OBJECTIVES: Central lines (CLs) are essential for the delivery of modern cancer care to children. Nonetheless, CLs are subject to potentially life-threatening complications, including central line–associated bloodstream infections (CLABSIs). The objective of this study was to assess the feasibility of a multicenter effort to standardize CL care and CLABSI tracking, and to quantify the impact of standardizing these processes on CLABSI rates among pediatric hematology/oncology inpatients.

METHODS: We conducted a multicenter quality improvement collaborative starting in November 2009. Multidisciplinary teams at participating sites implemented a standardized bundle of CL care practices and adopted a common approach to CLABSI surveillance.

RESULTS: Thirty-two units participated in the collaborative and reported a mean, precollaborative CLABSI rate of 2.85 CLABSIs per 1000 CL-days. Self-reported adoption of the CL care bundle was brisk, with average compliance approaching 80% by the end of the first year of the collaborative and exceeding 80% thereafter. As of August 2012, the mean CLABSI rate during the collaborative was 2.04 CLABSIs per 1000 CL-days, a reduction of 28% (relative risk: 0.71 [95% confidence interval: 0.55–0.92]). Changes in self-reported CL care bundle compliance were not statistically associated with changes in CLABSI rates, although there was little variability in bundle compliance rates after the first year of the collaborative.

CONCLUSIONS: A multicenter quality improvement collaborative found significant reductions in observed CLABSI rates in pediatric hematology/oncology inpatients. Additional interventions will likely be required to bring and sustain CLABSI rates closer to zero for this high-risk population. Pediatrics 2014;134:e1678–e1685

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KEY WORDS: bacteremia, catheter-related infections, cross infection, hospital oncology service, quality improvement

ABBREVIATIONS: CHA—Children’s Hospital Association; CL—central line; CLABSI—central line–associated bloodstream infection; NHSN—National Healthcare Safety Network; PHO—pediatric hematology/oncology; QI—quality improvement

Dr Bundy made substantial contributions to conception and design, acquisition of data, and analysis/interpretation of data; drafted the article; and revised it critically for important intellectual content. Drs Gaur and Billett made substantial contributions to conception and design, acquisition of data, and analysis/interpretation of data; drafted the article; and revised it critically for important intellectual content. Ms He and Dr Colantuoni made substantial contributions to analysis/interpretation of data and revised the article critically for important intellectual content. Ms He and Dr Colantuoni made substantial contributions to analysis/interpretation of data and revised the article critically for important intellectual content. Dr Miller made substantial contributions to conception and design, acquisition of data, and analysis/interpretation of data; she also revised the article critically for important intellectual content. All authors approved the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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(Continued on last page)
Central lines (CLs) are essential to the management of many pediatric patient populations, including children in ICU settings, those with chronic gastrointestinal conditions, and those with cancer and other chronic hematologic disorders. CLs can become infected, and their presence increases the risk of bloodstream infections and the associated morbidity and mortality. Bloodstream infections are the most common health care–associated infections in pediatric hematology/oncology (PHO) patients and are often associated with CLs (ie, central line–associated bloodstream infections [CLABSIs]). In addition to directly attributable morbidity, CLABSIs may introduce deleterious delays in the management of underlying malignancies.

The impact of “bundling” evidence-based or expert opinion–supported CL insertion and maintenance care practices on reducing CLABSIs has been well described in adult and pediatric ICU patients. Recent reports describe single-center successes with reducing CLABSIs in PHO inpatients with the use of standardized implementation of CL care and CL access practices. Whether CL maintenance care practices can be standardized for PHO inpatients across a diverse group of hospitals nationwide and similar gains in CLABSI reduction achieved in this patient population, which has other competing sources of bacteremia (eg, compromised skin and mucosal membranes), is unknown.

As part of a multicenter quality improvement (QI) initiative, PHO centers across the United States implemented and monitored adherence to a standardized CL maintenance care bundle and tracked CLABSIs by using standardized definitions for health care–associated infections. The present article describes the feasibility of such a multicenter effort and its impact on CLABSI rates in PHO inpatients.

**METHODS**

**Study Design**

The study was conducted as part of a multicenter collaborative, organized and operated by the Children’s Hospital Association (CHA). The collaborative was modeled on an earlier CHA PICU CLABSI collaborative and was orchestrated by a multidisciplinary team, including PHO physicians and nurses, infectious disease/infection prevention experts, QI experts, and CHA-based support and data management staff. All teams met in person semiannually for learning sessions directed by collaborative faculty. These 2-day learning sessions included education on QI, data review, teams’ “stories” of their successes and failures, and structured and unstructured networking time and exercises. In addition, teams interacted monthly on webinars in which collaborative data were reviewed, successes and stumbling blocks were presented by teams, and QI principles were reinforced. Thirty-two centers (as noted in the Acknowledgments) participated in the collaborative during the study period and shared their data for all PHO inpatients.

**Intervention**

The CL maintenance care bundle intervention developed by the collaborative faculty was an amalgamation of Centers for Disease Control and Prevention recommendations and standards, best practices derived from previous pediatric CLABSI prevention efforts and expert opinion. Recommended CL maintenance practices (Fig 1) included: (1) reduction of CL entries (eg, consolidate blood draws, change intravenous medications to oral); (2) sterile CL entry (eg, conduct proper hand hygiene before line entry, scrub cap with alcohol [15 seconds] or chlorhexidine [30 seconds]); and (3) standardized CL care practices (eg, date and time cap; dressing, needle, and tubing change; follow consistent procedure and change schedule).

**Measures**

**CLABSI**

Teams reported all existing baseline CLABSI data from January 2006 to October 2009, during the period before joining the collaborative. These data were compared with intervention period data from November 2009 to August 2012. CLABSIs were tracked as the number of CLABSI per 1000 CL-days per month for each center. To capture numerator data (CLABSIs), team members from each center applied standardized Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) surveillance definitions to determine whether positive blood culture results from PHO inpatients met CLABSI criteria. Two additional clarifications to the NHSN definitions were provided to participating centers during the intervention period: (1) CLABSIs “not present or incubating at admission” were defined as those occurring >48 hours after admission; and (2) date and time of first positive culture result were used to define a CLABSI as opposed to the NHSN criteria using onset of symptoms to capture date and time of CLABSI onset (due to the complexity of clinical manifestations in the PHO population). These clarifications are no longer required since implementation of the January 2013 updates to the NHSN CLABSI definition.

CLABSIs occurring >48 hours after hospital admission to <48 hours after hospital discharge were deemed inpatient events and were included in the analyses. To capture denominator data (CL days), per the NHSN guidelines, each team counted every PHO inpatient with ≥1 accessed CL as contributing 1 CL per day. In addition to measuring CLABSI rates, teams completed an event form (Supplemental Information A) for each CLABSI, which provided data on...
General care and maintenance
- The central venous catheter site should be visually assessed through the transparent dressing at least daily for signs and symptoms of infection or complications.
- Do not expose or submerge the dressing, catheter, cap, or tubing in water. Precautions should be taken to cover when bathing or showering.
- All procedures should be preceded by conscientious hand hygiene.

Procedure for all entries into catheter (via cap, tubing, or extensions) connected to the central venous catheter
- Consolidation, and elimination if possible, of catheter entries (eg, blood draws, flushes, medications) discussed with medical team.
- Nonsterile examination gloves (optional), no mask.
- Alcohol (15 s and 15 s dry time) or CHG (30 s and 30–60 s dry time)

External central venous catheter dressing change procedure
- Use dressing change kit/area defined by unit.
- Assess exit site when dressing removed for signs of infection or complications.
- Sterile gloves.
- Mask for all providers and assistants.
- Shield for patient’s face, endotracheal tube or tracheostomy with mask or drape.
- 30-s CHG scrub, then 30- to 60-s dry time for insertion site (2-min scrub if catheter in groin)
- No ointments at insertion site, unless dialysis catheter (per institution preference).
- Sterile transparent, semipermeable dressing: change every 7 d and PRN if soiled, damp, or loose.
- Gauze dressing for oozing or bleeding exit site: changed every 2 d for inspection, PRN if soiled, saturated, or loose.
- Labeling/documentation to indicate date dressing changed or due to be changed.

Access of IVAD port with needle and occlusive dressing procedure
- Use access/occlusion kit defined by unit.
- Assess site with dressing removed for signs of infection or complications.
- Sterile gloves.
- Mask for all providers and assistants.
- Shield for patients face, endotracheal tube or tracheostomy with mask or drape.
- 30-s CHG scrub, then 30- to 60-s dry time for insertion site (2-min scrub if catheter in groin)

FIGURE 1
CHG, chlorhexidine gluconate; CL, maintenance bundle; IVAD, implanted vascular access device.
*Institutional preference for CHG use for infant <2 months old.

the involved organism, patient attributes (eg, underlying diagnosis, presence of neutropenia), and recent care (eg, estimated number of line entries in the 72 hours preceding CLABSI incidence).

CL Maintenance Practices
CL maintenance practices were quantified monthly by using a standardized CL maintenance audit form (Supplemental Information B). Teams were encouraged to perform audits at least weekly and to develop a strategy that would capture the practices of the widest possible cross-section of nurses on all shifts and on all days of the week. Self-auditing was suggested, although any form of auditing was allowed.

Other Measures
Each center completed a unit profile survey annually that cataloged data on unit attributes, including patient volumes, staffing patterns, and other related practices that could impact or help better understand intercenter differences in CLABSI rates (eg, use of antibiotic prophylaxis, antimicrobial lock therapy).

Data Collection and Analysis
Teams electronically submitted CLABSI and CL maintenance audit data monthly to a centralized data repository managed by CHA. Exploratory data analysis included summarizing the total number of CLABSIIs and overall CLABSI rates during the precollaborative and collaborative periods, creating scatter plots of the monthly CLABSI rates during the study period with locally weighted regression smoother (lowess) and creating scatter plots of the monthly compliance to bundle elements during the postcollaborative period (with lowess). Characteristics of the units were summarized based on data collected via the unit profile survey. The primary analysis estimated and compared the CLABSI rates during the collaborative and precollaborative periods, by using a Poisson regression model for the monthly number of CLABSIIs offset by the reported monthly number of line days and a single predictor, an indicator for the collaborative period. An additional analysis estimated the monthly change in CLABSI during the precollaborative and collaborative periods separately by using a Poisson model that incorporated a linear spline with knots at the first month of the collaborative period. This model was used to determine whether the rate of CLABSI decline observed during the baseline period accelerated during the collaborative period. The
regression models were estimated via generalized estimating equations assuming an exchangeable correlation structure for the monthly measurements within a unit over time and a robust variance estimate. Sensitivity analyses included refitting the 2 aforementioned regression models but varying the number of months of precollaborative data that was included in the analysis to explore potential temporal issues (entire baseline, 34 months, 24 months, 12 months, and 9 months). In addition, the regression models were fit, including an indicator for the CLABSI definition change in January 2008,13,14 which required, among other things, 2 (instead of 1) positive blood culture results for common skin contaminants. To assess the difference in heterogeneity in CLABSI incidence before and during the intervention, we created an indicator for “no CLABSI event” for each unit in each month. We then fitted a logistic regression model with the intervention effect, while adjusting for total at risk time (ie, CL days). SEs were calculated by using robust variance estimates to adjust for clustering within the units. Stata version 11.2 (StataCorp, College Station, TX) was used for all analyses.

**Human Subjects**

The overall study was approved by the Johns Hopkins Medicine institutional review board. In addition, each team individually obtained approval (or exemption) locally.

**RESULTS**

**Participants**

Thirty-two units participated in the collaborative; 28 units completed the unit profile survey (Table 1). The most common unit configuration was hematology, oncology, and transplant combined (50%), with hematology and oncology alone the next most common (36%). Units varied widely in size (8–48 beds), and most housed patients in a single physical location (89%). Almost two-thirds of teams were operating in hospitals certified by the American Nurses Credentialing Center Magnet Recognition Program. A large majority (93%) of units managed afebrile, neutropenic, postintensive chemotherapy patients with acute myeloid leukemia in inpatient settings while awaiting count recovery, and none used antimicrobial-impregnated catheters. More than one-third used chlorhexidine gluconate baths

<table>
<thead>
<tr>
<th>TABLE 1 Participating Centers (N = 28)</th>
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<tr>
<td><strong>Center Attribute</strong></td>
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<tr>
<td><strong>Unit structure</strong></td>
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<tr>
<td>Unit type (n = 28)</td>
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<tr>
<td>Hematology, oncology, and transplant</td>
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<tr>
<td>Hematology and oncology</td>
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<tr>
<td>Oncology and transplant</td>
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<td>Annual patient-days (n = 25)</td>
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<td>Inpatients are housed in a single physical location (n = 28)</td>
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<td><strong>Staffing</strong></td>
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<td>Program includes an accredited hematology/oncology fellowship (n = 28)</td>
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<td>Float nurses used on the unit (n = 27)</td>
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<td>Traveling/contract nurses used on the unit (n = 25)</td>
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<td>Proportion of nurses CPHON-certified (mean (range)) (n = 28)</td>
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<td>Physician and nurse care practices (n = 28)</td>
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<td>Afebrile, neutropenic, post-intensive chemotherapy AML patients managed in inpatient setting while awaiting count recovery</td>
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<td>Patients at high risk of infection (including AML, relapsed ALL; excluding transplant) routinely receive antibacterial prophylaxis (other than PCP prophylaxis) while neutropenic</td>
</tr>
<tr>
<td>Antimicrobial-impregnated catheters</td>
</tr>
<tr>
<td>Not used</td>
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<tr>
<td>Used in a programmatically defined subset of patients</td>
</tr>
<tr>
<td>Routinely used in majority of patients</td>
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<tr>
<td>Chlorhexidine gluconate baths</td>
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<tr>
<td>Not used</td>
</tr>
<tr>
<td>Used in a programmatically defined subset of patients</td>
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<tr>
<td>Routinely used in majority of patients</td>
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<td>Participants in daily rounds</td>
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<td>Clinicians (eg, physicians, nurse practitioners, physician’s assistants, residents, fellows)</td>
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<td>Bedside nurses</td>
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<td>Research logistics (n = 25)</td>
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<td>Institutional review board designation</td>
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<td>Expedited review</td>
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<tr>
<td>Full review</td>
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<td>Have not been reviewed</td>
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</tbody>
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AML, with acute myeloid leukemia; CPHON, certified pediatric hematology oncology nurse; PCP, Pneumocystis carinii pneumonia.

a n refers to number of centers responding to that survey item.

b American Nurses Credentialing Center Magnet Recognition Program.
in at least some patients; more than one-half involved patients and families in daily rounds.

**CLABSI Rates**

Across 46 months of precollaborative data, the estimated CLABSI rate was 2.85 CLABSIs per 1000 CL-days (Fig 2). During the first 34 months of the collaborative, the estimated CLABSI rate decreased to 2.04 CLABSI per 1000 CL-days. This 28% reduction in CLABSI rates was statistically significant (relative risk: 0.71 [95% confidence interval: 0.55–0.92]). The estimated CLABSI rate during the precollaborative period decreased 10% per year, which was not statistically different from the estimated annual decrease of 9% during the collaborative period (P = .89). These findings were qualitatively unchanged when the duration of precollaborative data were varied from the entire precollaborative period to 34, 24, 12, or 9 months. The odds of “no CLABSI event” in a given unit in a given month during the intervention period was 2.59 times the corresponding odds during the pre-intervention period, comparing units with similar numbers of CL days (95% confidence interval: 1.26–5.33; P = .01), suggesting that the heterogeneity in the intervention period was significantly lower than that in the preintervention period.

**CL Maintenance Practices**

Compliance with recommended CL maintenance practices increased rapidly over the first year of the collaborative, from 38% at baseline to 79% by the end of the first year (Fig 2). After the first year of the collaborative, there was little change over time in maintenance compliance, with a consistent rate of 81% to 86% reported. Changes in self-reported maintenance compliance practices were not statistically associated with changes in observed CLABSI rates.

**DISCUSSION**

During the first 2.5 years of an ongoing PHO QI collaborative, we observed a 28% reduction in CLABSI incidence. This reduction suggests the elimination of ~290 CLABSIs during the collaborative period. Although the cost of a CLABSI in US PHO populations has not been reported, CLABSIs in PICU populations cost ~$40 000. Using this estimate, our observed CLABSI reduction represents a cost savings in excess of $11 million.

Previous reports have demonstrated reductions in CLABSI rates among hospitalized PHO patients at single centers, but the present study is the first, to our knowledge, to report such reductions across a large network of PHO centers. This study is also the first to demonstrate the feasibility of 32 PHO centers implementing a standardized CL maintenance care bundle, tracking CL infections by using standardized definitions, and generating benchmarking data. Other than a research trial design, such multicenter QI efforts are the next best way to standardize interventions and outcome assessments in a “real-world” setting and to deliberate on the impact of such standardized care practices on patient outcomes (eg, CLABSIs).

We are encouraged by the decline in collaborative-wide CLABSI rate and explain this outcome by making 3 comparisons: versus the multicenter PICU CLABSI reduction effort on which the current collaborative was based, versus the published single-center experience from several PHO centers, and, finally, versus the precollaborative data available from many of the collaborative centers.

**FIGURE 2**

CLABSIs per 1000 CL-days and self-reported CL maintenance bundle compliance. Each center (N = 32) contributes 1 data point (ie, dot) per month.
The current PHO QI collaborative was modeled on a parallel effort involving a large network of PICUs. Compared with the decline in CLABSI rate seen in the PICUs, the decline observed in PHO centers was modest. In the first year of the PICU effort, CLABSI incidence declined from 5.4 to 3.1 CLABSIs per 1000 CL-days. Notably, the precollaborative rate observed in the PHO collaborative (2.85 per 1000 CL-days) was lower than that reported at the end of the PICU collaborative’s first year. After 3 years, the PICU CLABSI rate declined further to 2.3 CLABSIs per 1000 CL-days, which is slightly higher than the PHO collaborative rate we report. In addition to substantial differences in underlying patient populations, the PHO and PICU collaboratives differed in other important ways. The PICU collaborative included a CL insertion bundle, in addition to the CL maintenance bundle. In the PHO setting, in which CLs are typically placed surgically (as opposed to at the bedside), insertion practices were deemed to be standardized to begin with. This point, combined with the relatively higher use of temporary versus permanent CLs, may explain both the higher baseline rate of CLABSIs in the PICU collaborative and the striking decline with standardizing CL insertion and maintenance practices. Similarly, 1 method of CLABSI reduction in both PICU and adult ICU studies is to remove CLs as quickly as possible when they are no longer needed or suspected to be infected. Salvage of infected CLs in PHO patients is not uncommon and there is a known risk of relapse of the same infection or a new infection with a different organism in these patients. Furthermore, early removal of CLs is not feasible in the PHO population because of ongoing treatment requirements for months to years. In January 2013, the NHSN recognized a subset of CLABSIs as attributable to translocation of bacteria from the skin and/or mucous membranes and defined them as mucosal barrier injury laboratory-confirmed bloodstream infections. These infections, which would be less amenable to prevention by CL care practices and are relatively frequent in PHO patients, occur much less frequently in critical care units (there were no mucosal barrier injury laboratory-confirmed bloodstream infections reported by any of the 38 adult critical care units in the study of See et al). These factors likely also influenced the more modest decline in CLABSI rate observed in the present study.

We are aware of 3 published single-center CLABSI reduction efforts in PHO patients, one of which involved a collaborative participant. All 3 were published in the past year and included standardization of CL care practices as part of their intervention. Two stated the CLABSI definition that they used (NHSN definition); 1 study did not clarify how CLABSI was defined. Of note, Choi et al used patient-days and not CL-days as their denominator; a difference not as significant in PHO patients, a majority of whom have a CL in situ; this difference is important because it underscores the point that differences in definitions used and variability in adjudication can confound comparisons of local data versus published reports. Although both groups that reported their CLABSI definition noted a decline in their postintervention CLABSI rate, for one this drop was statistically significant and for the other it was not; neither reduced CLABSI rates to zero. It is clear that, for a number of reasons (eg, the limitations of the NHSN CLABSI definition, even with the modifications made in January 2013), the prolonged immune-suppressed state of PHO patients, and the fact that these patients have a CL in situ for prolonged periods of time as they move between the hospital and ambulatory environments with different caretakers of the CL), a CLABSI rate of zero is a laudable goal achieved by few and sustained by even fewer. However, as shown at individual centers and from the collaborative-wide results we present, a reduction in CLABSI rate in PHO patients is possible and linked among other things to institution of CL maintenance care practices. There are a number of other practices and interventions “beyond the CL care bundle,” and significant differences in their use across North American PHO centers were reported in a recent survey. Choi et al note that their CLABSI rate in bone marrow transplant patients was not reduced with CL maintenance care practices alone until they discontinued the use of power ports and instituted chlorhexidine gluconate baths in their patients.

To assess the impact of participating in this QI collaborative on CLABSI rates, we present both pre-/post- and slope-based analyses. The former showed a statistically significant reduction in CLABSI rates but does not clearly demonstrate the contribution of the collaborative to observed reductions, acknowledging the observed reduction that was ongoing during the pre-collaborative period and the variability in the number of centers and the period of time for which precollaborative CLABSI data were available. The slope-based analysis aimed to determine whether the collaborative was associated with acceleration in CLABSI reduction. Although this analysis found no acceleration, it is not clear what the lowest theoretical CLABSI rate is in the PHO population and whether an asymptote is being reached such that further CLABSI reduction acceleration is no longer possible. We did, however, observe several teams that reported periods in excess of 6 consecutive months without a CLABSI, suggesting that the true floor for CLABSI in the PHO population may yet be lower than we have achieved as a collaborative. It should also be noted that many teams were already engaged in local CLABSI reduction QI efforts before joining the collaborative, potentially muting the observed...
difference between precollaborative and collaborative CLABSI rates. Several teams were also actively trialing or implementing other, noncollaborative CLABSI reduction strategies (eg, routine chlorhexidine gluconate bathing, antibiotic or ethanol lock therapy) before and during the collaborative. The effect of these additional strategies on CLABSI rates is unknown. Similarly, there was variability in non–CLABSI-focused care strategies (eg, empirical antibiotic prophylaxis) that might also have differentially affected CLABSI rates.

We looked for any association between changes in both individual and bundled self-reported CL maintenance practices and changes in CLABSI rates, and unlike in the PICU setting, did not see any. This outcome may in part be because reported maintenance compliance was high throughout all but the earliest months of the study. The limitations of a self-audit assessment of clinical care practices may have affected the validity of the high compliance rates reported for CL care practices across centers. Although this method is susceptible to biases in reporting, it is also a process highly valued by participating teams, who used audit tools not just for measurement but also for reminders and teaching to staff regarding appropriate maintenance practices. It is also possible that factors distinct from CL maintenance practices, such as improved overall attention to detail, enhanced emphasis on safety culture, and changes in belief systems on the inevitability of CLABSI among immunocompromised PHO inpatients, may have contributed to observed reductions in CLABSI rates.

CONCLUSIONS
In the largest study of its kind in PHO inpatients, we found that collaborative improvement efforts with the use of standardized approaches, tools, and definitions lowered CLABSI rates in this immunocompromised population. Although it cannot be said with certainty which bundle elements were most essential to minimizing CLABSI, which nonbundle elements can further drop the CLABSI rate, and whether the CLABSI rate using the current NHSN definition can realistically be maintained at zero in PHO patients, we have created robust benchmarking data that will facilitate future comparisons. Substantial future work remains, both to better understand the definitional and epidemiologic challenges of CLABSI reduction in this population, and also to extend the gains by the most successful of our teams to all centers. Maximizing the outcomes of children with cancer will require not only continued increases in cure rates from new therapies, but also steadfast focus on reducing the complications associated with treatment.

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(Continued from first page)

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Preventing CLABSIs Among Pediatric Hematology/Oncology Inpatients: National Collaborative Results

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