Impact of Staffing on Bloodstream Infections in the Neonatal Intensive Care Unit

Jeannie P. Cimiotti, DNS, RN; Janet Haas, MS; Lisa Saiman, MD, MPH; Elaine L. Larson, PhD

Objective: To examine the association between registered nurse staffing and healthcare-associated bloodstream infections in infants in the neonatal intensive care unit (NICU).

Design: Prospective cohort study.

Setting: Two level III-IV NICUs in New York, NY, from March 1, 2001, through January 31, 2003.

Participants: A total of 2675 infants admitted to the NICUs for more than 48 hours and all registered nurses who worked in the same NICUs during the study period.

Intervention: Hours of care provided by registered nurses.

Main Outcome Measure: Time to first episode of healthcare-associated bloodstream infection.

Results: A total of 224 infants had an infection that met the study definition of healthcare-associated bloodstream infection. In a multivariate analysis, after controlling for infants' intrinsic and extrinsic risk factors, a greater number of hours of care provided by registered nurses in NICU 2 was associated with a decreased risk of bloodstream infection in these infants (hazard ratio, 0.21; 95% confidence interval, 0.06-0.79).

Conclusion: Our findings suggest that registered nurse staffing is associated with the risk of bloodstream infection in infants in the NICU.

Arch Pediatr Adolesc Med. 2006;160:832-836

Author Affiliations: Center for Health Outcomes and Policy Research, School of Nursing, University of Pennsylvania, Philadelphia (Dr Cimiotti); School of Nursing (Ms Haas and Dr Larson) and Department of Pediatrics, College of Physicians and Surgeons (Dr Saiman), Columbia University, and Department of Epidemiology, New York–Presbyterian Hospital (Dr Saiman), New York, NY.

HEALTHCARE-ASSOCIATED infections are a significant cause of morbidity and mortality among infants in the neonatal intensive care unit (NICU).[1,2] Infants hospitalized in the NICU have the highest rates of healthcare-associated infection among the pediatric population, with infection rates ranging from 6 to more than 30 infections per 100 patient discharges.[3] Among infants in the NICU, the bloodstream is the most common site of healthcare-associated infection in all birth weight groups.[4]

Evidence of a significant association between nurse staffing and adverse patient outcomes has been reported.[5-7] However, to date only a few studies have examined the association between nurse staffing and healthcare-associated infections in infants.[8-11] Furthermore, no prospective studies, to our knowledge, have specifically examined the association between nurse staffing and bloodstream infections in the NICU. This study examined the association between registered nurse staffing and bloodstream infections among infants in the NICU.

METHODS

DESIGN

This cohort study used data collected as part of a larger clinical trial to assess the effects of 2 hand hygiene regimens on healthcare-associated infections in infants in the NICU.[12] The study used a randomly assigned crossover design in which either a traditional antiseptic soap containing 2% chlorhexidine gluconate or a waterless hand rinse containing 61% ethyl alcohol was used by all staff and visitors sequentially for half of the study period (11 months for each product).

SAMPLE AND SETTING

The study was conducted in 2 level III-IV NICUs located in New York, NY. Both NICU 1 (43 beds) and NICU 2 (50 beds) are affiliated with the New York–Presbyterian Hospital and provide specialized medical treatment to severely compromised infants. Data on nurse staffing were provided by the nurse staffing office of each NICU, and data were classified as follows: hours per day for full-time registered nurses, full-time other (ie, nurse managers), per-diem registered nurses, float registered nurses, and agency registered nurses. Staffing data were collected on all infants who were hospitalized in the NICU for more than 48 hours from March 1, 2001, through January 31, 2003. Institutional review board approval was obtained from the participating institutions.

DATA COLLECTION

In this study, we examined only the first episode of healthcare-associated bloodstream infection. Data on bloodstream infections were collected by the study nurse epidemiologist, and the National Nosocomial Infection Surveillance System definitions were used.[13] Clinical data were obtained from infants' medical records, and laboratory, radiology, and pharmacy data were collected from the hospitals' computer information systems (ECLIPSYS; Eclipsys Corp, Boca Raton, Fla; WEBCIS; Columbia University Department of Informatics, New York; HealthQuest; McKesson Information Solutions, Alpharetta, Ga; and Eagle; Siemens AG, Munich, Germany). A computerized list of all blood cultures positive for organisms from infants was generated by the clinical microbiology laboratories and reviewed twice weekly by the nurse epidemiologist, who also made unit rounds at least once weekly.

Interrater agreement ($\kappa = 0.97$) regarding presence or absence of bloodstream infection was established by comparing data collected simultaneously by the study nurse epidemiologist and the hospital infection control staff for 3 months. Discrepancies regarding infection status were resolved by the consensus of 2 physician coinvestigators (including L.S.).

RISK FACTORS

Four risk factors reported to be associated with bloodstream infection in infants were examined: birth weight,[14-17] intravascular catheterization,[16-19] major surgery,[20,21] and total parenteral nutrition.[17,19] Birth weight was stratified into 4 groups: less than 1000 g, 1000 to 1500 g, 1501 to 2500 g, and more than 2500 g. Catheters were classified as umbilical, tunneled (Hickman and Broviac), and peripherally inserted central. The performance of major surgery, defined as an operating room procedure other than circumcision or minor abdominal surgery,[22] was determined from the infant's diagnosis related group. Total parenteral nutrition was recorded as the number of days of total parenteral nutrition received before bloodstream infection, or on discharge in infants without a bloodstream infection.

Two additional variables were examined: (1) the hand hygiene product used by staff when each bloodstream infection was diagnosed and (2) registered nurse hours, defined as registered nurse care hours per infant per day. Registered nurse hours were adjusted for patient case mix based on diagnosis related group and nursing intensity weight as described elsewhere.[5-7,23] The 2001 nursing intensity weights, which reflect the amount of nursing care required for typical patients in each diagnosis related group, ranged from 1.96 to 32.40.

DATA ANALYSIS

Continuous variables were presented as the mean and standard deviation and categorical variables were expressed as percentages. Infant characteristics were compared by χ^2, Fisher exact, and unpaired *t* tests. Data from each day of each infant's admission were linked with the corresponding registered nurse staffing data (adjusted for case mix) for the same days before bloodstream infection or censoring (eg, death or discharged with no infection). The window of exposure was calculated as the mean of registered nurse hours from 48 to 144 hours before bloodstream infection.

A Cox proportional hazards regression model was used to identify risk factors associated with bloodstream infection. The proportional hazards assumption was validated both graphically and through fitting a discrete-time model as described by Allison.[24] Confounder selection was based on the criteria described by Mickey and Greenland[25]; variables significant ($P < .25$) in the preliminary analysis were included in the multivariate model. Intravascular catheterization, total parenteral nutrition, and registered nurse hours were modeled as time-dependent covariates.

In this analysis, the risk of bloodstream infection was modeled for each infant, and then parameter estimates of the covariates birth weight, intravascular catheterization, total parenteral nutrition, hand hygiene product, NICU site, and adjusted registered nurse hours were calculated for that same infant. If a neonate had more than one bloodstream infection, only the first was included in these analyses.

Because intravascular catheters in infants have been reported as a risk factor for bloodstream infection,[16-18] the incidence density was also defined as number of bloodstream infections per 1000 catheter days, as per National Nosocomial Infections Surveillance System protocol.[3] All calculations were performed with Stata release 9 statistical software (StataCorp LP, College Station, Tex).

RESULTS

A total of 3155 admissions to the study NICU were recorded during the study period. After excluding infants who were admitted for 48 hours or less, the final sample included 2675 admissions. Of these, 224 infants (8.4%) had a total of 298 bloodstream infections. Coagulase-negative staphylococci (45.0%) were the most common pathogens, followed by gram-negative bacteria (23.2%), yeast (13.5%), *Staphylococcus aureus* (9.5%), and enterococci (7.7%). The incidence rate of bloodstream infection was 6.11 per 1000 patient days and 16.56 per 1000 catheter days. Of the 48 infant deaths that occurred during this study, 16 involved infants with a bloodstream infection.

CHARACTERISTICS OF INFANTS

The characteristics of infants enrolled in this study are summarized in **Table 1**. Overall, 55.9% of the infants in this sample were male, their mean gestational age was 34.8 weeks (range, 23-42 weeks), and their mean birth weight was 2401 g (range, 428-5513 g). Overall, 309 infants (11.6%) had a birthweight of less than 1000 g; 330 (12.3%), 1000 to 1500 g; 812 (30.3%), 1501 to 2500 g; and 1224 (45.8%), greater than 2500 g. The length of stay before bloodstream infection ranged from 2 to 312 days (mean, 14.7 days). Central venous catheters were inserted in 1543 infants (57.6%): 783 (50.7%) were umbilical, 45 (2.9%) tunneled, and 715 (46.3%) peripherally inserted central catheters. In addition, 468 infants (17.5%) had major surgery and 1284 (48.0%) received total parenteral nutrition during their hospitalization.

CHARACTERISTICS OF REGISTERED NURSE STAFFING

Nursing acuity and registered nurse hours are summarized in **Table 2**. Overall, the mean nursing acuity in the 2 NICUs was 5.3 (range, 2.04-32.4). The mean number of infants occupying beds in the NICUs was 37 (range, 21-49), and the mean number of registered nurse hours per infant per day was 10.8 (range, 7.3-15.0).

Table 1. Characteristics of Study Population by Neonatal Intensive Care Unit (NICU)*

Characteristic	NICU 1 (n = 1550) No Infection	NICU 1 (n = 1550) Infection	NICU 2 (n = 1125) No Infection	NICU 2 (n = 1125) Infection
No. (%) of infants	1388 (89.5)	162 (10.5)	1063 (94.5)	62 (5.5)
Birth weight, No. (%), g				
<1000	134 (9.7)	75 (46.3)	66 (6.2)	34 (54.8)
1000-1500	153 (11.0)	32 (19.8)	131 (12.3)	14 (22.6)
1501-2500	433 (31.2)	22 (13.6)	349 (32.8)	8 (12.9)
>2500	668 (48.1)	33 (20.4)	517 (48.6)	6 (9.7)
Catheter, No. (%)				
Umbilical	394 (28.4)	98 (60.5)	253 (23.8)	38 (61.3)
Tunneled	18 (1.3)	4 (2.5)	15 (1.4)	8 (12.9)
Peripherally inserted central	372 (26.8)	116 (71.6)	178 (16.7)	49 (79.0)
Catheter days, mean (SD)	5.3 (11.4)	16.4 (16.7)†	3.8 (10.8)	19.0 (13.5)†
Total parenteral nutrition, No. (%)	823 (59.3)	154 (95.1)	200 (23.5)	57 (91.9)
Total parenteral nutrition days, mean (SD)	6.9 (20.0)	15.0 (13.4)†	3.0 (20.0)	15.9 (13.4)†
Surgery, No. (%)	305 (22.0)	39 (24.1)	111 (10.4)	13 (21.0)
Length of stay, mean (SD), d	12.8 (17.6)	16.7 (13.3)†	16.5 (17.6)	23 (13.3)†

*Because of rounding, percentages may not all total 100.
†Days to bloodstream infection.

Table 2. Nursing Acuity and Registered Nurse Staffing by Neonatal Intensive Care Unit (NICU)

Characteristic	Mean (SD) NICU 1 No Infection	Mean (SD) NICU 1 Infection	Mean (SD) NICU 2 No Infection	Mean (SD) NICU 2 Infection
Nursing intensity weight	5.3 (2.6)	7.8 (3.0)	4.7 (2.1)	8.5 (3.7)
Registered nurse h/d*	10.7 (1.0)	10.7 (1.0)	11.0 (1.0)	10.7 (1.2)
Infant census	39 (4)	39 (4)	34 (5)	34 (6)

*Indicates registered nurse hours per infant per day.

Table 3. Hazard Ratios Estimating the Risk of Bloodstream Infection

Variable	Hazard Ratio (95% CI)
Birth weight, g	
<1000	2.64 (1.77-3.94)
1000-1500	1.82 (1.15-2.89)
1501-2500	1.42 (0.85-2.38)
>2500	1.00
Peripherally inserted central catheter	1.83 (1.31-2.56)
Umbilical catheter	1.33 (0.88-2.02)
Total parenteral nutrition	12.62 (6.93-22.98)
Alcohol hand rub	1.15 (0.84-1.58)
Chlorhexidine gluconate	1.00
NICU 1	0.07 (0.005-1.02)
NICU 2	1.00
Registered nurse hours, NICU 1	1.53 (0.39-6.07)
Registered nurse hours, NICU 2	0.21 (0.06-0.79)

Abbreviations: CI, confidence interval; NICU, neonatal intensive care unit.

MULTIVARIATE ANALYSIS

In the preliminary analysis, surgery, tunneled catheters, and the hand hygiene product used by staff were not significantly associated with bloodstream infection (all $P > .25$). Risk factors significant in the preliminary analyses included birth weight, 2 catheter types (umbilical and peripherally inserted central catheters), total parenteral nutrition, NICU site, and registered nurse hours. We found a significant NICU site × registered nurse hours interaction effect (hazard ratio [HR], 7.12; 95% confidence interval [CI], 1.23-41.42). On the basis of this finding, we adjusted our model in an attempt to obtain an accurate representation of registered nurse staffing in each NICU as described by Greenland and Rothman.[26]

These significant variables and the hand hygiene product were further analyzed in the multivariate Cox regression model. The hand hygiene product, although not significant in the preliminary analysis ($P = .26$), was included in the multivariate model because it was the intervention in the parent clinical trial. A summary of results from the multivariate Cox regression model is provided in **Table 3**. In this model, 3 risk factors were independently associated with bloodstream infection. Birth weight of less than 1000 g (HR, 2.64; 95% CI, 1.77-3.94), birth weight of 1000 to 1500 g (HR, 1.82; 95% CI, 1.15-2.89), number of days of peripherally inserted central catheter use (HR, 1.83; 95% CI, 1.31-2.56), and number of days of total parenteral nutrition use (HR, 12.62; 95% CI, 6.93-22.98) were significantly associated with an increased risk of bloodstream infection. Among the 4 birth weight groups, infants weighing less than 1000 g were 2.64 times more likely to develop bloodstream infection than the highest birth weight group (>2500 g). Further analysis of the catheter data showed that infants with bloodstream infection had peripherally inserted central catheters in place for significantly more days than uninfected infants (mean, 12 and 3 days, respectively; $P<.001$).

In addition, the number of registered nurse hours in NICU 2 was significantly associated with a decreased risk (HR, 0.21; 95% CI, 0.06-0.79) of bloodstream infection. We found that more registered nurse hours per nursing intensity weight was associated with a 79% reduction in the risk of bloodstream infection in NICU 2. Umbilical catheter use, hand hygiene product, NICU site, and registered nurse hours in NICU 1 were not associated with risk of bloodstream infection. A survival curve comparing registered nurse hours at NICU 2 and number of days to first bloodstream infection is shown in the **Figure**.

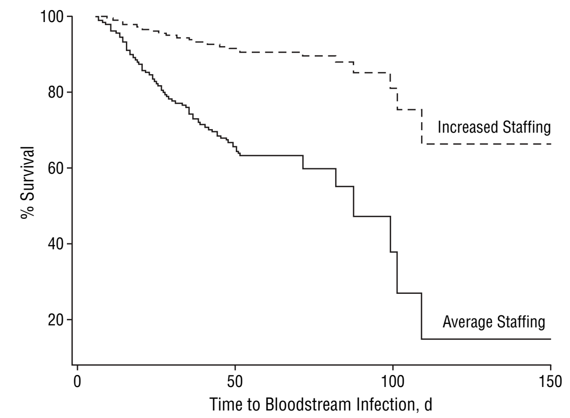

Figure. Survival estimates of 1125 infants in neonatal intensive care unit 2, showing the typical changes in survival after increasing registered nurse hours.

COMMENT

To our knowledge, this is the first prospective study to examine registered nurse staffing and the risk of endemic bloodstream infection in infants in the NICU. We found low birth weight, peripherally inserted central catheters, and total parenteral nutrition to be significantly associated with bloodstream infection. These findings are consistent with previous research on infants in the NICU.[17,19,27-33]

After controlling for infants' intrinsic and extrinsic risk factors, we found that the number of hours of care provided by registered nurses was significantly associated with the risk of bloodstream infection in one of our study NICUs. This finding is consistent with other studies on nurse staffing. Nursing workload has been associated with higher rates of infection[34-36] and increased mortality.[37,38] The use of pooled or temporary nurses has been significantly associated with infection,[8,34,39,40] possibly because of lapses in aseptic technique by those unfamiliar with the routine care policies of the nursing unit. In the NICU, it has been reported that bloodstream infection is associated with understaffing, overcrowding, and the moving of infants between rooms.[8,9,11] Furthermore, understaffing has been linked to several infectious outbreaks[8,11] and the transmission of antibiotic-resistant organisms among premature infants.[8,10] Our findings suggest that increasing registered nurse staffing by 1 full-time equivalent could possibly reduce the risk of bloodstream infection by 11% in NICU 2.

The fact that the number of registered nurse hours was not associated with bloodstream infection in NICU 1 (HR, 1.53; 95% CI, 0.39-6.07) may have several explanations. When compared with the infants in NICU 2, those in NICU 1 were significantly smaller and more acutely ill, with more invasive devices, which could outweigh the effect of registered nurse staffing. In addition, the infants in NICU 1 had consistently fewer registered nurse hours of care per day than those in NICU 2. This lack of variation in registered nurse hours in NICU 1 may have made it more difficult to detect an association between registered nurse hours and bloodstream infection in these infants. Surprisingly, we found that when nursing acuity increased, registered nurse hours remained the same in NICU 1 and decreased in NICU 2. This unrecognized increase in nursing acuity could have increased the risk of bloodstream infection in both NICUs. It has been reported that scores on acuity measures are associated with the risk of healthcare-associated infection in infants. Gray and colleagues[41] report in a study of low-birth-weight infants that assessing illness severity with the Score for Neonatal Acute Physiology provides information on the risk of bloodstream infection beyond that provided by birth weight alone. Griffin and Moorman[42] reported that Score for Neonatal Acute Physiology values rise 24 hours before bloodstream infection. It has also been reported that the Clinical Risk Index for Babies is predictive of bloodstream infection in low-birth-weight infants.[43] Hospital staffing decisions are typically determined by the number of patients in a unit; however, the foregoing findings suggest that hospitals should consider implementing a patient classification system that is acuity driven to determine nurse staffing need.

This study had several limitations. First, it was conducted in 2 NICUs with high-risk infants, which limits generalizability to other hospital units and patient populations. Second, although the level of nurse education has been associated with adverse patient outcomes,[44] the educational level of nurses was unmeasured in this study. Third, the 2 study NICUs were environmentally different in a number of ways (NICU 2 was newly renovated and more spacious than NICU 1).

In conclusion, our findings suggest that registered nurse staffing is associated with the risk of bloodstream infection among infants in the NICU. We hypothesize that inadequate nurse staffing and increased nurse workload in a critical care environment results in poor hand hygiene compliance, breaks in aseptic technique, or compromises in practice that might increase the risk of transmitting infection. Further research is warranted that examines the association between registered nurse staffing and healthcare-associated infection to improve the quality of care and the outcomes of infants in the NICU.

Accepted for Publication: January 17, 2006.
Correspondence: Jeannie P. Cimiotti, DNS, RN, Center for Health Outcomes and Policy Research, School of Nursing, University of Pennsylvania, 420 Guardian Dr, Philadelphia, PA 19104-6096 (jcimiott@nursing.upenn.edu).
Author Contributions: *Study concept and design:* Cimiotti, Saiman, and Larson. *Acquisition of data:* Cimiotti and Haas. *Analysis and interpretation of data:* Cimiotti. *Drafting of the manuscript:* Cimiotti. *Critical revision of the manuscript for important intellectual content*: Cimiotti, Haas, Saiman, and Larson. *Obtained funding:* Larson. *Administrative, technical, and material support:* Cimiotti, Haas, Saiman, and Larson. *Study supervision:* Saiman and Larson.
Funding/Support: This study was supported by grant 1 R01 NR05197-03 from the National Institute of Nursing Research, National Institutes of Health (Staff Hand Hygiene and Nosocomial Infection in Neonates).
Acknowledgment: Leo Lichtig, PhD (vice president, Aon Consulting), and Jack Needleman, PhD (associate professor, University of California at Los Angeles), acted as expert consultants on this study. John E. Marcotte, PhD (director, Statistical Computing Group, University of Pennsylvania), and Tim Cheney (data analyst, Center for Health Outcomes and Policy Research, School of Nursing, University of Pennsylvania) provided statistical support, and 3M Health Information Systems provided the DRG Finder software that was used in analysis. We are extremely grateful to the neonatal nurses and the management staff of New York–Presbyterian Hospital.

REFERENCES

1. Pessoa-Silva CL, Miyasaki CH, de Almeida MF, Kopelman BI, Raggio RL, Wey SB. Neonatal late-onset bloodstream infection: attributable mortality, excess of length of stay and risk factors. *Eur J Epidemiol*. 2001;17:715-720.
2. Stoll BJ, Hansen N. Infections in VLBW infants: studies from the NICHD Neonatal Research Network. *Semin Perinatol*. 2003;27:293-301.
3. NNIS System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2003, issued August 2003. *Am J Infect Control*. 2003;31:481-498.
4. Gaynes RP, Edwards JR, Jarvis WR, Culver DH, Tolson JS, Martone WJ. Nosocomial infections among neonates in high-risk nurseries in the United States: National Nosocomial Infections Surveillance System. *Pediatrics*. 1996;98:357-361.
5. Knauf RA, Lichtig LK, Risen-McCoy R, Singer AD, Wozniak L. *Implementing Nursing's Report Card: A Study of RN Staffing, Length of Stay and Patient Outcomes.* Washington, DC: American Nurses Association; 1997.
6. Lichtig LK, Knauf RA, Milholland DK. Some impacts of nursing on acute care hospital outcomes. *J Nurs Adm*. 1999;29:25-33.
7. Needleman J, Buerhaus P, Mattke S, Stewart M, Zelevinsky K. Nurse-staffing levels and the quality of care in hospitals. *N Engl J Med*. 2002;346:1715-1722.
8. Andersen BM, Lindemann R, Bergh K, et al. Spread of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive unit associated with understaffing, overcrowding and mixing of patients. *J Hosp Infect*. 2002;50:18-24.
9. Haley RW, Bregman DA. The role of understaffing and overcrowding in recurrent outbreaks of staphylococcal infection in a neonatal special-care unit. *J Infect Dis*. 1982;145:875-885.
10. Haley RW, Cushion NB, Tenover FC, et al. Eradication of endemic methicillin-resistant *Staphylococcus aureus* infections from a neonatal intensive care unit. *J Infect Dis*. 1995;171:614-624.
11. Harbarth S, Sudre P, Dharan S, Cadenas M, Pittet D. Outbreak of *Enterobacter cloacae* related to understaffing, overcrowding, and poor hygiene practices. *Infect Control Hosp Epidemiol*. 1999;20:598-603.
12. Larson EL, Cimiotti J, Haas J, et al. Effect of antiseptic handwashing vs alcohol sanitizer on health care–associated infections in neonatal intensive care units. *Arch Pediatr Adolesc Med*. 2005;159:377-383.
13. Horan TC, Emori TG. Definitions of key terms used in the NNIS System. *Am J Infect Control*. 1997;25:112-116.
14. Lehner R, Leitich H, Jirecek S, Weninger M, Kaider A. Retrospective analysis of early-onset neonatal sepsis in very low birth-weight infants. *Eur J Clin Microbiol Infect Dis*. 2001;20:830-832.
15. Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J, Angus DC. The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med*. 2003;167:695-701.
16. Urrea M, Iriondo M, Thio M, et al. A prospective incidence study of nosocomial infections in a neonatal care unit. *Am J Infect Control*. 2003;31:505-507.
17. Nagata E, Brito AS, Matsuo T. Nosocomial infections in a neonatal intensive care unit: incidence and risk factors. *Am J Infect Control*. 2002;30:26-31.
18. Wisplinghoff H, Seifert H, Tallent SM, Bischoff T, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in pediatric patients in United States hospitals: epidemiology, clinical features and susceptibilities. *Pediatr Infect Dis J*. 2003;22:686-691.
19. Brodie SB, Sands KE, Gray JE, et al. Occurrence of nosocomial bloodstream infections in six neonatal intensive care units. *Pediatr Infect Dis J*. 2000;19:56-65.
20. Oppido G, Napoleone CP, Formigari R, et al. Outcome of cardiac surgery in low birth weight and premature infants. *Eur J Cardiothorac Surg*. 2004;26:44-53.
21. Christie C, Hammond J, Reising S, Evans-Patterson J. Clinical and molecular epidemiology of enterococcal bacteremia in a pediatric teaching hospital. *J Pediatr*. 1994;125:392-399.
22. *AP-DRGs: All Patient Diagnosis Related Groups Definitions Manual.* Version 18.0. Wallingford, Conn: 3M Health Information Systems; 2000.
23. Lichtig LK, Knauf RA, Risen-McCoy R, Wozniak L. *Nurse Staffing and Patient Outcomes in the Inpatient Hospital Setting.* Washington, DC: American Nurses Association; 2000.
24. Allison PA. *Event History Analysis Regression for Longitudinal Event Data.* Newbury Park, Calif: Sage Publications; 1984.
25. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol*. 1989;129:125-137.
26. Greenland S, Rothman KJ. Concepts in interaction. In: Rothman KJ, Greenland S, eds. *Modern Epidemiology.* Philadelphia, Pa: Lippincott Williams & Wilkins; 1998:329-342.
27. Carrieri MP, Stolfi I, Moro ML; Italian Study Group on Hospital Acquired Infections in Neonatal Intensive Care Units. Intercenter variability and time of onset: two crucial issues in the analysis of risk factors for nosocomial sepsis. *Pediatr Infect Dis J*. 2003;22:599-609.
28. Pawa AK, Ramji S, Prakash K, Thirupuram S. Neonatal nosocomial infection: profile and risk factors. *Indian Pediatr*. 1997;34:297-302.
29. Moro ML, De Toni A, Stolfi I, Carrieri MP, Braga M, Zunin C. Risk factors for nosocomial sepsis in newborn intensive and intermediate care units. *Eur J Pediatr*. 1996;155:315-322.
30. Stoll BJ, Hansen N, Fanaroff AA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics*. 2002;110:285-291.
31. Stoll BJ, Gordon T, Korones SB, et al. Late-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. *J Pediatr*. 1996;129:63-71.
32. Avila-Figueroa C, Goldmann DA, Richardson DK, Gray JE, Ferrari A, Freeman J. Intravenous lipid emulsions are the major determinant of coagulase-negative staphylococcal bacteremia in very low birth weight newborns. *Pediatr Infect Dis J*. 1998;17:10-17.
33. Beck-Sague CM, Azimi P, Fonseca SN, et al. Bloodstream infections in neonatal intensive care unit patients: results of a multicenter study. *Pediatr Infect Dis J*. 1994;13:1110-1116.
34. Fridkin SK, Pear SM, Williamson TH, Galgiani JN, Jarvis WR. The role of understaffing in central venous catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol*. 1996;17:150-158.
35. Vicca AF. Nursing staff workload as a determinant of methicillin-resistant *Staphylococcus aureus* spread in an adult intensive therapy unit. *J Hosp Infect*. 1999;43:109-113.
36. Arnow P, Allyn PA, Nichols EM, Hill DL, Pezzlo M, Bartlett RH. Control of methicillin-resistant *Staphylococcus aureus* in a burn unit: role of nurse staffing. *J Trauma.* 1982;22:954-959.
37. Aiken LH, Clarke SP, Sloane DM, Sochalski J, Silber JH. Hospital nurse staffing and patient mortality, nurse burnout, and job dissatisfaction. *JAMA*. 2002;288:1987-1993.
38. Tarnow-Mordi WO, Hau C, Warden A, Shearer AJ. Hospital mortality in relation to staff workload: a 4-year study in an adult intensive-care unit. *Lancet*. 2000;356:185-189.
39. Li J, Birkhead GS, Strogatz DS, Coles FB. Impact of institution size, staffing patterns, and infection control practices on communicable disease outbreaks in New York State nursing homes. *Am J Epidemiol*. 1996;143:1042-1049.
40. Robert J, Fridkin SK, Blumberg HM, et al. The influence of the composition of the nursing staff on primary bloodstream infection rates in a surgical intensive care unit. *Infect Control Hosp Epidemiol*. 2000;21:12-17.
41. Gray JE, Richardson DK, McCormick MC, Goldman DA. Coagulase-negative staphylococcal bacteremia among very low birth weight infants: relation to admission illness severity, resource use, and outcome. *Pediatrics*. 1995;95:225-230.
42. Griffin MP, Moorman JR. Toward the early diagnosis of neonatal sepsis and sepsis-like illness using a novel heart rate analysis. *Pediatrics*. 2001;107:97-103.
43. Auriti C, Maccallini A, DiLiso G, DiCiommo V, Ronchetti MP, Orazalesi M. Risk factors for nosocomial infections in the neonatal intensive-care unit. *J Hosp Infect*. 2003;53:25-30.
44. Aiken LH, Clarke SP, Cheung RB, Sloane DM, Silber JH. Educational levels of hospital nurses and surgical patient mortality. *JAMA*. 2003;290:1617-1623.