

# Reduced central line infection rates in children with leukemia following caregiver training

## A quality improvement study

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### Abstract

Infections are a leading cause of morbidity and mortality in children with acute leukemia. Central-line (CL) devices increase this population's risk of serious infections.

Within the context of a quality improvement (QI) project, we tested the effect of caregiver education on CL management on the CL-associated bloodstream infection (CLABSI) rate among children with acute leukemia seen at a large referral center in Italy. The intervention consisted of 9 in-person sessions for education and practice using mannequins and children.

One hundred and twenty caregivers agreed to participate in the initiative. One hundred and five (87.5%) completed the training, 5 (4.1%) withdrew after the first session, and 10 (8.3%) withdrew during practical sessions. After educational intervention, the overall CLABSI rate was reduced by 46% (from 6.86 to 3.70/1000 CL-days). CLABSI rate was lower in children whose caregivers completed the training (1.74/1000 CL-days, 95% CI 0.43–6.94) compared with those who did not receive any training (12.2/1000 CL-days, 95% CI 7.08–21.0,  $P < 0.05$ ) or were in-training (3.96/1000 CL-days, 95% CI 1.98–7.91) at the time of infection.

Caregiver training in CL management, applied within a multifaceted QI approach, reduced the rate of CLABSI in children with acute leukemia. Specific training and active involvement of caregivers in CL management may be effective to reduce CLABSI in high-risk children.

**Abbreviations:** ALL = acute lymphocytic leukaemia, AML = acute myelogenous leukemia, CL = central line, CLABSI = central-line associated blood stream infection, DH = day hospital, PHO = pediatric hemato-oncology, QI = quality improvement.

**Keywords:** caregivers, children, CLABSI, education, leukemia

## 1. Introduction

Infections are a major cause of morbidity and mortality in children with acute leukemia, due to severe and prolonged cytopenia, hypogammaglobulinemia, severe mucositis, and gut microbial dysbiosis.<sup>[1–3]</sup> The threat to a patient's health is

related either directly to the infection itself or indirectly to interruption or delay of chemotherapy, prolonged hospitalization, and risk of nosocomial infections or malnutrition.<sup>[4]</sup>

Bloodstream infections are serious events and cause a prolongation of hospital stay, increased costs and high risk of mortality. Central line (CL)-associated bloodstream infection (CLABSI) rates in oncologic children vary between 0.7 and 7.4 episodes per 1000 central-line (CL) days, according to different studies.<sup>[5–8]</sup> However, the risk of infection is significantly linked with the patient's main diagnosis and underlying conditions, and duration of the CL.<sup>[5,6]</sup> Children with acute leukemia and children undergoing bone marrow transplantation show higher CLABSI rates when compared with children affected by other hematologic illnesses or solid tumors.<sup>[6]</sup> In studies on CL-related complications in European children with acute leukemia, infection rates ranged from 1.4 to 5.4/1000 CL days depending on CL characteristics (such as catheter type, site of insertion, and dwell time).<sup>[9]</sup>

Standard practices to prevent CLABSI have been disseminated by the US Centers for Disease Control and Prevention (CDC).<sup>[10]</sup> Previous studies demonstrated the efficacy of multifaceted interventions to reduce infections, and particularly CLABSI, in at-risk patients.<sup>[11,12]</sup> Implementation of evidence-based interventions, including hygiene measures and appropriate management of medical devices, likely significantly reduces the CLABSI rate in hemato-oncology patients.<sup>[8,13,14]</sup>

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Children with leukemia maintain a CL on average for 2 years, spending the majority of this time at home. Our working hypothesis was that maintaining appropriate CL hygiene and management through active involvement of the family may reduce the infection rate in this at-risk population. We tested the effect of caregiver training in CL management, as part of a larger quality improvement (QI) project, on the CLABSI rate in children with acute leukemia.

## 2. Methods

### 2.1. The working team

A multidisciplinary team was created to carry out a QI project to reduce CLABSI among children with acute leukemia. The QI team included pediatricians with expertise in infectious diseases and hemato-oncology, experts in QI methodology, microbiologists, surgeons, and nurses. Team members met regularly to define the study protocol and practice interventions based on CDC and the National Association of Children's Hospitals and Related Institutions (NACHRI) Quality Transformation Efforts guidance.<sup>[10,12]</sup> The QI team met regularly to discuss infection rates, systematically review new events, and discuss barriers to protocol implementation. The QI project was started in 2010. A caregiver training course was proposed and developed by the QI team in 2013 as a nested intervention to test once CLABSI rates had plateaued.

### 2.2. Setting and population

The study was done at Santobono-Pausilipon Children's Hospital, the largest pediatric medical center in Southern Italy, with over 35,000 pediatric admissions in 2014. It is a major referral center for children with leukemia, with about 350 children in follow-up and about 40 new diagnoses of acute leukemia annually. Care is provided predominantly on two units: The pediatric hemato-oncology (PHO) (average daily census 14 patients), and day hospital (DH) (average daily census 30 patients) units.

### 2.3. Operational definitions

Eligible patients were children with acute myelogenous leukemia (AML) or acute lymphocytic leukemia (ALL) aged 2 months to 18 years admitted to the PHO or DH. Patients admitted to the PHO for other diseases and patients undergoing bone marrow transplantation received care in a system separate from those with acute leukemia and were excluded from the analysis.

A fever episode was defined by a body temperature  $>38.5^{\circ}\text{C}$  in one measurement or by body temperature  $>38^{\circ}\text{C}$  in two consecutive measurements within 1 hour.

CLABSI was defined according to standard CDC/National Healthcare Safety Network (NHSN) definitions at the time of project start.<sup>[15]</sup> The same definition was used throughout the study to reduce variability in our outcome measure. The determination of each CLABSI event was made by members of the QI team.

Infections were identified and patient data extracted through daily monitoring of admitted patients and manual chart review of eligible patients admitted between March 2012 and March 2014. A research nurse trained in data collection and interpretation reviewed the list of admitted patients each weekday and enrolled those who met inclusion criteria. On Monday morning, the research nurse would also review patients admitted during the

weekend. CLABSIs were identified in real time with positive cultures. CL day and patient-day denominator data were obtained by measuring the number of children with leukemia, with or without CL, present in the unit at the same time each day.<sup>[10,15]</sup> Each patient with a CL contributed only 1 CL day even if the patient had more than 1 CL.<sup>[15]</sup>

All children were treated for their leukemia according to the protocol of the Italian Association of Pediatric Hematology and Oncology (AIEOP) for acute lymphoblastic and acute myeloid leukemia.<sup>[16]</sup>

### 2.4. Study design

In the initial phase of the QI project, a stable CLABSI rate of 6.7/1000 CL days was achieved among the study population within 2 years, and the existing protocol was moved to a sustain mode (key drivers for the overall QI project are shown in Table 1). In an effort to further reduce the CLABSI rate, a caregiver training course was proposed and developed, to be implemented in the context of the ongoing CLABSI prevention protocol. The SMART aim<sup>[17,18]</sup> was to decrease the CLABSI rate from 6.7/1000 CL days to 4.5/1000 CL days (30% reduction) within 1 year. The educational intervention was implemented and monitored in both the PHO and DH. Components were adjusted as needed using plan-do-study-act (PDSA) cycles.<sup>[17,18]</sup>

**Table 1**  
Key drivers and interventions for the overall CLABSI reduction quality improvement study.

| Key drivers                                     | Interventions   |
|---|---|
| Hygiene measures and management of central-line | Review and application of maximal sterile barrier precautions   |
|   | Promotion of hand hygiene<br>Alcohol-containing hand hygiene product dispenser at patients' bedside<br>Use of chlorhexidine for CL placement and management<br>Use of recommended insertion-site dressing practices<br>Removal of central lines when no longer needed<br>Visual score to assess the CL exit site<br>Checklist for CL daily management |
| Health-care personnel education and training    | Continuous education of health-care personnel   |
|   | Training course for nurses<br>Production of local protocol for CL management<br>Dissemination of the local protocol to other units having contacts with CL (e.g., radiology)<br>Checklist for surgical CL placement<br>Registered nurse dedicated to infection control  |
| Health care personnel feedback and performance  | Monitoring of nurse activities and feedback on success rate   |
|   | Monitoring of alcohol-containing hand hygiene product and chlorhexidine consumption<br>Daily measurement of fever episodes and CLABSI and monthly reporting of rates<br>Standardized review and classification of episodes<br>Sharing of infection monitoring results (run charts)  |
| Interaction with microbiology unit and pharmacy | Optimization in blood culture sampling strategies   |
|   | Replacement of povidone-iodine with chlorhexidine for skin preparation<br>Medical kits for CL medication and management   |

CL = central line, CLABSI = central line-associated bloodstream infection.

### 2.5. Educational intervention

Before implementation of the quality improvement initiative, patients' caregivers were not involved in CL care. During the first hospitalization, when typically a CL is placed to start chemotherapy, caregivers received general information about the role of CL in the overall management of their children and were made aware of the importance to keep the insertion site clean and to avoid handling the CL. None of caregivers was involved in CL dressing changes. Once a week, during routine hospital visits, nurses checked the CL insertion site and managed the CL dressing.

We set up a specific educational initiative to train caregivers/families in the management of CL and infection prevention. The 9-session training course lasted approximately 2 months based on caregiver autonomy and self-confidence. Each session was attended by 1 or 2 caregivers and lasted 60 to 90 minutes, and included ample time for questions and discussion. Session themes and topics are listed in Table 2. The first session consisted of an overview of infection prevention measures and CL care. The second and third sessions focused on individual and environmental hygiene measures. The remaining 6 sessions were practical experience on mannequins (3 sessions) and patients (3 sessions). At the final session, a locally produced video clip illustrating the procedures for asepsis and care of CL insertion site was provided to all training participants. Additionally, a checklist for CL management at home, similar to those used by inpatient providers, was developed and distributed to training participants (see supplemental content, <http://links.lww.com/MD/B64>—which illustrates the checklist for the management of central line).

During subsequent patient admissions, participants participated in CL care by supporting nurses during CL dressing, observing (and reporting to their bedside nurse) health care personnel compliance with the CLABSI prevention protocol on the study units as well as in other settings throughout the hospital, such as radiology or the surgery unit.

**Table 2**  
Caregiver training program.

| Session | Theme   | Topics  |
|---------|---|---|
| 1       | Overview  | Infection risk in children with leukemia<br>General infection prevention measures<br>Central lines and children with leukemia (prolonged dwell time, potential complications, principles of care)   |
| 2–3     | Hygiene measures (individual and environmental) | Review from previous session<br><br>Maximal sterile barriers precautions<br>Hand hygiene training and demonstration<br>Principles and process for preparation of a sterile environment at home<br>Distribution of pamphlet on CL care at home |
| 4–6     | Practical—mannequin                             | Review from previous sessions<br>Demonstration and practice of CL management on mannequin<br>Checklist for CL management at home<br>Discussion of local barriers (at home) and risks  |
| 7–9     | Practical—patient                               | Checklist for CL management at home review/revision<br>Practical session on patient<br>Video clip presentation<br>Questions and answers   |

### 2.6. Outcome measures

The primary outcome was CLABSI rate/1000 CL days in children with acute leukemia. To better evaluate the educational program effect, CLABSI rates were calculated among groups of caregivers stratified by training completed at the time of infection. Caregivers were classified as fully trained (all sessions attended, judged independent by trainers), in training (had not completed the training at the moment in which the infection occurred, but had begun the practical sessions), and not trained (declined training or did not intend to complete training).

The number of families completing the training and the number of central-line medication administrations performed in DH by nurses (rather than families) were used to indirectly measure the training program's efficacy.

### 2.7. Statistical analysis

We used statistical process control charts (*P*-charts) to track outcome measures and detect trends and special causes of variation.<sup>[15,17]</sup> The baseline rate was calculated based on the previous 12 months of the QI project (March 2012 and April 2013) and was compared with cumulative CLABSI rates computed with 95% confidence intervals (CI).

Cumulative rates with 95% CI were used to compare the CLABSI rate among stratified caregiver groups. Continuous variables were analyzed by analysis of variance.

### 2.8. Human subject protection

The Santobono-Pausilipon Children's Hospital institutional review board reviewed the project and considered it a local quality improvement initiative rather than research involving human subjects. Informed consent beyond the standard consent for treatment for all inpatients was not required. All families who agreed to participate to the CL training signed an informed consent before starting the educational program.

## 3. Results

A total of 118 children were diagnosed with acute leukemia and included in the study. Of the 118, 42 (35 ALL and 7 AML) (35.6%) children were admitted for fever episodes during the study period, and 50% of these (21/42) met the definition of CLABSI (Table 3).

Among ALL patients, those with a diagnosis of high-risk ALL and those who presented as a relapse were grouped together and classified as high risk ALL (ALL-HR).

Children with ALL had a slightly lower incidence of CLABSI compared with children with ALL-HR and AML, although this difference was not statistically significant (Table 3).

The baseline CLABSI rate was 6.86/1000 CL-days. Following implementation of the training, the CLABSI rate decreased to 3.70/1000 CL-days within the first 8 months with a 46.1% rate reduction attributable to the intervention alone (Fig. 1).

During the study period 120 caregivers of 118 children with acute leukemia agreed to participate to the training, including 2 families in which both parents asked to be trained. After the first session, 5 caregivers (4.1%) declined participation in the project. Ten additional families (8.3%) withdrew during the practical sessions because of self-described anxiety, fear, and a feeling of incompetence. The remainder of the caregivers completed the training.

**Table 3**  
**Features of children with febrile episodes and CLABSI.**

|  | ALL        | HR-ALL      | AML         | Total       | P    |
|--|------------|-------------|-------------|-------------|------|
| General characteristics  |            |             |             |             |      |
| Number of children admitted for febrile episode                | 14         | 21          | 7           | 42          | NA   |
| Number of children with CLABSI (%)                             | 7 (50)     | 11 (52)     | 3 (43)      | 21          |      |
| Gender (M/F)   | 10/4       | 11/10       | 2/5         | 23/19       | 0.16 |
| Age in months at the first episode*                            | 59 (44)    | 72 (72)     | 138 (141)   | 71 (82)     | 0.28 |
| Type of central line   |            |             |             |             |      |
| Hickman–Broviac  | 13         | 20          | 7           | 40          | 0.77 |
| Groshong   | 1          | 1           | 0           | 2           |      |
| Episodes of CLABSI   |            |             |             |             |      |
| Number of CLABSI/patient†                                      | 0.5 ± 0.52 | 0.76 ± 0.99 | 0.71 ± 1.11 | 0.67 ± 0.87 | 0.68 |
| Children with febrile episode (s) but no CLABSI (%)            | 7 (50)     | 10 (48)     | 4 (57)      | 21          |      |
| Children with febrile episode (s) and 1 CLABSI (%)             | 7 (50)     | 8 (38)      | 2 (29)      | 17          | 0.61 |
| Children presenting with febrile episode (s) and ≥2 CLABSI (%) | 0 (0)      | 3 (14)      | 1 (14)      | 4           |      |

ALL = acute lymphoblastic leukaemia, AML = acute myeloid leukaemia, CLABSI = central-line associated blood stream infection, HR-ALL = high-risk ALL including children with ALL classified as high risk and those who experienced a ALL relapse, NA = not applicable.  
 \* Age reported as median and interquartile range (IQR).  
 † Number of episodes reported as mean ± SD.

Cumulative CLABSI rate among patients whose caregivers were fully trained at the time of infection was lower (1.74/1000 CL-days) than those whose caregivers were not trained at the time of infection (12.2/1000 CL-days,  $P < 0.05$ ). An intermediate CLABSI rate was observed among children managed by in training caregivers at the time of infection (3.96/1000 CL-days). Fig. 2 reports the raw cumulative rates with 95% CI.

Following the intervention, the number of CL dressing changes performed by DH nurses decreased from an average of 25 to approximately 5 per day. The latter procedures were needed in children whose caregivers did not take part in the study or were unable/unwilling to manage CL.

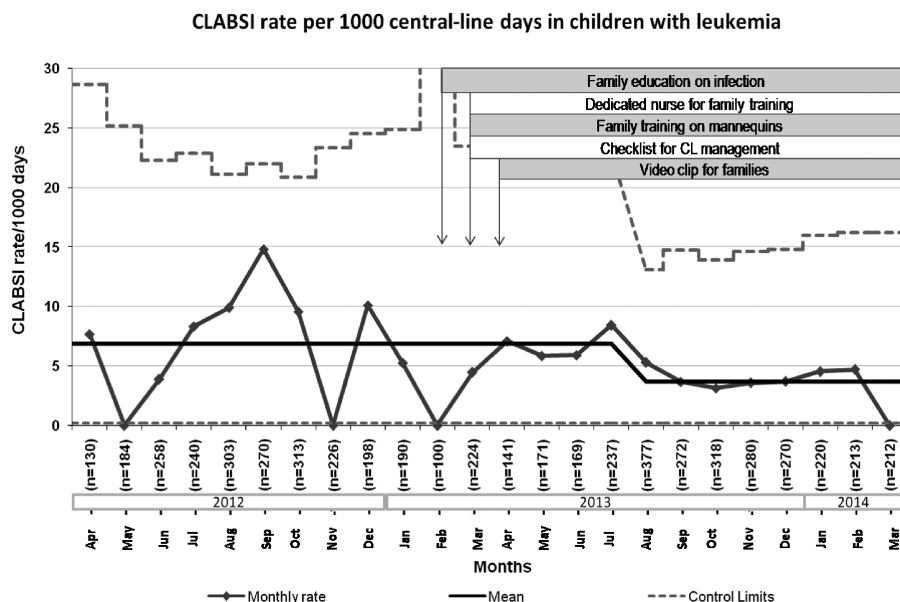
In 3 cases the CL was removed due to the severe clinical conditions of children affected by infections resistant to antimicrobial therapy (*Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Candida albicans*). All these cases occurred before

application of educational intervention. During the project, none of the caregivers (trained or those refusing training) was responsible for displacement or improper practice requiring new CL placement.

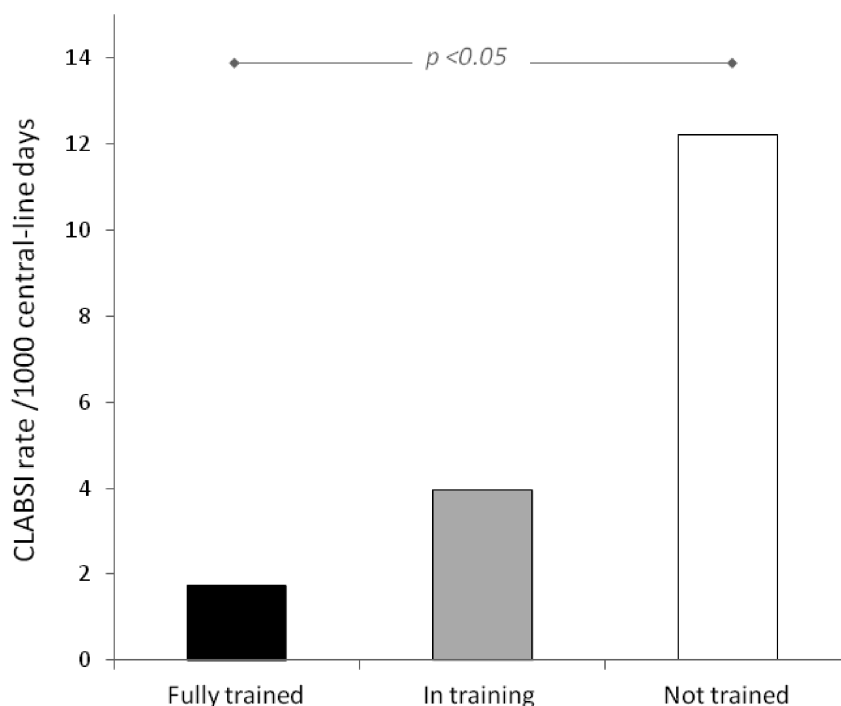
**4. Discussion**

We demonstrated that, in the context of a standard prevention protocol, training caregivers in CL management can further reduce CLABSI rates in children with acute leukemia.

Implementation of evidence-based interventions executed by healthcare providers has been shown to reduce CLABSI rates in pediatric and adult intensive care units.<sup>[11,19]</sup> On that basis, we applied standard CL placement and management bundles, designing, adapting, and monitoring interventions to prevent CLABSI in the study population for about 3 years (Table 1).



**Figure 1.** CLABSI rate per 1000 central-line days in children with leukaemia. CLABSI = central-line associated blood stream infection.



| Level of education | Number of CLABSI | Central-line days | CLABSI rate/1000 central-line days | 95%CI        |
|--------------------|------------------|-------------------|------------------------------------|--------------|
| Fully trained      | 2                | 1156              | 1.74                               | 0.43 to 6.94 |
| In training        | 8                | 2017              | 3.96                               | 1.98 to 7.91 |
| Not trained        | 13               | 1066              | 12.2                               | 7.08 to 21.0 |

Figure 2. CLABSI rates according to the level of family training. CLABSI=central-line associated blood stream infection.

More recently, a similar evidence-based protocol successfully reduced CLABSI rates in pediatric hemato-oncology patients.<sup>[20]</sup> While demonstrating significant progress in CLABSI prevention, there remain as yet unidentified factors that could further reduce and perhaps yield a zero rate among pediatric hemato-oncology patients. In search of these unidentified factors, we considered the prolonged CL dwell time typical of children with leukemia and the fact that most of that dwell time is spent at home or in outpatient settings.

We hypothesized that involving caregivers directly in CL management and CLABSI prevention would reduce CLABSI rates. We demonstrated both a 46% reduction in overall CLABSI rates and an 80% reduction in rate among fully trained versus not trained caregivers. This suggests that any caregiver involvement is effective, and that empowering all caregivers by transfer of CL management could have a dramatic impact on CLABSI rates in this vulnerable population globally.

Recent findings among families of oncology or non-oncology patients support family involvement in CL management to impact infection rate.<sup>[21,22]</sup> Although we did not specifically assess caregivers' compliance to the training, most families demonstrated dedication and accountability to the process (data not shown). The effect of our training on CLABSI rate further supports its efficacy.

Initially, all caregivers agreed to participate in the program and began the training sessions, indicating a belief among caregivers that home CL management is relevant and important. During the study period only a minority of families (12%) withdrew from the training program, demonstrating the educational intervention was both informative and feasible to complete. Of the caregivers who withdrew, most did so during the practical sessions, reporting anxiety, fear of causing pain to their children, and a feeling of incompetence. The high degree of interest in the didactic educational sessions, and our overall rate reduction, further support that basic education of caregivers on infection risk and CL management may be helpful for all families of children with leukemia.<sup>[22]</sup>

Therefore, caregiver training obviated the need for administration of medications in DH that could be done at home. This likely decreased the number of providers handling the CL as well as the number of CL accesses in the hospital. This may have reduced the risk of infection among at-risk patients, having an impact on final infection rate.

In addition to directly attributable morbidity, CLABSI may introduce deleterious delays in the management of underlying malignancies, resulting in delayed chemotherapy, prolonged hospitalization and, sometimes, central line removal or replacement.<sup>[20]</sup>



As a consequence of the reduced infection rate, the overall care of our patient likely improved in terms of time spent in the hospital ward and overall infection risk. Following the intervention, the number of CL dressing changes performed by DH nurses decreased by 80%, thus freeing the nurses to perform other tasks.

Our study has some limitations. The caregiver training intervention was nested in a QI project and therefore the reduction of the CLABSI rate should be considered as the result of a multifaceted intervention in which caregiver training represents an effective, additional intervention. The relatively small number of caregivers in the not trained group may be seen as a limitation because it may potentially reduce the reliability of our comparison. However, this number reflects the relatively high acceptance of the caregiver training and, actually, may be considered a strength of our intervention. Finally, CLABSI definitions have been updated since the completion of our study.<sup>[23]</sup> Although we cannot estimate the effects of these changes, it is likely that our interventions would be effective at preventing a portion of, if not most, CLABSIs by current criteria.

In conclusion, implementation of a standard protocol for CL management by caregivers through hands-on training reduced CLABSI rates in children with leukemia. More specifically, educational programs offered to caregivers, coupled with stringent hygiene and CL care bundles, were effective in reducing the CLABSI rate in children with leukemia. Caregiver training within a multifaceted implementation of evidence-based practices may result in a dramatic improvement of CLABSI rates, and in turn of survival in leukemic patients.

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## References

- Castagnola E, Molinari AC, Fratino G, et al. Conditions associated with infections of indwelling central venous catheters in cancer patients: a summary. *Br J Haematol* 2003;121:233–9.
- Perdikaris P, Petsios K, Vasilatou-Kosmidis H, et al. Complications of Hickman-Broviac catheters in children with malignancies. *Pediatr Hematol Oncol* 2008;25:375–84.
- Koh AY. Prolonged febrile neutropenia in the pediatric patient with cancer. *Am Soc Clin Oncol Educ Book* 2012. 565–9.
- Hughes WT. Bloodstream infections in cancer patients. *Eur J Cancer* 2005;41:1370–1.
- Rinke ML, Chen AR, Bundy DG, et al. Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. *Pediatrics* 2012;130:e996–1004.
- Choi SW, Chang L, Hanauer DA, et al. Rapid reduction of central line infections in hospitalized pediatric oncology patients through simple quality improvement methods. *Pediatr Blood Cancer* 2013; 60:262–9.
- Allen RC, Holdsworth MT, Johnson CA, et al. Risk determinants for catheter-associated blood stream infections in children and young adults with cancer. *Pediatr Blood Cancer* 2008;51:53–8.
- O'Grady NP, Alexander M, Dellinger EP, et al. Healthcare infection control practices advisory committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002;23:759–69.
- Handrup MM, Møller JK, Frydenberg M, et al. Placing of tunneled central venous catheters prior to induction chemotherapy in children with acute lymphoblastic leukemia. *Pediatr Blood Cancer* 2010; 55:309–13.
- O'Grady NP, Alexander M, Burns LA, et al. Healthcare infection control practices advisory committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52: e162–93.
- Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;355:2725–32.
- Miller MR, Griswold M, Harris JM2nd, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. *Pediatrics* 2010;125:206–13.
- Caselli D, Cesaro S, Livadiotti S, et al. Infection Study Group of the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP). Preventing transmission of infectious agents in the pediatric in-patients hematology-oncology setting: what is the role for non-pharmacological prophylaxis? *Pediatr Rep* 2011;3:e9.
- Livadiotti S, Milano GM, Serra A, et al. Infectious Diseases Working Group of the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP). A survey on hematology-oncology pediatric AIEOP centers: prophylaxis, empirical therapy and nursing prevention procedures of infectious complications. *Haematologica* 2012;97: 147–50.
- Centers for Disease Control and Prevention, Central Line-Associated Bloodstream Infection (CLABSI) EventDevice-associated module. *CLABSI* 2011;4:1–8.
- Italian Association for Pediatric Hematology and Oncology (AIEOP)—Scientific Committee for Infections, Castagnola E, Caselli D, Cesaro S, et al. Recommendations for the Management of Fever in Neutropenic Children with Hematooncologic Diseases. 2004;Version 2.0, September.
- Wiley, Langley GJ, Moen RD, Nolan KM, et al. *The Improvement Guide: A Practical Approach to Enhancing Organizational Performance*. 2nd ed. 2009;ISBN:9780470192412.
- Provost LP, Murray SK. *The Health Care Data Guide: Learning From Data for Improvement*. 1st ed. San Francisco, CA: Jossey-Bass; 2011.
- Miller MR, Niedner MF, Huskins WC, et al. National association of children's hospitals and related institutions pediatric intensive care unit central line-associated bloodstream infection quality transformation teams. Reducing PICU central line-associated bloodstream infections: 3-year results. *Pediatrics* 2011;128:e1077–83.
- Bundy DG, Gaur AH, Billett AL, et al. Children's hospital association hematology/oncology CLABSI collaborative. Preventing CLABSIs among pediatric hematology/oncology inpatients: national collaborative results. *Pediatrics* 2014;134:e1678–85.
- Muir A, Holden C, Sexton E, et al. Preventing bloodstream infection in patients receiving home parenteral nutrition. *J Pediatr Gastroenterol Nutr* 2014;59:177–81.
- Rinke ML, Chen AR, Milstone AM, et al. Bringing central line-associated bloodstream infection prevention home: catheter maintenance practices and beliefs of pediatric oncology patients and families. *Jt Comm J Qual Patient Saf* 2015;41:177–85.
- National Healthcare Safety Network (NHSN) Overview 2015. Available at: <http://www.cdc.gov/nhsn/acute-care-hospital/clabsi> (accessed June 8, 2016).