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Incidence Trends in Pathogen-specific, Central Line-associated Bloodstream Infections in US Intensive Care Units, 1990–2010

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Abstract

Objective—To quantify historical trends in rates of central line-associated bloodstream infections (CLABSIs) in U.S. intensive care units (ICUs) caused by major pathogen groups, including *Candida spp.*, *Enterococcus spp.*, specified Gram-negative rods, and *Staphylococcus aureus*.

Design—Active surveillance in a cohort of participating ICUs through the U.S. Centers for Disease Control and Prevention (CDC), National Nosocomial Infections Surveillance (NNIS) system during 1990–2004 and the National Healthcare Safety Network (NHSN) during 2006–2010.

Setting—ICUs

Patients or participants—Patients who were admitted to participating ICUs

Interventions—None

Results—The CLABSI incidence density rate for *S. aureus* decreased annually starting in 2002 and remained lower than for other pathogen groups. Since 2006, the annual decrease for *S. aureus* CLABSIs in non-pediatric ICU types was −18.3% (95% CI, −20.8% to −15.8%), whereas the incidence density rate for *S. aureus* among pediatric ICUs did not change. The annual decrease for all ICUs combined since 2006 was −17.8% (95% CI, −19.4% to −16.1%) for *Enterococcus spp.*, −16.4% (95% CI, −18.2% to −14.7%) for Gram-negative rods, and −13.5% (95% CI, −15.4% to −11.5%) for *Candida spp.*

Conclusions—Patterns of ICU CLABSI incidence density rates among major pathogen groups have changed considerably during recent decades. CLABSI incidence declined steeply since 2006, except for CLABSI due to *S. aureus* in pediatric ICUs. There is a need to better understand CLABSIs that still do occur based on microbiological and patient characteristics. New prevention approaches may be needed in addition to central line insertion and maintenance practices.

INTRODUCTION

Central-line associated bloodstream infections (CLABSIs) are among the most common types of healthcare-associated infections (HAIs). A coordinated effort by state and federal agencies, professional societies, and health-care personnel to implement proven best practices for the insertion of central lines has been associated with an approximately 60%

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decrease in overall CLABSI incidence rates in U.S. intensive care units (ICUs) during the last decade. [1–4] Additionally, population-based surveillance has shown that the incidence of hospital-onset, methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections decreased approximately 11% per year during 2005–2008.[5] However, an estimated 18,000 CLABSIs still occur each year in U.S. ICUs, and contribute to poor patient outcomes and increased healthcare costs.[1]

The Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) is used to track progress toward meeting federal, state, and facility level HAI prevention goals. In 2009, the U.S. Department of Health and Human Services announced its Action Plan to Prevent HAIs, which set goals for a 50% decrease in CLABSI incidence and 100% adherence to recommended central line insertion practices by 2013.[6,7] Also, the Centers for Medicare & Medicaid Services (CMS) and more than half of all states now require public reporting of CLABSIs by healthcare facility; in most states and nationally, this reporting is being accomplished through use of NHSN. Facility-level CLABSI data reported to CMS via NHSN are now publicly available on the CMS "Hospital Compare" website. Mandated, public reporting of CLABSI data is expected to accelerate progress toward CLABSI elimination.

Previous analyses of NHSN CLABSI surveillance data have tended to focus on overall CLABSI or *S. aureus* incidence density rates. Additional microbiological information is needed to help direct future CLABSI prevention efforts. A comparison of 2009 versus 2001 CLABSI surveillance data showed greater declines in the incidence of *S. aureus* CLABSIs than for other pathogen groups.[1] This observation suggests there have been differences in the recent success of CLABSI prevention depending on the causative pathogen; better description and understanding of CLABSI rate trends could inform new approaches to prevention that may be needed to make an impact on preventing CLABSIs associated with specific pathogens. To further investigate this finding and better understand the historical context concerning the microbiology of CLABSIs in U.S. ICUs, we analyzed 20 years of CDC CLABSI surveillance data to characterize pathogen-specific trends in CLABSI incidence density rates.

METHODS

CLABSI Surveillance Systems and Reporting Environment

CLABSI data were reported by participating ICUs through the CDC's National Nosocomial Infections Surveillance (NNIS) system during 1990–2004 and the NHSN during 2006–2010. Data are unavailable from 2005 because of a transition year between the systems. CLABSI reporting was mainly voluntary until several states implemented reporting mandates through NHSN starting in November 2006 and culminated in 21 states and the District of Columbia with CLABSI reporting mandates by October 2010 (written communication, Cathy Rebmann, CDC, March 2012). Overall, 25 states had at least one ICU that participated in CLABSI surveillance in 1990, 41 in 2000, and 50 in 2010. All data included in this analysis were submitted prior to any CMS CLABSI reporting requirement as a condition of participation in the CMS Hospital Inpatient Quality Reporting Program. We analyzed data from 7 ICU types: Cardiothoracic, Coronary, Medical, Surgical, combined Medical-Surgical

units in facilities with a major medical school teaching program affiliation, combined Medical-Surgical units in facilities without such an affiliation, and non-neonatal Pediatric units.[8]

Definitions and Data Collection

NHSN data are maintained electronically at CDC. For each month of surveillance, participating hospital units submit microbiologic and other information about all CLABSI events as well as the monthly total of patient-days and central line-days for that location.[9] Detailed descriptions of NNIS and NHSN CLABSI surveillance methods and definitions are available.[8,10,11] In brief, a CLABSI is a primary bloodstream infection in a patient who had a central line at the time of, or within the 48 hours before the onset of the infection.[11] For the recognized pathogens included in this analysis, a laboratory-confirmed bloodstream infection means that the pathogen must be cultured from one or more blood cultures, and the organism cultured from blood is not related to an infection at another site.[11] NHSN CLABSI surveillance methodology distinguishes between recognized pathogens and common commensals (*e.g.*, coagulase-negative *Staphylococci*); because we limited our analysis to recognized pathogens, no correction was needed for a 2008 protocol change that only applied to common commensals.[12] The most commonly isolated CLABSI pathogens were grouped into 4 categories: *Candida* species; *Staphylococcus aureus; Enterococcus* species; and Gram-negative rods including *Acinetobacter baumanii*, *Enterobacter* species, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. CLABSIs with more than one pathogen could be reported in multiple pathogen categories. In sub-analyses, additional pathogen-specific incidence rates were analyzed for *C. albicans,* non-*albicans Candida* spp., *E. faecalis*, *E. faecium*, and 2 subgroups of Gram-negative rods corresponding to *Enterobacteriaceae* (*Enterobacter* spp., *E. coli*, and *Klebsiella* spp.) or the common environmental organisms, *A. baumanii* and *P. aeruginosa*.

Statistical Analysis

For each pathogen category included in our study, we calculated the pooled mean CLABSI incidence density rate per 1000 central line-days per year, by ICU type. We also calculated the annual device utilization rate (DUR; total central line-days ÷ total patient-days) to assess whether CLABSI trends were related to changes in central line usage.[13] We used Poisson regression to model trends in pathogen-specific CLABSI incidence. The NNIS and NHSN periods were modeled separately to more accurately characterize CLABSI trends. The variables year, ICU type, and an interaction term for year and ICU type were included in the preliminary models for each pathogen category. ICU types were subsequently collapsed into mutually exclusive groups if preliminary analyses indicated a similar direction (increase, decrease, or no change) in the CLABSI trend; given a similar direction in trend, ICU types were only separated into different groups if their slope estimates differed at a higher level of statistical significance ($P<.01$). The final ICU groups for the NNIS period were Medical-Surgical ICUs (with or without major medical school affiliation) and non-Medical-Surgical ICUs (Cardiothoracic, Coronary, Medical, Pediatric, and Surgical ICUs) for each pathogen category, except that all ICU types were combined for *Enterococcus* spp. For the NHSN period, all 7 ICU types were grouped together for each pathogen category, except that Pediatric ICUs were analyzed separately from other ICU types for *S. aureus*.

To evaluate whether our findings could be explained by migration into or out of the surveillance network, a sensitivity analysis was conducted using data from NNIS continuous reporters, defined as ICUs that participated in CLABSI surveillance for at least one month in ≥14 of 15 NNIS surveillance years, and NHSN continuous reporters, which participated in CLABSI surveillance for at least one month during each of the 5 NHSN years. A participating ICU was defined as one that reported ≥50 central line-days in a given year.

Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina). *P* values are reported at a 2-sided significance level of ≤.05. The (former) National Center for Preparedness, Detection, and Control of Infectious Diseases, CDC, conducted an ethical review and approved the routine reporting of health care–associated infection data to NNIS and NHSN, determining that such reporting constitutes surveillance and not research, and therefore is not subject to IRB review requirements. Our examination of temporal trends in these surveillance data is within the scope of routine surveillance activities, and likewise is not subject to further institutional review.

RESULTS

Characteristics of Participating ICUs

The number of participating ICUs grew from 127 in 1990 to 3,474 in 2010, and 89% of that increase occurred after 2006, when some states started to mandate CLABSI reporting. Corresponding growth was observed in the number of facilities, ICU patient-days and central line-days under surveillance. The overall DUR was 0.51 central line-days per patient-days per year and did not vary considerably across the years (range, 0.49 to 0.53). When looking at the annual number of participating ICUs and total reported central line-days by ICU type, substantial growth in participation was observed for all ICU types (Table 1). However, the largest relative increase occurred for Medical-Surgical units without a major medical school affiliation, and the smallest relative increase occurred for Surgical units.

Pooled Mean CLABSI Incidence Density by Pathogen Category

The pooled mean CLABSI incidence density rate per 1,000 central line-days is shown by pathogen category (Figure 1). The 2010 pooled mean overall ICU CLABSI incidence density rate was 1.3 CLABSIs per 1,000 central line-days. When looking at the distribution of pathogens across time (Figure 1), *S. aureus* CLABSI incidence had no clear pattern during the majority of the NNIS period but decreased starting in 2002 and remained lower than other pathogen categories. The *Candida* spp. CLABSI incidence density rate was lower than other groups during much of the NNIS period but converged with Gram-negative rod and *Enterococcus spp.* incidence during NHSN years. The *Enterococcus* spp. CLABSI incidence density rate increased from the lowest to highest incidence of the 4 categories by 2000 and remained so into 2010. The differences discussed between these pathogen groups are based on analysis of reported surveillance data and were not tested for statistical significance.

The unadjusted 2010 pathogen-specific incidence density rates for *Candida* spp., *Enterococcus* spp., Gram-negative rods, and *S. aureus* were 0.25, 0.28, 0.26, and 0.14

CLABSIs per 1,000 central line-days, respectively. In 2010, 42% of *Candida* spp. CLABSIs were due to *C. albicans* and 59% to non-*albicans Candida* spp. Forty-five percent of *Enterococcus* spp. CLABSIs were due to *E. faecalis*, 44% to *E. faecium*, and 13% to other species. Thirty-six percent of Gram-negative rod CLABSIs were associated with *Klebsiella* spp., 22% with *P. aeruginosa*, 20% with *Enterobacter* spp., 14% with *E. coli,* and 12% with *A. baumanii*.

Pathogen-Specific Trends in CLABSI Incidence Density Rates

For each pathogen and ICU group used in the final analysis, the modeled trend is shown with the reported, annual CLABSI incidence density rates for the NNIS and NHSN surveillance periods (Figure 2). Table 2 displays the magnitude of the model-estimated annual percent changes for each pathogen group reflected in Figure 2.

During the NNIS period, the *S. aureus* incidence density rate declined in non-Medical-Surgical ICUs, and *Enterococcus spp.* incidence increased for all ICU types. For *Candida* spp. and Gram-negative rods, the slight decrease observed among Medical-Surgical ICUs was not confirmed by the sensitivity analysis among continuously-reporting ICUs. In contrast, during the NHSN period significant and substantial annual decreases were detected within all pathogen and ICU groups except for the *S. aureus* incidence density rate among Pediatric ICUs, which did not change (Table 2). The sensitivity analysis confirmed these findings, although the decreases were somewhat smaller among continuously reporting ICUs than for all reporters. During the NHSN period, the declines were greatest for *S. aureus* (non-Pediatric ICUs) and more modest for Gram-negative rods and *Candida* spp.

DISCUSSION

Our results demonstrate that historical decreases in pathogen-specific CLABSI rates in U.S. ICUs are largely attributable to steep annual declines that have occurred since 2006. Though overall declines were observed for the major pathogens in our analysis, the relative incidence of CLABSIs due to these pathogens has changed considerably during the last decade. The *S. aureus* CLABSI incidence density rate has fallen below those of *Candida* spp., *Enterococcus* spp., and Gram-negative rods, with the exception that *S. aureus* CLABSI incidence in pediatric ICUs has not decreased. Furthermore, the incidence rates for these non-*S. aureus* pathogen groups have converged. These changes reflect an evolution in the success of CLABSI prevention measures.

The incidence density rate of CLABSIs caused by *Candida* spp., *Enterococcus* spp., and Gram-negative rods has remained higher than for *S. aureus* since 2004. A likely explanation for this finding is that central line insertion practices may be less effective at preventing bloodstream infections caused by *Candida* spp., *Enterococcus* spp., and *Enterobacteriaceae*, because some of these infections occur as a result of contamination of the catheter at the hub or needleless connector, while others arise from the gastrointestinal tract through compromised mucosal barriers.[14,15] It may be prudent to turn our attention to infections due to these other pathogen groups that may require different approaches to prevention; for example, optimizing central line maintenance practices.[1,8] Changes in NHSN surveillance

definitions to allow separate reporting of bloodstream infections likely related to mucosal barrier injury are in development for use beginning in 2013.

The increase in enterococcal CLABSI rates during the late 1990s may reflect the increasing prevalence of vancomycin-resistant Enterococci (VRE) in ICUs during this period.[16,17] The subsequent declines in enterococcal CLABSI rates could reflect the effects of targeted environmental decontamination, patient isolation, and improved availability of effective antimicrobial therapy, in addition to central line insertion practices.[18,19] Although *Candida* CLABSI incidence density rates were substantially lower than for *S. aureus* earlier in the study period, they have been higher than for *S. aureus* since 2004. The effect of central line-based CLABSI prevention strategies on the epidemiology of *Candida* CLABSIs deserves further study.

The lack of recent improvement in *S. aureus* CLABSI incidence density rates in Pediatric ICUs stands in contrast to other ICU types. It has been reported elsewhere that the incidence of healthcare-associated, invasive methicillin-resistant *S. aureus* infections has declined in adults but not in children.[20] The adoption of central line insertion and maintenance bundles reduces overall CLABSI rates by approximately 40%–60% in Pediatric ICUs, but no pediatric study has reported the near-elimination of CLABSIs that has been observed with similar interventions in some adult ICUs.[21–23] Proposed reasons for this difference include host factors and longer catheter dwell times for pediatric ICU populations versus adults.[24] Focused attention on daily maintenance and care of central lines may be required to effect major reductions in CLABSI rates in Pediatric ICUs, where maximizing compliance with insertion practices alone is unlikely to significantly reduce CLABSIs.[25]

Reporting mandates have driven explosive growth in participation in NHSN CLABSI surveillance, especially by smaller, non-academic hospitals. This growth will provide more representative national surveillance data while also posing challenges to the interpretation of long-term CLABSI and other HAI trends.

The microbiologic categories and ICU groups chosen for this analysis are not intended to be definitive concerning the use of CLABSI data to evaluate pathogen- or healthcare location-specific concerns. Microbiologic CLABSI data are collected at the species level and provide a powerful tool to provide insight into the etiology and preventability of CLABSI or other HAIs reported to NHSN. Likewise, the rapid growth in NHSN CLABSI reporting may support future analyses involving a broader range of ICU types (e.g., burn units) as well as hospital wards and specialty care areas, including hematology/oncology units.

Our analysis has several limitations. First, in looking at historical trends, the interpretation of earlier findings is based on the relatively small number of participating ICUs. We thus cannot rule out that migration into or out of the system had a substantial impact on findings. Due to the length of the study period and the need to consider pathogen- and ICU-specific trends, we were unable to identify a substantial cohort of continuous reporters across the entire 20-year surveillance period. Second, though ICU type and medical school teaching affiliation may broadly represent certain patient characteristics, we could not account for patient morbidities or other factors that influence CLABSI risk and are likely to be highly

variable across facilities. Thus our findings may not necessarily reflect trends at the facility or regional level. Third, problems with inter-observer reliability could impact the integrity of CLABSI surveillance data. Fourth, CLABSI reporting does not require users to indicate the source of the positive blood culture. Therefore, changes over time may reflect improvements in central line hub management, thereby reducing intraluminal catheter colonization and the likelihood that blood cultures drawn through central lines will be positive. And fifth, we were unable to assess the extent to which recent CLABSI public reporting mandates acted as a negative incentive for facilities to identify and report CLABSIs.

Though overall CLABSI incidence density rates continue to decline, there is a need to better understand CLABSIs that still do occur. Microbiological data submitted to NHSN such as those presented here help inform the interpretation of measures of prevention success. For some scenarios, new prevention approaches may be needed in addition to central line insertion and maintenance practices. Also, evaluation is ongoing concerning areas of the current CLABSI definition that may be overly sensitive concerning bloodstream infections that can be acquired through routes other than the central line. Finally, as more and more healthcare facilities achieve excellent compliance with guidelines around central line insertion and maintenance, greater attention may need to be given to healthcare-associated BSIs that are occurring as a result of other primary, non-device-associated HAIs.

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Author Contributions: Dr. Fagan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Fagan, Edwards, Park, Fridkin, Magill

Acquisition of data: Edwards

Drafting of the manuscript: Fagan, Edwards, Park, Fridkin, Magill

Critical revision of the manuscript for important intellectual content: Fagan, Edwards, Park, Fridkin, Magill

Statistical analysis: Fagan, Edwards

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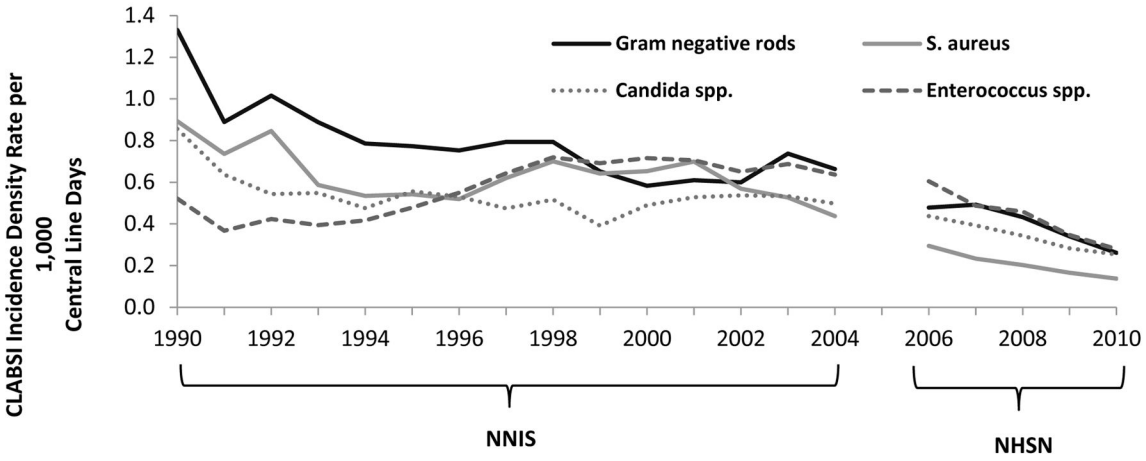

Figure 1.

Pathogen-Specific Pooled Mean CLABSI Incidence Density Rate per 1,000 Central-Line Days among 7 ICU Types,* NNIS (1990–2004) and NHSN (2006–2010) CLABSI Surveillance Data

*Cardiothoracic, Coronary, Medical, Medical-Surgical without Major Medical School Affiliation, Medical-Surgical with Major Medical School Affiliation, Pediatric, and Surgical ICUs

Figure 2a. *Staphylococcus aureus*

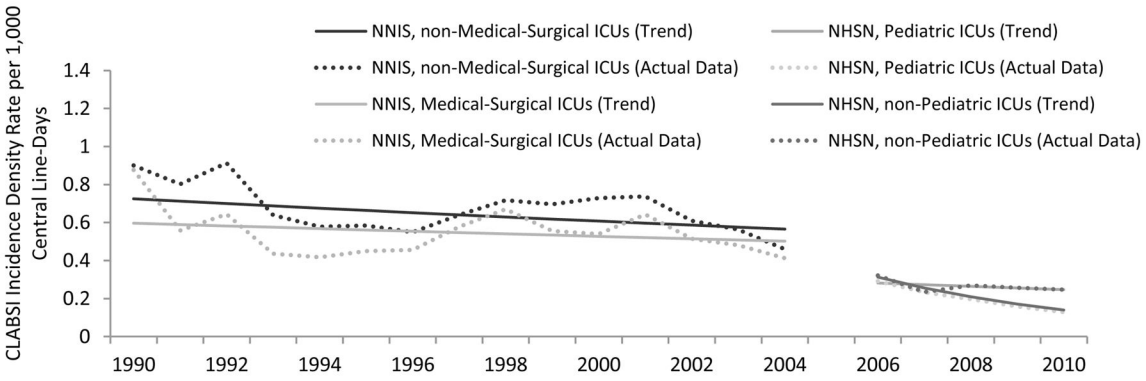

Figure 2b. *Candida spp*.

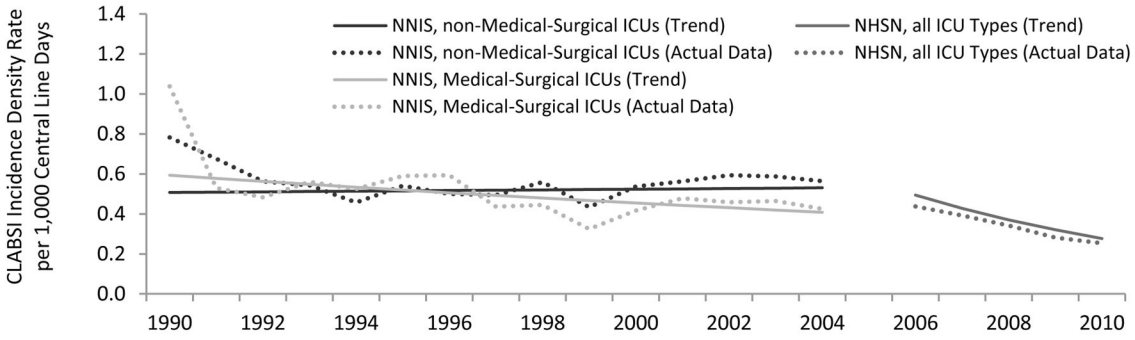

Figure 2c. Gram negative rods

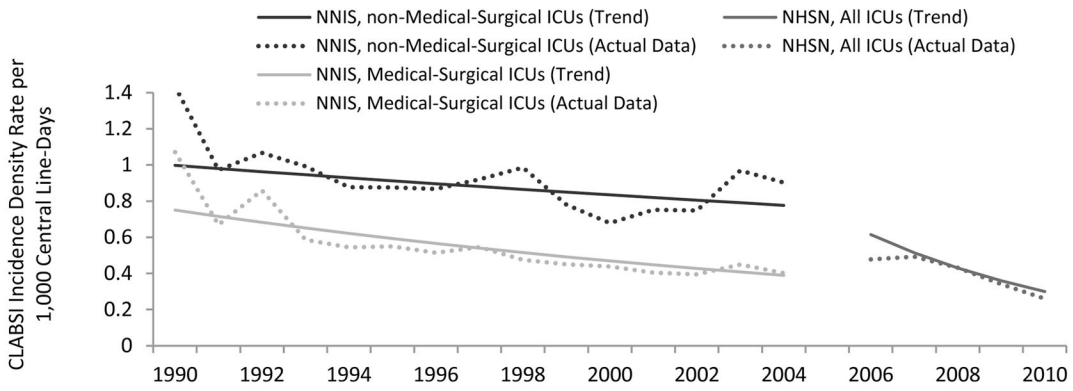

Figure 2d. *Enterococcus spp*.

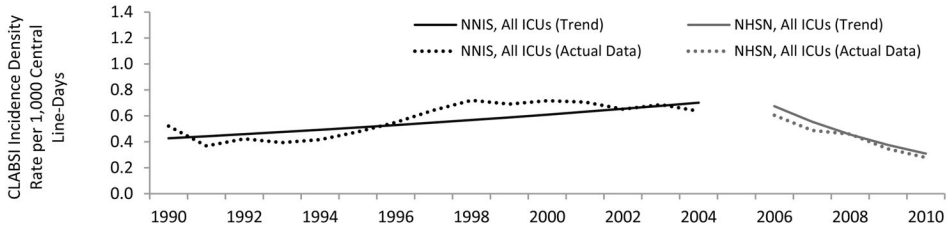

Figure 2.

Parts a–d Pathogen-Specific Pooled Mean CLABSI Incidence Density Rate per 1,000 Central-Line Days among 7 ICU Types,* NNIS (1990–2004) and NHSN (2006–2010) CLABSI Surveillance Data: Figure 2a, *Staphylococcus aureus*; Figure 2b, *Candida spp.*; Figure 2c, Gram negative rods (*Acinetobacter baumanii*, *Enterobacter* species, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumonia*, or *Pseudomonas aeruginosa*); and Figure 2d, *Enterococcus spp.*

*Cardiothoracic, Coronary, Medical, Medical-Surgical without Major Teaching Affiliation, Medical-Surgical with Major Teaching Affiliation, Pediatric, and Surgical ICUs

Table 1

No. (%) of Intensive Care Units and Central-Line Days Reported to the Centers for Disease Control and Prevention by ICU Type and 5-Year Period, 1990–2010*

	ICU Type						
				Medical-Surgical			
	Cardiothoracic	Coronary	Medical	Without Major Teaching Affiliation	With Major Teaching Affiliation	Pediatric	Surgical
No. (%) of Participating ICUs by 5-Year Period**							
1990–1994 (n=465)	28 (6)	73 (16)	81 (17)	96 (21)	53 (11)	46 (10)	88 (19)
1995–1999 (n=753)	60 (8)	97 (13)	126 (17)	153 (20)	104 (14)	71 (9)	142 (19)
2000–2004 (n=691)	59 (9)	80 (12)	116 (17)	136 (20)	114 (17)	64 (9)	122 (18)
2006–2010 (n=3,787)	326 (9)	326 (9)	482 (13)	1797 (47)	254 (7)	281 (7)	321 (8)
No. (%) of Central-Line Days × 10^3 by 5-Year Period							
1990–1994	117 (10)	87 (8)	185 (16)	192 (17)	114 (10)	102 (9)	354 (31)
1995–1999	328 (10)	203 (6)	545 (17)	666 (21)	459 (14)	233 (7)	745 (23)
2000–2004	388 (10)	235 (6)	631 (16)	942 (23)	805 (20)	312 (8)	746 (18)
2006–2010	1,669 (11)	1,142 (8)	2,318 (16)	5,407 (36)	1,571 (11)	1,085 (7)	1,715 (12)

* No CLABSI surveillance data from 2005 due to transition year from NNIS to NHSN

** An ICU that reported at least once during the 5-Year Period

Table 2

Estimated Annual Percent Changes in Pathogen-Specific Pooled Mean CLABSI Incidence Density Rate per 1,000 Central-Line Days among 7 ICU Types,* NNIS (1990–2004) and NHSN (2006–2010) CLABSI Surveillance Data

	NNIS (1990–2004)		NHSN (2006–2010)	
	All ICUs	Continuous Reporters	All ICUs	Continuous Reporters
Pathogen-specific ICU Grouping**	**Annual % Change (95% CI)**	**Annual % Change (95% CI)**	**Annual % Change (95% CI)**	**Annual % Change (95% CI)**
S. aureus				
Medical-Surgical ICUs	−1.2 (−2.6, 0.1)	3.8 (0.2, 7.5)		
Non-Medical-Surgical ICUs	−1.8 (−2.6, −0.8)	−3.6 (−5.3, −1.8)		
Pediatric ICUs			−3.3 (−12.2, 6.7)	−1.5 (−15.8, 15.1)
Non-Pediatric ICUs			−18.3 (−20.8, −15.8)	−16.9 (−21.0, −12.6)
Candida spp.				
Medical-Surgical ICUs	−2.6 (−4.0, −1.2)	4.5 (0.7, 8.5)		
Non-Medical-Surgical ICUs	0.3 (−0.7, 1.3)	−0.9 (−2.7, 0.9)		
All ICU Types			−13.5 (−15.4, −11.5)	−10.8 (−14.1, −7.4)
Gram negative rods				
Medical-Surgical ICUs	−4.6 (−5.9, −3.2)	0.0 (−3.8, 4.0)		
Non-Medical-Surgical ICUs	−1.8 (−2.5, −1.0)	−3.3 (−4.7, −2.0)		
All ICU Types			−16.4 (−18.2, −14.7)	−10.1 (−13.2, − 7.0)
Enterococcus spp.				
All ICU Types	3.6 (2.8, 4.4)	4.6 (2.9, 6.3)	−17.8 (−19.4, −16.1)	−14.1 (−17.2, −11.6)

*Cardiothoracic, Coronary, Medical, Medical-Surgical without Major Medical School Affiliation, Medical-Surgical with Major Medical School Affiliation, Pediatric, and Surgical ICUs

**Medical-Surgical ICUs include ICUs designated as Medical-Surgical with or without Major Medical School Affiliation; non-Medical-Surgical ICUs include Cardiothoracic, Coronary, Medical, Pediatric, and Surgical ICUs

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