Nosocomial Bloodstream Infections

Secular Trends in Rates, Mortality, and Contribution to Total Hospital Deaths

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Background: Nosocomial bloodstream infections occur at a rate of 1.3 to 14.5 per 1000 hospital admissions and are believed to lead directly to 62 500 deaths per year in the United States. Measures of the incidence and the proportion of all hospital deaths related to deaths from these infections provide estimates of their impact. The objectives of the study were to characterize the secular trends in nosocomial bloodstream infection at a single institution and to estimate the population-attributable risk for death among patients experiencing the infection.

Methods: A 12-year retrospective study using prospectively collected data from a hospital-wide surveillance system for nosocomial infections in a 900-bed tertiary care institution. All patients (N=260 834) admitted to the institution between 1980 and 1992 were included in the study. Bloodstream infection rates were calculated for the 10 leading groups of pathogens, and trends were analyzed using simple linear regression. In-hospital mortality rates from patients who did or did not develop nosocomial bloodstream infections were compared.

Results: Between 1980 and 1992, a total of 3077 patients developed 3464 episodes of nosocomial bloodstream infection. The crude infection rates increased linearly from 6.7 to 18.4 per 1000 discharges (0.83 to 1.72 episodes per 1000 patient-days) during the 12-year study period (r=.87). Increases in the infection rates were due to gram-positive cocci (r=.96) and yeasts (r=.95) and essentially explained by infections caused by coagulase-negative staphylococci, *Staphylococcus aureus*, enterococci, and *Candida* species, respectively. Although the crude mortality in patients with nosocomial bloodstream infections decreased from 51% in 1981 to 29% in 1992, the in-hospital population-attributable mortality among infected patients increased from 3.55 deaths per 1000 discharges in 1981 to 6.22 per 1000 discharges in 1992 (r=.67). The etiologic fraction or the proportion of deaths in patients with bloodstream infection to all deaths occurring in the hospital increased from 11.4% in 1981 to 20.4% in 1992 (r=.59).

Conclusions: The incidence, the etiologic fraction, and the population-attributable risk for death among patients experiencing nosocomial bloodstream infections increased progressively during the last decade.

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EACH YEAR, among the 35 million patients admitted to US hospitals, at least 2.5 million will develop a nosocomial infection, almost 250 000 of which will be bloodstream infections. The attack rate for nosocomial bloodstream infections ranges from 1.3 to 14.5 per 1000 hospital admissions,[1] varying with the type of population studied, the size of the institution, the length of hospital stay, and the ward location within an institution.[2-8]

Recently, the National Center for Health Statistics reported that the percentage of discharge diagnoses that included both community- and hospital-acquired bacteremias increased from 74 cases per 10 000 patients in 1979 to 176 per 10 000 in 1987.[9] Furthermore, according to vital statistics reports, the age-adjusted death rates from septicemia have increased exponentially during the past four decades.[10] Banerjee and colleagues,[7] at the Centers for Disease Control and Prevention, Atlanta, Ga, recently reported secular trends in nosocomial "primary" bloodstream infections for institutions in the National Nosocomial Infections Surveillance system during the period from 1980 to 1989. The rates of infection increased from 1.85 per 1000 discharges in 1980 to 3.48 per 1000 in 1989. The

See Methods on next page

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METHODS

HOSPITAL SETTING

The University of Iowa Hospitals and Clinics (UIHC), Iowa City, is a 902-bed institution serving Iowa and the border areas of surrounding states. An average of 22 000 patients was admitted annually during the study period. The UIHC is a tertiary health care center. During the study period, a maximum of 220 beds were reserved for critical care. This number has been reduced over time. The current distribution is as follows: medical intensive care unit (ICU) (10 beds), coronary ICU (24 beds), cardiovascular ICU (10 beds), stroke unit (22 beds), adult and pediatric bone marrow transplantation unit (12 and eight beds, respectively), burn unit (14 beds), transplantation units (eight beds), and surgical ICU (26 beds). Pediatric critical care wards include the pediatric ICU (eight beds), the neonatal ICU (10 beds), the intermediate nursery ICU (27 beds), and some other units with critical care beds. Currently, a total of 213 beds are reserved for critical care at UIHC.

SURVEILLANCE METHODS

Continual prospective surveillance for nosocomial infections began in 1976, and recent studies using standard methods have estimated the sensitivity and specificity of this hospital-wide reporting of nosocomial infection activities to be 81 and 97%, respectively.[14]

All patients admitted to UIHC between July 1, 1980, and June 30, 1992, were included in the study. Only patients admitted for at least 24 hours in surveyed areas were considered. Patients with bloodstream infections were identified through the nosocomial infection surveillance program.[14] Surveillance data are routinely stored on computer tapes and available for review. Additional chart reviews were performed for data completion when necessary (n=332, almost 10%); all charts but one were found.

STUDY OBJECTIVES

The primary objectives of the study were (1) to characterize the secular trends in nosocomial bloodstream infection rates for all pathogens as well as by pathogen group at a single institution and (2) to estimate the population-attributable risk for death among patients experiencing nosocomial bloodstream infection.

Bloodstream infection rates were calculated for the following pathogen groups: coagulase-negative staphylococci (CNS), *Staphylococcus aureus*, streptococci, enterococci, *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Candida* species, and others. Other analyses also included larger groups: gram-positive cocci, aerobic gram-negative bacilli, fungi, and others. Rates were calculated for each year using as the denominator the total number of patients discharged (or the total number of patient-days of care) during the surveillance period.

The primary outcome measure examined was in-hospital mortality in patients who did or did not develop nosocomial bloodstream infections. In the event that the same patient developed more than one episode of bloodstream infection, only the first episode was considered in

rates of infection were the highest in the largest teaching institutions.

Mortality rates associated with nosocomial bloodstream infections are higher than those associated with community-acquired infections.[3,11,12] In the largest community-based study published so far,[3] 51% of the 2978 episodes of bacteremia documented were hospital-acquired, and the mortality associated with these infections was twice that associated with community-acquired infections. The crude mortality associated with bloodstream infection approximates 35%, ranging from 12% to 80%.[3,5,11-13] Secular trends in mortality associated with nosocomial bloodstream infections have not yet been reported.

The primary objectives of this study were to examine the secular trends in rates of nosocomial bloodstream infection in a single tertiary care institution and to quantify the population-attributable risk for death among patients experiencing the disease.

RESULTS

SECULAR TRENDS IN BLOODSTREAM INFECTION RATES

Between 1980 and 1992, a total of 260 834 patients were admitted to UIHC, averaging almost 22 000±4500 (mean±SD) patients a year (median, 20 097 patients; range, 16 806 to 31 434 patients) and representing a total of 2 383 118 patient-days of care. During the 12-year study period, 3464 episodes of nosocomial bloodstream infections were identified. The latter include both primary and secondary bloodstream infections. The overall bloodstream infection rates increased linearly (r=.87, $P<.001$) from 6.7 per 1000 discharges in 1981 to 18.4 per 1000 discharges in 1992, with a peak in 1991 (21.3 per 1000 discharges, **Figure 1**).

Marked changes in pathogen-specific groups were observed during the study period (**Figure 2** and **Table 1**). Aerobic gram-negative rods were the most common organisms causing bloodstream infection in 1981 to 1983, constituting 52% (342/663) of the bloodstream isolates. By 1990 to 1992, the proportion of bloodstream infections caused by aerobic gram-negative rods fell to 29% (376/1291). By contrast, the proportion of isolates of gram-positive cocci progressively increased from 42% to 54% during the study period, representing a 1.4-fold increase. Staphylococci were the leading pathogens involved in 29% of the infections in 1981 to 1983 and rose to 43% of the infections by 1990 to 1992. Coagulase-negative staphylococci were the leading pathogens from 1984 to 1992; the proportion of infections caused by CNS isolates increased 2.5-fold, from 12% to 30% during the study period. *Staphylococcus aureus* was the second most common pathogen, involved in 12% to 17% of all episodes of bloodstream infections. Marked increases in the propor-

the analysis of mortality, except when death occurred more than 28 days after bloodstream infection. In the latter situation, mortality of the subsequent episode was considered. We excluded from the analysis of mortality patients whose blood cultures were obtained after death.

DEFINITIONS

We defined a patient with nosocomial infection as one who had at least one positive blood culture at least 72 hours after admission associated with clinical signs of sepsis.[15] Thus, each episode of nosocomial bloodstream infection was associated with a clinical picture of sepsis according to standard definitions proposed by the Centers for Disease Control and Prevention.

Primary bloodstream infection refers to a bacteremia (or fungemia) for which there was no documented distal source; the infection was either a laboratory-confirmed bloodstream infection (99.4%) or clinical sepsis (0.6%).[7,15] Primary bloodstream infections include those resulting from intravenous or arterial line infections. *Secondary bloodstream infection* defines an infection that develops subsequent to a documented infection with the same microorganism at another body site. *Polymicrobial bloodstream infection* refers to infections in which more than one microorganism has been recovered from the blood culture within a 48-hour period.[16,17]

The crude mortality defines the ratio of the number of patients who died with nosocomial bloodstream infection to the total number of patients with the infection.

The *etiologic fraction* is the proportion of all deaths in the target population attributable to the exposure of interest, in this case, bloodstream infection.[18] This concept allows one to place the relative risk in a public health perspective.[19] In this study, the etiologic fraction was calculated as the ratio of the deaths occurring within 28 days after an episode of bloodstream infection to the total number of in-hospital deaths; 28- or 30-day mortality is the most commonly recommended outcome for assessing mortality rates from bloodstream infection or for evaluating the impact of new compounds for the treatment of sepsis.[11,20,21] The *population-attributable risk for death*, also known as the *population-attributable mortality*, refers to the risk (or mortality, respectively) ratio of the number of deaths in the target population (bloodstream infection) to the number of patients admitted.[19]

STATISTICAL ANALYSIS

The sum of all nosocomial bloodstream infections (episodes) or of all bloodstream isolates documented in each fiscal year (from July 1 to June 30) have been considered in statistical analyses. Rates per 1000 discharges or per 10 000 patient-days were calculated. Linear trends were analyzed using the simple linear regression analysis (least-squares method), with year considered as an independent variable and numbers of bloodstream infection episodes or isolates, respectively, as dependent variables.

Odds ratios and 95% confidence interval (CI) for death were assessed with χ^2 tests. Adjusted odds ratios were assessed with use of the Mantel-Haenszel procedure. All statistical analyses were performed using EPISTAT and SYSTAT software (version 5.2, Systat Inc, Evanston, Ill). All tests were two-tailed, and $P<.05$ was considered significant.

tion of bloodstream infections caused by enterococci (from 1.1% to 5.3%) and *Candida* species (from 2.5% to 7.1%) between 1981 to 1983 and 1990 to 1992 were observed. These represented 4.8- and 2.8-fold increases, respectively, during the study period. The proportion of the infections involving streptococci or other gram-positive organisms did not change during the study period. Noteworthy, most of the increase in the overall bloodstream infection rate was due to increases in the four pathogen groups (**Table 2**): CNS ($P<.001$), *S aureus* ($P=.009$), enterococci ($P<.001$), and *Candida* species ($P=.001$).

Although the proportion of infections due to aerobic gram-negative rods decreased significantly ($P<.05$) from 52% in 1981 to 1983 to 29% in 1990 to 1992, the annual number of bloodstream infection episodes remained stable (131±25 [mean±SD] episodes per year); the rates of infections averaged 6.74±1.6 (mean±SD) episodes per 10 000 patient-days (range, 4.4 to 9.1 episodes). The proportion of polymicrobial bloodstream infections increased during the study period; in addition, the rates of infection increased from 8.3 to 19.8 episodes of polymicrobial bloodstream infection per 10 000 patient-days in 1981 and 1992, respectively ($P<.001$, Figure 2).

CHANGES DURING THE STUDY PERIOD

The following changes that occurred during the study period were examined: average length of stay, surveillance activities, definitions of nosocomial infection, and microbiologic laboratory techniques. Between 1980 and 1992, the average length of stay remained stable; the length of stay averaged 8.17±0.21 (mean±SD) days (median, 7 days; range, 7.87 to 8.48 days). Neither surveillance activities nor definitions of nosocomial bloodstream infection changed during the study period. Between January 1, 1980, and October 1, 1987, the BACTEC 460 (BACTEC System, Johston Laboratories Inc, Towson, Md) radiometric system was used and a 5-mL blood culture inoculum was standard. After October 1, 1987, the BACTEC 660 (BACTEC System) nonradiometric system was used. After April 1, 1988, the standard blood culture inoculum doubled from 5 to 10 mL. It is estimated that an enhanced recovery of 33% occurred with the newer system utilizing a 10-mL inoculum plus a nonradiometric system.[22]

PRIMARY AND SECONDARY BLOODSTREAM INFECTIONS

During the 12 years of the study period, 2034 (59%) of the 3464 episodes of infection were primary bloodstream infections. The proportion of primary bloodstream infections increased progressively from 51% in 1981 to 71% in 1992, ranging from 43% to 71% during the study period. Among those infections, at least 20% were associated with intravascular device infections, par-

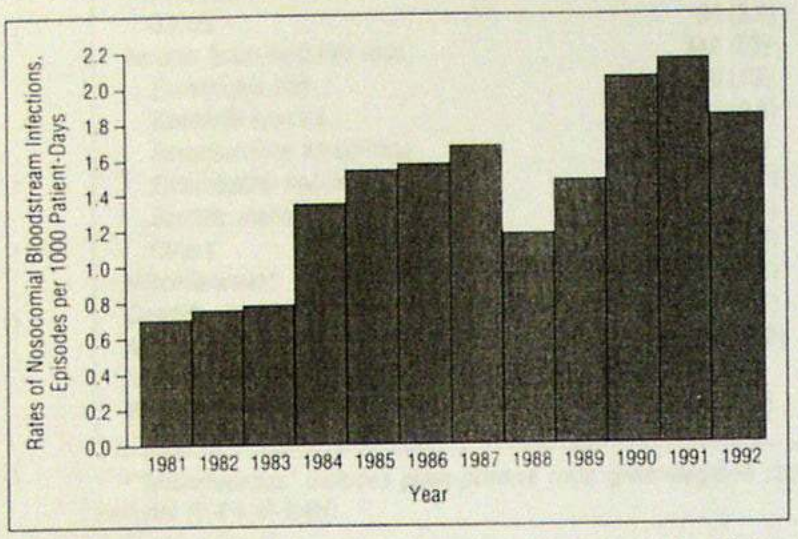

Figure 1. *Secular trends in nosocomial bloodstream infection rates. Rates of nosocomial bloodstream infections at the University of Iowa Hospitals and Clinics, Iowa City, between 1981 and 1992 demonstrate a linear increase (r=.87, P<.001).*

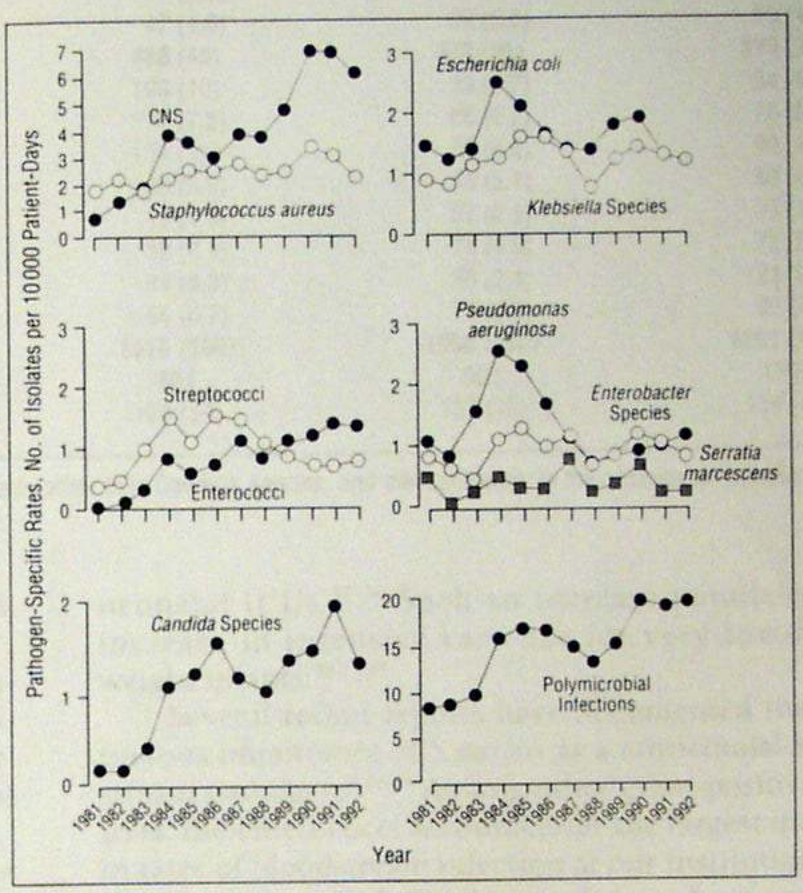

Figure 2. *Secular trends in rates of selected bloodstream isolates. Rates of four pathogen groups demonstrated statistically significant increases during 1981 to 1992: coagulase-negative staphylococci (CNS, P<.001), Staphylococcus aureus (P=.009), enterococci (P<.001), and Candida species (P=.001). Rates of polymicrobial bloodstream infections also increased linearly during the study period (P<.001).*

ticularly intravenous catheters. Intravenous lines may well be responsible for a larger proportion of primary bloodstream infections, but appropriate catheter tip cultures were not performed or the patient failed to meet the clinical criteria for intravascular-associated infections as defined by the Centers for Disease Control and Prevention.[15]

A total of 1430 bloodstream infection episodes were secondary to a previously documented nosocomial infection (1430/3464 [41%]). The leading sources of infection were lower respiratory tract infections (29%), surgical wound infections (25%), and urinary tract infections (20%).

CRUDE AND POPULATION-ATTRIBUTABLE MORTALITY

Among 3077 patients with bloodstream infections, 1150 died; the crude mortality associated with the infections averaged 39% during the study period. Importantly, the crude mortality in patients with nosocomial bloodstream infections (**Figure 3**, top) decreased significantly from 51% in 1981 to 32% in 1992 ($P<.01$). In marked contrast, the in-hospital mortality among patients who did not acquire bloodstream infections was markedly lower, averaging 2.9% (range, 1.8% to 3.7%), but did not vary significantly during the study period ($P=.98$).

Although the crude mortality in patients with bloodstream infection decreased during the study period, the in-hospital mortality among patients experiencing bloodstream infections—the population-attributable mortality—increased linearly from 3.56 per 1000 discharged in 1981 to 5.15 per 1000 discharged in 1992 ($r=.64$, $P=.024$, Figure 3, bottom). In contrast, no significant change was observed in the population-attributable mortality from patients who did not experience bloodstream infections ($r=.001$, $P=.99$).

Patients with nosocomial bloodstream infections showed a risk ratio for death eightfold to 24-fold higher than those who did not develop the infection. Overall, exposure to bloodstream infection was associated with estimated odds ratios for death of 20.45 (95% CI, 18.9 to 22.1; Mantel-Haenszel, $P<.0001$).

ETIOLOGIC FRACTION

The etiologic fraction is the proportion of all deaths in the hospital population attributable to bloodstream infection. In this study, it was calculated as the ratio of the death occurring within 28 days after an episode of nosocomial bloodstream infection to the total number of in-hospital deaths. The etiologic fraction averaged 12.9% during the study period (range, 7.2% to 20.4%). The etiologic fraction increased ($r=.59$) from 11.4% in 1981 to 20.4% in 1992 ($P=.046$). These figures are crude because not all deaths among patients with bloodstream infection are directly attributable to the bloodstream infection. Instead, approximately 70% of deaths among patients with nosocomial bloodstream infection are attributable to the infection.[23] Thus, an estimate of the adjusted 1992 etiologic fraction might be 14% (70% of 20%).

COMMENT

The trends in pathogen-specific rates of nosocomial bloodstream infections at our institution parallel those observed in large teaching National Nosocomial Infections Surveillance hospitals from 1980 to 1989.[7] The increase in rates (almost threefold during the study period) occurred linearly during a time when neither our definitions of infection nor our surveillance activities changed. Important microbiologic laboratory changes occurred after 1987. They would be expected to increase rates no more than 33% only after they were instituted.[22] These data suggest that the increases in rates oc-

Table 1. Nosocomial Bloodstream Isolates at the University of Iowa Hospitals and Clinics, Iowa City, 1981 to 1992

Isolates	No. (%)			
	1981-1983	1984-1986	1987-1989	1990-1992
Gram-positive cocci	**276** (42)	**448** (44)	**586** (55)	**700** (54)
Coagulase-negative staphylococci	79 (12)	175 (17)	254 (24)	391 (30)
Staphylococcus aureus	115 (17)	120 (12)	150 (14)	167 (13)
Streptococci	39 (5.9)	69 (17)	68 (6.4)	41 (3.2)
Enterococci	7 (1.1)	37 (3.6)	61 (5.7)	48 (5.3)
Others	36 (5.4)	47 (4.6)	53 (5.0)	53 (4.1)
Aerobic gram-negative rods	**342** (52)	**458** (45)	**370** (35)	**376** (29)
Escherichia coli	89 (13)	106 (10)	93 (8.7)	84 (6.5)
Klebsiella species	64 (9.6)	77 (7.5)	66 (6.2)	76 (5.9)
Pseudomonas aeruginosa	77 (12)	114 (11)	55 (6.2)	62 (4.8)
Enterobacter species	43 (6.5)	60 (5.9)	55 (5.1)	59 (4.6)
Serratia marcescens	19 (2.8)	19 (1.9)	27 (2.5)	23 (1.8)
Others	50 (7.5)	82 (8.1)	74 (6.9)	72 (5.6)
Miscellaneous*	28 (4.2)	44 (4.3)	36 (3.4)	123 (9.6)
Candida species	17 (2.5)	68 (6.7)	74 (6.9)	92 (7.1)
All Pathogens	**663 (100)**	**1018 (100)**	**1066 (100)**	**1291 (100)**
No. of episodes	593	861	903	1107
Polymicrobial infections	63 (11)	124 (14)	137 (15)	154 (14)

* *"Miscellaneous" includes gram-positive rods, gram-negative cocci, yeasts other than* Candida *species, and clinical sepsis in the absence of positive blood cultures (0.4% of total).*

curred very likely as a result of an increasingly high-risk hospital population.

Most of the increase in the rates of bloodstream infections occurred in four groups of pathogens: CNS, *S aureus*, enterococci, and *Candida* species. A similar observation was made for primary bloodstream infections at National Nosocomial Infections Surveillance hospitals.[7] These data also confirm and extend the observations for the trends previously observed in Virginia, where CNS and *Candida* species were the two pathogens that demonstrated statistically significant increases in bloodstream infection rates during the period from 1978 to 1984.[4]

Coagulase-negative staphylococci currently account for one fourth of nosocomial bloodstream infections,[7,8,24] and several reports have documented their increasing importance as bloodstream pathogens.[4,25,26] Three major reasons may be advanced to account for such an increase. Surveillance artefact combining both the greater recognition and reporting of CNS, as well as an increased frequency in performing blood cultures, has been suggested.[27,28] Although no important change has been noted in our surveillance technique, some reporting bias—placement of increased clinical importance of CNS over time—may have contributed to the increase in the observed rates. Recent studies have shown that only a single blood culture positive for CNS is frequently associated with clinically relevant episodes of bloodstream infection.[29-31] The widespread use of broad-spectrum antibiotics that parallels the increase in the proportion of CNS resistant to methicillin or its derivatives may be partly responsible for the selection of CNS as bloodstream pathogens. However, a major factor responsible for such an increase certainly is the use of multiple invasive devices, particularly in critically ill patients. A worldwide increase in the current number of CNS bloodstream infections has been detected in neonatal ICUs.[32-36] Such an increase paralleled the increase in intensive care use for very-low-birth-weight infants.[28,37,38]

Several recent reports have documented the continuous importance of *S aureus* as a nosocomial bloodstream pathogen.[7,24,39] Among other gram-positive bacteria, the enterococci accounted for the largest increase in rates of bloodstream infection at our institution during the study period. Similar trends have been reported earlier at different institutions as well as nationwide.[7,24,39-41] Enterococcal colonization facilitated by the use of broad-spectrum β-lactam antimicrobial agents for either therapy or surgical prophylaxis certainly constitutes a major cause for the rising importance of enterococci as bloodstream pathogens.[41,42]

Rates of candidemia increased 12-fold during the study period; the most common fungal pathogen isolated was *C albicans*, which accounted for 56% of the total number of *Candida* strains isolated. These data confirm and extend previous observations in patients with cancer[43,44] as well as in patients nationwide.[1,4,7] Prolonged treatment with multiple antimicrobial agents facilitating *Candida* species colonization, the use of multiple indwelling devices, and prolonged neutropenia in patients with cancer have been demonstrated to be independent risk factors for the acquisition of nosocomial candidemia and certainly accounted for the dramatic increases observed in our study.[45-48]

The reason for the observed increase in the proportion of polymicrobial infection remains unclear. Polymicrobial bacteremia is a serious problem in patients with malignant neoplasms[49-51] and has been reported at higher rates in the geriatric population[52,53] as well as in infants in the neonatal ICUs.[54] The high proportions of elderly patients and patients with cancer admitted at UIHC may have contributed to the observed increase in polymicrobial bloodstream infection. The changes described in the

Table 2. Secular Trends in Nosocomial Bloodstream Isolates by Pathogen-Specific Groups at the University of Iowa Hospitals and Clinics, Iowa City, 1981 to 1992*

	F Ratio	*P*	R^2
Significant trends			
All pathogens	15.6	.003	0.61
Gram-positive cocci	30.2	<.001	0.75
Yeasts	21.3	.001	0.68
Coagulase-negative staphylococci	69.2	<.001	0.82
Enterococci	69.8	<.001	0.88
Staphylococcus aureus	10.4	.009	0.51
Candida species	21.5	.001	0.68
Polymicrobial infections	25.6	<.001	0.72
No significant trends			
Gram-negative rods	0.01	.92	0.01
Escherichia coli	0.28	.61	0.03
Klebsiella species	0.93	.36	0.08
Enterobacter species	0.71	.42	0.07
Serratia marcescens	0.08	.78	0.01
Pseudomonas aeruginosa	1.05	.18	0.09
Streptococci	0.02	.88	0.01

**Data were tested for significance using simple linear regression analysis (least-squares method), with year considered as an independent variable and numbers of respective isolates as dependent variables. Rates of bloodstream infection were calculated as the number of bloodstream isolates per 10 000 patient-days. Most of the increase in the overall bloodstream infection rate was due to increases in the four pathogen groups: coagulase-negative staphylococci (P<.001, S aureus (P=.009), enterococci (P<.001), and Candida species (P=.001). No significant trend in the rates of infection due to aerobic gram-negative rods showed a statistically significant trend in the rates of infection during the study period.*

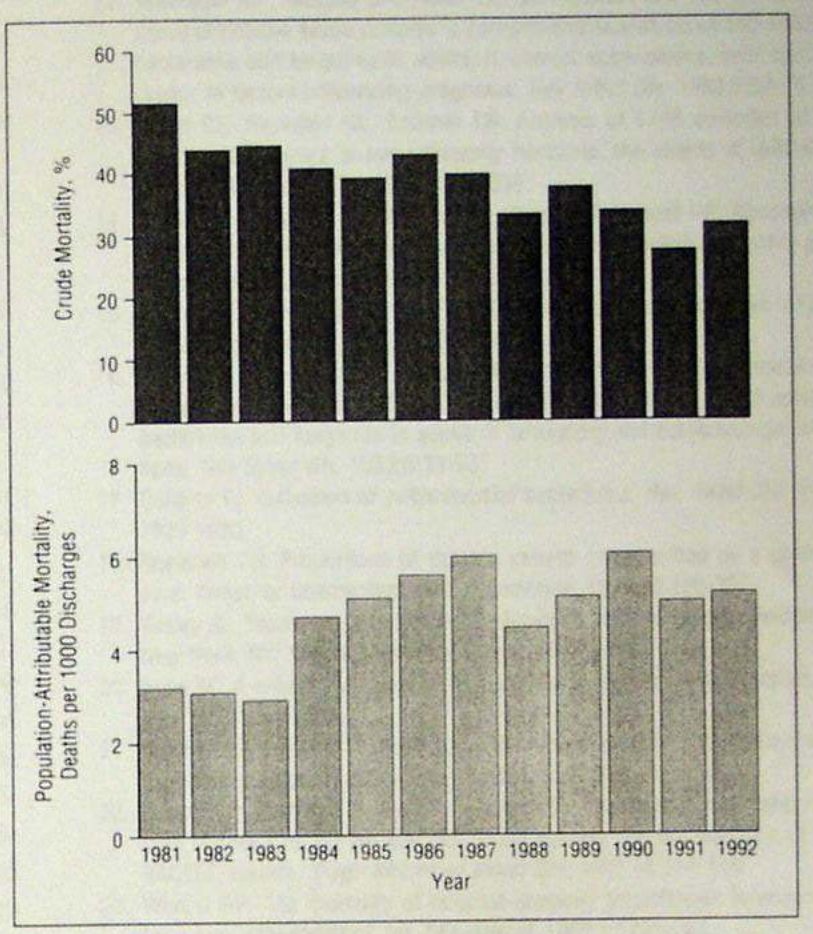

Figure 3. *Crude (top) and population-attributable (bottom) mortality from nosocomial bloodstream infection. In-hospital mortality (crude mortality) in patients with nosocomial bloodstream infections refers to the ratio of the number of patients who died with nosocomial infection to the total number of patients with the infection. The population-attributable mortality refers to the ratio of the number of deaths in patients with bloodstream infections to the total number of patients admitted.*

blood culture technique may have contributed in a minor way to our findings. Polymicrobial infections are associated with higher mortality rates than are monomicrobial infections,[11,55,56] even after controlling for confounding variables.[57]

Rates of bloodstream infection reported in our study are among the highest reported thus far.[1] We attribute such high rates as well as increases observed in the overall incidence of bloodstream infection to several factors: accurate surveillance that has been validated,[14] a high proportion of critical care beds, possibly the advanced age (mean, 59 years) of our infected patients, and possibly an increased severity of illness associated with the need to justify admission to the hospital in the current era of scrutiny by third-party payers. In contrast to the National Nosocomial Infections Surveillance program that reports only primary infections, we report both secondary and primary bloodstream infections.

Elderly patients experience an increased daily rate of nosocomial infection compared with younger patients.[58] In a recently reported study,[27] rates of both hospital- and community-acquired bloodstream infection were three times higher in patients older than 65 years, reaching 23.5 episodes per 1000 admissions in 1987. Importantly, 55% of the patients with bacteremia were in the Medicare age group (>65 years). We reported age to be an independent predictor for acquiring a nosocomial bloodstream infection in a population-based study that included all patients admitted between 1987 and 1990 at UIHC.[59]

The endemic rates of nosocomial infections vary markedly among areas of the same hospital. It has been reported that bloodstream infection is 7.4 times more likely to occur in patients in the ICU as in those on the wards.[60] Bloodstream infection accounts for the higher proportion of all nosocomial infections in ICUs.[30,61] Data from a statewide surveillance system in Virginia indicated rates of nosocomial bloodstream infection that ranged from five to 15 per 1000 admissions in ICUs other than burn units. At UIHC between 1987 and 1990, more than 50% of the bloodstream infection episodes occurred in five critical care units, which housed 24% of the patients admitted during this period; the rates of infection were three times higher in patients admitted in critical care units vs all other locations within the hospital.[59] The attributable mortality rate from nosocomial bloodstream infection was recently estimated to be 35% (95% CI, 25% to 45%) in a cohort of critically ill surgical patients admitted to UIHC between 1988 and 1990.[62]

According to a recent national vital statistics report,[63] septicemia was responsible for almost 1% of all deaths occurring in the United States in 1989. Analysis of the changes in age-adjusted death rates for the 15 leading causes of death from 1979 to 1989 demonstrated a 78% increase; these changes constituted the highest increase reported among all causes of death during the decade. Age-adjusted death rates from septicemia demonstrated an exponential increase from 0.3 per 100 000 population in 1950 to 7.9 deaths per 100 000 population in 1993.[10] This analysis included community- and

hospital-acquired bacteremias; the latter are associated with higher mortality rates.[3,11,12,64] Because cases of nosocomial bloodstream infection account for a large portion—perhaps 60% or more—of cases of septicemia, it is not surprising that an increase in septicemia rates would be paralleled by an increase in bloodstream infection rates such as we observed. To our knowledge, our study is the largest series of nosocomial bloodstream infections and the first to analyze secular trends in mortality rates associated with infection.

Although the crude mortality in patients with bloodstream infection decreased during the study period, the in-hospital mortality among patients with the infection increased linearly. In-patients with nosocomial bloodstream infection were at significantly greater risk of death than were those without this infection. The adjusted risk of death revealed that patients who developed a bloodstream infection carried a risk of dying that was 20-fold greater than that of those who did not develop the infection (odds ratio, 20.45; 95% CI, 18.9 to 22.1). These data extend recent information derived from national statistics[9] showing a decrease from 31% to 25% in the overall fatality rates for patients with either community- or hospital-acquired bacteremia during the period from 1979 to 1987; patients with septicemia, however, carried a significantly greater risk of death than those without this discharge diagnosis (relative risk, 8.6; 95% CI, 8.5 to 9.1).

The results of our study demonstrate a progressive increase in the etiologic fraction during the 12 years of the study. These data allow us to calculate the potential impact of effective efforts aimed at the prevention of nosocomial bloodstream infections. In 1992, the crude proportion of deaths in the hospital population that would have been averted in the absence of bloodstream infections was estimated to be 20%, and the adjusted figure was estimated to be 14%.

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Correction

Statistical Errors in Text and in Table 2. In the article titled "Flavonoid Intake and Long-term Risk of Coronary Heart Disease and Cancer in the Seven Countries Study," published in the February 27, 1995, ARCHIVES (1995;155:381-386), on page 383, left-hand column, the first sentence should read as follows: Mean flavonoid intake was positively associated with percentage of smokers (r=.54, P=.03), with the logarithm of alcohol intake (r=.39, P=.14), and with the intake of β-carotene (r=.30, P=.26), and inversely with the intake of saturated fat (r=−.49, P=.06), dietary fiber (r=−.48, P=.06), ascorbic acid (r=−.42, P=.10), and vitamin E (r=−.32, P=.23). In Table 2, the SFA intake was 21.8 g/d in the cohort in Corfu, Greece; 28.0 g/d in Crete, Greece; 28.4 g/d in Rome railroad, Italy; 39.9 g/d in Dalmatia, Croatia; and 69.1 g/d in Slavonia, Croatia. In addition, Dr Menotti was affiliated with the Laboratory of Epidemiology and Biostatistics, National Institute of Health, Rome, Italy, and not with the Institute of Food Sciences and Nutrition in Perugia, Italy, at the time the study was conducted.