ORIGINAL ARTICLE

Impact of a Central Line Infection Prevention Bundle in Newborn Infants

Rowena McMullan, FRACP;[1,2] Adrienne Gordon, PhD[1,2]

OBJECTIVE. To compare central line use and central line–associated bloodstream infection in newborn infants before and after the introduction of a central line infection prevention bundle in order to determine the effectiveness of the bundle and to identify areas for further improvement.

DESIGN. Retrospective cohort analysis of prospectively collected data.

SETTING. Level 5 neonatal intensive care unit in Sydney, Australia.

PATIENTS. Newborn infants admitted to the Royal Prince Alfred Hospital Neonatal Intensive Care Unit who had a central venous catheter (CVC) inserted.

METHODS. Data regarding clinical characteristics, CVC use, and infection were collected before and after the introduction of a bundle of interventions. The bundles encompassed (1) insertion of CVC, (2) maintenance of CVC, (3) an education program, and (4) ongoing surveillance and feedback.

RESULTS. Baseline and intervention groups were comparable in clinical characteristics. The number of CVCs inserted was reduced in the intervention group (central line utilization rate, 0.16 vs 0.2, $P < .0001$). Overall CVC dwell time was reduced, resulting from significant reduction in peripherally inserted CVC dwell time (6 days [95% CI, 5.0–11.8 days] vs 7.3 days [4.0–10.4 days], $P = .0004$). Central line–associated bloodstream infections were significantly reduced, predominantly secondary to decreased peripherally inserted CVC–related bloodstream infections (1.2/1,000 central line–days vs 11.5/1,000 central line–days, $P < .0001$).

CONCLUSION. This central line infection bundle was effective in reducing CVC use, dwell time, and central line–associated bloodstream infections.

Infect Control Hosp Epidemiol 2016;37:1029–1036

Safe and reliable vascular access is a necessary part of care for sick infants in the neonatal intensive care unit (NICU). Central venous catheters (CVCs) are commonly used to provide long-term venous access. They provide critical nutrition for growth as well as a portal for other vital intravenous fluids and medications. They provide improved nutrition and avoid repeated painful procedures associated with the use of peripheral venous cannulas.[1,2] CVCs used in the NICU include umbilical venous catheters (UVCs) and peripherally inserted CVCs (PCVCs). PCVCs are inserted via a peripheral vein and threaded so that the tip of the catheter lies in a large central vein. UVCs also have the tip sited in a large central vein but are inserted via the umbilical vein.

There are a number of complications associated with CVC use, varying from minor and easily treatable to life-threatening. The most frequent complication is central line–associated bloodstream infection (CLABSI). The Centers for Disease Control and Prevention defines a CLABSI as "a primary blood stream infection in a patient that had a central line within the 48-hour period before the development of the blood stream infection, and is not related to an infection at another site."[3] The incidence of CLABSI varies widely within the population studied and definition used, but is 1.6–15 per 1,000 central line–days in NICUs in high income countries.[4–6] Incidence increases with decreasing birthweight and gestational age.[7] Infection usually occurs via skin commensals that migrate via the catheter entry site or cannula hub, the predominant causative organism being coagulase-negative *Staphylococcus*.[8,9] The umbilical stump is particularly heavily colonized, but a recent retrospective cohort analysis demonstrated that UVC CLABSI rate is similar to that in PCVC.[10] CLABSI is responsible for 69% of all late-onset infections in preterm babies.[11] Late-onset neonatal sepsis is a significant risk factor for increased mortality and prolonged hospital stays,[12] although mortality is variable and related to the implicated pathogen.[13] In those who survive, there is poorer long-term

Affiliations: 1. Department of Newborn Care, Royal Prince Alfred Hospital Women and Babies, Sydney, Australia; 2. Charles Perkins Centre, University of Sydney, Sydney, Australia.

Received February 23, 2016; accepted May 8, 2016; electronically published June 13, 2016

 0899-823X/2016/3709-0004. DOI: 10.1017/ice.2016.127

growth and developmental outcomes,[14,15] with associated increased morbidity and increasing healthcare costs.[16]

Prevention of CLABSI is a key objective for improvement of patient safety and reduction of mortality, hospital stay, and costs. Preventing and controlling healthcare-associated infection is one of the 10 Australian National Safety and Quality Health Service standards, highlighting the national commitment to these preventable infections.[17] Fortunately, CLABSI has been shown to be highly modifiable with "bundles" of health care interventions.[18,19] A bundle is defined as "a limited number of specific practices, each essential for effective and safe patient care and that, when implemented together, result in additional improvements in patient outcomes."[20] These multidisciplinary, evidence-based best practice recommendations are effective in reducing CLABSI in the NICU.[20,21]

An audit of CLABSI rates in 2012 at our institution[22] showed 8.5 CLABSI/1,000 central line-days, and 13.4/1,000 central line–days for infants less than 29 weeks' gestation. Comparative data combining rates from all the other level 5 NICUs in New South Wales over the same period using the same definition of CLABSI showed a CLABSI rate of 8.3/1,000 central line–days at less than 29 weeks' gestation.[23] The audit identified a number of areas for improvement: the implementation of standardized practices, central line policy revision, and a structured education program. Following this, a bundle of CLABSI prevention interventions was introduced. The aim of this study was to compare CLABSI rates before and after the introduction of the CLABSI prevention bundle to determine its effectiveness and to identify areas for further improvement.

METHODS

Study Setting and Design

This was a retrospective cohort analysis of prospectively collected data. Eligible infants were admitted to the Royal Prince Alfred Hospital NICU and had a CVC inserted. The study periods were January 1, 2012-December 31, 2012 (baseline) and August 1, 2013-July 31, 2014 (intervention). The bundle of interventions commenced during March-August 2013.The intervention period was chosen as the most recent fully audited data available. This hospital is a major obstetric tertiary referral center. The hospital currently averages approximately 5,500 deliveries per year and covers an inner-city, multicultural population. It provides a level 5 NICU service[24] with an average of approximately 900 admissions to the nursery each year. This study was approved prospectively by the Sydney Local Health District ethics committee.

Process and Interventions

Following the audit, a multidisciplinary team of staff with an interest in quality improvement and infection control was formed. Areas where CLABSI prevention had failed were reviewed, and solutions were proposed. These were based upon current best evidence, and largely upon the recommendations from the Provincial Infectious Diseases Advisory Committee, Ontario.[25] A fishbone diagram was used to highlight the issues (Figure 1).

The baseline and intervention central line practices are documented in Table 1. It must also be noted that probiotics were introduced into routine newborn care from October 2012 for all infants less than 30 weeks' gestation, or greater than 29 weeks' gestation with additional risk factors placing them at higher risk for necrotizing enterocolitis. There were no other relevant changes in policy or definitions during the study periods.

Implementation Strategy

The bundle of interventions was implemented via a structured education program. There is a strong background within this

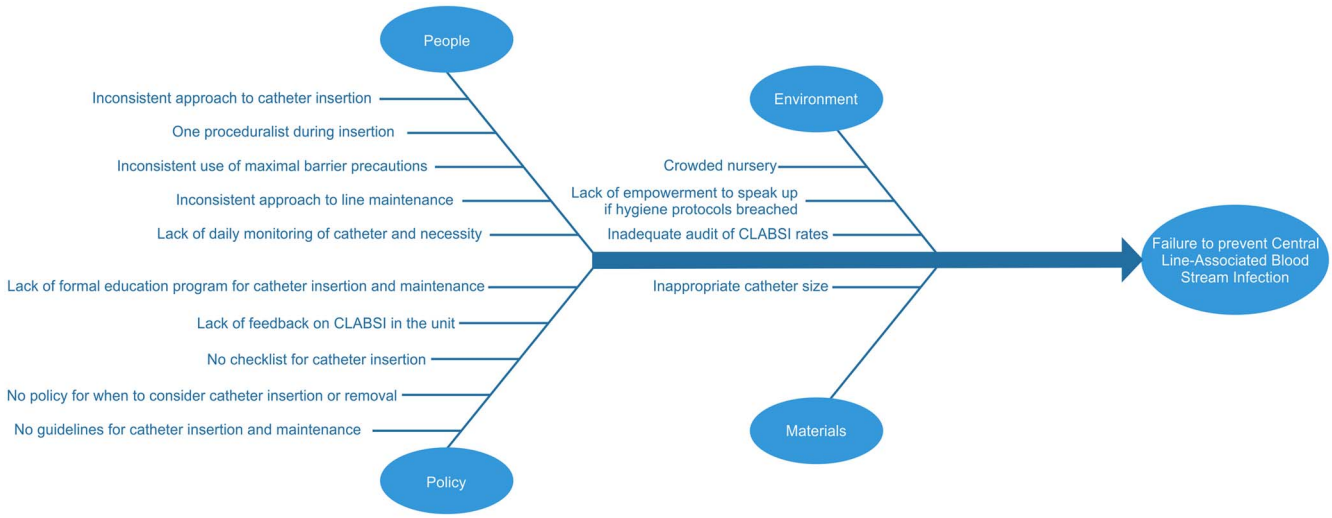

FIGURE 1. Fishbone diagram highlighting process failures in prevention of central line-associated bloodstream infection (CLABSI).

https://doi.org/10.1017/ice.2016.127 Published online by Cambridge University Press

TABLE 1. Baseline and Intervention Central Line Practices

Baseline	Intervention
Insertion bundle	
No formalized CVC discussions.	Daily discussions as part of clinical handover regarding CVC necessity.[a]
CVC left in situ for 24 hours after full feeds reached at 150 mL/kg/day.	Removal of CVC at earliest opportunity.
If TPN indicated, CVC placed if likely to require TPN for more than 5 days.	
Inconsistent approach to sterile precautions.	Use of maximal sterile precautions including use of hat, mask, double glove, and gown for anyone within 1 m of sterile field.
Only 1 person scrubbed.	Isolating bed space with a screen.
No hat or mask worn.	3-minute WHO surgical hand scrub before gowning.
Procedure performed through doors of the incubator.	2 people scrubbed per line insertion.
No isolation of bed space.	Draping of entire patient, using open care or incubator with side down.
Inconsistent choice of CVC or site of insertion.	2-Fr CVC as preferred access. 1-Fr only for <1 kg, or if unable to insert a larger CVC.
	Sites of preference: lower limb > upper limb > scalp.
Supervision recommended but not mandated in policy.	Inexperienced staff to be directly supervised at all times. Only senior staff to insert CVC in infants <750 g.
Clean twice with aqueous 0.015% chlorhexidine and allow to air dry for 3 minutes.	Unchanged.
Practitioner makes entry into medical records after the procedure. Inconsistent details recorded.	Use of a checklist and sticker to add to medical records.
Maintenance bundle	
Central line stop cocks/ hubs (eg, medication). Sealed nutrition and bags and use of 3-way taps. 48-hour TPN. Minimize line breaks. Maximum sterile precautions for line breaks. Scrub the hub for 15–30 seconds with chlorhexidine 0.5% solution and allow to dry.	Unchanged.
Dressing replaced when soiled or integrity compromised.	If dressing compromised then replaced if appropriate under full sterile precautions. Otherwise CVC removed.
Surveillance bundle	
Inconsistent hand hygiene monitoring with minimal feedback.	Observed moments of hand hygiene with quarterly feedback to all staff.
Infections coded by staff specialists ad hoc.	Monthly infection meeting of all senior staff with hospital microbiologist to discuss and code infection data.
Attendance at some ward rounds of external infectious diseases specialist.	Weekly attendance on ward rounds of local infectious diseases specialist.
Annual feedback from statewide data, provided >1 year after data collected.	Real-time monthly feedback of CLABSI rates to senior staff. Quarterly feedback provided to all staff via education program.
Irregular audit.	Second yearly audit and formal report detailing CVC use and CLABSI rates.
Education bundle	
Ad hoc teaching provided 3–6 times/ month. Different educators would utilize different teaching styles and materials and focus on different topics within CVC use.	Structured and formalized education program, based on the SCORPIO method of teaching[26] and covering CVC use, insertion, maintenance, and prevention of CLABSI. Includes formative assessment and evaluation. Consistent education materials prepared in advance.

NOTE. CLABSI, central line–associated bloodstream infection; CVC, central venous catheter; Fr, French; SCORPIO, Structured, Clinical, Objective Referenced, Problem-based, Integrated, and Organized; TPN, total parenteral nutrition; WHO, World Health Organization.

[a]Daily discussion included both initial decision to insert a CVC as well as ongoing requirement for it to remain in situ. There was a concerted effort to avoid CVC in larger and mature infants likely to tolerate enteral nutrition well.

unit with the SCORPIO[26] (Structured, Clinical, Objective Referenced, Problem-based, Integrated, and Organized) method of teaching. This approach uses interactive problem-focused learning to teach specific skills and has been adapted for adult postgraduate learning.[27] It was the successful foundation of the SEA-URCHIN Project[28] (South East Asia–Using Research for Change in Healthcare-Associated Infections) that was also initiated by this unit, with which our bundle had similar objectives and some shared materials. Education sessions were conducted every 3 months, covering all new staff and providing updates to all staff at least yearly. There were 3 workshops, each lasting 1.5–2.5 hours and containing an introduction, a number of skills-focused stations, an objective structured clinical examination, and formative assessment. Each workshop had a coordinator and a number of facilitators, who were medical staff and nurse educators with an interest in infection control. The central line workshop contained an introduction with an overview of CLABSI and 4 stations: (1) preparation to handle or insert lines, (2) CVC insertion, (3) CVC maintenance, and (4) local and state audit feedback of CLABSI. The infection control workshop consisted of 4 stations: (1) hand hygiene, (2) infection control at birth, (3) nursery admission, and (4) nursery environment. A hand hygiene workshop consisted of an introduction with local audit feedback and 3 stations: (1) the World Health Organization's 5 Moments for Hand Hygiene,[29] (2) effective hand hygiene, and (3) assertiveness training.

Data Collection

Information was identified and obtained from the neonatal clinical database. Data were extracted for every infant who had a CVC placed during his or her NICU admission. If further clarification was required, there was validation of data with the full medical record. Data regarding clinical characteristics, CVC use, and details of any bloodstream infection were collected. Infections are coded monthly by a committee of attending neonatologists and the hospital microbiologist using the following definitions.

Definitions

Central line was defined as a venous line inserted via either the umbilical or a peripheral vein, such that the line tip is placed into a large central venous vessel.[30] Central lines included UVC and PCVC.

Proven bloodstream infection was defined as growth of a certain pathogen in blood and treated by the clinicians as infection. If the pathogen could be a potential contaminant, there must be a pure growth of that organism, with either confirmatory laboratory evidence or growth of the same organism on repeat culture.

CLABSI was defined as a proven bloodstream infection associated with a central venous line when a central line has been in use 48 hours before signs and symptoms of an infection with no apparent source other than the central line. A culture of the same organism in any sample within 13 days is counted as a single infection. This definition was unchanged throughout the studied periods.

Early-onset infection was defined as a proven bloodstream infection with initial symptoms occurring sooner than 48 hours after birth.

Late-onset infection was defined as a proven bloodstream infection with initial symptoms occurring at least 48 hours after birth.

Babies were analyzed as part of gestational cohort groups. These groups included less than 29, 29–31, 32–36, and at least 37 weeks' gestation.

Statistical Analysis

Data were managed with an electronic spreadsheet (Excel 2013; Microsoft) and analyzed using Prism, version 5.0 for Windows (GraphPad). The central line utilization ratio was calculated as the number of central line–days/number of patient-days. CLABSI rates were calculated as number of CLABSI/central line–days × 1,000.[7] Continuous data were expressed as mean (SD) or median (interquartile range) according to the distribution. Data were compared with the Mann-Whitney test or the unpaired *t* test as appropriate. Categorical data were expressed as count and proportion and compared with the χ^2 or Fisher exact test. One-way analysis of variance (Kruskal-Wallis test) was used to compare more than 2 groups. All reported *P* values are 2 sided, and significance was assumed at $P < .05$.

RESULTS

Clinical Characteristics

Patient demographic characteristics are shown in Table 2. There were no significant differences between the groups in any of the parameters recorded.

Central Line Use

With regard to central line insertion, 353 CVCs (177 UVCs and 176 PCVCs) were inserted in 214 newborns during the baseline period, compared with 260 CVCs (142 UVCs and 118 PCVCs) inserted in 162 newborns during the intervention period. There were significantly fewer CVC inserted in the intervention period; the central line utilization rate was 0.11 in the intervention period vs 0.2 at baseline (Fisher exact test, $P = .0001$).

Overall, median dwell time of CVCs was significantly shorter in the intervention period compared with the baseline period; 4.4 (95% CI, 2.2–6.7) vs 5.0 (2.9–8.2) days (Mann-Whitney test, $P = .01$). A reduction in PCVC dwell time underlies this difference: 6 (5.0–11.8) vs 7.3 (4.0–10.4) days (Mann-Whitney test, $P = .0004$) (Figure 2). UVC dwell times were not significantly different in intervention and baseline

https://doi.org/10.1017/ice.2016.127 Published online by Cambridge University Press

TABLE 2. Characteristics of Infants With Central Lines Inserted

Characteristic	Baseline ($n = 214$)	Intervention ($n = 162$)	P
Male sex	134 (63)	95 (59)	.46
Gestation, median (IQR), weeks	32 (23–41)	31 (24–41)	.52
Birthweight, median (IQR), g	1,660 (1,155–2,781)	1,644 (1,176–2,530)	.85
Singleton	176 (82)	126 (78)	.30
Antenatal steroids <37 weeks	143/165 (87)	117/126 (93)	.12
Delivery by Caesarean	130 (61)	110 (68)	.16
Chorioamnionitis	65 (30)	62 (38)	.12
Ex-utero transfer	34 (16)	29 (18)	.68

NOTE. Data are no. (%) of infants unless otherwise indicated. IQR, interquartile range.

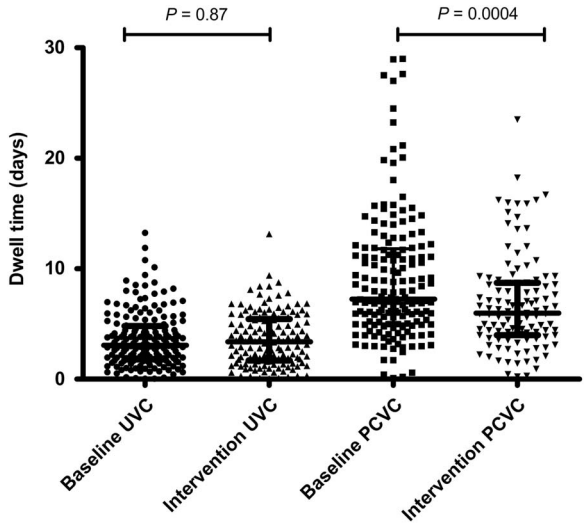

FIGURE 2. Dwell time of central venous catheters in the baseline and intervention groups. PCVC, peripherally inserted central venous catheter; UVC, umbilical venous catheter.

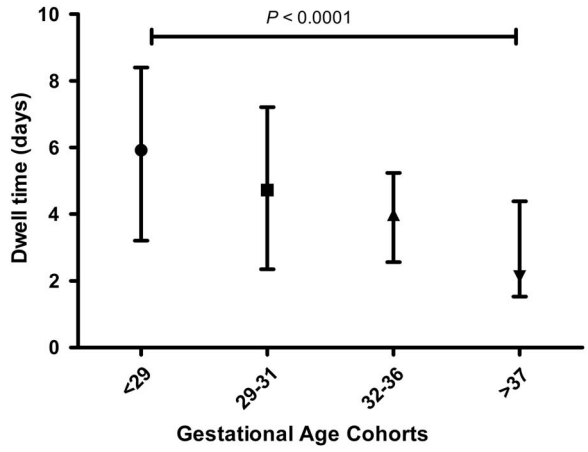

FIGURE 3. Reduction in central venous catheter dwell time in the intervention period across gestational age cohorts.

groups (3.1 [1.8–4.8] vs 3.4 [1.7–5.4], $P = .87$). Dwell time was not different in babies less than 31 weeks' gestation (5.9 [2.9–10.4] vs 5.5 [2.9–7.8] days, $P = .19$) but was significantly shorter for those babies at least 31 weeks' gestation in the intervention period (3.7 [1.9–5.5] vs 4.2 [2.8–6.8] days, $P = .05$). Dwell time was longer in preterm infants in comparison with term and was inversely proportional to gestational age (1-way analysis of variance, $P < .0001$) (Figure 3).

Most babies less than 29 weeks' gestation had more than 1 CVC placed during their admission, with the median number of lines placed in this cohort being 2. One infant in this cohort had 5 CVCs placed. After 29 weeks' gestation, most infants had only 1 CVC placed. Compared with baseline, there was no difference in the number of CVCs per patient either overall or when analyzed per gestational age cohort.

Infection

There were 15 positive blood cultures with clinical signs of infection in the intervention period: 4 were early-onset and 11 were late-onset sepsis. Of the 11 with culture-positive late-onset sepsis, 3 were CLABSI, all with a pure growth of coagulase-negative *Staphylococcus*. One other patient had a CVC in situ at the time of deterioration but had a diagnosis of necrotizing enterocolitis with perforated bowel and blood culture grew *Enterococcus faecalis*. The remaining patients did not have a CVC in situ within 48 hours of bloodstream infection. At baseline, there were 22 bloodstream infections. One of these infections was an early-onset infection, confirmed from blood cultures of samples collected at birth with the same organism isolated in the mother. Another was in a baby without a central line following laser therapy for retinopathy of prematurity. The remaining 20 infections were CLABSI. Of 20 infections, 19 were caused by coagulase-negative *Staphylococcus* and 1 by *Escherichia coli*.

Overall there was a significant decrease in CLABSI rates from 8.5 per 1,000 central line–days to 2.3 per 1,000 central line–days (Fisher exact test, $P = .004$) (Table 3). Three (1.2%) of 260 CVC were implicated in infection compared with 20 (5.7%) of 353 CVC in the baseline data. The run chart of total CLABSI over time is shown in Figure 4 and was extended post hoc to include 2014–2015 data to highlight continued reduced CLABSI rates.

https://doi.org/10.1017/ice.2016.127 Published online by Cambridge University Press

TABLE 3. Central Line–Associated Infection Rates

	Baseline ($n = 214$)		Intervention ($n = 162$)			
Variable	Rate per 1,000 CL-days	CLABSI per total CL-days	Rate per 1,000 CL-days	CLABSI per total CL-days	*P*	Relative risk (95% CI)
Overall	8.5	20/2,357	2.3	3/1,333	.004	0.3 (0.1–0.86)
<29 weeks	13.4	13/966	1.89	1/530	.009	0.16 (0.02–1.1)
<32 weeks	11.4	19/1,664	1.1	1/946	.0003	0.11 (0.02–0.8)
≥32 weeks	1.4	1/693	5.2	2/387	.57	N/A
UVC	1.4	1/704	3.9	2/513	.59	N/A
PCVC	11.5	19/1,653	1.2	1/820	<.0001	0.1 (0.01–0.65)

NOTE. CL, central line; CLABSI, central line–associated bloodstream infection; N/A, not applicable; PCVC, peripherally inserted central venous catheter; UVC, umbilical venous catheter.

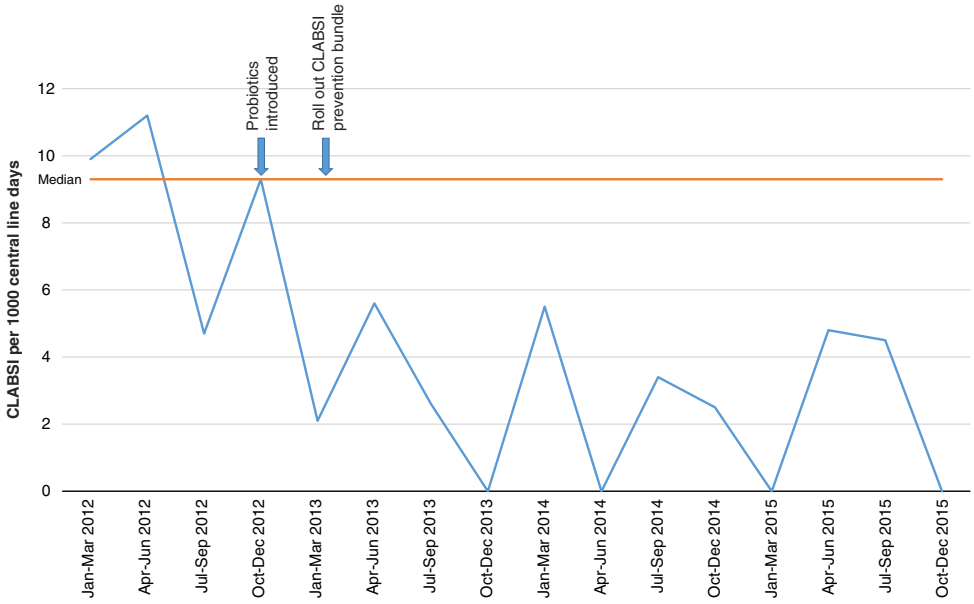

FIGURE 4. Run chart of central line–associated bloodstream infections (CLABSI) per 1,000 central line–days 2012–2015.

Of interest, 2 of the 3 CVCs in the intervention group that caused clinical sepsis were UVCs, both in infants between 32–34 weeks' gestation. There was only 1 CLABSI seen related to a PCVC, which was in an infant of 25 weeks' gestation who had 5 PCVC in total. There were too few CLABSI in the intervention cohort to perform any further analysis.

DISCUSSION

The major findings of this study are that adoption of a coordinated training, education, and review program in a busy Australian neonatal unit has resulted in change in clinical practice, and that this behavioral change translated into significant reductions in clinical complications associated with CVC use. The reductions in the number of CVCs inserted, CVC dwell time, and CLABSI rates provide further data in support of CLABSI prevention intervention bundles. The reduction of healthcare-associated infection is a nationally important issue, and we have demonstrated the substantial impact that can be made within a single unit with a bundle of interventions.

The intervention package is generalizable to many NICUs in resource-rich countries. Although analyzed retrospectively, data are entered prospectively, infections are coded by the clinical team and the hospital microbiologist, and data are validated by a dedicated audit officer.

Limitations of this study include the relatively small data set, particularly regarding the number of CLABSI. The reduction in infection is, however, in keeping with similar infection prevention bundles in larger studies.[20,21] It is not a randomized trial and therefore is prone to bias. However, the demographic characteristics of infants in the baseline and intervention groups showed no significant differences. There was no measurement of compliance to the bundle, and in consequence we

https://doi.org/10.1017/ice.2016.127 Published online by Cambridge University Press

cannot confirm that the interventions described were adhered to and are directly responsible for the reduction in CLABSI. Documentation in medical records has been insufficient to provide other relevant process outcomes. There has been a reduction in sepsis statewide, which has been attributed to a focus on timely data feedback and quality improvement.[23] Therefore, it is possible that the reduction in CLABSI seen in this study is a reflection of the general trend seen across the state. However, our hospital has shown the largest and most consistent decrease in infection rates statewide[23] and was the first to implement a bundle of interventions using a structured education program. Ongoing audit will be necessary to document sustained effects. We acknowledge that the introduction of probiotics is a potential confounder. It is possible that both by a direct beneficial effect of probiotics on the immune system[31] and by reducing times to full feeds,[32] probiotics may have reduced CLABSI in vulnerable infants by reducing the need for or dwell time of central lines.

CVCs are necessary in many infants, in particular in preterm infants who may take prolonged periods to tolerate full enteral feeds. However, median dwell time of CVCs was 4.4 days overall and just 2.1 days in term infants. There are a number of clinical factors other than time to reach enteral feeds that may influence the decision to insert a CVC, such as difficult peripheral venous access, or the infusion of hyperosmolar or other irritant fluids or medications. The short dwell time seen in this study may reflect a high rate of CVC-related complications and subsequent reinsertion, although the reasons for insertion and removal of CVCs are not routinely collected in our unit. The short dwell time suggests that at least some CVCs were not necessary. CVC dwell time was significantly shorter in infants at least 31 weeks' gestation in the intervention group than at baseline. This may be a consequence of the policy both to avoid CVCs, utilizing peripheral venous access instead, and to remove CVCs at the earliest opportunity, especially in those who are likely to tolerate and reach full feeds more quickly.

There were only 3 CLABSI in the intervention group and consequently too few to perform adjusted analysis or comment further upon the associations or impacts of the CLABSI seen in the intervention period. Only 1 PCVC was related to CLABSI in 1 year of data collection, in a 25-week infant. However, 2 UVCs were implicated in CLABSI, both in more mature babies. This contrasts with the baseline data, in which most cases of CLABSI were related to PCVC use. This may reflect the emphasis that has been placed on PCVC insertion and maintenance, with a focus on the smallest and most vulnerable infants. Ongoing quality improvement in this unit now focuses on both UVC and PCVC, and the education program emphasizes the importance of the maintenance and insertion bundles in all infants with central lines, regardless of gestation or line type. Further regular audit is important to continue to identify areas of change and should measure compliance to interventions.

Although global incidence of NICU CLABSI is decreasing,[7,33] central line infection still represents a major risk at an individual level and contributes significantly to length of hospital stay and associated costs. As incidence decreases, it is becoming more important to tackle CLABSI and institute best practices via neonatal networks, such as the Australia and New Zealand Neonatal Network or the Vermont Oxford Network. Walshe demanded that "our expectations of the evidence base for [quality improvement] methodologies should be on a par with our expectation in relation to other forms of healthcare interventions."[34(p.153)] These networks offer the potential to replicate successful education programs and perform robust interventional studies in this area of quality improvement.

ACKNOWLEDGMENTS

Financial support. None reported.

Potential conflicts of interest. Both authors report no conflicts of interest relevant to this article.

Address correspondence to Rowena McMullan, FRACP, Department of Newborn Care, Royal Prince Alfred Women and Babies, Missenden Rd, Camperdown, NSW 2050, Australia (rowenamcm@gmail.com).

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