidence, aetiology and microbial profiles of CLABSI.[18] In a German NEOKISS analysis among preterm infants born between 2012 and 2016, median CLABSI rates were 8.62, 5.29 and 2.35 per 1000 central line days in those with a BW of ≤499 grams, 500–999 g and 1000–1499 g, respectively.[18-20] For infants weighing >2500 g, the pooled mean CLABSI rate was approximately 0.6, as indicated by the National Healthcare Safety Network (NHSN) in their 2012 annual report.[21]

Coagulase-negative Staphylococci (CoNS) are the most commonly isolated pathogens in nosocomial bacteremia, accounting for up to 77.9% and 35.7% of NIs in developed and developing countries, respectively.[22,23] CoNS are also mainly associated with CLABSI, as they are common components of normal skin flora.[4] CoNS possess less virulence properties than gram-negative bacteria and fungi, resulting in relatively lower rates of immediate infectious complications and continued speculation as to whether CoNS positive cultures represent true infection or contamination.[24,25] Other common pathogens responsible for neonatal NI include *S. aureus*, *Enterococcus* spp and *E. coli*, accounting for respectively

TABLE 1 Definitions and incidence proportions of nosocomial infections from large neonatal network studies

				Definition of NI[a]					Incidence	
Author	Country	Study population	No. of neonates	Onset	Clinical symptoms	Antibiotic treatment	Clinical infection[b]	Inclusion CoNS	Year(s)	%
Ronnestad et al.[c 32]	Norway	BW <1000 gr or 22-$27^{6/7}$ wks GA	462	>6 d	No	No	No	Yes	1999–2000	17.3
Hornik et al.[d 33]	USA (Pediatrix Medical Group)	BW <1500 gr	99,796	4–120 d	No	No	No	Yes	1997–2010	12.2
Morioka et al.[14]	Japan	BW <1,000 gr	378	>72 h	Yes	No	No	Not mentioned	2006–2008	5.6
Boghossian et al.[e 13]	USA (NICDH)	BW <401–1000 gr or 22-$28^{6/7}$ wks GA	15,178	>72 h	No	≥ 5 d	No	Yes	2002–2008	25
Leistner et al.[78]	Germany (NEOKISS)	BW <1500 gr	33,048	>72 h	Yes	No	No	Yes	2007–2011	17.4
Wojkowska-Mach et al.[f 12]	Poland (Polish Neonatology Surveillance Network)	BW <1501 gr	1243	>72 h	Yes	No	Yes	Yes	2009–2011	34.4[G]
Stoll et al.[31]	USA (NICDH)	BW <401–1000 gr or 22–28 wks GA	29,252	>72 h	No	≥ 5 d or intent to treat but death <5 d	No	Not mentioned	1993–2012	32
Escalante et al.[36]	South America (NEOCOSUR)	BW 500–1500 gr	13,821	>72 h	No	No	No	Yes	2001–2013	22.2

Abbreviations: BW, birth weight; CoNS, coagulase-negative staphylococci; d, days; GA, gestational age; gr, grams; h, hours; NI, nosocomial infection; No, number; VLBW, very low birth weight; wks, weeks.

[a]Definition NI: a positive blood culture is a prerequisite for all included studies.

[b]Pertains to culture-negative infection.

[c]Cohort comprised of extremely premature infants who received very early full milk feeding. Five of the 21 neonatal departments were academic departments.

[d]All participating units consisted of NICUs managed by large private groups of neonatologists.

[e]Reported infection rate for singleton births only.

[f]All participating units consisted of tertiary care NICUs in teaching hospitals.

[g]Infection rate constitutes number of infection episodes. Number of infants with an infection not mentioned.

1.6–17%, 2.9–13% and 0.6–11% of NIs.[25] Out of all causative microorganisms, *Pseudomonas aeruginosa* is typically associated with the highest infection-related mortality (56%), followed by *E. coli* (20%), *Klebsiella pneumoniae* (13%), *S. aureus* (12%) and *Candida* spp (7.5%).[13,25] However, the distribution of causative microorganisms differs greatly by site and hospital location and is subject to continuous change depending on local patient demographics, colonisation of the nosocomial environment, definitions and surveillance techniques, and antibiotic treatment guidelines.[24]

A longstanding conviction regarding the origin of late-onset neonatal infections is the concept of microbial translocation as a result of intestinal hyperpermeability. Whereas staphylococcal infections most often derive from the immature impaired skin barrier, evidence has shown that late-onset infections may also be preceded by colonisation of the immature neonatal gut by certain highly invasive organisms (group B *Streptococcus*, *Serratia marcescens*), underscoring the need for prevention efforts such as microbial surveillance and decontamination strategies.[26]

1.2 | Comparability and definition

Despite the growing list of studies describing the epidemiology of neonatal NIs and the increasing interest among researchers and clinicians in the development of prevention strategies, establishing a clear epidemiological overview can be a difficult task. The presence of large inter centre and inter regional variability in incidence rates limits comparability between studies (Table 1). One of the primary reasons for this variability is the lack of consensus regarding disease definition. While NIs are often defined as those occurring 72 hours after birth, a cut-off time point considered to adequately differentiate NI from infections acquired via vertical transmission (ie early-onset sepsis), others apply 48 hours or even 7 days as threshold.[27-30] Moreover, a positive culture is a prerequisite for NI in all studies, while the presence of clinical signs and symptoms is only included in a select few.[2,13,28-36] The same holds true for the criterium of ≥5 days of antibiotic treatment, predominantly utilised in studies based on large cohorts, which may have excluded CLABSI episodes that were only treated through line removal or short course antibiotic therapy. Although the lack of a uniform definition for NI remains a critical issue, we may still find some level of comparability between studies. Given that the peak incidence of hospital-acquired infections is typically between the 10th and 22nd day of life, setting the threshold at 48 or 72 hours as onset should only pose minor issues, particularly if cases that manifest on day 3 postpartum are responsible for this discrepancy.[13,37] Caution should nevertheless be taken when comparing NI definitions, especially if CoNS are excluded or require two blood samples for confirmation, as management of CoNS positive cultures will substantially influence infection rates.[38,39]

Other important elements when looking at epidemiological trends are the population used as a denominator and the type of units from which the data are collected. For example, Gkentzi et al. (2018) described the epidemiology of neonatal infections for all infants admitted to 16 Greek neonatal units while Grisaru et al. (2014) restricted their analysis to singleton, VLBW infants born between 24–32 weeks' gestation in 28 Israelian units.[28,35] Similarly, while Stoll et al.[31] reported infection rates for extremely preterm infants born at US Neonatal Research Network (NRN) hospitals with expertise in caring for high-risk infants and extensive experience in multicentre clinical trials, Cailes et al.[29] summarised neonatal infection data from the UK neonIN infection surveillance network containing both intensive care and regular neonatal units. Thus, reported cohorts range from selected preterm populations admitted to tertiary academic centres to neonates with medium-low dependency care.

Although many neonatal network studies report epidemiological associations and changes over time, the changing number of neonatal units contributing annual data to these networks form a potential source of bias, as the addition of new units with lower incidence rates may have a larger impact on overall declining infection rates.[29] Additionally, the majority of these networks rely on voluntary reporting of infections, thus risking data incompleteness and inconsistent quality of reporting.[29] Hence, a robust and pragmatic definition for nosocomial infections in neonates is needed to reduce subjective variations in care and bolster prevention efforts.

1.3 | Importance of quality improvement collaboratives and benchmarking

Despite continued improvements in perinatal care, challenges in closing the gap between quality of care and clinical outcomes persist. Quality improvement (QI) collaboratives are commonly used as a strategy to identify performance gaps and promote the translation of evidence from clinical research into practice.[40] Even though collaborative networks are difficult to establish and not widespread, there are examples of multiple neonatal networks that demonstrated improvement in NI rates through collaborative efforts. For example, unadjusted rates of late-onset infections decreased by more than 50% (from 22% in 2005 to 10% in 2014) within the Vermont Oxford Network with 756-member NICUs,[39] illustrating the level of improvement that can be achieved through dissemination of evidence-based neonatal care practices, such as the use of less invasive respiratory support methods and acknowledging the importance of human milk feeding for preterm infants.[41] Although international consensus on the definition of ventilator-associated pneumonia (VAP) among neonates and its long-term implications remains to be established, many QI initiatives have focused on reducing the burden of VAP. A nursing-led QI initiative consisting of education, bundled intervention implementation (ie strict hand hygiene, limiting circuit breaks, systematic oral care, among others) and staff empowerment led to a 71% and 31% reduction in VAP and total ventilation days, respectively.[42] These projects share certain qualities which contributed to their success including establishment of quantifiable project metrics, cultivation of multidisciplinary team efforts, use of proper data collection technology, shared learning opportunities, transparency

and respect for local cultures.[39,40] Overall, the QI model provides a much-needed basis for an effective collaborative framework for data comparison and multicentre improvement for high-risk neonatal populations. Further efforts are warranted to define practices that, when standardised across NICUs, achieve the largest and sustained improvement in outcomes.

1.4 | General prevention strategies

Even with major recent advancements in neonatal intensive care management of preterm infants, rates of late-onset infections have shown a progressive decrease, largely as a result of effective infection control measures. Below we discuss some of the most common and widely implemented prevention strategies within the neonatal population.

1.4.1 | Hand hygiene

Hand hygiene (HH) is currently recognised as the single most important measure to prevent NIs. The association between NI and the lack of HH dates back to the mid-1800s, when Ignaz Semmelweis provided the first evidence that contaminated hands play a role in the nosocomial transmission of bacteria.[43] At a maternity clinic in a Viennese hospital, Semmelweis recommended that hands be cleansed with a chlorinated lime solution prior to entering delivery suites, resulting in a reduction in the mortality rate of puerperal fever from 16% to 3%.[43] However, compliance with HH practices has been shown to be difficult to achieve and sustain. Following the implementation of a problem based, task oriented education programme, Lam et al. (2004) found an increase in HH compliance from 40% to 53% with a concomitant decrease in the NI rate from 11.3 to 6.2 per 1,000 patient-days.[44] In contrast, Raskind et al. (2007) reported a return to the baseline compliance rate (89%) after initial full compliance (100%).[45] Despite many examples of successful interventions consisting of different mixtures of education, performance feedback and periodic reminders, achieving substantial and lasting effects remains a challenge, with the most common barriers for adherence consisting of lack of familiarity or awareness, sense of self-efficacy, and shortages of time and resources. Moreover, HH compliance rates differ considerably between healthcare professionals because of differing influencing factors such as guideline knowledge, risk perception and social norms, thus illustrating the importance of designing interventions tailored to specific healthcare workers.

A relatively new measure to boost HH compliance is the 'nudge,' or friendly push to encourage desired behaviour.[45] Several nudges in health care have proved successful.[46-48] A controlled before-after trial assessing the effect of behavioural nudges displayed as posters above alcohol dispensers on the use of alcohol-based hand rub in two adult non-intensive care units found an increase in its overall use (relative risk: 1.6, 95% CI: 1.2–2.2).[45] A theoretical framework which focusses on obstacles that impede change and strategies designed at introducing an organisational and behavioural change effort is required to achieve long-lasting changes in HH practices and reduce NI rates.

1.4.2 | Human milk feeding

Another extensively studied preventive measure is the use of human milk (HM) feeding. HM contains a large number of substances and bioactive compounds with putative antimicrobial actions and numerous studies have shown that HM feedings reduce the incidence of NI in preterm and VLBW infants, even though their optimal dose and timing for maximum protection remain to be identified.[49,50] A systematic review and meta-analysis of 44 studies comparing the effect of exclusive HM versus exclusive preterm formula found evidence for a potential reduction in NI in infants born <28 weeks' gestation and/or with a birth weight <1500 g given a 100% HM diet (RR 0.71; 95% CI 0.49–1.05; n = 776), although publication bias was not assessed and the near-significant trend may have been caused by the relatively large number of comparisons performed in the study.[51] Similarly, Cortez et al. (2018) found a reduced incidence of late-onset sepsis in preterm infants fed exclusively HM compared to those fed exclusively preterm formula (9/63 vs. 19/55, $p < 0.05$).[52]

1.4.3 | Antibiotic stewardship programmes

Up to 72% of neonates admitted to the NICU are treated with one or more courses of antibiotics, with inappropriate use constituting nearly 26% of all prescriptions.[53-55] Diagnostic challenges, including the presence of nonspecific signs and symptoms and lack of blood culture sensitivity, have complicated rational antibiotic use in neonatal ICUs.[9] As a result, a growing list of epidemiologic studies have linked antibiotic overexposure to infections due to multi-resistant organisms, invasive candidiasis, necrotising enterocolitis and even late-onset sepsis, likely due to the altered colonisation of the gastrointestinal tract and consequent increased predisposition to the emergence of nosocomial pathogens.[56,57] One of the largest studies to establish this link is a retrospective cohort study from the Canadian Neonatal Network comprising >14,000 VLBW infants which found an association between prolonged antibiotic treatment (4–7 days) and a composite outcome of mortality and morbidity, including late-onset sepsis.[55] In an effort to stimulate a more prudent use of antibiotics, antibiotic stewardship programmes (ASPs) have become regular practice in many institutions. While several studies implementing different strategies to optimise the use of antibiotics in the NICU have reported successful outcomes,[58,59] sustainment remains a challenge due to large practice variation among clinicians and opposing clinical outcome metrics used to assess the impact of ASPs. Improvements in diagnostic testing as well as continuous assessment of antibiotic consumption in NICUs are needed to reduce the burden of neonatal infections.

1.4.4 | Single-room care

Over the past few years, increased attention has been given to the importance of healthcare facility design as a basic component of infection prevention. Several factors related to the hospital environment including physical layout, functional elements (sink and alcohol dispenser location) and patient-healthcare worker interaction are believed to impact nosocomial transmission of infectious organisms.[60] Moreover, other factors such as lighting, noise and separation from parents may also affect infant morbidity, particularly adverse neurodevelopmental outcomes.[61] As a result, NICU ward design has responded by gradually shifting away from open bay (OBU) to single-room units (SRU). Although studies comparing these two models of care within the NICU population are sparse, several have reported beneficial effects of the SRU, including lower age at full enteral feed, reductions in length of stay, rehospitalisation, physiological stress, apneic events and mortality, and increases in parental involvement and breastfeeding rates.[62-66] Nevertheless, evidence regarding the effect of room privatisation on infection rates remains inconclusive.[60,63] In addition, it remains unclear whether the reported changes in infection rates can be entirely attributed to the new ward design, as other factors may have confounded the results including annual variation in regional infection rates and concomitant modifications to infection control and antibiotic prescribing practices. Clearly, more evidence is needed before the single-room model of care can be broadly endorsed.

1.4.5 | Probiotics

In addition to human milk feeding, another strategy to reduce the burden of NI consists of repopulating the preterm infant's gut via enteral probiotic supplementation. However, despite numerous randomised controlled trials and systematic reviews and meta-analyses, clinical data regarding the safety and efficacy of probiotic administration remain inconsistent. A Cochrane meta-analysis of trial data (19 studies, 5338 preterm infants) found no significant reduction in nosocomial sepsis after probiotic supplementation.[67] In contrast, a meta-analysis of 37 randomised controlled trials (n = 9416) showed that probiotics lead to a significantly reduced risk of late-onset sepsis in preterm infants (RR 0.86, 95% CI, 0.78–0.95).[68] Given the wide variety of different probiotic strains and the lack of consensus regarding optimal timing, dosage and duration of supplementation, many institutions have refrained from recommending probiotics in the prevention of NI.

1.5 | Central line–associated Bloodstream Infections

Bloodstream infections are the leading cause of sepsis in the NICU, with central lines being the prevailing source.[8] Over the last decade, several successful strategies for the sustainable reduction of CLABSI in the NICU have been reported.

1.5.1 | Insertion and maintenance bundles

One of these strategies is the development and implementation of central line insertion and maintenance bundles consisting of small groups of evidence-based interventions derived from best practice recommendations categorised according to the quality of supporting evidence (Tables 2 and 3). Key components of these bundles typically include hand hygiene, maximum barrier precautions, skin antisepsis, methods for dressing assessment and change, replacement of administration sets and catheter hub disinfection.[1] Timely line removal and reduction in overall central line utilisation, both of which rely upon the early initiation of enteral feeds and rapid advancement to full enteral feeds, are also often mentioned as essential elements for reducing CLABSI.[69] The application of bundles is considered an all-inclusive approach, in which adherence to all individual components is fundamental.[1] As such, an overall compliance of ≥95% to all bundle elements is considered necessary to establish an associated reduction in CLABSI.[70] Although care bundles conceptually manage areas of uncertainty by providing a practical and dependable solution during the process of care, they may also contain a certain level of inefficiency as not all elements may be presumptively related to the bundle's objectives.

1.5.2 | Insertion and maintenance teams

Another CLABSI prevention strategy is the implementation of dedicated insertion and maintenance teams where the responsibility for all central line related activities is placed into the hands of a small group of proficient individuals, thereby reducing practice variability, the labour-intensive task of training and reskilling medical and bedside nursing staff and, ultimately, the risk of line-associated complications.[71] Holzmann-Pazgal et al.[71] investigated the effect of a dedicated central line maintenance team consisting of highly trained nursing staff in a level II-III NICU and found an overall reduction of 65% in CLABSI rate (11.6 to 4 per 1000 central line days; $p < 0.0001$). Even though introduction of the maintenance bundle prior to the formation of the maintenance team had no effect on CLABSI rates, use of the same bundle led to a significant and sustained decrease in CLABSI.[71] Evidently, the implementation of a committed group carrying out and taking responsibility for the same tasks under a consistent level of skill has the potential to lead to fewer central line related adverse outcomes.

1.5.3 | Antimicrobial-impregnated central lines and prophylactic antibiotics during central line use and upon removal

Other methods that focus on the prevention of CLABSI include the continuous administration of low dose prophylactic antibiotics during line use (either alone or in combination with parenteral nutrition) and the use of antibiotic lock solutions or antimicrobial-coated

TABLE 2 Best-practice components of central line insertion bundles

1. Use of dedicated and trained team for insertion procedure[a,b]
Designation of only trained staff who demonstrate competence for the insertion and maintenance of central lines[a]
Insertion training course including indications for central line insertion, proper sterile techniques, hand hygiene, use of maximum sterile barrier precautions and proper skin disinfection[b]
Periodic evaluation of knowledge and adherence to guidelines for those involved in central line insertion and maintenance procedures[a]
Ensuring appropriate nursing staff levels in ICUs. Observational studies suggest that an elevated patient-to-nurse ratio is associated with CLABSI[a]
2. Performance of proper hand hygiene[a,b]
Hand washing with regular soap and water or application of alcohol-based hand rub before and after contact with central line insertion sites or dressings. Palpation of the insertion site should not be performed after the application of an antiseptic, unless aseptic technique is maintained[a]
3. Utilisation of maximum sterile barrier precautions (ie mask, gown, cap, sterile gloves, sterile full body cape) [a,b]
Sterile gloves worn for the insertion of the central line[a]
Maximum sterile barrier precautions used[a]
Recommendation to wear face mask when within 3 feet of sterile field[b]
4. Availability of all necessary supplies at bedside prior to central line insertion[b]
5. Selection of best insertion site to minimise infection risk and noninfectious complications[a]
In paediatric patients, the upper or lower extremities or the scalp (in neonates or young infants) can be used as insertion site[a]
6. Preparation of skin with an antiseptic (ie 70% alcohol, CHG or PI)[b]
No recommendation can be made regarding the safety or efficacy of CHG in infants <2 months of age[a]
Recommendation to perform cutaneous antisepsis with a > 0.5% CHG solution with alcohol for the majority of patient populations prior to central line insertion or dressing changes. In case of a contraindication for CHG use, tincture of iodine or 70% alcohol can be used as alternative[a]
Application for 30 seconds and allowed to dry according to manufacturer's recommendation before central line insertion[a,b]
7. Empowerment of staff to stop non-emergent procedure when sterile conditions have been violated[b]

Abbreviations: CHG, chlorhexidine gluconate; CLABSI, central line–associated bloodstream infection; IV, intravenous; PI, povidone-iodine.

[a]Based on the 2011 Centers for Disease Control (CDC) guidelines for prevention of intravascular catheter-associated bloodstream infections.[79]

[b]Based on the California Perinatal Quality Care Collaborative Nosocomial Infection Prevention Toolkit (2007).[80]

TABLE 3 Best-practice components of central line maintenance bundles

1. Performance of daily assessment and documentation of whether central line placement or continued use is necessary as part of multidisciplinary rounds[b]
Recommendation to use a peripherally inserted central line instead of a short peripheral central line when the duration of i.v. therapy is likely to exceed 6 days [a]
Timely removal of a central line that is no longer necessary [a]
Consider removal when ≥120 ml/kg/day enteral feed is reached [b]
Consider discontinuing lipids when >2.5 g/kg/day of enteral fat intake is reached [b]
2. Performance of proper hand hygiene [a]
Hand washing with conventional soap and water or application of alcohol-based hand rub before and after palpating central line insertion sites or dressings [a]
3. Assessment of the integrity of central line dressing and insertion site daily and if necessary, performance of dressing change[a,b]
Replacement of dressing if damp, loosened or visibly soiled [a]
Daily evaluation of the insertion site by palpation through dressing to discern tenderness and by inspection if dressing is transparent[a]
In case of local tenderness or other signs of a possible CLABSI, opaque dressings should be removed and site inspected visually [a]
Removal of peripheral central lines if the patient develops signs of phlebitis, infection or in case of central line malfunction [a]
Antiseptics allowed to dry according to the manufacturer's recommendations[a]
4. Assemblance and configuration of standardised IV tubing set-up using proper antiseptic technique[a,b]
In patients not receiving blood products or fat emulsions, continuously used administration sets, secondary sets and add-in devices should be replaced no more than at 96-hour intervals, but at least every 7 days [a]
Replacement of tubing used to administer blood products or fat emulsions within 24 hours of starting the infusion. Those combined with amino acids and glucose are to be infused separately or transformed into a 3-in−1 admixture [a]
5. Scrubbing of IV tubing connector using proper antiseptic technique for at least 15 seconds[a,b]
Minimisation of contamination risk by scrubbing access port with a proper antiseptic (CHG, PI, iodophor or 70% alcohol). Port is only accessed with sterile devices [a]

Abbreviations: CHG, chlorhexidine gluconate; CLABSI, central line–associated bloodstream infection; IV, intravenous; PI, povidone-iodine.

[a]Based on the 2011 Centers for Disease Control (CDC) guideline for prevention of intravascular catheter-associated bloodstream infections.[79]

[b]Based on the California Perinatal Quality Care Collaborative Nosocomial Infection Prevention Toolkit (2007).[80]

central lines. A Cochrane review conducted by Jardine et al.[72] concluded that prophylactic vancomycin given as 5 mg/kg twice daily or in combination with parenteral nutrition at a dose of 25 microg/mL in neonates with a central line, decreased the rate of suspected or proven bacterial sepsis (RR 0.40; 95% CI 0.20–0.78), despite having no effect on mortality. More recent studies have demonstrated that elective administration of prophylactic antibiotics upon central line removal positively contributes to preventing CLABSI.[73,74]

A prospective randomised trial conducted by Hemels et al.[74] in which preterm infants were randomised to receive either two doses of cefazolin during line removal or a placebo, demonstrated that the administration of the anti-staphylococcal agent was effective in the prevention of CoNS-related sepsis. A more recent Cochrane review however regarded this trial as being underpowered and having a high risk of bias due to unclear randomisation and inadequate blinding, thereby concluding that current evidence is insufficient to recommend antibiotic administration at the time of central line removal.[75] A similar, related approach is the use of antibiotic-impregnated central lines. Despite being part of US and UK national guidelines for paediatric and adult patients at highest risk of infection,[76,77] trial evidence regarding the effectiveness of antibiotic-impregnated central lines in reducing bloodstream infection risk among newborn infants is sparse. The combination of insufficiently conclusive research outcomes regarding the true clinical benefits, and the possible development of resistant organisms resulting from the liberal use of systemic antimicrobial therapy makes that these approaches currently cannot be recommended.

2 | CONCLUSION

Nosocomial infections are a major source of morbidity and mortality in the NICU. Surveillance data from large neonatal networks demonstrate that some progress in tackling neonatal NI has been made, although study comparability is complicated by variability in definitions, baseline populations and institutional practices. Most successful prevention efforts have focused on implementing evidence-based practices, eliminating outdated strategies based on tradition, dogmas or unsystematic experience in favour of more effective ones. Perhaps the most promising model for lasting improvement has been demonstrated through QI collaboratives and benchmarking, which have achieved substantial reductions in infection rates through the identification and implementation of best practices, selection of measurable outcomes and fostering of a sense of community and transparency. Despite this progress however, continued work towards improved prevention methods is required if further progress is to be made on the road to zero neonatal infections.

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CONFLICTS OF INTEREST

None declared.

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