ORIGINAL ARTICLE

Changes in the incidence and antimicrobial susceptibility of healthcare-associated infections in a New York hospital system, 2006-2012

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Keywords

Antimicrobial resistance • Multidrug-resistant organisms • Bloodstream infections • Surgical site infections • Urinary tract infections

Summary

Introduction. *National efforts to curtail healthcare-associated infections (HAI) proliferated recently, though data detailing progress over time are limited. This retrospective cohort study aims to describe changes in incidence and antimicrobial susceptibility of HAI in four New York City hospitals over seven years.*
Methods. *Electronic data were collected retrospectively for all patients discharged from 2006 through 2012. Previously validated computerized algorithms based on National Healthcare Safety Network criteria detected bloodstream infections, pneumonia, surgical site infections, and urinary tract infections with Enterococcus spp., Staphylococcus aureus, Streptococcus pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumoniae. Antimicrobial susceptibilities were obtained from electronic laboratory records. Logistic regression was used to assess changes in odds of acquiring an HAI and odds of antimicrobial resistance over time, controlling for age, gender, severity of illness, previous hospitalizations, and admission source.*
Results. *In total, 19,052 HAI were identified among 761,426 discharges. HAI rates fell for all organisms, all infection types, and within all hospitals. Odds of acquiring an HAI decreased significantly over time for all organisms. Resistance levels were stable for Enterococcus spp., S. aureus, A. baumannii, and S. pneumoniae. Multidrug resistance increased for P. aeruginosa and decreased for K. pneumoniae, though imipenem resistance among K. pneumoniae climbed sharply in 2011.*
Conclusions. *This study suggests that HAI incidence rates are falling, possibly due to increased federal, state and local attention to healthcare quality and patient safety. Though we found no substantial reductions in resistance, recent national attention towards antimicrobial stewardship may precipitate a change in coming years.*

Introduction

Healthcare-associated infections (HAI) remain endemic in U.S. healthcare facilities despite growing emphasis on infection prevention and control programs designed to curtail their spread [1]. The latest national data released by the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NSHN) show notable decreases for some HAI including central line-associated bloodstream infections (BSI) and certain types of surgical site infections (SSI) [2]. However, national longitudinal data are available only for the selected types of HAI tracked by the NHSN, which are limited primarily to procedure- and device-associated infections. The NHSN data also reveal substantial differences across regions and states, emphasizing the importance of monitoring trends at the local level [2].

Antimicrobial resistance among common healthcare pathogens is similarly persistent in hospitals, even with advances in stewardship efforts and transmission-based precautions for patients with drug-resistant organisms [3-5]. Multidrug-resistant phenotypes are implicated in more than 20% of HAI nationally, though prevalence varies considerably by region and institution [6]. The CDC's most recent comprehensive report on antimicrobial susceptibilities shows only slight changes in resistance for most organisms over the past several years, but data are likewise limited to specific types of HAI and trends are evaluated for only a short time period [6].

In light of the need for longitudinal data at the local level following a period of sharp increases in regional Gram-negative resistance, this study aims to describe changes in the epidemiology of HAI in four New York City hospitals over a seven year period from 2006 through 2012. Specifically, this study assesses changes in incidence of HAI, prevalence of antimicrobial resistance, and patient-level factors at admission that are associated with these outcomes for six of the most common bacterial pathogens in healthcare settings.

Methods

Sample and setting

Data were collected from four hospitals in a single academically-affiliated network located in New York, NY. The facilities included a 221-bed community hospital, a 283-bed pediatric acute care hospital, a 647-bed adult tertiary/quaternary care hospital, and a 914-bed adult and pediatric tertiary/quaternary care hospital. All discharges occurring from January 1, 2006 through December 31, 2012 were included in the analyses. Although some patients were admitted multiple times throughout the seven-year study period, the unit of analysis for this study was each patient discharge.

Data collection

All data were collected retrospectively from the network's Clinical Data Warehouse, which stores information from a variety of electronic sources shared by the four hospitals [7]. Dates of hospital admission and discharge, source of admission, and previous in-network hospitalizations were obtained from the admission-discharge-transfer (ADT) record. Complete lists of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes associated with each admission were obtained from billing records. Time-stamped culture results and antimicrobial susceptibility patterns were obtained from clinical microbiology laboratory records. All data were linked using patients' unique medical record numbers and admission dates.

Definitions of infections, antimicrobial resistance, and patient characteristics

Four types of infections were included in this analysis: BSI, SSI, urinary tract infections (UTI), and pneumonia. Algorithms for identifying infections in the electronic data were designed in accordance with the NHSN guidelines for surveillance of HAI [8]. Figure 1 illustrates criteria used to adjudicate cases of each infection type: BSI were identified by blood cultures; SSI by post-operative wound cultures and documentation of an NHSN operating room procedure; pneumonia by respiratory culture and ICD-9-CM diagnosis code for pneumonia; and UTI by either urine culture 10^3-10^5 colony forming units per milliliter (CFU/mL) and less than two other species and pyuria within a 48 hour window before or after culture collection, or urine culture with at least 10^5 CFU/mL and less than two other species.

Dates of culture collection and hospital admission were used to determine whether infections were healthcare-associated, i.e., developed at least two days after hospital admission.

This study included HAI associated with *Staphylococcus aureus*, *Acinetobacter baumannii*, *Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis* and *Enterococcus faecium*. Binary classifications of antibiotic resistance were defined for *S. aureus* (oxacillin), *S. pneumoniae* (penicillin), *A. baumannii* (ampicillin-sulbactam), and *E. faecalis* and *E. faecium* (vancomycin). For *P. aeruginosa* we assessed resistance to cefepime, gentamicin, levofloxacin, meropenem, piperacillin/tazobactam, and tobramycin. For *K. pneumoniae* we assessed resistance to cefepime, ceftriaxone, gentamicin, imipenem, levofloxacin, meropenem, piperacillin/tazobactam, tobramycin, and trimethoprim/sulfamethoxazole. Multidrug resistance for *P. aeruginosa* and *K. pneumoniae* was defined as resistance to at least three antibiotic classes among those assessed [9]. Resistance to each antibiotic was determined by the hospitals' clinical microbiology laboratories.

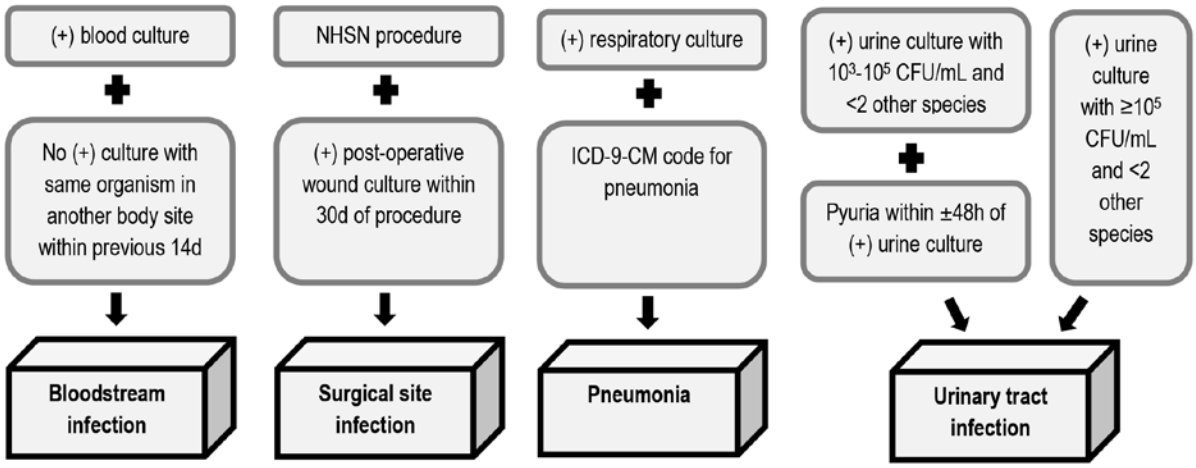
Patient characteristics at admission were assessed using several measures. A weighted Charlson Comorbidity Index was created using ICD-9-CM diagnosis codes for conditions indicated as being present upon hospital admission [10]. Patients who had at least one within-network inpatient hospitalization in the previous year were identified using ADT records. In addition, ADT records were used to determine patients' admission source, defined as either healthcare (i.e., transfer from another hospital, ambulatory surgery center, skilled nursing facility, hospice center) or non-healthcare (e.g., from home). Patient age, sex, admission hospital, and admission year were also collected from the Clinical Data Warehouse.

Statistical analysis

To assess changes in HAI over time we tabulated the number of HAI occurring each year and stratified by organism and body site of infection. Percent changes in HAI incidence per 10,000 discharges between 2006 and 2012 were calculated. Multiple logistic regression was used to evaluate changes in odds of infection over time, controlling for hospital, age (continuous), sex, within-network hospitalization in the previous year, admission source, and Charlson Comorbidity Index. A separate model was constructed for each of the six organisms. Patients who had an infection in more than one body site with the same organism during a single admission were represented only once in each multivariable model. In order to evaluate whether patient characteristics associated with HAI changed throughout the study period, we also assessed interaction between year and age, sex, prior hospitalization, admission source and Charlson Comorbidity Index for each body site of infection.

To assess changes in antibiotic sensitivities over time, we tabulated the annual proportion of infections resistant to each of the antibiotics identified *a priori* for each organism. Multiple logistic regression was used to evaluate changes in the odds of resistance over time, controlling for hospital, age, sex, within-network hospitalization in the previous year, admission source, and Charlson Comorbidity Index. Each organism was modeled separately. Patients who had an infection at more than one body site with the same organism during a single admission were represented only once in each multivariable model and were considered to have a resistant infection if at least one of the infections was caused by a resistant organism.

Fig. 1. Algorithms for identifying four types of infections using electronically available data from laboratory records and International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes. Definitions are based on the Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) guidelines for surveillance of HAIs [7]. ICD-9-CM codes for pneumonia included 003.22, 020.3-020.5, 021.2, 022.1, 031.0, 039.1, 052.1, 055.1, 073.0, 083.0, 112.4, 114.0, 114.4, 114.5, 115.05, 115.15, 115.95, 130.4, 136.3, 480.0-480.3, 480.8, 480.9, 481, 482.0-482.3, 482.30-482.32, 482.39, 482.4, 482.40, 482.41, 482.42, 482.49, 482.8, 482.81-482.84, 482.89, 482.9, 483, 483.0, 483.1, 483.8, 484.1, 484.3, 484.5-484.8, 485, 486, 513.0, and 517.1. CFU/mL, colony forming units per milliliter.



Results

Characteristics of the 761,426 patient discharges that occurred during the study period are described by year in Table I. A total of 19,052 HAI with the six organisms of interest were identified. Forty-nine percent were UTI (N = 9,319), 23% were pneumonia (N = 4,414), 19% were BSI (N = 3,602), and 9% were SSI (N = 1,717). From 2006 to 2012, incidence per 10,000 discharges fell for each type of HAI within all four hospitals and for each of the six organisms included in this study (Fig. 2). Table II displays results of the multivariable regression analyses modeling the association between advancing year and odds of HAI. For each organism there was a statistically significant decrease in the odds of HAI over time, controlling for hospital and patient characteristics. Patients with a healthcare admission source were significantly more likely to develop an HAI with all organisms except *S. pneumoniae*, for which a positive but not statistically significant association was found. Within-network hospitalization in the previous year significantly increased the odds of developing an HAI with all organisms except *S. pneumoniae*, for which a statistically significant negative association was found. Advancing age and greater severity of illness were significantly associated with development of HAI for all organisms. Male patients were significantly more likely to develop an HAI with *S. aureus, P. aeruginosa, S. pneumoniae* and *A. baumannii,* while female patients were significantly

Tab. I. Characteristics of hospitalized patients by year.

Year	2006	2007	2008	2009	2010	2011	2012
N	104,645	106,783	105,177	109,631	112,656	112,122	110,412
% (no.) admitted to each hospital							
Community	13.1 (13,668)	12.6 (13,476)	12.7 (13,376)	11.7 (12,803)	11.6 (13,072)	11.2 (12,557)	11.1 (12,225)
Pediatric acute care	15.8 (16,507)	17.1 (18,281)	18.0 (18,959)	15.2 (16,694)	14.6 (16,487)	14.5 (16,260)	14.9 (16,405)
Adult tertiary/quaternary care	31.9 (33,355)	31.7 (33,839)	31.4 (33,054)	31.9 (35,005)	32.2 (36,283)	31.7 (35,579)	31.3 (34,608)
Adult/pediatric tertiary/quaternary care	39.3 (41,115)	38.6 (41,187)	37.8 (39,788)	41.2 (45,129)	41.6 (46,814)	42.6 (47,726)	42.7 (47,174)
% (no.) admitted from healthcare source*	9.6 (10,044)	10.5 (11,228)	10.7 (11,287)	17.3 (18,983)	16.7 (18,798)	17.5 (19,653)	16.6 (18,270)
% (no.) hospitalized within previous year**	22.6 (23,658)	32.4 (34,601)	37.2 (39,069)	40.2 (44,054)	43.3 (48,772)	44.4 (49,747)	45.1 (49,800)
Mean (standard deviation) Charlson Comorbidity Index	1.4 (2.75)	1.6 (2.95)	1.6 (2.93)	1.6 (2.99)	1.7 (3.08)	1.8 (3.30)	1.8 (3.36)
Mean (standard deviation) age in years	44.5 (27.82)	44.3 (27.89)	44.4 (27.99)	44.6 (28.11)	44.8 (28.11)	45.5 (28.3)	45.4 (28.46)
% (no.) male sex	44.9 (46,989)	44.5 (47,511)	44.2 (46,473)	44.4 (48,717)	44.3 (49,930)	44.5 (49,939)	44.4 (48,989)

*Admission from another hospital, ambulatory surgery center, skilled nursing facility, or hospice center.

**Within-network hospitalizations only.

Tab. II. Relationships between advancing year and odds of healthcare-associated infection, odds of antimicrobial resistance at four New York City hospitals, 2006-2012.

Organism	*Enterococcus faecalis and Enterococcus faecium*	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Streptococcus pneumoniae*
Relationship between advancing year and odds of healthcare-associated infection[1]						
N	6,301	4,399	4,116	2,758	688	195
Year (continuous, 2006-2012)	0.86 [0.85,0.87]	0.89 [0.88,0.90]	0.89 [0.87,0.90]	0.90 [0.88,0.92]	0.88 [0.85,0.92]	0.85 [0.79,0.92]
Hospital*						
Community	0.44 [0.40,0.48]	0.59 [0.52,0.66]	0.55 [0.49,0.63]	0.49 [0.42,0.56]	0.76 [0.56,1.02]	0.82 [0.49,1.36]
Pediatric acute care	0.57 [0.51,0.65]	0.70 [0.61,0.79]	1.01 [0.86,1.17]	0.85 [0.71,1.02]	0.78 [0.54,1.13]	0.60 [0.32,1.13]
Adult/pediatric tertiary/ quaternary care	0.54 [0.51,0.57]	0.80 [0.75,0.86]	1.27 [1.20,1.36]	0.80 [0.74,0.87]	1.37 [1.15,1.61]	0.94 [0.69,1.30]
Healthcare admission source**	2.08 [1.96,2.21]	1.91 [1.78,2.05]	1.88 [1.75,2.02]	2.23 [2.05,2.43]	2.63 [2.23,3.10]	1.39 [0.96,2.00]
Hospitalized within previous year***	1.75 [1.66,1.85]	1.47 [1.39,1.57]	1.49 [1.40,1.59]	1.64 [1.52,1.78]	1.39 [1.19,1.63]	0.68 [0.50,0.93]
Charlson Comorbidity Index (continuous)	1.08 [1.075,1.085]	1.08 [1.07,1.09]	1.08 [1.07,1.09]	1.06 [1.05,1.07]	1.08 [1.07,1.09]	1.08 [1.05,1.11]
Age in years (continuous)	1.017 [1.016,1.018]	1.009 [1.007,1.010]	1.021 [1.019,1.022]	1.022 [1.020,1.024]	1.01 [1.007,1.014]	1.006 [1.00,1.01]
Male sex	0.87 [0.83,0.91]	1.57 [1.48,1.67]	0.81 [0.77,0.87]	1.11 [1.03,1.20]	1.42 [1.23,1.65]	1.84 [1.37,2.46]
Relationship between advancing year and odds of antimicrobial resistance for patients with healthcare-associated infections[2]						
N (%) resistant	2,716 (43.1)	1,964 (44.7)	404 (9.8)	165 (5.6)	276 (40.1)	75 (38.5)
Year (continuous, 2006-2012)	0.98 [0.95,1.01]	0.94 [0.91,0.97]	0.86 [0.82,0.91]	1.45 [1.32,1.59]	0.95 [0.88,1.03]	0.86 [0.73,1.01]
Hospital*						
Community	0.61 [0.49,0.76]	1.30 [1.03,1.65]	0.63 [0.42,0.95]	0.48 [0.20,1.13]	0.98 [0.52,1.85]	0.88 [0.28,2.76]
Pediatric acute care	0.40 [0.29,0.55]	1.34 [0.98,1.83]	0.17 [0.09,0.34]	0.34 [0.16,0.74]	0.11 [0.03,0.50]	0.67 [0.16,2.78]
Adult/pediatric tertiary/ quaternary care	2.77 [2.46,3.11]	1.00 [0.87,1.14]	0.37 [0.29,0.47]	0.78 [0.55,1.12]	2.01 [1.42,2.84]	0.74 [0.36,1.53]
Healthcare admission source**	1.36 [1.21,1.54]	1.28 [1.10,1.48]	1.98 [1.58,2.49]	1.47 [1.04,2.08]	1.05 [0.74,1.49]	2.26 [0.97,5.27]
Hospitalized within previous year***	1.46 [1.31,1.63]	1.62 [1.42,1.84]	1.59 [1.28,1.98]	1.18 [0.84,1.66]	0.82 [0.59,1.14]	1.40 [0.70,2.79]
Charlson Comorbidity Index (continuous)	1.04 [1.03,1.05]	1.01 [1.00,1.03]	1.00 [0.98,1.03]	0.98 [0.94,1.03]	1.00 [0.96,1.04]	1.12 [1.03,1.21]
Age in years (continuous)	1.002 [0.999,1.005]	1.017 [1.014,1.020]	0.99 [0.98,1.00]	0.98 [0.97,0.99]	1.00 [0.99,1.01]	0.99 [0.97,1.00]
Male sex	0.84 [0.75,0.93]	0.99 [0.87,1.13]	1.26 [1.02,1.56]	1.08 [0.78,1.49]	1.25 [0.91,1.73]	2.14 [1.11,4.14]

Results of logistic regression analyses controlling for hospital and patient characteristics. Data are odds ratios (95% confidence intervals).
[1] N for each organism is less than the total incidence for each organism because some patients had infections with the same organism in multiple body sites.
[2] Antimicrobial resistance was defined as resistance to: oxacillin for *Staphylococcus aureus;* penicillin for *Streptococcus pneumoniae;* ampicillin-sulbactam for *Acinetobacter baumannii;* vancomycin for *Enterococcus faecalis* and *Enterococcus faecium;* and ≥ 3 antibiotic classes for *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.*
* Reference: adult tertiary/quaternary care
**Admission from another hospital, ambulatory surgery center, skilled nursing facility, or hospice center.
***Within-network hospitalizations only.

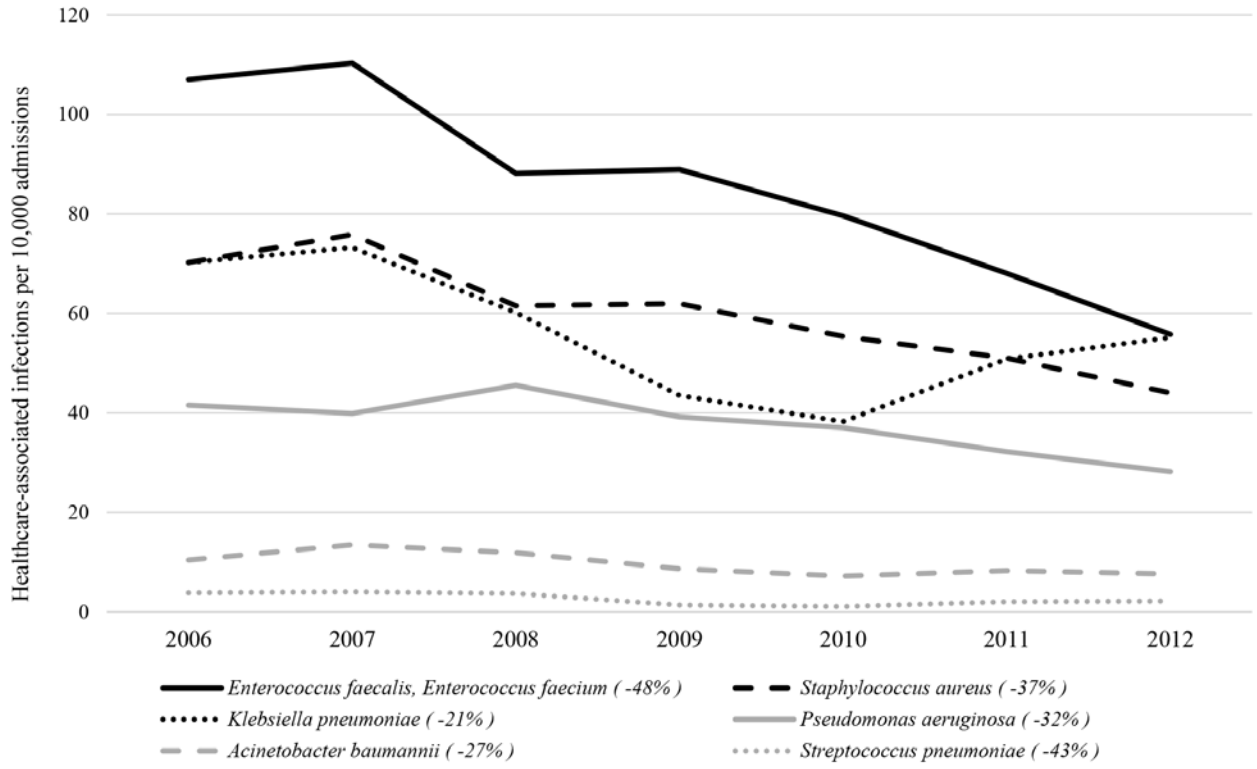
more likely to develop an HAI with *K. pneumoniae* and *E. faecalis/E. faecium*.

The impact of admission source and within-network hospitalization in the previous year decreased significantly over time, with the magnitude of association between HAI and admission source decreasing steadily throughout the study period and the magnitude of association between HAI and previous hospitalization decreasing steadily through 2010 and then rising slightly. Statistically significant interaction with year was not identified for any other factor.

The annual proportion of HAI caused by antibiotic-resistant organisms is presented in Table III. The multivariable logistic regression analyses show no appreciable change in levels of antibiotic resistance for any organism except *P. aeruginosa*, for which multidrug resistance increased significantly over the study period and *K. pneumoniae*, for which multidrug resistance decreased significantly (Table II). Resistance to all tested antibiotics increased for *P. aeruginosa*. For *K. pneumoniae,* resistance decreased slightly for all tested antibiotics except for tobramycin, for which resistance increased by 10%, and imipenem, for which there was a sharp increase from an average of 20% in 2006-2010 to over 70% in 2011.

Patients with a healthcare admission source were significantly more likely to develop a resistant infection for all organisms except *S. pneumoniae* and *A. baumannii*. Resistance was significantly associated with within-network

Fig. 2. Annual incidence of healthcare-associated infections per 10,000 admissions in four New York City hospitals, 2006-2012. The percent decrease in infection rate between 2006 and 2012 is displayed for each organism.



hospitalization in the previous year for *K. pneumoniae, S. aureus,* and *E. faecalis/E. faecium*. Odds of resistance were significantly higher for males among those infected with *K. pneumoniae* and *S. pneumoniae* and significantly higher for females among those infected with *E. faecalis/E. faecium*. There was a small but significant positive association between severity of illness and resistance among *S. pneumoniae* and *E. faecalis/E. faecium* infections. Advancing age was associated with resistance among *S. aureus* infections, while younger age was associated with resistance among *P. aeruginosa* infections.

Discussion

Using data from four hospitals in a major metropolitan center, we observed persistent and statistically significant declines in the incidence of healthcare-associated BSI, SSI, UTI, and pneumonia between 2006 and 2012. The reductions in BSI, SSI, and pneumonia paralleled trends tracked at the national level for selected conditions including central line-associated BSI, BSI with methicillin-resistant *S. aureus*, ventilator-associated infections, and SSI following common orthopedic, cardiac, gastrointestinal, and gynecological procedures [2, 11-13]. Though U.S. rates of catheter-associated UTI climbed in 2009-2012, our study sites continued to experience annual reductions of total UTI [2, 11].

The reduced incidence of HAI across the study institutions is noteworthy, particularly in light of changes to the patient population which occurred in tandem. Though severity of illness remained stable over the course of the study, the proportion of patients admitted from other healthcare facilities and who had been hospitalized in-network within the previous year increased considerably, rising from 23% to 45% and from 10% to 17%, respectively. Patients who have had prolonged contact with the healthcare system tend to be more vulnerable to infection and more likely to enter the hospital already having been colonized with common healthcare-associated pathogens [14]. Yet, the observed reductions in HAI were robust despite the demographic shift to include a higher burden of these patients. In fact, the results of the interaction models indicate that rates of HAI are falling even more among patients who had previous healthcare exposures compared with other patients, suggesting that the overall decline in HAI may be due, in part, to a reduced risk among this subset. Improved screening procedures for patients admitted from healthcare sources or with known history of hospitalization may have contributed to falling HAI rates, possibly because a higher proportion of infections that were present upon hospital admission would have been diagnosed within the first 48 hours and therefore not counted as HAI, or because interventions such as decolonization were effective at preventing HAI [15]. Similarly, the slight decrease in *S. pneumoniae* may be due to faster diagnosis

Tab. III. Changes over time in the proportion of healthcare-associated infections resistant to antibiotics, 2006-2012.

	2006	2007	2008	2009	2010	2011	2012	% change in proportion of resistant infections, 2006 to 2012
Enterococcus faecalis and *Enterococcus faecium* (N = 6,476)	483/1,120 (43)	529/1,178 (45)	361/927 (39)	406/975 (42)	425/897 (47)	322/763 (42)	279/616 (45)	+ 5%
Staphylococcus aureus (N = 4,553)	346/735 (47)	395/810 (49)	282/647 (44)	296/679 (44)	295/624 (47)	241/572 (42)	192/486 (40)	– 15%
Klebsiella pneumoniae (N = 4,237)	69/735 (9)	118/782 (15)	85/633 (13)	29/477 (6)	30/431 (7)	37/570 (7)	43/609 (7)	– 22%
Pseudomonas aeruginosa (N = 2,859)	3/435 (1)	7/426 (2)	11/479 (2)	35/430 (8)	42/417 (10)	34/361 (9)	33/311 (11)	+ 1,000%
Acinetobacter baumannii (N = 731)	34/109 (31)	69/144 (48)	69/125 (55)	38/95 (40)	32/81 (40)	40/93 (43)	24/84 (29)	– 6%
Streptococcus pneumoniae (N = 196)	15/40 (38)	21/43 (49)	19/39 (49)	2/15 (13)	0/12 (0)	10/23 (43)	9/24 (38)	0%
Total (N = 19,052)	950/3,174 (30)	1,139/3,383 (34)	827/2,850 (29)	779/2,671 (29)	824/2,462 (33)	684/2,382 (29)	580/2,130 (27)	– 10%

Data are no. resistant isolates/no. total isolates (% resistant). Antimicrobial resistance was defined as resistance to: oxacillin for *Staphylococcus aureus*; penicillin for *Streptococcus pneumoniae*; ampicillin-sulbactam for *Acinetobacter baumannii;* vancomycin for *Enterococcus faecalis* and *Enterococcus faecium*; and ≥ 3 antibiotic classes for *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

and appropriate classification as non-HAI, since these infections are more likely to be acquired in the community. Changes in infection prevention practices at the study institutions such as hand hygiene improvement and implementation of a central line care bundle may have contributed to declining infection rates overall, though it is difficult to evaluate the impact of specific policies since they varied throughout the course of the study.

In addition to risk differences between patients with and without previous healthcare contact, we also identified risk differences based on gender. That male patients had higher odds of developing HAI caused by *S. aureus, P. aeruginosa, S. pneumoniae* and *A. baumannii* while female patients had higher odds of *K. pneumoniae* and *E. faecalis/E. faecium* may be related to the types of infections that these organisms are most likely to cause. For example, *S. aureus* is a common cause of bloodstream infections, which are more common in male patients, and *E. faecalis/E. faecium* have emerged as common causes of UTI, which are more common in female patients [16-18]. The fact that female patients were more likely to have a vancomycin-resistant strain of *E. faecalis/E. faecium* may be the result of previous antibiotic treatment for recurring UTI [19]. *S. pneumoniae* has been reported to occur more frequently among men, possibly due to higher rates of smoking and underlying conditions such as chronic heart and lung diseases [20]. Previous antibiotic treatment for *S. pneumoniae* and other causes of pneumonia may explain why resistance was found to be higher among men [21].

While the incidence of HAI was greatly reduced, little progress was made with regard to reducing antimicrobial resistance. The strongest trend occurred among *P. aeruginosa*, for which resistance to aminoglycoside, carbapenem, cephalosporin, and fluoroquinolone antibiotics increased and beta-lactamase inhibitor activity decreased. The proportion of multidrug-resistant *P. aeruginosa* isolates grew from less than 1% in 2006 to over 10% in 2012, and statewide data suggest that this upward trajectory has continued in recent years [22]. For *K. pneumoniae* we observed moderate decreases in resistance to aminoglycoside, cephalosporin, fluoroquinolone, and sulfonamide antibiotics as well as increased beta-lactamase activity, though resistance to imipenem more than tripled in 2011 following an outbreak of carbapenem-resistant *K. pneumoniae*. It's likely that this outbreak contributed to the overall rise in *K. pneumoniae* infections that occurred in 2011 after several years of steadily falling rates. The considerable uptick in carbapenem resistance is reflective of a national epidemic of *K. pneumoniae* carbapenemase, which first appeared in New York City in the early 2000s [23, 24]. Still, the percent of *K. pneumoniae* isolates that were multidrug-resistant was lower than statewide reports of 25% and decreased throughout the study period [22]. This discrepancy may be due to differences in the definition of multidrug resistance and the specific drugs for which antimicrobial activity was assessed. Similar to trends reported at the state and national levels, methicillin resistance among *S. aureus* remained relatively stable after 2007, following precipitous declines in

the previous decade [3, 6, 22, 25, 26]. Consistent with data available from the CDC, no meaningful changes in vancomycin resistance among *Enterococcus* spp. occurred in the study facilities during the observed time frame [6, 22].

This study was conducted during a period of heightened attention toward HAI prevention [1]. The application of evidence-based practices and bundles coupled with the adoption of new reimbursement policies that reframed many healthcare-associated conditions as fully preventable events likely played a role in reducing HAI [27, 28]. However, since many changes to infection prevention practice have been introduced during the last decade, it is not feasible to isolate the effects of any single initiative. Moreover, it is unlikely that any one factor was solely responsible for the reduction [29]. Analogous broad efforts towards reducing antimicrobial resistance among healthcare-associated pathogens were also introduced during this timeframe. Antimicrobial stewardship programs may have had some effect with regard to halting the upward trends in resistance for many organisms; nonetheless, data suggest that they have not yet had much impact with regard to lessening the burden of resistance at the state or national level [6, 16, 30]. The evidence of such impact is likely to require longer periods of time than other practices associated with prevention of HAI.

One of the major strengths of this analysis is its application of a consistent methodology for identifying HAI over time. Unlike other sources of longitudinal data, the electronic algorithms used to define infections in this study were not sensitive to changes in case definitions, infection prevention personnel training, or financial and regulatory incentives that may have altered reporting practices [31]. The algorithms were created and validated by an interdisciplinary team that included an infectious disease physician, and infection prevention nurse, an epidemiologist, a database manager, and an IT systems manager with expertise in hospital administrative data [7, 32, 33]. Still, the gold standard for diagnosis of an infection is clinician adjudication after full chart review, and disadvantages to using electronic data sources have been identified [34]. The SSI algorithm was designed to include only infections associated with NHSN operative procedures, so infections resulting from other procedures were not identified. Previous studies have reported low sensitivity for some of the ICD-9-CM codes used to create the Charlson Comorbidity Index, though specificity is generally high [35]. Data on previous out-of-network hospitalizations were not available, and it is possible that some within-network hospitalizations were not captured due to erroneous assignment of new medical record numbers to patients who were readmitted within one year. This type of misclassification, however, could only lessen the magnitude of the observed association between previous admission and odds of HAI. As the quality and availability of electronic patient data improves, the validity of some data elements may have changed over time, though we are not aware of any specific changes to the way data were collected or recorded that would have affected the study variables.

In addition to issues of data quality, there are also some limitations to our statistical analyses. We were unable to account for previous use of antibiotics, which is a known risk factor for resistance and may also confound the associations between infection and prior hospitalization or admission from a healthcare source, since patients with previous healthcare contact may be more likely to have taken antibiotics [36]. In addition, the multivariable model predicting antimicrobial resistance for *S. pneumoniae* was not adequately powered to detect differences over time.

Conclusion

Overall, this study provides strong support for the observation that the incidence of HAI is falling and that the reduction in HAI is not limited to device and procedure-associated infections. Although we were unable to measure the impact of any specific policy or practice changes due to the overlapping nature of their implementation, the reduction may be the result of increased federal and state attention to healthcare quality and patient safety. Accordingly, although we have yet to observe substantial reductions in antimicrobial resistance, the recent uptick in national attention towards antimicrobial monitoring and stewardship may precipitate a change in coming years.

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The authors have no conflicts of interest.

Authors' contributions

B.C. performed the analysis and wrote the manuscript. J.L. collected, prepared, and managed the data. E.L. oversaw the project and advised on the study design, analysis, and manuscript preparation.

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