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Rapid Reduction of Central Line Infections in Hospitalized Pediatric Oncology Patients Through Simple Quality Improvement Methods

Sung W. Choi, MD,[1]* Lawrence Chang, MD,[1] David A. Hanauer, MD, MS,[2] Jacqueline Shaffer-Hartman, MPH, CIC,[3] Daniel Teitelbaum, MD,[4] Ian Lewis, MD,[5] Alex Blackwood, MD,[6] Nur Akcasu, NP,[1] Janell Steel, RN,[7] Joy Christensen, NP,[7] and Matthew F. Niedner, MD[8]

Background. Pediatric hematology–oncology (PHO) patients are at significant risk for developing central line-associated bloodstream infections (CLA-BSIs) due to their prolonged dependence on such catheters. Effective strategies to eliminate these preventable infections are urgently needed. In this study, we investigated the implementation of bundled central line maintenance practices and their effect on hospital-acquired CLA-BSIs. ***Materials and Methods.*** CLA-BSI rates were analyzed within a single-institution's PHO unit between January 2005 and June 2011. In May 2008, a multidisciplinary quality improvement team developed techniques to improve the PHO unit's safety culture and implemented the use of catheter maintenance practices tailored to PHO patients. Data analysis was performed using time-series methods to evaluate the pre- and post-intervention effect of the practice changes. ***Results.*** The pre-intervention CLA-BSI incidence was 2.92 per 1,000-patient days (PD) and coagulase-negative *Staphylococcus* was the most prevalent pathogen (29%). In the post-intervention period, the CLA-BSI rate decreased substantially (45%) to 1.61 per 1,000-PD ($P < 0.004$). Early on, blood and marrow transplant (BMT) patients had a threefold higher CLA-BSI rate compared to non-BMT patients ($P < 0.033$). With additional infection control countermeasures added to the bundled practices, BMT patients experienced a larger CLA-BSI rate reduction such that BMT and non-BMT CLA-BSI rates were not significantly different post-intervention. ***Conclusions.*** By adopting and effectively implementing uniform maintenance catheter care practices, learning multidisciplinary teamwork, and promoting a culture of patient safety, the CLA-BSI incidence in our study population was significantly reduced and maintained. Pediatr Blood Cancer 2013;60:262–269. © 2012 Wiley Periodicals, Inc.

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INTRODUCTION

Central line-associated bloodstream infections (CLA-BSIs) remain a significant cause of treatment-related morbidity, mortality, and increased healthcare costs in hospitalized patients [1,2]. Over the last decade, it has become increasingly evident that reliable implementation of established, ''simple'' interventions, such as hand-washing and procedural checklists, can reduce the incidence of CLA-BSIs [1]. In 2004, the efficacy of five such interventions in the adult intensive care unit (ICU) setting was reported [3]. Importantly, the interventions were accompanied by policies and procedures that inculcated a culture of patient safety and health care quality among the clinical care team [4]. The merits of these processes were demonstrated in a landmark study of 108 ICUs across the state of Michigan that led to significant reductions in CLA-BSIs from a baseline of 7.7 infections per 1,000 catheter days to 1.4 [5] which persisted up to 3 years after the interventions were implemented [6], and was associated with improved awareness [7].

Public reporting and pay-for-performance incentive programs for quality measures have significantly encouraged improved health care processes [8–10]. Notably, bundled central line care practices have been used to provide an organized framework for catheter insertion procedures, resulting in better outcomes [11,12], although the majority of the work has been validated in adult ICU patients. Recent reports have shown that it is possible to attain a reduction in CLA-BSIs in pediatric ICUs, and even across an entire pediatric hospital [13–16]. In contrast to the adult ICU experience, the application of catheter insertion processes alone was not sufficient to reduce infection rates in children. The development and application of a central line maintenance bundle reduced pediatric ICU CLA-BSI rates by almost half [14]. There has been growing interest in reducing the incidence of CLA-BSIs outside of the ICU setting for both adults [17,18] and children [19]. However, little is known of the applicability of the interventions developed in the ICU to other care settings or populations.

In the pediatric ICU setting, a primary oncologic diagnosis more than doubles the risk of developing a CLA-BSI [20]. The rate of CLA-BSIs among hospitalized pediatric hematology–oncology (PHO) patients has been reported to range from 2.3 to 4.6

[1]Pediatric Hematology–Oncology, Department of Pediatrics, University of Michigan, Ann Arbor, Michigan; [2]General Pediatrics and Informatics Core of the Comprehensive Cancer Center, Department of Pediatrics, University of Michigan, Ann Arbor, Michigan; [3]Department of Infection Control, University of Michigan, Ann Arbor, Michigan; [4]Division of Pediatric Surgery, Department of Surgery, University of Michigan, Ann Arbor, Michigan; [5]Division of Pediatric Anesthesiology, Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan; [6]Division of Pediatric Infectious Diseases, Department of Pediatrics, University of Michigan, Ann Arbor, Michigan; [7]Department of Nursing, University of Michigan, Ann Arbor, Michigan; [8]Division of Pediatric Critical Care, Department of Pediatrics, University of Michigan, Ann Arbor, Michigan

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*Correspondence to: Sung W. Choi, MD, Blood and Marrow Transplant Program, University of Michigan, 1500 E. Medical Center Drive, 5303 Cancer Center, Ann Arbor, MI 48109-5942.
E-mail: sungchoi@med.umich.edu

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infections per 1,000 catheter days [21]. Accordingly, CLA-BSIs may account for the single largest cause of nosocomial infections in this high-risk population [22]. Furthermore, the risk of life-threatening infection in these patients is potentially exacerbated by prolonged neutropenia resulting from immunosuppressive chemotherapy [23–25]. Other risk factors for the development of CLA-BSIs that are common among children with cancer include blood product exposure, parenteral nutrition, and younger age [23,26–33]. Little data exist about effective approaches for reducing the incidence of CLA-BSIs in this vulnerable population. In this study, we tested the hypothesis that implementing a bundled set of care practices for the daily maintenance of central lines in PHO patients would reduce the rate of CLA-BSIs. We further hypothesized that iterative root cause analyses (RCA) of residual CLA-BSIs in PHO patients would help refine the bundle and identify additional prevention strategies.

METHODS

Study Setting

The PHO service at the University of Michigan Mott Children's Hospital is a 26-bed unit. There are approximately 100 new pediatric oncology diagnoses and over 600 admissions to the PHO unit annually. The average daily census is 12 patients under the PHO service and 7 patients under the blood and marrow transplant (BMT) service. As a part of routine institutional infection control practices, all PHO patients with a central line catheter in place during their inpatient admission were prospectively followed for the development of a CLA-BSI throughout the period under analysis (January 2005 through June 2011). The institutional review board approved the study and waived the need for informed consent.

Study Design

A multidisciplinary CLA-BSI Working Group was developed in January 2008 with the aim to reduce the CLA-BSI rate in PHO patients. This team included pediatric physicians specializing in PHO, infectious diseases, anesthesiology, and surgery, as well as an infection-control professional, a phlebotomy service leader, and several PHO nursing leaders. During the first 4 months of the project, the team members met regularly and received training in the study design, the practice interventions, and the expected effect of these interventions according to the CDC and Pediatric ICU NACHRI Quality Transformation Efforts [14]. Team members developed techniques to improve the safety culture associated with central line catheter care, identified best practices for the insertion and maintenance of catheters, and disseminated the information to clinical care providers. In May 2008, a central line maintenance bundle specific to PHO/BMT patients was implemented to promote adherence to key practices (Table I). These catheter care practices were tailored to non-ICU, PHO patients, and adapted to the general care inpatient setting. Maintenance bundle forms were distributed weekly to all bedside nurses and served both as a retrospective audit (for care processes already completed during the shift) as well as a prospective checklist (to drive adherence to preferred standard practices in the remainder of the shift).

In order to identify common factors in patients who developed CLA-BSIs, a RCA was conducted for every CLA-BSI event. Patient variables, catheter variables, contextual factors, and system issues were systematically reviewed to characterize CLA-BSI events and identify drivers and common themes. A summary of the findings and the overall incidence of CLA-BSIs were reviewed at monthly meetings. In July 2009 (14 months after the initial intervention), power peripherally inserted central catheters (PICC) were discontinued as a result of a suspected association with CLA-BSIs. As part of ongoing Plan-Do-Study-Act quality improvement work, daily chlorhexidine gluconate (CHG) cleansing [34–36] was also implemented in January 2010 (20 months after the initial intervention).

TABLE I. Central Line Catheter Maintenance Bundle

Hand hygiene
Proper hand cleansing before every catheter/tubing/dressing interaction
Dressings changed appropriately
Recommended intervals: at 7 days for transparent dressings or 3 days for gauze
Other indications: soiled, damp, loose, unknown date/time of last change
Recommended practices: chlorhexidine gluconate skin antisepsis when dressing changed
Intravenous tubing changed appropriately
Recommended intervals: at $\geq$96 hours since last tubing change or 24 hours if blood/lipid exposure
Other indications: Medication hang-time expiration, unknown date/time of last change
Bathing or showering performed
Chlorhexidine used for bath or shower
Dressing and catheter covered during bath or shower
Dressing changed immediately after bath or shower if dressing change due by date
Caps/tape changed on unaccessed lumens after bath or shower
Central lines entered appropriately
Minimized entries through batching of medication administration and lab draws
Maintained closed intravenous system (e.g., pre-pierced ports/caps, and bifuse extension sets)
Cleansed access points with alcohol scrub prior to each line entry

Data Collection

The project's process measure was maintenance bundle compliance which was self-reported by bedside nurses through completion of the weekly forms. The project outcome measure was the CLA-BSI rate, calculated by dividing the number of monthly CLA-BSI events by the number of patient days (PD) in that month. The Agency for Healthcare Research and Quality's Hospital Survey on patient safety culture was administered bi-annually and served as a contextual measure for the project.

CLA-BSIs were identified prospectively by a trained, hospital-based, infection control professional following National Healthcare Safety Network (NHSN) methods [37]. The surveillance methods and personnel utilized were consistent during the pre-intervention and post-intervention phases, and determinations of CLA-BSI events were made by an infection control professional independently from the clinical team [38]. The NHSN definition for CLA-BSI used to identify events during the study period included the following common-practice modifications: (i) only

laboratory confirmed primary bloodstream infections were included; (ii) the date of onset was defined as the date of the first positive blood culture; and (iii) CLA-BSIs identified in the first 48 hours of admission were excluded as present or incubating at admission. In 2008 (during the study period), the NHSN definition for CLA-BSI was revised, notably to require two positive cultures for organisms considered to be common skin contaminants [38,39]. To assess and correct for the effect of this change on CLA-BSI determinations, all cases of CLA-BSI prior to 2008 were re-adjudicated using the revised 2008 definition.

Analysis

Between January 2005 and June 2011, the monthly CLA-BSI rate was plotted on annotated control charts. After March 2008, all-or-none compliance with central line maintenance practices was collected and summarized by time period in tabular form. Statistical process control was employed for real-time insight into the data, and natural break points were identified through special cause variation using the four conventional rules, at which point mean lines were adjusted [40]. These mean lines were used to establish early and late steady-state CLA-BSI rates. For the purposes of this analysis, the CLA-BSI rates of two additional time periods were defined and analyzed: pre-intervention (January 2005–April 2008) and post-intervention (May 2008–June 2011). Wilcoxon rank sum and *t*-tests were used as appropriate to generate *P* values.

RESULTS

CLA-BSI Rates and Blood Culture Isolates

The PHO CLA-BSI rate from 2005 through 2007 (pre-implementation) using the CDC/(NHSN) definition in effect at the time was 3.59/1,000 patient-days (PD). Adjudication of the 80 CLA-BSI cases prior to 2008 identified 12 that no longer met the revised definition. Excluding cases not satisfying the updated CDC/NHSN definition, the 2005–2007 CLA-BSI rate was 2.92/1,000 PD, yielding an 18.6% rate reduction attributable to the definition change alone. All further analyses were performed with only cases meeting the current CDC/NHSN definition for analytic consistency and contemporary relevance. Culture isolates are summarized in Table II.

TABLE II. CLA-BSI Blood Culture Isolates 2005–2011, Based on Revised NHSN Definition*

	All PHO	Non-BMT	BMT
Counts (n)	(***130***)	(***60***)	(***70***)
Number of concurrent isolates	***%***	***%***	***%***
One organism	*72.7*	*67.4*	*76.8*
Two organisms	*22.2*	*20.9*	*23.2*
Three organisms	*5.1*	*11.6*	—
Gram positive cocci	***71.7***	***66.9***	***74.2***
Staphylococcus	34.6	28.4	40.0
coagulase (−)[a]	29.2	21.7	35.7
aureus	5.4	6.7	4.3
Streptococcus	21.6	23.4	18.5
pneumoniae	0.8	—	1.4
mitis[a]	10.8	15	7.1
alpha-hemolytic NOS[a]	6.2	6.7	5.7
oralis[a]	1.5	—	2.9
sanguis[a]	1.5	1.7	1.4
salvarius[a]	0.8	—	1.4
Enterococcus	14.7	13.4	15.7
faecalis	6.2	6.7	5.7
faecium	8.5	6.7	10
Micrococcus[a]	0.8	1.7	—
Gram negative bacilli	**22.5**	**28.4**	**16.9**
Pseudomonas	6.2	3.3	8.5
aeruginosa	5.4	3.3	7.1
oryzihabitans	0.8	—	1.4
Klebsiella	5.4	8.3	2.8
oxytoca	3.1	5	1.4
pneumonia	2.3	3.3	1.4
Enterobacter	3.1	5	1.4
cloacae	2.3	3.3	1.4
species NOS	0.8	1.7	—
Escherichia coli	3.1	6.7	—
Stenotrophomonas maltophilia	0.8	1.7	—
Acinetobacter species NOS	0.8	1.7	—
Alcaligenes xylosoxidans	0.8	—	1.4
Leptotrichia buccalis	0.8	—	1.4
Proteus mirabilis	1.5	1.7	1.4
Fungal	**3.1**	**5.1**	**1.4**
Candida	3.1	5.1	1.4
krusei	1.5	1.7	1.4
parapsilosis	0.8	1.7	—
glabrata	0.8	1.7	—
Gram positive bacilli	**3.2**	—	**5.6**
Bacillus cereus[a]	0.8	—	1.4
Clostridium perfringens	0.8	—	1.4
Lactobacillus species NOS	0.8	—	1.4
Microbacterium	0.8	—	1.4

NHSN, National Healthcare Safety Network; NOS, not otherwise specified; [a]Organisms considered to be common skin contaminants in the revised NHSN definition; *The revised NHSN definition required two positive blood cultures for organisms considered common skin contaminants.

Bundle Compliance

Self-reported adherence to recommended maintenance bundle practices was generally high (>90%) in most domains, both in the early ramp-up period as well as during the later sustaining period, and all-or-none compliance increase by 35% (Table III). The only two domains with <90% compliance during the early ramp-up period (bathing practices and strategies to reduce line entry) both showed marked improvement over time. Pre-implementation compliance data were not collected.

Subgroup Analysis

The CLA-BSI rate dropped significantly after bundle implementation in the PHO population overall, as well as in the BMT and non-BMT subgroups (Table IV and Fig. 1). Out of 102 total PHO CLA-BSIs, more than half (58%) occurred in BMT patients, although BMT patients comprised a minority (30%) of PD. Overall, BMT patients were three times more likely to develop a CLA-BSI per patient-day than non-BMT patients ($P < 0.033$). However, comparing the late steady state rates, BMT patients were only 1.33 times as likely to develop a CLA-BSI than non-BMT patients, and this difference lost statistical significance.

TABLE III. Compliance With Central Line Maintenance Practices

	Early ramp-up over 6 months (4/08–9/08)	Sustained period over 17 months (10/08–2/10)
Self-reported compliance audits, count (n)	235	221
Dressing change practices	97%	99%
Intravenous tubing change practices	100%	99%
Bathing practices	57%	89%
Practices to reduce central line entries	71%	97%
Access point hygiene practices	97%	90%
Hand hygiene before all central line care and entries	98%	92%
All-or-none compliance (i.e., completely compliant)	51%	86%

TABLE IV. CLA-BSI Rates in All Patients and Subgroups, Pre- and Post-Intervention

	All PHO	BMT	Non-BMT
Aggregate CLA-BSI events (n)	(102)	(57)	(45)
Pre-intervention CLA-BSI rate[a]	2.92	5.55	1.81
Post-intervention CLA-BSI rate[a]	1.61	2.96	1.04
Pre/post-CLA-BSI rate reduction (%)	45%	47%	43%
P comparing pre- vs. post-intervention	*<0.004*	*<0.037*	*<0.035*
Early steady state CLA-BSI rate[a]	2.77	5.25	1.82
Late steady state CLA-BSI rate[a]	1.23	1.33	1.00
Early/late CLA-BSI rate reduction (%)	56%	75%	45%
P comparing early vs. late steady state	*<0.002*	*<0.007*	*<0.007*

PHO, pediatric hematology/oncology; BMT, blood and marrow transplant; CLA-BSI, central line-associated bloodstream infection; [a]Rate expressed as CLA-BSIs per 1,000 patient-days.

CLA-BSI rates are displayed in annotated control chart format in Figure 1 for the aggregate PHO population as well as the BMT/non-BMT subgroups. All three control charts demonstrate special cause variation consistent with the intended effects of the prevention bundle, although signals emerged in different timeframes. In the non-BMT population, significant CLA-BSI reduction occurred immediately following implementation of the bundle. However, it was not until after elimination of power PICCs and implementation of daily CHG bathing that a significant and sustained CLA-BSI rate reduction was appreciated in the BMT population.

Common Variables in the CLA-BSI RCA

Patient characteristics and catheter variables of those who met the criteria for CLA-BSI following implementation of the maintenance bundle checklist are summarized in Table V. There were 36 CLA-BSI events that occurred in 32 patients. Four patients experienced greater than one CLA-BSI. Twenty-one CLA-BSI events occurred in BMT recipients (58%) and 15 in PHO patients (42%). The median time from catheter insertion to CLA-BSI event was 47 days (interquartile range, IQR, 15–116). The median age of the study population was 12 years (IQR 4–18), and 72% were male. The majority of patients had either hematologic malignancies (58%) or solid tumors (36%).

Safety Culture

The PHO nursing responses to the AHRQ Hospital Survey on patient safety culture reflected improvement in nearly all domains when comparing the pre-intervention with the post-intervention data. This included positive perceptions of: overall unit safety (rose from 40% to 89%, $P < 0.07$), organizational learning and continuous improvement (rose from 64% to 85%, $P < 0.31$), teamwork within the unit (rose from 79% to 95%, $P < 0.37$), and hospital management support for patient safety (rose from 51% to 93%, $P < 0.25$). Survey sample sizes were small with low response rates (12–32%), and comparisons did not meet statistical significance.

DISCUSSION

Rapid improvements in health care performance metrics commonly result from the reliable implementation of evidence-based science into daily practice more than implementing novel methods of care. The growing pressure to reduce nosocomial CLA-BSIs has led to more effective adoption of evidence-based clinical practice guidelines that have significantly improved patient safety in both adult and pediatric ICU settings [5,14]. Herein, we demonstrate that the application of daily maintenance catheter care bundles to pediatric patients with an underlying diagnosis of hematologic malignancy roughly halved CLA-BSIs. In contrast to adult ICU experiences, where bedside percutaneous catheter insertion practices are key drivers of CLA-BSI, our findings reinforce the importance of daily catheter maintenance practices for sustainably reducing rates of infection in catheters with prolonged dwell times. Three quarters of the CLA-BSIs we observed occurred more than 2 weeks out from central line insertion. The importance of daily catheter maintenance practices may well hold true for the adult oncology population in whom

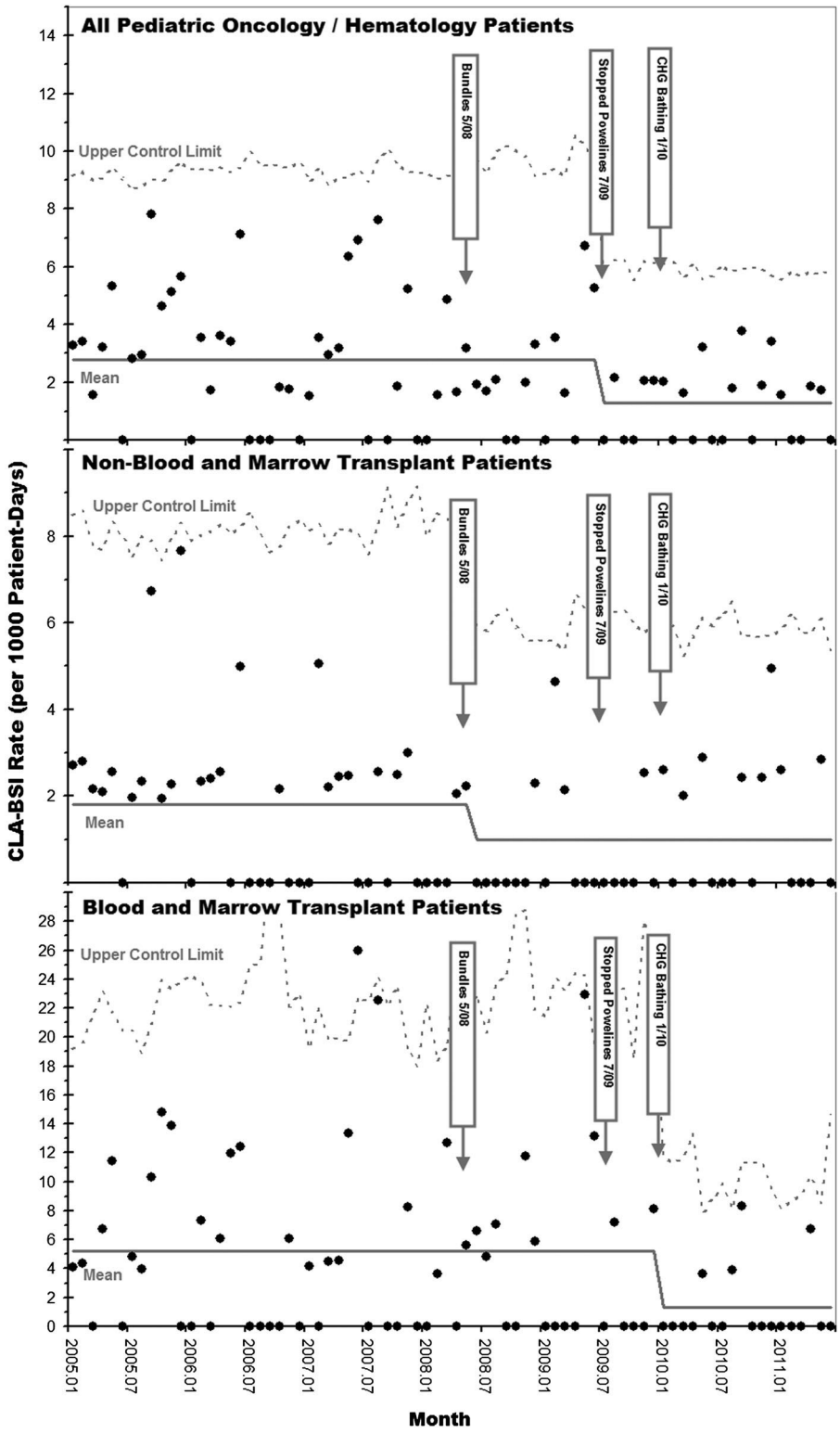

Fig. 1. CLA-BSI rate for all pediatric hematology/oncology and subsets.

CLA-BSIs temporally related to surgically implanted catheters are also uncommon.

The early steady-state CLA-BSI rate for our entire study population was 2.77 per 1,000 PD, and within the BMT and non-BMT patients, the rates were 5.25 and 1.82 per 1,000 PD, respectively—nearly a threefold difference. In line with published literature [41], we considered BMT as a potential risk factor for CLA-BSI. Interestingly, during the late steady-state period, the

TABLE V. Characteristics of CLA-BSI Events (May 2008–June 2011)

Patient category, count (%)		
All CLA-BSI events	36	100%
Occurring in BMT patients	21	58%
Occurring in non-BMT patients	15	42%
Patient demographics		
Age in years, median (IQR)	12	[4–18]
Male:female, count (%)	26:10	72%:28%
Diagnosis, count (%)		
Hematologic malignancy	21	58%
ALL	10	—
AML	9	—
MDS	2	—
Solid tumors	13	36%
Non-malignancy (aplastic anemia/PNH)	2	6%
Blood counts at time of CLA-BSI event		
WBC in cells/μl, median (IQR)	250	100–2,075
Leukopenic with WBC <450 cells/μl, count (%)	28	78%
ANC in cells/μl, median (IQR)	0	0–1,650
Neutropenic with ANC <500 cells/μl, count (%)	24	67%
Temporal association to antecedent events, count (%)		
Operation or procedure <7 days prior to CLA-BSI event	8	22%
Transfusions		
Red blood cells <7 days prior to CLA-BSI event	27	75%
Platelets <7 days prior to CLA-BSI event	26	72%
Chemotherapy		
<7 days prior to CLA-BSI event	21	58%
<30 days prior to CLA-BSI event	35	97%
Stem cell infusion		
<7 days prior to CLA-BSI event	8	38%[a]
<30 days prior to CLA-BSI event	14	67%[a]
Post-BMT day number at time of CLA-BSI, median (IQR)[b]	+5	0 to +15
Catheter dwell time prior to CLA-BSI event, median days (IQR)	47	15–116
Temporal association to subsequent events, count (%)		
Patient death		
<7 days after CLA-BSI event	1	3%
<30 days after CLA-BSI event	3	8%
Within the same hospitalization of CLA-BSI event	7	19%
Patient transfer to ICU <7 days after CLA-BSI event	8	22%
Catheter type, count (%)		
Neostar	12	34%
Broviac	8	22%
Power PICC	9	25%
Port	4	11%
PICC, standard	3	8%

CLA-BSI, central line-associated bloodstream infection; BMT, blood and marrow transplant; IQR, interquartile range; ALL, acute lymphoblastic leukemia; AML, acute myelogenous leukemia; MDS, myelodysplastic syndrome; PNH, paroxysmal nocturnal hemoglobinuria; WBC, white blood cell count; ANC, absolute neutrophil count; PICC, peripherally inserted central catheter; [a]Percentages are of events are among BMT patients only; [b]Of 36 CLA-BSI events, 21 occurred in BMT patients of which 4 (19%) occurred between 1–3 days prior to transplant date.

rates between the BMT and non-BMT patients were 1.33 (45% reduction) and 1.00 (75% reduction) per 1,000 PD, respectively. As time went on and further infection control strategies were implemented, the CLA-BSI rate in BMT patients became insignificantly different from non-BMT patients, demonstrating that similar CLA-BSI outcomes can be achieved in these populations despite their differences in risk [42].

In contrast to recent studies reporting decreased rates of CLA-BSI with PICCs [43,44], we initially observed overrepresentation of PICCs in our RCAs. Nine of seventeen CLA-BSIs were associated with power PICCs within the first 14 months of implementing bundled checklists. However, this finding should be interpreted with caution as we eliminated these lines early in the study period during process improvements. It is possible that over time with further adherence to standardized catheter care techniques, we would have observed similar CLA-BSI rates across catheter types. Based on our RCA, there were no other suggested associations between catheter variables (type, number of lumens, and material) and the risk for developing CLA-BSIs. A reduction in the BMT CLA-BSI rate was observed after cessation of power PICCs and implementation of CHG bathing [34,36]. However, a causal relationship can only be inferred by temporal association. The addition of CHG bathing may have led to uniform and better monitored bathing practices. Alternatively, it may

have coincided with a time period when standardized best-catheter practices were more reliably established.

It is intuitive that children with cancer and blood disorders, particularly those undergoing a BMT, would be at increased risk for CLA-BSI because of their immunocompromised state. In fact, the median WBC and ANC at the time of CLA-BSI in our patient population were 250 and 0 μl^{-1}, respectively. However, despite the severe neutropenia, our findings suggest that rigorous implementation of PHO-specific central line maintenance bundles reduced the incidence of CLA-BSIs significantly. Consistent with published data [5,14,42], this reduction occurred without hiring additional staff or significantly increasing nursing workload. Nonetheless, our RCA findings suggest that future areas of study are needed particularly regarding the apparent associations with blood product transfusions, stem cell infusions, and male gender. For instance, during periods of neutropenia, one could consider prophylactically locking central lines with antibiotics [41] or ethanol solutions [45,46] much as other neutropenic prophylaxis is initiated in this population. Similarly, perhaps more rigorous aseptic techniques for blood product transfusions should be adopted during periods of neutropenia, such as more rapid expiration of intravenous tubing exposed to blood products.

The CDC/NHSH definition for CLA-BSI changed in January 2008, which led to an attributable rate reduction of 18% in our study population, consistent with other reports [14,16,20,41]. The most common pathogen excluded as a likely skin contaminant was coagulase-negative *Staphylococcus* (CNS). Nonetheless, gram-positive bacteria still caused the majority of CLA-BSI in our study, and CNS remained the predominant organism. It is possible that immunocompromised hosts are more susceptible to less virulent isolates or microcontamination that immune competent hosts might spontaneously clear [20]. Importantly, the revised CDC/NHSN definition is less sensitive to catheters infected with common skin contaminants. While this may reduce false positives in other care settings, it may falsely exclude real line infections in immunocompromised children. In such vulnerable populations, a clinical adjudication of CLA-BSI with CNS or other skin flora should always be entertained, even if infection control specialists would not categorize an event as a laboratory-confirmed CLA-BSI.

There are several limitations of our study. First, given the non-randomized study design and lack of controls, we cannot conclude with certainty that the implementation of maintenance bundle checklists was responsible for the reduction in CLA-BSIs, nor that the temporal associations were causal. However, our findings are consistent with successful implementation of evidence-based practices. Second, the CDC definition of CLA-BSI primarily relates to hospital-acquired bloodstream infections. As such, our data do not capture PHO patients who acquire CLA-BSIs on the outpatient setting and are then hospitalized for further management. Similarly, the hospital-based surveillance system functions by geography, not diagnostic category, so there were undoubtedly a non-trivial number of CLA-BSIs that occurred in this population, specifically in the pediatric ICU, that are not reflected in our reported data. Therefore, the true incidence (as well as the associated morbidity and mortality) of CLA-BSIs may be underrepresented in our study. Third, CLA-BSI rates in our PHO unit were expressed with a denominator of PD because nearly all of our patients have central lines (catheter day data were not collected). If our CLA-BSI rate were expressed in central line days, our rate would likely be slightly higher. Nonetheless, PD remained a consistent denominator throughout the study period. Lastly, this is a single-institution study focused on (i) transferring current evidence into new populations, (ii) identifying local phenomena to guide specific quality improvement countermeasures, and (iii) unit-level contextual forces that may have facilitated success. Therefore, extrapolation to other PHO units warrants careful consideration. Ongoing multi-center collaborative efforts in PHO units [47] should help further illuminate reproducible best practices.

In summary, efforts to eradicate CLA-BSIs, which were initially implemented in adult and pediatric ICUs [5,14] are now being extended into other high-risk populations. Our study supports that CLA-BSIs are also preventable in PHO patients. The significant reduction is sustainable with day-to-day adherence to evidence-based guidelines and continued re-evaluation of catheter care practices. We developed an optimal maintenance bundle specific to our patient population, which required a multidisciplinary-collaborative effort to enact. Over the 3-year post-implementation period, our CLA-BSI incidence was significantly reduced by eliminating defects in best practices through quality improvement methods, specifically, multidisciplinary team-based problem solving, iterative RCA, and ongoing Plan-Do-Study-Act cycles. Notably, it is believed that the sustained reductions in CLA-BSI rates in both patient populations resulted from: (i) promoting a culture of patient safety, (ii) adopting uniform catheter care practices, (iii) learning multidisciplinary teamwork, and (iv) communicating effectively between patients, families, physicians, nurses, phlebotomists, and infection control specialists. Arenas where standardized best practice catheter care guidelines could be studied in the future include the outpatient clinical setting, home health interfaces, and in patients' homes where families or the patients themselves are the catheter care providers.

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REFERENCES

1. Mermel LA. Prevention of intravascular catheter-related infections. Ann Intern Med 2000;132: 391–402.
2. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1994;271:1598–1601.
3. Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. Crit Care Med 2004;32:2014–2020.
4. Sexton JB, Berenholtz SM, Goeschel CA, et al. Assessing and improving safety climate in a large cohort of intensive care units. Crit Care Med 2011;39:934–939.
5. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med 2006;355:2725–2732.
6. Pronovost PJ, Goeschel CA, Colantuoni E, et al. Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: Observational study. BMJ 2010;340:c309.
7. Pronovost PJ, Berenholtz SM, Goeschel CA, et al. Creating high reliability in health care organizations. Health Serv Res 2006;41:1599–1617.
8. Institute of Medicine. To Err is Human: Building a Safer Health System. 1999. http://www.iom.edu/Reports/1999/To-Err-is-Human-Building-A-Safer-Health-System.aspx. Accessed on February 28, 2012.
9. Institute of Medicine. Rewarding Provider Performance: Aligning Incentives in Medicare. 2006. http://iom.edu/Reports/2006/Rewarding-Provider-Performance-Aligning-Incentives-in-Medicare.aspx. Accessed on February 28, 2012.
10. Lindenauer PK, Remus D, Roman S, et al. Public reporting and pay for performance in hospital quality improvement. N Engl J Med 2007;356:486–496.
11. Murray LJ, Lee R, Martens C. In vivo cytokine gene expression in T cell subsets of the autoimmune MRL/Mp-Ipr/Ipr mouse. Eur J Immunol 1990;20:163–170.

12. Iscove NN, Sieber F. Erythroid progenitors in mouse bone marrow detected by macroscopic colony formation in culture. Exp Haematol 1975;3:32–43.
13. Costello JM, Morrow DF, Graham DA, et al. Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. Pediatrics 2008;121:915–923.
14. Miller MR, Griswold M, Harris JM II, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. Pediatrics 2010;125:206–213.
15. Chuengchitraks S, Sirithangkul S, Staworn D, et al. Impact of new practice guideline to prevent catheter-related blood stream infection (CRBSI): Experience at the Pediatric Intensive Care Unit of Phramongkutklao Hospital. J Med Assoc Thai 2010;93:S79–S83.
16. Wheeler DS, Giaccone MJ, Hutchinson N, et al. A hospital-wide quality-improvement collaborative to reduce catheter-associated bloodstream infections. Pediatrics 2011;128:e995–e1004, quiz e1004-1007.
17. Kallen AJ, Patel PR, O'Grady NP. Preventing catheter-related bloodstream infections outside the intensive care unit: Expanding prevention to new settings. Clin Infect Dis 2010;51:335–341.
18. Marra AR, Cal RG, Durao MS, et al. Impact of a program to prevent central line-associated bloodstream infection in the zero tolerance era. Am J Infect Control 2010;38:434–439.
19. Advani S, Reich NG, Sengupta A, et al. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: Extending risk analyses outside the intensive care unit. Clin Infect Dis 2011;52:1108–1115.
20. Niedner MF, Huskins WC, Colantuoni E, et al. Epidemiology of central line-associated bloodstream infections in the pediatric intensive care unit. Infect Control Hosp Epidemiol 2011;32:1200–1208.
21. Edwards JR, Peterson KD, Mu Y, et al. National Healthcare Safety Network (NHSN) report: Data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009;37:783–805.
22. Simon A, Fleischhack G, Hasan C, et al. Surveillance for nosocomial and central line-related infections among pediatric hematology–oncology patients. Infect Control Hosp Epidemiol 2000;21:592–596.
23. Wurzel CL, Halom K, Feldman JG, et al. Infection rates of Broviac–Hickman catheters and implantable venous devices. Am J Dis Child 1988;142:536–540.
24. Farr BM. Vascular catheter related infections in cancer patients. Surg Oncol Clin N Am 1995;4:493–503.
25. Link H, Bohme A, Cornely OA, et al. Antimicrobial therapy of unexplained fever in neutropenic patients–guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO), Study Group Interventional Therapy of Unexplained Fever, Arbeitsgemeinschaft Supportivmassnahmen in der Onkologie (ASO) of the Deutsche Krebsgesellschaft (DKG-German Cancer Society). Ann Hematol 2003;82:S105–S117.
26. Abbas AA, Fryer CJ, Paltiel C, et al. Factors influencing central line infections in children with acute lymphoblastic leukemia: Results of a single institutional study. Pediatr Blood Cancer 2004;42:325–331.
27. Wylie MC, Graham DA, Potter-Bynoe G, et al. Risk factors for central line-associated bloodstream infection in pediatric intensive care units. Infect Control Hosp Epidemiol 2010;31:1049–1056.
28. Ingram J, Weitzman S, Greenberg ML, et al. Complications of indwelling venous access lines in the pediatric hematology patient: A prospective comparison of external venous catheters and subcutaneous ports. Am J Pediatr Hematol Oncol 1991;13:130–136.
29. McLean TW, Fisher CJ, Snively BM, et al. Central venous lines in children with lesser risk acute lymphoblastic leukemia: Optimal type and timing of placement. J Clin Oncol 2005;23:3024–3029.
30. Adler A, Yaniv I, Solter E, et al. Catheter-associated bloodstream infections in pediatric hematology–oncology patients: Factors associated with catheter removal and recurrence. J Pediatr Hematol Oncol 2006;28:23–28.
31. Adler A, Yaniv I, Steinberg R, et al. Infectious complications of implantable ports and Hickman catheters in paediatric haematology–oncology patients. J Hosp Infect 2006;62:358–365.
32. CDC. National Vital Statistics; 2009. http://www.cdc.gov/HAI/bsi/bsi.html. Accessed on February 28, 2012.
33. Scott RD., The Direct Medical Costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention: CDC. http://www.cdc.gov/ncidod/dhqp/pdf/Scott_CostPaper.pdf; 2009. Accessed on February 28, 2012.
34. Vernon MO, Hayden MK, Trick WE, et al. Chlorhexidine gluconate to cleanse patients in a medical intensive care unit: The effectiveness of source control to reduce the bioburden of vancomycin-resistant *Enterococci*. Arch Intern Med 2006;166:306–312.
35. Bleasdale SC, Trick WE, Gonzalez IM, et al. Effectiveness of chlorhexidine bathing to reduce catheter-associated bloodstream infections in medical intensive care unit patients. Arch Intern Med 2007;167:2073–2079.
36. Peterson LR, Singh K. Universal patient disinfection as a tool for infection control: Rub-a-dub-dub, no need for a tub. Arch Intern Med 2006;166:274–276.
37. CDC. Central Line-Associated Bloodstream Infection (CLABSI): Event Guidelines and Procedures for Monitoring CLABSI. NHSN Manual 2010. http://www.cdc.gov/nhsn/psc_da.html. Accessed on February 28, 2012.
38. CDC. Catheter-Associated Bloodstream Infection Definitions: http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrentpdf 2008. Accessed on February 28, 2012.
39. Srinivasan A, Bell WM, Cardo M, et al. Central Line-Associated Blood Stream Infections—United States, 201, 2008, and 2009. MMWR 2011;60:243–248.
40. Company WE. Statistical quality control handbook. 1956:OCLC 33858387.
41. Kelly M, Conway M, Wirth K, et al. Moving CLABSI prevention beyond the intensive care unit: Risk factors in pediatric oncology patients. Infect Control Hosp Epidemiol 2011;32:1079–1085.
42. Miller MR, Niedner MF, Huskins WC, et al. Reducing PICU central line-associated bloodstream infections: 3-Year results. Pediatrics 2011;128:e1077–1083.
43. Mollee P, Jones M, Stackelroth J, et al. Catheter-associated bloodstream infection incidence and risk factors in adults with cancer: A prospective cohort study. J Hosp Infect 2011;78:26–30.
44. Hatakeyama N, Hori T, Yamamoto M, et al. An evaluation of peripherally inserted central venous catheters for children with cancer requiring long-term venous access. Int J Hematol 2011;94:372–377.
45. Valentine KM. Ethanol lock therapy for catheter-associated blood stream infections in a pediatric intensive care unit. Pediatr Crit Care Med 2011;12:e292–e296.
46. Blackwood RA, Klein KC, Micel LN, et al. Ethanol locks therapy for resolution of fungal catheter infections. Pediatr Infect Dis J 2011;30:1105–1107.
47. http://www.childrenshospitals.net/AM/Template.cfm?Section=Collaboratives1& Template=/CM/HTMLDisplay.cfm&ContentID=60780. Accessed on February 28, 2012.