ORIGINAL ARTICLE

# The Burden of Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection among Hematology, Oncology, and Stem Cell Transplant Patients

Kristen E. Metzger, MPH, CIC;[1] Yvonne Rucker, RN, MSN;[2] Mary Callaghan, RN, MN, APN;[2] Michelle Churchill, RN, MSN, ANP-BC;[2] Borko D. Jovanovic, MS, PhD;[3] Teresa R. Zembower, MD, MPH;[1,4] Maureen K. Bolon, MD, MS[1,4]

OBJECTIVE. To evaluate the impact and burden of the new National Healthcare Safety Network surveillance definition, mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI), in hematology, oncology, and stem cell transplant populations.

DESIGN. Retrospective cohort study.

SETTING. Two hematology, oncology, and stem cell transplant units at a large academic medical center.

METHODS. Central line–associated bloodstream infections (CLABSIs) identified during a 14-month period were reviewed and classified as MBI-LCBI or non-MBI-LCBI (MBI-LCBI criteria not met). During this period, interventions to improve central line maintenance were implemented. Characteristics of patients with MBI-LCBI and non-MBI-LCBI were compared. Total CLABSI, MBI-LCBI, and non-MBI-LCBI rates were compared between baseline and postintervention phases of the study period.

RESULTS. Among 66 total CLABSI cases, 47 (71%) met MBI-LCBI criteria. Patients with MBI-LCBI and non-MBI-LCBI were similar in regard to most clinical and demographic characteristics. Between the baseline and postintervention study periods, the overall CLABSI rate decreased from 3.37 to 3.21 infections per 1,000 line-days (incidence rate ratio, 0.95; 4.7% reduction, $P = .84$), the MBI-LCBI rate increased from 2.08 to 2.61 infections per 1,000 line-days (incidence rate ratio, 1.25; 25.3% increase, $P = .44$), and the non-MBI-LCBI rate decreased from 1.29 to 0.60 infections per 1,000 line-days (incidence rate ratio, 0.47; 53.3% reduction, $P = .12$).

CONCLUSIONS. Most CLABSIs identified among hematology, oncology, and stem cell transplant patients met MBI-LCBI criteria, and CLABSI prevention efforts did not reduce these infections. Further review of the MBI-LCBI definition and impact is necessary to direct future definition changes and reporting mandates.

*Infect Control Hosp Epidemiol* 2015;36(2):119–124

## BACKGROUND

Central line–associated bloodstream infections (CLABSIs) lead to increased patient morbidity, mortality, and length of stay and have been estimated to cost between $3,700 and $39,000 per infection.[1–4] CLABSIs identified in intensive care unit patients are publicly reportable through the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) and affect reimbursement by the Centers for Medicare and Medicaid Services.[5] Given the increasing significance of this quality metric, the application of a valid, standardized surveillance definition is imperative. Limitations of the NHSN CLABSI surveillance protocol, especially when applied to immunocompromised patient populations, have been well described.[6–10] Although evidence-based prevention guidelines[11–12] have led to significant reductions in CLABSI rates in recent years,[13] many institutions continue to struggle with high CLABSI rates in hematology, oncology, and stem cell transplant patients.[14] One possible explanation for elevated rates in this population is that treatment with cytotoxic chemotherapy regimens, or graft-versus-host disease, may compromise the mucosal barriers and lead to translocation of oral and gastrointestinal flora into the bloodstream.[15] Although these events are usually unrelated to

Affiliations: 1. Department of Healthcare Epidemiology and Infection Prevention, Northwestern Memorial Hospital, Chicago, Illinois; 2. Department of Nursing, Northwestern Memorial Hospital, Chicago, Illinois; 3. Department of Preventative Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois; 4. Department of Medicine, Division of Infectious Diseases, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Present affiliation: Palliative Care Division, NorthShore University Health System, Glenview, Illinois [M. Churchill].

Received August 12, 2014; accepted October 20, 2014; electronically published December 18, 2014

 0899-823X/2015/3602-0001. DOI: 10.1017/ice.2014.38

the presence of a central line, they are nonetheless classified as CLABSIs per the NHSN definitions. In response to concerns, the CDC convened a workgroup to optimize the CLABSI surveillance protocol. The workgroup developed a modified CLABSI definition and then evaluated it in a multicenter field test.[16] Consequently, CDC released a revised NHSN surveillance protocol for CLABSI in January 2013.[17] In addition to the definition for laboratory-confirmed bloodstream infection (LCBI, hereafter referred to as non-MBI-LCBI), the revised protocol specified a new category of infection known as mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI).

The main objective of this study was to evaluate the burden of MBI-LCBI among hematology, oncology, and stem cell transplant patients at a large academic medical center. Our specific aims were to (1) determine the proportion of CLABSIs classified as MBI-LCBI vs non-MBI-LCBI; (2) describe the clinical characteristics of patients who developed CLABSI, comparing MBI-LCBI cases with non-MBI-LCBI cases; and (3) evaluate how CLABSI prevention efforts affect rates of MBI-LCBI and non-MBI-LCBI.

## METHODS

Infection preventionists at our facility applied the revised 2013 NHSN CLABSI surveillance protocol to all CLABSI cases identified during the 14-month period from July 2012 through August 2013 on 2 inpatient hematology, oncology, and stem cell transplant units (72 total beds). The definition was retrospectively applied to CLABSI cases identified before January 2013; to reduce bias in retrospectively applying the new definition and ensure that all bloodstream infections were correctly classified, candidate blood cultures during this period were re-reviewed. Cases were classified as MBI-LCBI (mucosal barrier injury criteria met) or non-MBI-LCBI (mucosal barrier injury criteria not met). A retrospective review of medical records was conducted to collect demographic and clinical data on each case.

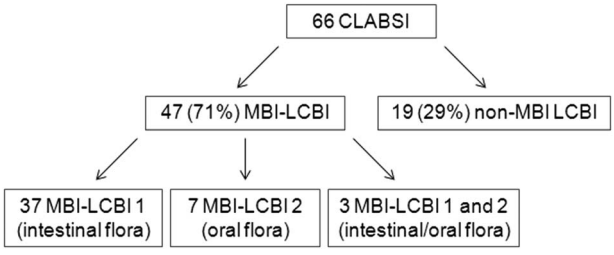


FIGURE 1. Classification of central line–associated bloodstream infections (CLABSIs) as meeting mucosal barrier injury laboratory-confirmed bloodstream infection criteria (MBI-LCBI) or not meeting mucosal barrier injury laboratory-confirmed bloodstream infection criteria (non-MBI-LCBI). MBI-LCBI were further differentiated according to National Healthcare Safety Network definitions.

Because baseline data revealed that most infections occurred long after line insertion, targeted interventions to improve central line care and maintenance were initiated in January 2013. Interventions included re-education; implementation of a standardized schedule for central line dressing, tubing, and injection cap changes (ie, activities occurred on specified days of the week); weekly documentation and practice audits; and the introduction of alcohol impregnated port protectors.

TABLE 1. Characteristics of Central Line–Associated Bloodstream Infection (CLABSI) Cases Meeting Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection Criteria (MBI-LCBI) or Not Meeting Such Criteria (Non-MBI-LCBI)

| | MBI-LCBI ($n=47$) | Non-MBI-LCBI ($n=19$) | $P$ value[a] |
|---|---|---|---|
| Demographic and clinical characteristics | | | |
| Male sex | 30 (64) | 9 (47) | .27 |
| Age, median (range), y | 60 (23–72) | 57 (25–71) | .94 |
| Primary disease type | – | – | .002 |
| Leukemia[b] | 28 (60) | 2 (11) | – |
| Lymphoma | 6 (13) | 8 (42) | – |
| Multiple myeloma | 11 (23) | 6 (32) | – |
| Other[c] | 2 (4) | 3 (16) | – |
| SCT during current admission | 23 (49) | 9 (47) | > .99 |
| Neutropenic within 3 days before CLABSI | 44 (94) | 14 (74) | .04 |
| Neutropenia duration, median (range), d | 14 (4–57) | 11.5 (5–51) | .57 |
| Gastrointestinal GVHD (any grade) | 4 (9) | 0 (0) | .32 |
| Mucositis (any grade) | 19 (40) | 9 (47) | .78 |
| Chemotherapy during admission | 44 (94) | 15 (79) | .10 |
| Clinical outcomes | | | |
| Length of stay, median (range), d | 32 (13–109) | 36 (10–56) | .72 |
| ICU transfer within 7 days after infection | 9 (19) | 3 (16) | > .99 |
| Death during current hospitalization | 7 (15) | 0 (0) | .18 |
| Line(s) removed owing to CLABSI | 30 (64) | 14 (74) | .57 |
| Localized signs and symptoms of infection[d] | 8 (17) | 2 (11) | .71 |

NOTE. Data are no. (%) of cases unless otherwise indicated. GVHD, graft-versus-host disease; ICU, intensive care unit; SCT, stem cell transplant.

[a]2-sided $P$ values were calculated using the Fisher exact test for binary variables, Pearson $\chi 2$ test for primary disease type, and Mann-Whitney test for continuous variables.

[b]Myelodysplastic syndrome is included in the leukemia category.

[c]Includes bladder cancer, Devic's disease, Crohn disease, aplastic anemia, and systemic amyloidosis.

[d]Includes documentation of redness, tenderness, and/or purulent drainage at central line insertion site.

https://doi.org/10.1017/ice.2014.38 Published online by Cambridge University Press

The baseline phase was defined as July 1, 2012, through January 31, 2013, and the postintervention phase was defined as February 1, 2013, through August 31, 2013. Monthly rates of total CLABSI, MBI-LCBI, and non-MBI-LCBI were calculated per 1,000 line-days.

Clinical characteristics of patients with MBI-LCBI and non-MBI-LCBI were compared using the Fisher exact test, Pearson $\chi^2$ test, or Mann-Whitney test, as appropriate. Poisson regression was used to calculate an incidence rate ratio (IRR) to compare baseline and postintervention CLABSI rates. Two-sided *P* values ≤.05 were considered statistically significant. Data analysis was performed using PASW Statistics, version 18.0 (PASW) and Stata, version 12 (StataCorp). This study was approved by Northwestern University's Institutional Review Board.

TABLE 2. Distribution of Organisms Cultured among Central Line–Associated Bloodstream Infection (CLABSI) Cases Meeting Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection Criteria (MBI-LCBI) or Not Meeting Such Criteria (Non-MBI-LCBI)

| MBI-LCBI organisms cultured | No. (%) of MBI-LCBI cases ($n = 47$ cases with $n = 53$ organisms isolated) |
|---|---|
| *Escherichia coli* | 15 (32) |
| *Enterococcus faecium* | 14 (30) |
| Viridans group streptococci | 10 (21) |
| *Klebsiella pneumoniae* | 3 (6) |
| *Enterococcus faecalis* | 3 (6) |
| *Candida* species | 2 (4) |
| *Enterobacter aerogenes* | 1 (2) |
| *Enterobacter cloacae* | 1 (2) |
| *Enterococcus gallinarum* | 1 (2) |
| *Fusobacterium* species | 1 (2) |
| *Klebsiella oxytoca* | 1 (2) |
| *Bacterioides thetaiotaomicron* | 1 (2) |
| **Non-MBI-LCBI organisms cultured** | **No. (%) of non-MBI-LCBI cases ($n = 19$ cases with $n = 20$ organisms isolated)** |
| *Staphylococcus aureus* | 5 (26) |
| *Staphylococcus epidermidis* | 4 (21) |
| *Pseudomonas aeruginosa* | 3 (16) |
| *Candida parapsilosis* | 1 (5) |
| *Capnocytophaga sputigena* | 1 (5) |
| *Escherichia coli* | 1 (5) |
| Viridans group streptococci | 1 (5) |
| *Gemella* species | 1 (5) |
| *Lactobacillus* species | 1 (5) |
| *Enterococcus faecium* | 1 (5) |
| *Streptococcus agalactiae* | 1 (5) |

## RESULTS

A total of 66 CLABSIs were identified during the study period; 47 (71%) were classified as MBI-LCBI and 19 (29%) were classified as non-MBI-LCBI (Figure 1). Of the 47 MBI-LCBI cases, 44 (94%) met the definition based on neutropenia criteria, while 3 (6%) met the definition based on the receipt of an allogeneic hematopoietic stem cell transplant in the previous year with grade 3–4 graft-versus-host disease or greater than 1 L of diarrhea documented in a 24-hour period. Per NHSN definitions based on the type of organisms isolated, among MBI-LCBI cases, 37 (79%) were classified as MBI-LCBI 1 (intestinal flora), 7 (15%) were classified as MBI-LCBI 2 (oral flora), and 3 (6%) were classified as both MBI-LCBI 1 and MBI-LCBI-2 (Figure 1). Most clinical and demographic characteristic were similar between MBI-LCBI and non-MBI-LCBI cases; however, significant differences were noted in regard to the presence of neutropenia (94% of MBI-LCBI cases vs. 74% of non-MBI-LCBI case, $P = .04$) and primary disease type ($P = .002$, Table 1). The most common organisms cultured from patients with MBI-LBCI were *Escherichia coli* (32%), *Enterococcus faecium* (30%), and viridans group streptococci (21%), whereas the most common organisms cultured from patients with non-MBI-LCBI were *Staphylococcus aureus* (26%), *Staphylococcus epidermidis* (21%), and *Pseudomonas aeruginosa* (16%) (Table 2). As shown in Table 3, between the baseline and postintervention periods, the overall CLABSI rate

TABLE 3. Central Line–Associated Bloodstream Infection (CLABSI) Rates and Incidence Rate Ratios (IRRs) before and after the Implementation of CLABSI Reduction Interventions

| | Baseline period | Postintervention period |
|---|---|---|
| Overall CLABSI | | |
| Rate per 1,000 line-days | 3.37 (34 infections/ 10,090 line-days) | 3.21 (32 infections/ 9,969 line-days) |
| IRR (95% CI) | – | 0.95 (.59–1.54) |
| % Change | – | −4.70% |
| *P* value | – | .84 |
| MBI-LCBI | | |
| Rate per 1,000 line-days | 2.08 (21 infections/ 10,090 line days) | 2.61 (26 infections/ 9,969 line days) |
| IRR (95% CI) | – | 1.25 (.71–2.23) |
| % Change | – | 25.30% |
| *P* value | – | .44 |
| Non-MBI-LCBI | | |
| Rate per 1,000 line-days | 1.29 (13 infections/ 10,090 line days) | 0.60 (6 infections/9,969 line days) |
| IRR (95% CI) | – | 0.47 (.18–1.23) |
| % Change | – | −53.30% |
| *P* value | – | .12 |

NOTE. MBI-LCBI, mucosal barrier injury laboratory-confirmed bloodstream infection; Non-MBI-LCBI, not meeting mucosal barrier injury laboratory-confirmed bloodstream infection criteria.

https://doi.org/10.1017/ice.2014.38 Published online by Cambridge University Press

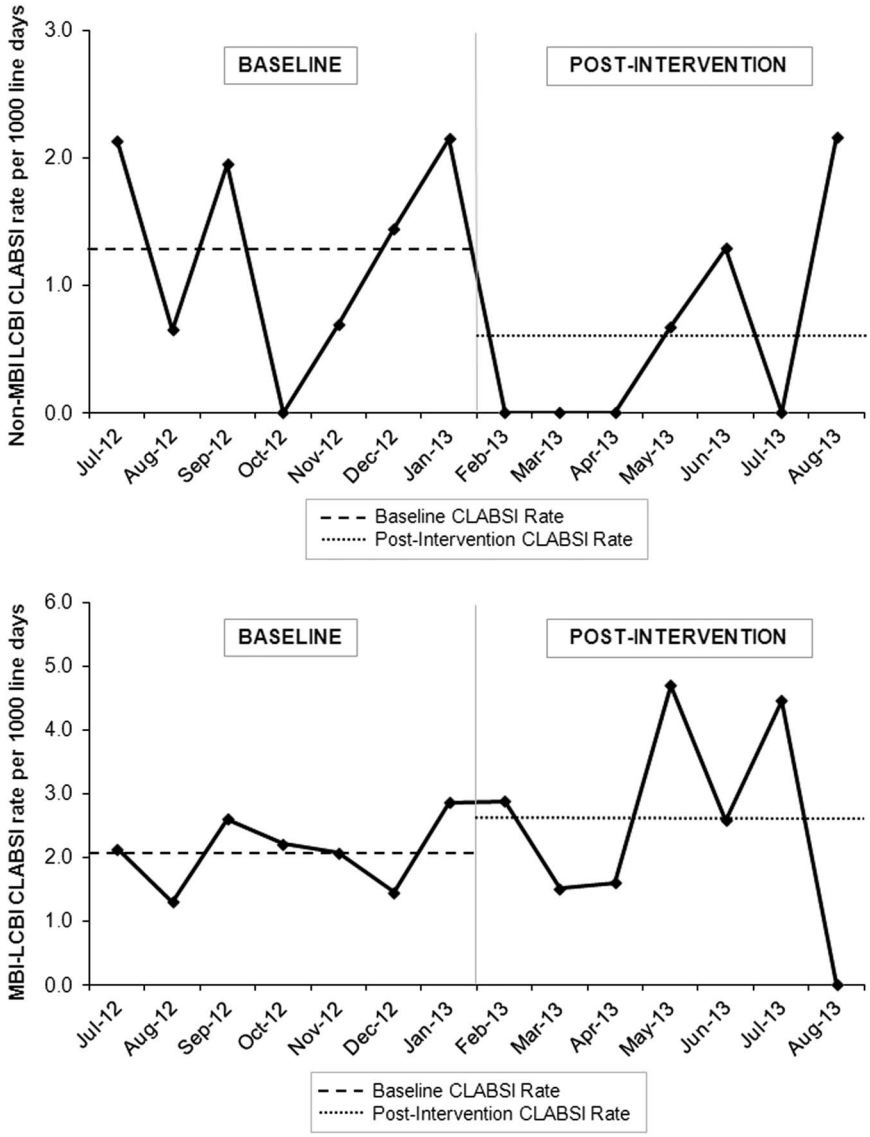


FIGURE 2. Monthly rates of central line–associated bloodstream infections (CLABSIs) that meet criteria as mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI) and that do not meet such criteria (non-MBI-LCBI), comparing periods before and after the implementation of line maintenance interventions.

decreased from 3.37 to 3.21, the MBI-LCBI rate increased from 2.08 to 2.61, and the non-MBI-LCBI rate decreased from 1.29 to 0.60. Figure 2 shows the monthly rates of non-MBI-LCBI and MBI-LCBI, comparing baseline and postintervention periods. During the postintervention period, a non-MBI-LCBI rate of zero was achieved for 4 of 7 months.

## DISCUSSION

Our data show that MBI-LCBI cases account for most of the CLABSI cases identified in hematology, oncology, and stem cell transplant patient populations. Overall, clinical and demographic characteristics were similar between patients who developed MBI-LCBI and non-MBI-LCBI. As expected on the basis of the surveillance definition, neutropenia was more prevalent in patients with MBI-LCBI, but surprisingly, the majority of patients with non-MBI-LCBI were also neutropenic. Thus, in this population, the organism isolated from blood cultures was often the deciding factor in the classification of MBI-LCBI or non-MBI-LCBI.

After the implementation of CLABSI prevention interventions focused on improving line maintenance practices, we observed little change in overall CLABSI rate, an increase in the MBI-LCBI rate, and a substantial decrease in the non-MBI-LCBI rate. Although the reduction in non-MBI-LCBI did not reach statistical significance, likely in part owing to a small sample size, we believe that the reduction was clinically significant. On the basis of our experiences, we recommend

https://doi.org/10.1017/ice.2014.38 Published online by Cambridge University Press

that facilities separate MBI-LCBI from non-MBI-LCBI for internal tracking and data reporting purposes. Aggregating the 2 types of infections can mask reductions in arguably more preventable non-MBI-LCBI, lead to misinterpretation of intervention efforts, undermine credibility of infection preventionists, and reduce caregiver morale.

Although MBI-LCBI may not be amenable to line care interventions, these infections often still lead to significant patient morbidity and mortality. As demonstrated in our data, the prevalence of these infections is high in oncology patients, and the number of infections actually increased during the intervention period. Interventions that have shown some benefit in the prevention of gastrointestinal or oral mucositis, such as oral cryotherapy, low-level laser therapy, prophylactic drugs, probiotics, and basic oral and bowel care regimens[18–19] may also hold promise in preventing MBI-LCBI. In order to improve patient outcomes, additional research into the prevention of MBI-LCBI is warranted.

In the era of public reporting and pay-for-performance programs, a thorough evaluation of the use and interpretation of the MBI-LCBI definition is necessary. Although CLABSIs identified outside intensive care units do not currently affect reimbursement, future inclusion is anticipated and could significantly impact hospitals with large oncology populations. Moreover, we often see MBI-LCBI "spill-over" to intensive care units: in a recent 22-month period 12% of intensive care unit CLABSIs were classified as MBI-LCBI at our institution. The CDC is currently evaluating preliminary MBI-LCBI data submitted to NHSN and stated their "intention to remove MBI-LCBI from CLABSI data used for public reporting starting in January 2015" (CLABSI workshop at Association of Professionals in Infection Control and Epidemiology Annual Conference, June 8, 2014, Katherine Allen-Bridson and Nicola Thompson, CDC). Additionally, since NHSN's list of MBI-LCBI eligible organisms is likely not inclusive of all organisms that may cause bloodstream infection owing to translocation across compromised oral or gastrointestinal mucosa, careful review of this component of the definition is crucial to ensure data validity and accurate interfacility comparison.

The results of this retrospective study demonstrate the impact of the revised CLABSI surveillance protocol in hematology, oncology, and stem cell transplant patients and show that CLABSI prevention measures are unlikely to affect rates of MBI-LCBI. Although further analysis of national MBI-LCBI data is still necessary, our results lend support to CDC's intention to separate MBI-LBCI data from CLABSI data used for reporting purposes.

## ACKNOWLEDGMENTS

We thank all individuals who participated in or supported the project team to reduce CLABSIs in the oncology population, including all oncology nurses and physicians.

*Financial support.* None reported.

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

Address correspondence to Kristen E. Metzger, MPH, CIC, Department of Healthcare Epidemiology and Infection Prevention, Northwestern Memorial Hospital, 645 N. Michigan Ave., Suite 900, Chicago, IL 60611 (kmetzger@nm.org).

Presented in part: Association of Professionals in Infection Control and Epidemiology Annual Conference; Anaheim, CA; June 7, 2014 (Abstract 413).

## REFERENCES

1. Digiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. *Am J Respir Crit Care Med* 1999;160:976–981.
2. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med* 2006;34:2084–2089.
3. Mermel LA. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000;132:391–402.
4. Elward AM, Hollenbeak CS, Warren DK, Fraser VJ. Attributable cost of nosocomial primary bloodstream infection in pediatric intensive care unit patients. *Pediatrics* 2005;115:868–872.
5. Centers for Disease Control and Prevention. Operational guidance for acute care hospitals to report central line-associated bloodstream infection (CLABSI) data to CDC's NHSN for the purpose of fulfilling CMS's Hospital Inpatient Quality Reporting (IQR) requirements. Available at: http://www.cdc.gov/nhsn/PDFs/FINAL-ACH-CLABSI-Guidance.pdf. Accessed October 11, 2013.
6. Steinberg JP, Robichaux C, Chernetsky Tejedor S, Dent Reyes M, Jacob JT. Distribution of pathogens in central line-associated bloodstream infection among patients with and without neutropenia following chemotherapy: evidence for a proposed modification to the current surveillance definition. *Infect Control Hosp Epidemiol* 2013;34:171–175.
7. Steinberg JP, Coffin SE. Improving the central line-associated bloodstream infection surveillance definition: a work in progress. *Infect Control Hosp Epidemiol* 2013;34:777–779.
8. Pehar M, Ristaino P, Budd AP, et al. Application of the National Healthcare Safety Network (NHSN) central line-associated bloodstream infection (CLA-BSI) definition to oncology patients: impact in the trenches. Presented at Fifth Decennial Conference on Healthcare-Associated Infections; Atlanta, Georgia; March 18-22, 2010 (Abstract 660).
9. Sexton DJ, Chen LF, Anderson DJ. Current definitions of central-line associated bloodstream infections: is the emperor wearing clothes? *Infect Control Hosp Epidemiol* 2010;31:1286–1289.
10. Fraser TG, Gordon SM. CLABSI rates in immunocompromised patients: a valuable patient centered outcome? *Clin Infect Dis* 2011;52:1446–1450.
11. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter–related infections. *Am J Infect Control* 2011;39:S1–S34.
12. Marschall J, Mermel LA, Fakih M, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35:753–771.
13. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related BSIs in the ICU. *N Engl J Med* 2006;355:2725–2732.
14. Dudek MA, Weiner LM, Allen-Bridson K, et al. National Healthcare Safety Network (NHSN) report, data summary

for 2012, device-associated module. *Am J Infect Control* 2013;41:1148–1166.
15. Tancrede CH, Andremont AO. Bacterial translocation and gram-negative bacteremia in patients with hematological malignancies. *J Infect Dis* 1985;152:99–103.
16. See I, Iwamoto M, Allen-Bridson K, Horan T, Magill SS, Thompson ND. Mucosal barrier injury laboratory-confirmed bloodstream infection: results from a field test of a new National Healthcare Safety Network definition. *Infect Control Hosp Epidemiol* 2013;34:769–776.
17. Centers for Disease Control and Prevention. Central line–associated bloodstream infection (CLABSI) event. Available at: http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf. Accessed October 2, 2013.
18. Lalla RV, Bowen J, Barasch A, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer* 2014;120:1453–1461.
19. Gibson RJ, Keefe DM, Lalla RV, et al. Systematic review of agents for the management of gastrointestinal mucositis in cancer patients. *Support Care Cancer* 2013;21:313–326.