The Economic Impact of *Staphylococcus aureus* Infection in New York City Hospitals

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We modeled estimates of the incidence, deaths, and direct medical costs of *Staphylococcus aureus* infections in hospitalized patients in the New York City metropolitan area in 1995 by using hospital discharge data collected by the New York State Department of Health and standard sources for the costs of health care. We also examined the relative impact of methicillin-resistant versus -sensitive strains of *S. aureus* and of community-acquired versus nosocomial infections. *S. aureus*-associated hospitalizations resulted in approximately twice the length of stay, deaths, and medical costs of typical hospitalizations; methicillin-resistant and -sensitive infections had similar direct medical costs, but resistant infections caused more deaths (21% versus 8%). Community-acquired and nosocomial infections had similar death rates, but community-acquired infections appeared to have increased direct medical costs per patient ($35,300 versus $28,800). The results of our study indicate that reducing the incidence of methicillin-resistant and -sensitive nosocomial infections would reduce the societal costs of *S. aureus* infection.

Each year approximately two million hospitalizations result in nosocomial infections (1). In a study of critically ill patients in a large teaching hospital, illness attributable to nosocomial bacteremia increased intensive care unit stay by 8 days, hospital stay by 14 days, and the death rate by 35% (2). An earlier study found that postoperative wound infections increased hospital stay an average of 7.4 days (3).

Staphylococcus aureus was the most common cause of nosocomial infections reported in the National Nosocomial Surveillance System between 1990 to 1996 (4). The leading cause of nosocomial pneumonia and surgical site infections and the second leading cause of nosocomial bloodstream infections (4), *S. aureus* also causes community-acquired infections (e.g., osteomyelitis and septic arthritis, skin infections, endocarditis, and meningitis). More than 95% of patients with *S. aureus* infections worldwide do not respond to first-line antibiotics such as penicillin or ampicillin (5). Additionally, methicillin-resistant strains of *S. aureus* (MRSA) are common. First reported in the 1960s (6), MRSA has become increasingly prevalent since the 1980s (7,8) and is now endemic in many hospitals and even epidemic in some, with resistance in approximately 30% of all *S.aureus* infections (8).

Vancomycin is the only drug that can consistently treat MRSA. However, beginning in 1989, hospitals have reported a rapid increase in vancomycin resistance in enterococci (VRE) (9). Increased vancomycin use helps select for VRE, and even a small increase in incidence of VRE infection could lead to cross-resistance in *S. aureus*, since genes conferring vancomycin resistance might be transferred from VRE (10). In 1996, Japan reported the first case of *S. aureus* infection with intermediate resistance to vancomycin (11). In 1997, two unrelated cases of *S. aureus* infection with intermediate resistance to vancomycin were reported in the United States (Michigan and New Jersey) (12). In both cases, patients had been treated with multiple courses of vancomycin for repeated MRSA infections over the 6 months before the *S. aureus* infection with intermediate resistance to

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vancomycin; additionally, VRE colonization had been diagnosed 7 months before the *S. aureus* infection with intermediate resistance to vancomycin in the New Jersey patient. The emergence of *S. aureus* infection with intermediate resistance to vancomycin in the United States suggests that *S. aureus* strains are constantly evolving and full resistance may develop (12).

The various ways of controlling MRSA (13) are still being debated. The elimination of endemic MRSA in hospitals is difficult and costly (14-17). In general, infection control in the United States is less stringent than in Canada and in some European countries, where identification of known carriers, prospective surveillance of patients and hospital workers, and use of nasal mupirocin have helped control drug-resistant *S. aureus* infection rates (18).

Knowledge of the scope of the problem is helpful for hospital administrators, insurers, and medical personnel who make policy decisions on control measures to prevent the spread of MRSA and the emergence of vancomycin-resistant *S. aureus*. However, the economic cost of *S. aureus* infections is not well known. Many studies focus on the cost of nonorganism-specific nosocomial infections (2,19,20). Moreover, the reported cost of a nosocomial infection varies because of the wide range of study populations, sites of infection, and methods used (16,21). The few investigations into the cost of *S. aureus* infections have focused on the differential cost of MRSA and MSSA infections (22,23) and are case studies of outbreaks in single hospitals. Thus, they do not provide perspective on the scope of the problem for a population over time.

We estimated the incidence, death rate, and cost of *S. aureus* infections associated with hospitalization in the New York City metropolitan area in 1995. We selected this geographic region because of its high prevalence of multidrug-resistant infections (24,25). We also compared the relative contributions of nosocomial versus community-acquired infections and methicillin-sensitive (MSSA) versus methicillin-resistant *S. aureus*.

The Study

Data

The 1995 Statewide Planning and Research Cooperative System (SPARCS) Administratively Releasable File was the primary source of data (26). SPARCS is a database of all hospital discharges in New York state, as reported by hospitals to the State of New York Department of Health, and the Administratively Releasable File contains discharge information on hospital location, patient characteristics (age, sex, race, ethnicity), and visit characteristics (primary diagnosis, secondary diagnoses, primary procedure, secondary procedures, length of stay, total charges, patient status, and disposition). We analyzed data for hospitals in the following New York City metropolitan area counties: Bronx, Dutchess, Kings, Manhattan, Nassau, Orange, Putnam, Queens, Richmond, Rockland, Suffolk, Ulster, and Westchester. Data on infection incidence or resource use not in SPARCS were obtained through a comprehensive literature search or estimated by a clinical panel consisting of four physicians specializing in infectious disease. Other sources for cost information were the 1995 Medicare Fee Schedule (27) for physician fees and the 1995 Red Book (28) for outpatient pharmaceutical average wholesale prices.

Definitions

We identified patients with the most common types of hospital-associated *S. aureus* infections: pneumonia, bacteremia, endocarditis, surgical site infections, osteomyelitis, and septic arthritis (Table 1) from SPARCS, which uses the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes (29). With the exception of ICD-9-CM code 482.4 (staphylococcal pneumonia) and 038.1 (staphylococcal septicemia), these codes are not organism-specific.

To identify *S. aureus* infections, we used the nonorganism–specific codes in conjunction with an additional ICD-9-CM code to identify the bacterial agent (i.e., 041.11 bacterial infection due to *S. aureus* in conditions classified elsewhere and of unspecified site). Patients with multiple infections were counted only once in the overall incidence rate. Their primary or first occurrence of a diagnosis of interest was used.

Because source of infection (nosocomial versus community-acquired) is not reported in SPARCS, we assumed that specific types of disease were either nosocomial or community-acquired on the basis of the clinical panel opinion (Table 2).

Table 1. ICD-9-CM codes used to identify infections in Statewide Planning and Research Cooperative System

Type of Infection	ICD-9-CM[a]	Description
Pneumonia	482.4	Pneumonia due to staphylococcus
Bacteremia	038.1	Staphylococcal septicemia
	790.7	Bacteremia
	996.62	Infection and inflammatory reaction due to internal vascular device, implant, and graft
Endocarditis	421.0	Acute and subacute bacterial endocarditis
	996.61	Infection and inflammatory reaction due to cardiac device, implant, and graft
Surgical site infection	998.3	Disruption of operation wound
	998.5	Postoperative infection
Osteomyelitis	730.01-730.09	Acute osteomyelitis
	730.10-730.19	Chronic osteomyelitis
Septic arthritis	711.00-711.09	Pyogenic arthritis
	996.66	Infection and inflammatory reaction due to internal joint problems

[a]International classification of diseases, 9th Revision, Clinical Modification, 1995.

Table 2. Definitions of nosocomial or community-acquired *Staphylococcus aureus* infections

Type of Infection	Nosocomial	Community-acquired
Pneumonia	Secondary diagnosis[a]	Primary diagnosis[a]
Bacteremia	Catheter- or surgery-associated infections[b]	Noncatheter- and nonsurgical-associated infections
Endocarditis	Prosthetic valve infections	Natural valve infections
Surgical site infection (SSI)	All SSIs	None
Osteomyelitis	None	All
Septic arthritis	Prosthetic joint infections	Natural joint infections

[a]ICD-9-CM 482.4 as the primary diagnosis vs. 482.4 as one of several other diagnoses.
[b]ICD-9-CM 996.62, or 038.1 associated with a surgical ICD procedure code, or 790.7 associated with a surgical ICD procedure code.

Modeling the Incidence Rate

ICD-9-CM code 041.11 (bacterial infection due to *S. aureus*) is not widely used by reporting hospitals. Therefore, the incidence of *S. aureus* infections based on the counts of 041.11 in SPARCS would underestimate the number of cases. We estimated the incidence of *S. aureus* infections (except pneumonia) as follows (Table 3): the total incidence of each type of infection (e.g., endocarditis) in SPARCS was multiplied by the

Table 3. Incidence of *Staphylococcus aureus* infections from research or clinical panel

Type of infection	Description	*S. aureus* %	Reference
Bacteremia	Staphylococcal septicemia	50	30
	Bacteremia	15	31,32
	Infection and inflammatory reaction due to internal vascular device, implant, and graft	16	4
Endocarditis	Acute and subacute bacterial endocarditis	30	Clinical panel
	Infection and inflammatory reaction due to cardiac device, implant, and graft	14	33
Surgical site infection	Disruption of operation wound and postoperative infection	20	4
Osteomyelitis	Acute and chronic osteomyelitis	50	34,35
Septic arthritis	Pyogenic arthritis	11 (age <5 yr) 33 (age 5-18 yr) 55 (age >18 yr)	33
	Infection and inflammatory reaction due to internal joint prosthesis	25	33

estimated percentage attributable to *S. aureus* (determined by research or clinical panel opinion) to give the total number of infections due to *S. aureus*. The incidence of pneumonia was equated with the occurrence of the ICD-9-CM code 482.4 (staphylococcal pneumonia). For ICD-9-CM code 038.1 (staphylococcal septicemia), we assumed that only 50% of infections were attributable to *S. aureus* (with the remainder attributable to *S. epidermidis*) (30).

Modeling Death Rates

The death rates attributable to bacteremia, endocarditis, or community-acquired pneumonia were assumed to be equal to the death rates found when these infections were coded as a primary diagnosis in SPARCS and 041.11 was used as a secondary diagnosis. For nosocomial pneumonia, however, we assumed that the attributable death rate was a percentage of the actual death rate—for ventilator-associated pneumonia patients, death rate is a function of both the severity of underlying disease and the pneumonia. A series of matched-cohort studies have demonstrated that the death rate attributable to ventilator-associated pneumonia is 0% to 57% of the actual death rate (36-39). On the basis of this research and expert panel judgment, nosocomial pneumonia in ventilator-associated pneumonia patients (identified by ICD-9-CM V46.0 or V46.1) was assumed to have an attributable death rate of 50% of the death rate found in SPARCS (30,40). We assumed that the attributable death rate of nonventilator-associated pneumonia was the death rate found in SPARCS. On the basis of the low death rate found in SPARCS (approximately 2%), we assumed that no deaths were attributable to osteomyelitis, septic arthritis, or surgical site infections.

Modeling Direct Medical Costs

Direct medical costs were defined as hospital costs attributable to *S.aureus* infection, professional fees incurred during hospitalization, and costs of other infection-related medical services provided after discharge. For each infection, total direct medical costs were calculated by multiplying the average direct medical cost per patient by the incidence of disease. Average hospital costs attributable to *S. aureus* per patient were assumed to be equal to the average hospital charge from SPARCS when the infection (e.g., pneumonia, bacteremia) was coded as a primary diagnosis and 041.11 was used as a secondary diagnosis. Professional fees incurred during hospitalization include physician visits and consultations for evaluation and management, as well as radiologic, surgical, and anesthesiologic costs. The average frequency of physician services per patient was based on clinical panel estimates. Costs of these services were based on 1995 Medicare Payment Rates for the Long Island, New York, area as an intermediate point between New York City costs and those of outlying counties.

Costs of medical services after discharge include those of postdischarge complications (e.g., abscesses, aneurysms) requiring rehospitalization, home-based intravenous antibiotic therapy, and outpatient oral antibiotic therapy. The average frequency of other medical services provided per patient was based on clinical panel estimates. Costs of hospital readmission were based on SPARCS charges; costs of home-based intravenous therapy were based on literature estimates (40,41); and costs of outpatient medications were based on average wholesale prices (25).

Modeling MRSA and MSSA *S. aureus* Infections

SPARCS does not identify MRSA or MSSA infections, and a code for infection with a drug-resistant organism (V09) is rarely used. Therefore, we modeled the comparative incidence, death rate, and cost of MRSA and MSSA. We computed the incidence of MRSA and MSSA infections by using the estimate that 29% of infections were due to MRSA (8). The clinical panel estimated that 10% of community-acquired infections were due to MRSA (includes infections acquired at long-term care facilities).

The number of deaths for MRSA and MSSA infections was estimated as follows: the clinical panel estimated a risk ratio for death rates of MRSA and MSSA infections, and deaths due to MRSA and MSSA infections were calculated from the estimated risk ratio and the overall number of deaths due to *S. aureus* infection. We estimated the direct medical cost per patient for MRSA and MSSA infections as follows: differences in resource use for those with MRSA and MSSA infections were identified by the clinical panel; these differences were converted into differences in cost using a method similar to that described above for modeling direct medical costs; and average costs for MRSA and MSSA infections were calculated by using the average cost for an *S. aureus* infection and the average difference in cost between MRSA and MSSA infections.

Incidence, Death Rate, and Attributable Costs

S. aureus Infection

Of 1,351,362 nonobstetrical hospital discharges in SPARCS for New York City in 1995, an estimated 13,550 (1.0%) were discharges of patients with *S. aureus* infections (Table 4). The total direct medical costs incurred by these patients was an estimated $435.5 million—average length of stay nearly 20 days, direct cost of infection, $32,100 (Table 4). The number of deaths was estimated at 1,400 (a 10% death rate). In contrast, the hospital charges for the average hospital stay in SPARCS (for all nonobstetrical discharges) were $13,263—average length of stay 9 days, death rate 4.1%. Thus, patients with *S. aureus* infection had approximately twice the cost, length of stay, and death rate of a typical hospitalized patient.

Pneumonia and bacteremia represented most *S. aureus* infections and accounted for 60% of the total direct medical costs and 97% of the number of deaths. Endocarditis caused the longest stay (26 days) and highest direct cost per patient ($47,200); surgical site infection caused the shortest stay (14 days) and lowest direct cost per patient ($21,810). Hospital charges were an average of $29,000 (90% of the total costs); professional fees were an average of $2,300 (7%); and postdischarge costs represented $800 (3%) (Table 5).

Table 4. Incidence, length of stay, costs, and death rates of *Staphylococcus aureus* infections by type of infection

Type of infection	Incidence	Length of stay (days)	Direct Medical Cost Total ($M)	Direct Medical Cost Per patient ($)	Deaths Total	Deaths %
Pneumonia	3,600	22.2	128.3	35,400	890	25
Bacteremia	4,400	18.0	137.0	31,300	470	11
Endocarditis	550	25.9	25.8	47,200	40	7
Surgical site infection	2,300	13.6	50.5	21,800	ND[a]	ND
Osteomyelitis	2,000	23.9	68.4	35,000	ND	ND
Septic arthritis	700	22.0	25.5	35,100	ND	ND
Total or average	13,550	19.8	435.5	32,100	1,400	10

[a]ND=no data.

Table 5. Direct medical charges—average hospital facility charges, professional fees, and postdischarge costs per case

Type of infection	Hospital charges $ (%)	Professional fees $ (%)	Postdischarge costs $ (%)	Total $
Pneumonia	33,400 (94)	2,000 (6)	ND[a]	35,400
Bacteremia	27,900 (89)	2,100 (7)	1,300 (4)	31,300
Endocarditis	41,700 (88)	4,300 (9)	1,200 (3)	47,200
Surgical site infection	20,200 (93)	1,600 (7)	ND	21,800
Osteomyelitis	30,000 (86)	3,200 (9)	1,800 (5)	35,000
Septic arthritis	30,600 (87)	3,100 (9)	1,400 (4)	35,100
Average	29,000 (90)	2,300 (7)	800 (3)	32,100

[a]ND=no data.

Nosocomial Infection

Nosocomial infections accounted for 46% of the total incidence of *S. aureus* infections (6,300 infections), while community-acquired infections accounted for 54% (7,250 infections) (Table 6). Community-acquired pneumonia as a primary diagnosis accounted for 12% (1,500) of the total cases. If community-acquired pneumonia is assumed to be mostly acquired in long-term care facilities, most infections (58%) were acquired institutionally. The cost attributable to community-acquired infections ($35,300) was approximately $6,500 higher on a per patient basis than the cost attributable to nosocomial infections ($28,800). The death rates attributable to community-acquired and nosocomial infections were similar (10.5% and 10.1%).

MRSA Infection

MRSA infections accounted for 21% (2,780) of the total *S. aureus* infection incidence (29% of 6,300 nosocomial infections plus 10% of 7,250 community-acquired infections), while MSSA infections accounted for 79% (10,770) of total infections (Table 6). The attributable cost of a patient with MRSA was approximately $2,500 higher than the attributable cost of a patient with MSSA ($34,000 versus $31,500). The higher cost of MRSA infections is due to the higher cost of vancomycin, longer hospital stay, and the cost of patient isolation procedures. For nosocomial infections alone, the cost attributable to MRSA was approximately $3,700 higher on a per patient basis than the cost attributable to MSSA infections ($31,400 versus $27,700). The death rate attributable to MRSA infections was estimated at more than 2.5 times higher than that attributable to MSSA infections (21% versus 8%).

Table 6. Incidence, length of stay, costs, and deaths of *Staphylococcus aureus* infections by source of infection and degree of resistance

Source of infection	Incidence	Direct medical cost: Total ($M)	Direct medical cost: Per patient ($)	Deaths: Total	Deaths: (%)
Nosocomial	6,300	181.0	28,800	640	10
Community	7,250	254.5	5,300	760	11
Pneumonia	1,500	51.7	34,900	380	25
Non-pneumonia	5,750	202.8	35,400	380	7
MRSA[a]	2,780	94.5	34,000	590	21
MSSA[b]	10,770	339.4	31,500	810	8

[a]Methicillin-resistant strains of *S. aureus*.
[b]Methicillin-sensitive strains of *S. aureus*.

Sensitivity Analyses

Although assumed to be underused in SPARCS, the ICD-9-CM code 041.11 represents a lower boundary of the total incidence of *S. aureus* infection. In SPARCS, code 041.11 was used 7,366 times associated with a diagnosis of interest (e.g., endocarditis) and represented a total cost of $236.4 million and a death rate (740 deaths) of 2% (Table 7). The upper boundary of the total cost of *S. aureus* infections was calculated by assuming that all hospital charges and deaths of patients with *S. aureus* infections were attributable to the infection, representing a total cost of $599 million and a death rate of 14.5% (1,960 deaths). We conducted sensitivity analyses (varying the percentage of nosocomial MRSA; percentage of patients isolated; difference in length of stay between patients with MRSA and MSSA; attributable length of stay for patients with ventilator-associated pneumonia; number of *S. aureus* catheter infections; and percentage of *S. aureus*–caused bacteremia, septicemia, and postoperative infections) and found that the difference in cost per case between MRSA and MSSA infections was $1,700 to $5,100.

Table 7. Sensitivity analyses

	Direct medical cost ($)	Deaths
Study results	435.5	1,400
Lower boundary: only 041.11 cases	236.4	740
Upper boundary: all costs attributable	599.0	1,960

Comments

Our sensitivity analysis shows that we did not vastly over- or underestimate the direct medical costs of *S. aureus* infections in New York City. However, the study had several limitations; it was retrospective, and the data sources were not validated by other means (e.g., interviews or chart review). Therefore, coding errors in this database may affect the results. The clinical panel estimates we used to model differences between MRSA and MSSA may lead to some inaccuracy in those difference estimates. Thus, our comparison of costs and deaths between MRSA and MSSA should be viewed as a best approximation in the absence of case-control data or a multivariate analysis of a well-defined patient population.

Our estimates of the cost per infection are generally higher than estimates in studies reviewed by Jarvis (19). A major reason may be our focus on New York City, where costs are much higher than in other areas of the United States. In addition, earlier studies have used only hospital costs. Our perspective was societal; therefore, we included physician fees and outpatient costs, as well as hospital charges. Finally, most of these studies focused on non–organism-specific nosocomial infections; *S. aureus* infections may have a higher average cost per episode than infections of other organisms (42).

On the other hand, we used conservative estimates for certain costs. Medicare prices for professional services are generally lower than commercial rates. Also, we did not account for postdischarge complications that did not lead to hospitalization. Additionally, our societal estimates did not include the cost of dying or lost productivity associated with these illnesses.

Despite its limitations, this study shows that hospitalizations associated with *S. aureus* are serious and have high medical costs and death rates. The average length of stay attributable to *S. aureus* infection for these patients was very high, 20 days—nearly three times the average for any other type of hospitalization (43). The increased length of stay in turn leads to increases in direct medical costs, with an average cost per case of $32,100 in 1995.

Treating an MRSA infection costs 6% to 10% more than treating an MSSA infection ($2,500 to $3,700 per case). This cost difference does not reflect MRSA's greater virulence; rather, it reflects the increased cost of vancomycin use and isolation procedures (if used). These estimates are slightly lower than the difference of $5,104 found by Wakefield et al. (21), perhaps because they focused on the cost of serious *S. aureus* infections, while our analysis examined all hospitalizable *S. aureus* infections.

Patients with MRSA infections have a high average attributable death rate of 21% versus 8% for an MSSA infection. Some of the death rate difference may be related to the underlying condition of patients who become infected with MRSA (e.g., older patients, drug users, sicker patients, patients previously exposed to other antibiotics) (44) and to the lack of effectiveness of vancomycin itself in curing MRSA. (Vancomycin has a narrow therapeutic index that allows little room for increasing blood concentration without incurring substantial losses in tolerance [45]).

Both MSSA and MRSA infections are associated with high costs and large numbers of deaths in the New York City metropolitan area. The costs and deaths associated with *S. aureus* infections may dramatically increase if the newly isolated *S. aureus* infection with intermediate resistance to vancomycin spreads or if VRSA emerges. For example, after penicillin-resistant *S. aureus* appeared in the 1950s, the death rate of bacteremia increased from 28% to 50% at the University of Minnesota (Figure) (46). After methicillin was introduced, the death rate decreased (47). Efforts should be directed toward reducing the incidence of MRSA and MSSA nosocomial infections to reduce their economic impact on society.

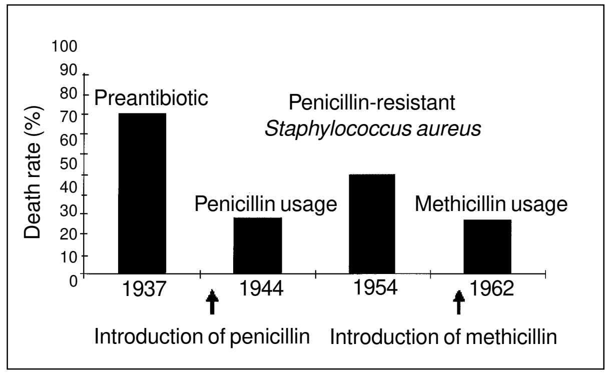

Figure. Death rate of staphylococcal bacteremia over time. (Data from 46, 47.)

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