

A quality improvement initiative to reduce central line infection in neonates using checklists

Jacqueline E. Taylor^{1,2} · Susan J. McDonald³ · Arul Earnest⁴ · Jim Buttery⁵ · Bree Fusinato² · Samantha Hovenden² · Andrea Wallace² · Kenneth Tan^{2,4}

Received: 28 July 2016 / Revised: 21 February 2017 / Accepted: 26 February 2017 / Published online: 10 March 2017
© Springer-Verlag Berlin Heidelberg 2017

Abstract Central line associated blood stream infections (CLABSI) are the most common complication of central catheters in neonates. These infections increase length of hospital stay, hospital costs and impact on mortality and morbidities. We performed a quasi-experimental study, over 24 months, utilising a pre-post design to determine the impact checklists had on central line infections. We introduced checklists for insertion, daily maintenance and procedural access based on the existing clinical guideline. Infections and compliance were monitored and reported back to the unit each month. We utilised the interrupted time series analysis to evaluate the impact of introduction of the checklists. Over the 24 months, 318 infants were included with a total of 509 central lines inserted. In the post intervention phase, definite CLABSI rates declined by 41%, from 13.8 definite CLABSIs per 1000 central-line days to 7.8 definite CLABSIs per 1000 central-line days. There was significant change in the mean levels in the post intervention

phase (coefficient crude -0.01015 ; 95% CI -0.01980 – 0.00051 , p value 0.039). Checklist compliance for insertion was 70%, and daily maintenance compliance overall mean was 66%.

Conclusion: Our quality improvement initiative using checklists, supported with education and feedback, significantly reduced CLABSI in our neonatal unit.

What is Known:

- Central line associated blood stream infection (CLABSI) continue to cause mortality and morbidity in the neonatal population.
- Bundles of intervention use quality improvement methodology to reduce CLABSI and checklists can assist with the introduction of these.

What is New:

- Checklists assist with reducing central line infection.
 - To ensure the success of checklists, robust education, leadership and continuous feedback are vital.
-

Revisions received: 21 December 2016; 17 February 2017; 22 February 2017

Communicated by Patrick Van Reempts

✉ Jacqueline E. Taylor
Jacquie.taylor@monashhealth.org

Susan J. McDonald
S.McDonald@latrobe.edu.au

Arul Earnest
Arul.earnest@monash.edu.au

Jim Buttery
Jim.Buttery@mcri.edu.au

Bree Fusinato
Bree.fusinato@monashhealth.org

Samantha Hovenden
Samantah.Hovenden@monashhealth.org

Andrea Wallace
Andrea.wallace@monashhealth.org

Kenneth Tan
Kenneth.tan@monashhealth.org

¹ LaTrobe University, Bundoora, Victoria, Australia

² Monash Newborn, Monash Health, Monash medical Centre, 246 Clayton Road, Clayton, Victoria 3168, Australia

³ Midwifery Professorial Unit, Mercy Hospital for Women, Heidelberg, Victoria, Australia

⁴ Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

⁵ Paediatric infectious diseases, Monash Health, Clayton Rd, Clayton, Victoria, Australia

Keywords Central venous catheter · Infection · Infant newborn · Quality improvement · Checklist

Abbreviations

ANTT	Aseptic non touch technique
BSI	Bloodstream infection
ANZNN	Australian and New Zealand Neonatal Network
CDC	Centers for Disease Control and Prevention
CLABSI	Central line associated bloodstream infection
CONS	Coagulase negative staphylococcus
CVC	Central venous catheter
ELBW	Extremely low birth weight
HAI	Hospital acquired infection
LOS	Late onset sepsis
NHSN	National Healthcare Safety Network
PICC	Peripherally inserted central catheter
UVC	Umbilical venous catheter
VICNISS	Victorian Infection Surveillance System

Introduction

In the USA, there has been a 50% reduction in central line associated blood stream infections (CLABSIs) between 2008 and 2014; however, hospital-acquired infection (HAI) costs remain significant. Preventable CLABSIs have significant attributable cost; however, these vary widely due to different study designs. A recent German study demonstrated median attributable cost per central venous catheter (CVC) bloodstream infection (BSI) was €29,909 [7]. Similarly, a study from the USA showed CVC infection was associated with longer length hospital stay (+7 days) and an additional \$129,000 in costs [1]. A study of blood stream infection, in infants with a birth weight <1500 g, demonstrated an increase in average hospital costs, per infant, by \$5875 to a total of \$12,480 [9]. Every incidence of hospital-acquired infection (HAI) in extremely low birth weight (ELBW) infants increases the risk of neurodevelopment impairment; 41% of infants with an infection will develop at least one adverse neurodevelopmental outcome at 18–22 months of corrected age [15]. Furthermore, ELBW infants with a history of sepsis are four times more likely to develop cerebral palsy [16]. Central venous catheters are life saving devices; however, they are not without complications, infection being the most prevalent [8].

There are numerous strategies to prevent and reduce infections in CVCs and these are detailed in guidelines published by the Centers for Disease Control and Prevention (CDC) in the USA [8].

Pronovost and colleagues introduced checklists in adult intensive care units across Michigan and demonstrated reduced CLABSIs to zero, and maintained this for 18 months. The overall median rate of catheter-related bloodstream infection decreased from 2.7 infections per 1000 catheter-days at baseline to 0 at 3 months after implementation of the study intervention and was sustained at 0 during the 18 months of follow-up [11].

Prior to this study, checklists have been used in neonatal units to change clinical practice using bundles of interventions to reduce catheter infections. A state-wide initiative across New York introduced central-line insertion and maintenance bundles and agreed to use checklists to monitor maintenance-bundle adherence and report checklist use. CLABSI rates decreased by 67% state-wide, however did not reach zero [14]. Other studies have found similar success when introducing bundles supported with checklists [2, 6]. Prior to commencing this study, we noted our infection rates could be improved. A review of the clinical guidelines at Monash Newborn, Clayton, Victoria, found they were based on the best available evidence; nevertheless, CLABSI rates were noted to be higher than other similar neonatal units. We hypothesised that checklists would increase awareness with the existing guideline and thereby decrease CLABSI rates. No other changes to clinical practice were made during the study period. To our knowledge, this is the first study to use checklists, in conjunction with education, in neonates, to reduce infection without changing the clinical guideline or introducing changes to clinical practice.

Methods

Setting

Monash Newborn, Clayton, Victoria, Australia is a medical and surgical neonatal unit, with a total of 54 beds, 24 of which are intensive care beds. The intensive care unit divided into three rooms, eight beds in each, and the special care beds are divided between five rooms. The unit has one medical director and one assistant medical director, six neonatologists, 21 junior doctors, two nurse unit managers, three nurse educators and 219 clinical nurses.

Inclusion/exclusion

In this report, we describe data for patients with a CVC in situ, admitted to the neonatal unit from May 2013 till April 2015. Patients admitted from other referring centres with a CVC in situ were included in the study; however, we planned to exclude infection if they occurred within 48 h of arrival to the unit.

Design

We used a quasi-experimental study utilising a pre-post design, over 24 months, between May 2013 and May 2015, to determine if insertion and maintenance checklists reduced confirmed and suspected infections CLABSIs in the neonatal unit. The specific aim to reduce infection was supported with change design and key drivers (see Fig. 1). The key drivers were designed to be flexible and allow for continual improvements. The key points were feedback, education and engagement. The design changed focused on the checklists and an education program that emphasised the evidence behind the best practice points. Being able to monitor infection rates and compliance enabled the feedback program to be up to date and thus clinically relevant.

Checklists

Three checklists were designed for insertion, daily maintenance and procedural line access. The insertion and daily maintenance followed those produced by The Joint Commission, USA [4] and modified for neonatal use following Monash Newborn’s clinical guideline. The procedural line access checklist was developed using the aseptic non touch technique (ANTT) framework [13] and was in line with Monash Newborn’s clinical procedure. ANTT is a standardised aseptic technique which is widely used internationally, to reduce preventable infection. The technique prevents contamination of key parts and key sites by hand hygiene, non-touch technique, using sterilised equipment and cleaning of the key parts prior to use. Key parts and sites are the pieces of equipment or site that if contaminated with micro-organisms increase the risk of infection [12]. The insertion checklist was further modified to contain only a YES

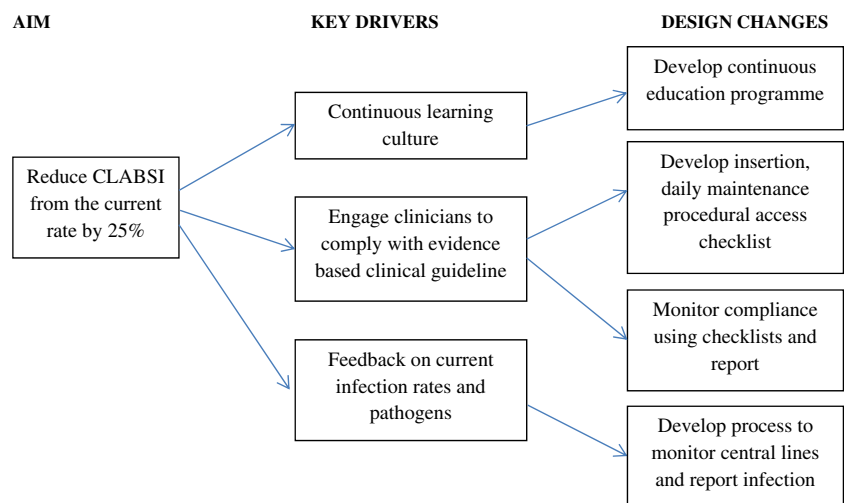
column to emphasise not negotiable. The daily maintenance checklist was to be completed each shift and covered a daily review of necessity of CVC, shift review of the site and dressing and line change regimen reminders. The procedural checklist was to be used every time the CVC was accessed and the operator observed to check that appropriate asepsis is followed. All three checklists are a one page document and contain the essential best practice points at the bottom to serve as a reminder. The insertion and procedural checklists were completed by an independent observer and the daily maintenance checklist was completed by the allocated bedside nurse.

Prior to implementation of the checklists in May 2014, education was provided to both the medical and nursing team on principles of insertion and line management, the use of checklists and ANTT refresher training. From May 2014 to April 2015, monthly education sessions on CVCs and infection prevention were delivered. Education was delivered using didactic teaching for the theoretical updates and work stations for staff to practice the ANTT skills. Feedback on checklist compliance and infection rates was provided, both verbally and on a notice board (monthly update). Verbal presentations were at the monthly staff meeting and twice a month during the dedicated nurse education session. The presentations included current infection rates, type of line and time in situ, organism type, infant’s characteristics and a discussion on infection prevention strategies. Run charts were utilised and the date of last infection clearly displayed.

Definitions

Prior to commencing the project, CLABSI needed to be defined. There is no consensus across the literature on CLABSI and research definitions vary from surveillance definitions. In the state of Victoria, we report to the

Fig. 1 Specific aim and key driver diagram developed by the study team



Victorian Infection Surveillance System (VICNISS) and the definitions of infection follow those of the National Healthcare Safety Network (NHSN). However, this definition can potentially lead to under reporting, as coagulase negative staphylococcus (CONS) sepsis requires two positive blood cultures obtained on the same day and this is not routine practice in Monash Newborn. Furthermore, Monash Newborn is part of the Australian and New Zealand Neonatal Network (ANZNN) and all late onset sepsis (LOS) are reported to enable benchmarking and practice improvement. For definite CLABSI, we used the ANZNN LOS definition [3] with the addition of a CVC in situ. For this project, we defined infection as below.

Definite CLABSI

Isolation from an organism from at least one peripheral blood culture. Coagulase negative staphylococcus must not be mixed or contain other skin flora and two or more signs of infection must be present and signs and symptoms are not related to an infection at another site and treatment with antibiotic therapy for ≥ 5 days and a CVC in situ or within 48 h post removal

Suspected CLABSI

No positive blood culture obtained and two or more signs of infection must be present and signs and symptoms are not related to an infection at another site and treatment with antibiotic therapy for ≥ 5 days and a CVC in situ or within 48 h post removal

Data collection

The project team collected all information on central lines, including type of CVC, days in situ, definite and suspected CLABSIs, time to infection and compliance of checklist usage, along with demographic data. Prior to commencing the project, CLABSI incidence rates, common pathogens and CVC utilisation rates, were unclear. Information was collected retrospectively from May 2013 to April 2014. All clinical records of infants who had a CVC were accessed and assessed using the set criteria. During the post intervention phase, CVC data and checklists were collected and analysed on an ongoing basis. The data collection tool, criteria and data collectors were the same in both phases. Furthermore, all data was reviewed and verified by the primary author.

For insertion checklists to be counted as compliant, they needed to be fully completed and follow all the practice recommendations. Daily maintenance checklists and a complete procedural access checklist (when required) were counted as compliant when they were fully completed on a shift by shift basis. All compliance with checklist completion is expressed as a percentage.

Data collected was entered into REDCap (Research Electronic Data Capture), a secure web application for maintaining databases [5].

Statistical analysis

CLABSI, the primary outcome metric, was measured using the predefined criteria. Infant demographics were compared between the pre and post intervention phase using the chi-squared for categorical variables, and Student *t* test or the Mann-Whitney test for continuous variables. Interrupted time series analysis models were used to quantify the pre and post intervention change in slopes in terms of proportion of monthly definite infections. In addition, we calculated the difference in mean proportion of definitive infections post versus pre intervention. The intervention started in May 2014. We used the autoregressive integrated moving average (ARIMA) model with an autocorrelation order of 1 to account for possible temporal correlation in the data. In February 2015, probiotics (Infloran, Laboratorio Farmaceutico S.I.T.) became standard care for all neonates less than 1500 g and 32 weeks gestation; therefore, we ran two different models (one without any adjustment, and another adjusting for monthly probiotic use). We also repeated the models for suspected infections and total infections. Run charts, designed by the Institute for Healthcare Improvement were also utilised. Run charts assist with reporting infection rates to the team to demonstrate how well a process is performing and give direction about the value of the change implemented. Data analysis was performed in Stata V14.0 (Stata Corp, College Station, TX, USA) and level of significance was set at 5%.

Results

In the pre intervention phase May 2013 to April 2014, 158 infants required a CVC with a total of 248 CVCs inserted. The use of checklists commenced in May 2014 and between May 2014 and April 2015, 160 infants required a CVC with a total of 261 CVCs inserted. The demographics of the infants are shown in Table 1. There were no differences between the groups, except for TPN days which were greater in the pre intervention phase. A point of interest is in the pre intervention phase, there were 23 infants (15.8%) born between 23 and 25 weeks and in the post intervention phase, there was an increase to 37 infants (23.1%); however, this was not statistically significant (*p* value 0.568). Nevertheless, a 7.3% increase in extreme prematurity is a clinically significant increase. Monash Newborn CVC practises do not vary across gestational age and birthweight.

Overall definite CLABSI rates declined by 41%, from 13.8 definite CLABSIs per 1000 central-line days to 7.8 definite CLABSIs per 1000 central-line days (see Table 2). Central

Table 1 Patient demographics

	Pre intervention (May 13–April 14)		Post intervention (May 14–April 15)		<i>p</i> value
	Mean	Median	Mean	Median	
Gestation	31.1	29	30.6	29	0.16
Weight	1822.7	1294.5	1703.7	1151	0.21
Male	83		100		0.069
CRIB II score	9.2	9.5	9.4	10	0.47
TPN days	27.9	16.5	30.3	24	0.02
IVAB days	34.5	22	36.9	29	0.25
Intubated days	13.1	5	11.7	4	0.59
Non-invasive ventilation days	27.1	13	32.6	15	0.47
NICU days	42.2	19.5	45.9	26.5	0.99
Hospital days	73.3	69	78	63.5	0.40

CRIB II score clinical risk index score for babies

line utilisation rates (number of central-line days/number of patient days) were the same in both pre and post intervention period; 0.24 in both.

The run charts for total CLABSIs (definite and suspected) and definite CLABSIs demonstrate a reduction in infection rates pre and post intervention (see Fig. 2). A signal of effective change was determined by a shift, six consecutive points below the median. The median was recalculated at the point of the signal.

We performed the interrupted time series analysis (Table 3) and noted no statistical significance in the change in the post intervention slope despite the reduction in infection. This may be due to relatively small numbers of catheter infections. However, there was a significant change in mean levels in the post intervention phase for definite infections (coefficient crude -0.01015 ; 95% CI -0.01980 – 0.00051 , *p* value 0.039); this remained significant when adjusted for the commencement of probiotics in the February of the post intervention phase.

In the pre intervention phase six infants died, two infants due to septic shock. No infants died in the post intervention phase.

Checklist compliance (measured by checklist completion)

To be counted as compliant, each practice point was to be adhered to and documented on the checklist. Overall insertion compliance was 70%; however, this varied between UVCs and PICCs, UVCs at 57% and PICCs at 83%. Compliance to the daily maintenance checklist varied with an overall compliance

rate of 66%. In total, there were 23 CLABSIs identified during the post intervention, the majority with UVCs [15] and PICCs [5]. Interestingly, when we compared checklist compliance for insertion and maintenance, with infection rates, there was no statistically significant association between compliance with the checklist completion and reduction in infection (*p* values 0.704 and 0.970, respectively).

Pathogens causing CLABSIs

The breakdown of specific pathogens causing CLABSI in the pre and post intervention phase is shown in Fig. 3. The most common pathogen in our unit was coagulase-negative staphylococci (CONS) in both the pre and post intervention phase. The proportion of CONS infection was virtually identical (61 vs 60%). These results are comparable to other neonatal units [14].

Discussion

This quality report demonstrates a significant reduction in CLABSI from the introduction of checklists, supported with extensive education and feedback. Apart from the introduction of probiotics in February 2015, no clinical changes were made during this time. This study demonstrates that a robust guideline alone is insufficient to ensure good clinical practice.

Table 2 CLABSI rates

	Pre intervention		Post intervention	
	Number of infections	Per 1000 central line days	Number of infections	Per 1000/central line days
CLABSI definite	39	13.8	23	7.8
CLABSI suspected	26	9.2	15	15

Fig. 2 Run charts displayed, updated each month to show improvements/failures

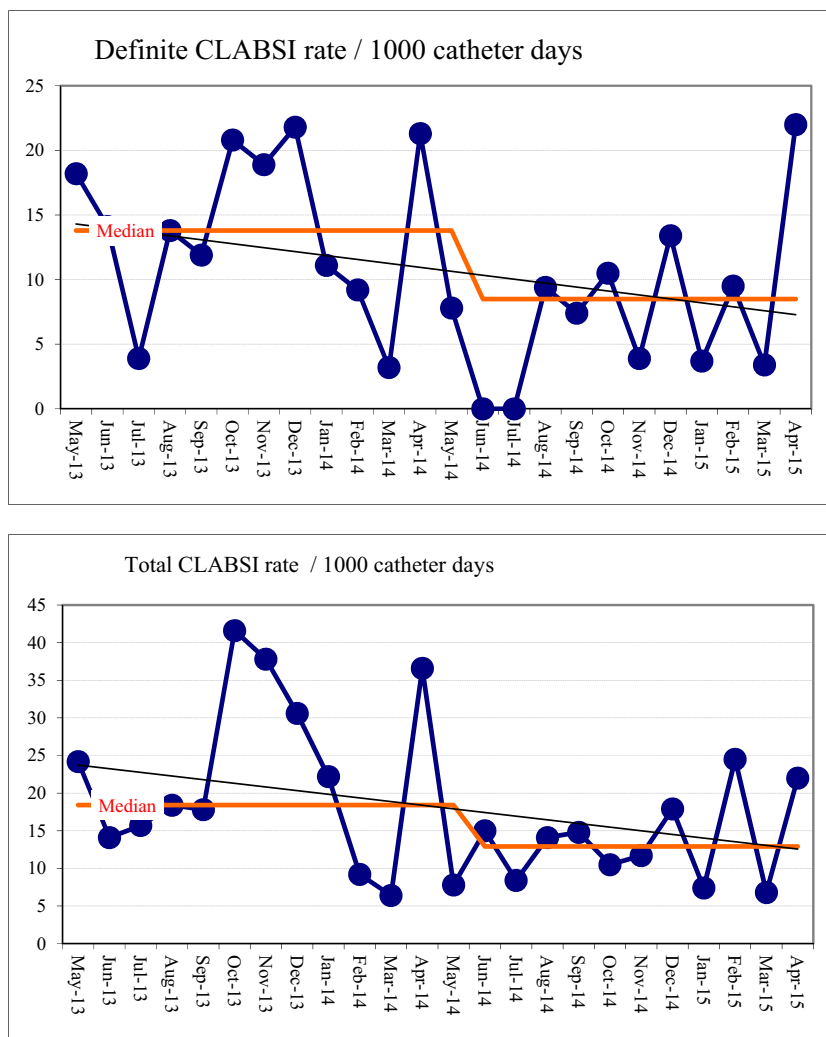
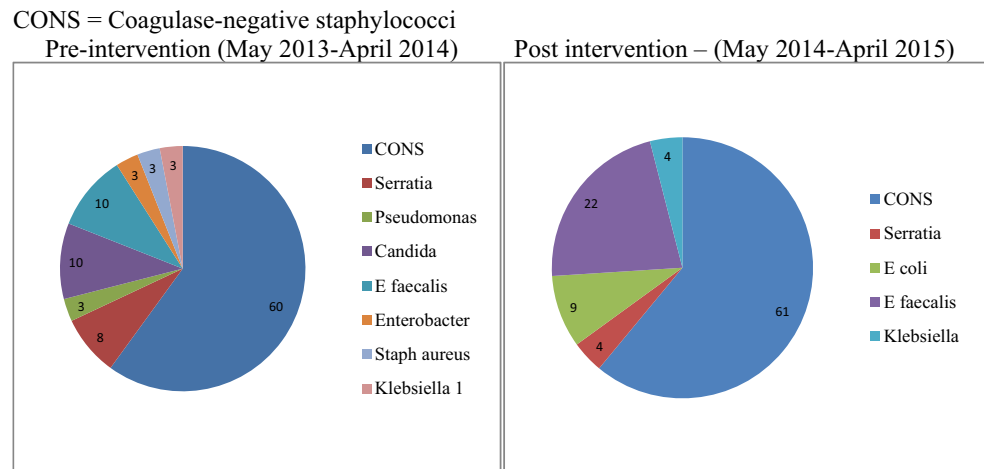


Table 3 Results from interrupted time series analysis looking at change in slopes and mean levels of infection before and after intervention

Variable	Coefficient crude	95% CI	<i>p</i> value	Coefficient adjusted for probiotics	95% CI	<i>p</i> value
Proportion definite infections						
Pre intervention slope	-0.00021	-0.00095 0.00053	0.585	-0.00019	-0.00090 0.00051	0.589
Change in post intervention slope	0.00126	0.00001 0.00250	0.048	0.00180	-0.00078 0.00437	0.172
Change in mean levels post intervention	-0.01015	-0.01980 0.00051	0.039	-0.01119	-0.02153 -0.00085	0.034
Proportion suspected infections						
Pre intervention slope	-0.00003	-0.00081 0.00074	0.936	-0.00002	-0.00076 0.00071	0.948
Change in post intervention slope	-0.00054	-0.00221 0.00114	0.531	-0.00137	-0.00503 0.00228	0.462
Change in mean levels post intervention	0.00108	-0.01031 0.01247	0.852	0.00231	-0.01236 0.01698	0.757
Proportion total infections						
Pre intervention slope	-0.00027	-0.00160 0.00105	0.688	-0.00028	-0.00160 0.00105	0.683
Change in post intervention slope	0.00079	-0.00300 0.00457	0.684	0.00029	-0.00775 0.00833	0.944
Change in mean levels post intervention	-0.00884	-0.03661 0.01893	0.532	-0.00793	-0.03802 0.02216	0.605

Fig. 3 Pathogens causing CLABSIs in the pre-post intervention period, expressed as a percentage



Evidence-based clinical guidelines are essential to ensure standardised evidenced-based care; nevertheless, these are not self-implementing. The availability of a guideline does not ensure it is being used in clinical practice. There are many contextual factors that affect the implementation of clinical guidelines at the bedside. Guidelines are often lengthy documents, which potentially may impede uptake. The checklists provided the clinician with a one-page document outlining all the essential parts of CVC insertion and maintenance. They are cost effective, provide a tool to fill the evidence practice gap, enabled performance measurement and assist with identifying failures in clinical care that may result in harm. It is important to note that the fall in infection rates from the introduction of checklist cannot solely be attributed to the checklists. The education program targeted all the medical and nursing staff and its impact should not be overlooked.

Checklist compliance was measured by completion of the checklist and all practice points adhered to. If the practice varied from the checklist, self-reported, or the checklist was not completed, this was classified as non-compliant. Checklist compliance varied and surprisingly, the analysis of the checklist compliance did not show reduction in infection as compliance increased. This may be due to a relatively small sample size. However, checklist completion may not be a true indicator of compliance. It could be assumed that the healthcare professional followed the best practice standards and the failure was to complete the checklist or conversely the checklist was completed even when best practice standards were not met. Nevertheless, despite the variation in compliance, the introduction of the checklist reduced infection rates. However, this reduction appears to be more than just the completion of a checklist. Clinicians need to be engaged and committed to embrace the concepts behind the checklists [10]. A vital part in the implementation of the checklists was education. Before the checklists were implemented, education on the best practice points was required to raise awareness of the guideline and to provide an opportunity to clear up areas of

ambiguity. This enabled the team to feel part of the change and involved in the process.

Despite the significant reduction in CLABSIs, central line infections continued to occur, thus highlighting further measures could be taken. To improve compliance to the checklists and subsequently the clinical procedure, the systems in place were scrutinised for potential factors that may impede adherence. Limited nursing availability was highlighted as a potential reason for poor compliance in completing the checklists. Changes implemented included all non-urgent CVCs and all fluid and line changes to be inserted in double nursing staff time, 13:00 to 15:30. This allowed more nurse availability to observe these procedures and ensure checklist completion and adherence to best clinical practice. The change required multi system involvement, including pharmacy as TPN delivery times required changing, financial department as the purchasing of more procedural trolleys were required, medical teams to ensure availability to insert CVCs in the specified times and nursing agreement to be available at those times. This was implemented in May 2015 and up to June 2016; checklist compliance has increased to 90% for insertion and 75% for daily maintenance and CLABSIs have reduced further to 3.5/1000 catheter days for definite infections.

Limitations

The pre-post design of the study reduces the robustness to make a connection between the invention and the reduced rates of CLABSI. However, a randomised controlled trial of the intervention was not feasible. It would have been unethical to purposefully insist some patients receive evidence-based care and not the others. Secondly, our QI initiative was limited to a single centre; therefore, the results may not be generalizable to other institutions with a different population. Thirdly, education could be an effect modifier for the impact of checklists. It is difficult to determine if the effect of the change was because of the checklists or the increase in education.

We would recommend units that introduce checklists, support the introduction with a strong education program. Finally, including inborn and outborn infants could potentially be seen as a high risk for confounding results; however, the number of outborn infants are minimal and would not have affected the results.

Conclusion

Using checklists, supported with education and feedback, significantly reduced CLABSI in our neonatal unit. However, avoidable CLABSIs continue to occur and by further improving systems and processes may assist with further reducing infection rates.

Authors' contributions Ms. Taylor conceptualised and designed the study, designed the data collection tools, checklists, coordinated and supervised data collection, analysed and interpreted the data, drafted the initial manuscript and approved the final manuscript as submitted.

Professor McDonald supervised and assisted in the conceptualisation and design of the study, critically reviewed the manuscript and approved the final submission.

Dr. Earnest analysed and interpreted the data and critically reviewed the manuscript and approved the final submission.

Dr. Tan supervised and assisted in the conceptualisation and design of the study, analysed and interpreted the data and critically reviewed the manuscript and approved the final submission.

Dr. Buttery supervised and assisted in the conceptualisation and design of the study, and critically reviewed the manuscript and approved the final submission.

Ms. Fusinato, Ms. Hovenden and Ms. Wallace collected the data, critically revised the manuscript and approved the final manuscript.

Compliance with ethical standards Prior to commencing our quality improvement project, we obtained ethics approval from Monash Health Human Research Ethics Committee and La Trobe University Human Ethics

Funding No external funding for this manuscript.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

References

1. Brunelli SM, Turenne W, Sibbel S et al (2016) Clinical and economic burden of bloodstream infections in critical care patients with central venous catheters. *J Crit Care* 35:69–74
2. Butler-O'Hara M, D'Angio C, Hoey H et al (2012) An evidence-based catheter bundle alters central venous catheter strategy in newborn infants. *J Pediatr* 160(6):972–977
3. Chow SSW (2013) Report of the Australian and New Zealand Neonatal Network 2011
4. Commission. TJ (2013) Preventing Central Line–Associated Bloodstream Infections: Useful Tools, An International Perspective. Nov 20, 2013. (accessed 05/01/2014)
5. Harris PA, Taylor R, Thielke R et al (2009) Research electronic data capture (REDCap) a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 42(2):377–381
6. Kaplan HC, Lannon C, Walsh MC et al (2011) Ohio statewide quality-improvement collaborative to reduce late-onset sepsis in preterm infants. *Pediatrics* 127(3):427–435
7. Leistner R, Hirsemann E, Bloch A et al (2014) Costs and prolonged length of stay of central venous catheter-associated bloodstream infections (CVC BSI): a matched prospective cohort study. *Infection* 42(1):31–36
8. O'Grady NP, Alexander M, Burns L et al (2011) Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 52:1–32
9. Payne NR, Carpenter JH, Badger GJ et al (2004) Marginal increase in cost and excess length of stay associated with nosocomial bloodstream infections in surviving very low birth weight infants. *Pediatrics* 114(2):348–355
10. Pronovost P (2013) Enhancing physicians' use of clinical guidelines. *JAMA* 311(25):2501–2502
11. Pronovost P, Needham D, Berenholtz S et al (2006) An intervention to decrease catheter-related bloodstream infections in the ICU. [Erratum appears in *N Engl J Med*. 2007 Jun 21;356(25):2660]. *N Engl J Med* 355(26):2725–2732
12. Rowley S, Clare S (2009) Improving standards of aseptic practice through an ANTT trust-wide implementation process: a matter of prioritisation and care. *J Infect Prev* 10:S18–S23
13. Rowley S, Clare S (2011) ANTT: a standard approach to aseptic technique. *Nurs Times* 107(36):12–14
14. Schulman J, Stricof R, Stevens TP et al (2011) Statewide NICU central-line-associated bloodstream infection rates decline after bundles and checklists. *Pediatrics* 127(3):436–444
15. Stoll BJ, Hansen N, Adams-Chapman I et al (2004) Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. *JAMA* 292(19):2357–2365
16. Wheeler M, Rennie JM (2000) Perinatal infection is an important risk factor for cerebral palsy in very-low birth weight infants. *Dev Med Child Neurol* 42:364–367