Original Investigation

National Burden of Invasive Methicillin-Resistant *Staphylococcus aureus* Infections, United States, 2011

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IMPORTANCE Estimating the US burden of methicillin-resistant *Staphylococcus aureus* (MRSA) infections is important for planning and tracking success of prevention strategies.

OBJECTIVE To describe updated national estimates and characteristics of health care– and community-associated invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections in 2011.

DESIGN, SETTING, AND PARTICIPANTS Active laboratory-based case finding identified MRSA cultures in 9 US metropolitan areas from 2005 through 2011. Invasive infections (MRSA cultured from normally sterile body sites) were classified as health care–associated community-onset (HACO) infections (cultured ≤3 days after admission and/or prior year dialysis, hospitalization, surgery, long-term care residence, or central vascular catheter presence ≤2 days before culture); hospital-onset infections (cultured >3 days after admission); or community-associated infections if no other criteria were met. National estimates were adjusted using US census and US Renal Data System data.

MAIN OUTCOMES AND MEASURES National estimates of invasive HACO, hospital-onset, and community-associated MRSA infections using US census and US Renal Data System data as the denominator.

RESULTS An estimated 80 461 (95% CI, 69 515-93 914) invasive MRSA infections occurred nationally in 2011. Of these, 48 353 (95% CI, 40 195–58 642) were HACO infections; 14 156 (95% CI, 10 096-20 440) were hospital-onset infections; and 16 560 (95% CI, 12 806-21 811) were community-associated infections. Since 2005, adjusted national estimated incidence rates decreased among HACO infections by 27.7% and hospital-onset infections decreased by 54.2%; community-associated infections decreased by only 5.0%. Among recently hospitalized community-onset (nondialysis) infections, 64% occurred 3 months or less after discharge, and 32% of these were admitted from long-term care facilities.

CONCLUSIONS AND RELEVANCE An estimated 30 800 fewer invasive MRSA infections occurred in the United States in 2011 compared with 2005; in 2011 fewer infections occurred among patients during hospitalization than among persons in the community without recent health care exposures. Effective strategies for preventing infections outside acute care settings will have the greatest impact on further reducing invasive MRSA infections nationally.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be one of the most common antimicrobial-resistant pathogens causing invasive infections, both in health care settings and in the community.[1-4] In the United States, MRSA is the predominant pathogen causing skin and soft tissue infections,[5] and reports using administrative data documented increases in the number of estimated hospitalizations in which *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes indicating MRSA infection were present.[6,7]

However, recent reports of surveillance programs in geographically distinct areas suggest there have been recent declines in the incidence of the most serious types of MRSA infections (ie, bloodstream infections), including those among critical care patients in US hospital settings[2,8] and both community- and hospital-onset MRSA bacteremia among military families, active duty personnel, and military retirees starting in 2005.[9] The Emerging Infections Program–Active Bacterial Core surveillance system (EIP-ABCs) at the Centers for Disease Control and Prevention (CDC) has been tracking invasive MRSA infections in 9 diverse US metropolitan areas since 2005. Reports using this system documented an 11% annual decline in the incidence of hospital-onset MRSA bloodstream infections between 2005 and 2008 in these metropolitan areas.[2] The cause of these declines is uncertain but may be due to improvements in hospital-based infection prevention practices, improved early management of noninvasive infections, or changes in the virulence of the circulating strains.

A prior CDC study estimated the national burden of invasive MRSA in 2005[3]; however, this report did not adjust for dialysis or include patients with recurrent infections.[10] Therefore, to better understand the current national burden of these most serious MRSA infections, spanning both community and health care settings, we used EIP-ABCs' data and updated methodology to describe the types and outcomes of invasive MRSA infections in 2011 and to estimate the infection burden in the United States in 2011 and 2005. These estimates are necessary to improve the assessment of invasive MRSA infection nationally, to inform prevention policies in health care settings, and to measure progress toward public health goals.[11]

Methods

Human Subjects Considerations
This surveillance activity was reviewed by human subject personnel at the CDC and was determined to be nonresearch. Local institutional review boards also reviewed when indicated and approved this activity.

Invasive MRSA Surveillance
The EIP-ABCs is a population-based surveillance system used by the CDC and collaborating agencies and organizations to estimate the incidence of invasive MRSA infections in selected counties in 9 US states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee). The methods of surveillance have been described previously,[3] with modifications to include recurrent infections (ie, multiple infections in a single patient during the calendar year) in incidence calculations. In brief, surveillance personnel at participating sites investigated all laboratory reports where MRSA was isolated. An invasive MRSA case was defined as a positive MRSA culture from a normally sterile site in a surveillance area resident at least 30 days apart of an initial invasive MRSA culture. For each invasive MRSA case, information on hospitalization and health care risk factors (ie, culture obtained after hospital day 3; presence of a central vascular catheter [CVC] at the time of infection; and history of MRSA infection or colonization, surgery, hospitalization, dialysis, or residence in a long-term care facility in the 12 months preceding the culture) were collected. Underlying conditions were obtained and used to calculate the Charlson index.[12]

Study Population
We used MRSA surveillance data from January through December of 2005 and 2011. The surveillance areas represented 16 489 254 and 19 393 677 persons in 2005 and 2011, respectively.[13,14]

Definitions
Cases were classified as (1) "hospital onset," if culture was obtained after hospital day 3 (with admission being day 1), (2) "health care–associated community onset" (HACO) if culture was obtained as an outpatient on or before hospital day 3 in a patient with a documented health care risk factor, or (3) "community associated" if culture was obtained as an outpatient on or before hospital day 3 in a patient without documentation of a health care risk factor. Of note, the definition of hospital-onset infections differ from previous reports where MRSA culture was obtained after hospital day 2 in prior methods; this refinement is consistent with classifying MRSA bloodstream infections as hospital-onset in the National Healthcare Safety Network's (NHSN) Laboratory Identified Event Reporting and is applied to all analysis in this article.

Cases were classified as a bloodstream infection if they had a positive blood culture for MRSA. Bloodstream infection cases were further classified as either (1) an access infection (physician-documented arteriovenous fistula, dialysis access site, or CVC exit site infection), an infection of uncertain focus either (2) with a CVC present or (3) without a CVC present, or (4) as having other infection foci if there were either positive MRSA cultures from sterile sites other than blood or additional infectious clinical diagnosis in the admission or discharge summary. An MRSA clinical diagnosis of bacteremia, pneumonia, osteomyelitis, or other infection was assigned to each case based on documentation of such diagnosis in the admission or discharge summary or by the sterile site from which MRSA was isolated. Each case was assigned additional MRSA clinical diagnosis if multiple diagnoses (eg, bacteremia and osteomyelitis) were documented within 30 days of the initial MRSA culture. Health care–associated infection criteria defined by the NHSN were not applied to cases because NHSN definitions only apply to infections not present on admission.

Cases with a clinical diagnosis of pneumonia were further classified as having confirmed lower respiratory tract infections if radiographic evidence was present (ie, broncho-

pneumonia, pneumonia, air space density or opacity, or new or changed infiltrates documented in a radiologist report) and the patient had MRSA recovered from a respiratory tract specimen within 3 days of the sterile site MRSA culture.

Statistical Analysis

Differences in baseline characteristics among cases in each epidemiologic category (hospital onset, HACO, and community associated) were analyzed using the χ^2 test or Fisher exact test (where appropriate) for categorical variables and the Wilcoxon rank sum test for continuous variables.

Overall, 9% of cases were reported with unknown race in medical charts. To facilitate extrapolation to national estimates, cases for which the race was unknown were assigned a race based on the known population distributions of race by sex, age, and receipt of chronic dialysis in each surveillance site. National estimates were determined by calculating EIP-ABC-specific incidence rates stratified by age group, race, sex, and receipt of dialysis, and extrapolated nationally by multiplying each stratum-specific incidence rate by the national population estimate for each stratum based on US census and US Renal Data System data.[15-18] In previous reports and publications, national estimates were adjusted for only age, race, and sex.[3] Confidence intervals for nationally estimated incidence rates of disease and mortality were calculated based on the gamma distribution.[19] Analyses were performed using SAS statistical software, version 9.3 (SAS Institute Inc), and Stata version 11.1 (StataCorp). We defined statistical significance as $P \leq .05$ for a 2-tailed test.

Results

Case Characteristics

The EIP-ABCs sites reported 4872 cases of invasive MRSA infections among 4445 persons (8% had >1 infection) in 2011. Among these cases, 4746 cases (97%) were classified into epidemiological classes: 2912 (60%) were HACO, 868 (18%) were hospital onset, and 966 (20%) were community associated (Table 1).

The median age of cases was 61 years (range, 0-103 years) (Table 1). The majority of cases were male (60%) and of either white (56%) or black (32%) race. Diabetes was a diagnosis in 41% of cases. There was receipt of hemodialysis or peritoneal dialysis within the year before invasive MRSA infection in 21% of cases (61% of cases receiving dialysis also had diabetes).

Most invasive MRSA infections had a positive blood culture (3907 [80%]) and were classified as a bloodstream infection (Table 2). Overall, 55% of infections had a nonvascular focus, and 45% had a vascular or nonspecific focus (Table 2). Among the 760 invasive MRSA infections with clinician-defined pneumonia, based on radiographic and respiratory specimen findings, 293 (31%) had confirmed MRSA lower respiratory tract infections (eTable in the Supplement). Other common MRSA syndromes included skin infections (1081 [22%]) and osteomyelitis (629 [13%]) (Table 2). There were 650 in-hospital deaths (13%), and the majority of these were within 7 days of initial MRSA culture (393 [60%]).

Health Care–Associated Infections

Health Care–Associated Community-Onset Infections

Of the 3780 health care-associated cases, 2912 (77%) had onset in the community and were classified as HACO; median age was 64 years, 59% were male, and 34% were black (Table 1). The median Charlson index score was 3 (range, 0-12), with specific underlying conditions including diabetes (1355 [47%]), decubitus and/or pressure ulcers (394 [14%]), chronic renal insufficiency (1260 [43%]), prior stroke (430 [15%]), and dementia (388 [13%]) all more prevalent compared with cases in other epidemiologic categories. Receipt of dialysis was recorded in 891 cases (31%) in the prior year; a significantly higher proportion compared with hospital-onset cases. Most had resided at a private residence (1812 [62%]) (Table 2), or long-term care facility (876 [30%]) at the time of culture. Few had resided in long-term acute care hospitals, or were homeless, incarcerated, or transferred from another hospital or acute care facility (1%-3% each). Hospitalization in the prior year was a common source of health care exposure (2291 [79%]) (Table 1), especially among those not receiving dialysis (1622 [80%]). Most cases in this latter group had been hospitalized in the 12 weeks prior to their MRSA infection (1042 [64%]) (Figure 1), and nearly a third of those cases (331 [32%]) were residents of a long-term care facility.

Hospital-Onset Infections

Underlying conditions among hospital-onset cases were similar to health care-associated community-onset cases except as previously noted. Among hospital-onset cases, 26% were in the intensive care unit, whereas 49% were in other inpatient wards (Table 2). The median length of hospitalization prior to MRSA infection was 7 days (range, 3-366 days). Bloodstream infection was the most common type of hospital-onset infection (619 [71%]), and had either a physician-diagnosed arteriovenous fistula or CVC exit site infection (21 [3%]), an uncertain focus with a CVC (137 [22%]) or without a CVC present (175 [28%]), or other infection foci (286 [46%]). Seven day all-cause mortality was more common among cases with hospital-onset infections (103 [12%]) compared with other epidemiologic categories, as was in-hospital all-cause mortality (182 [21%]).

Community-Associated Infections

Community-associated cases were more commonly male (619 [64%]) and younger than were cases in other epidemiologic categories (54 years) ($P < .001$) Table 1. Cases had significantly fewer comorbidities, with a median Charlson index score of 0 (range, 0-12). However, this group had a higher proportion of smoking (294 [30%]) (Table 1), intravenous drug use (133 [14%]), and human immunodeficiency virus (HIV)/AIDS (60 [6%]). Most cases lived in private residences prior to positive culture (910 [94%]) (Table 2). This group also had higher proportions of several infection types, including invasive infections associated with skin infections (241 [33%]), arthritis, joint infection, or bursitis (157 [16%]), or nonskin or internal abscess (133 [14%]), compared with cases in other epidemiologic categories. Community-associated cases had a lower in-hospital

Table 1. Demographics of Health Care–Associated Community-Onset (HACO), Hospital-Onset (HO), and Community-Associated (CA) MRSA Infection[a] Reported to the Emerging Infections Program–Active Bacterial Core Surveillance, United States, 2011

Demographic	Infections, No. (%)				P Value[c]
	HACO	HO	CA	Total[b]	
Total	2912 (100)	868 (100)	966 (100)	4872 (100)	
Sex					
Male	1724 (59)	527 (61)	619 (64)	2934 (60)	
Female	1185 (41)	341 (39)	347 (36)	1935 (40)	.03
Not specified	3 (0)	0	0	3	
Age, y					
<1	9 (0)	12 (1)	22 (2)	50 (1)	
1-17	18 (1)	17 (2)	51 (5)	87 (2)	
18-34	156 (5)	64 (7)	122 (13)	349 (7)	
35-49	401 (14)	135 (16)	216 (22)	769 (16)	...[d,e,f]
50-64	920 (32)	288 (33)	290 (30)	1536 (32)	
≥65	1408 (48)	345 (40)	265 (27)	2081 (43)	
Median (range)	64 (0-103)	60 (0-96)	54 (0-103)	61 (0-103)	
Race					
White	1610 (55)	480 (55)	576 (60)	2743 (56)	.046
Black	996 (34)	295 (34)	230 (24)	1542 (32)	<.001
Other	80 (3)	18 (2)	24 (2)	126 (3)	.54
Unknown	226 (8)	75 (9)	136 (14)	461 (9)	<.001
Dialysis within 1 y					
Yes	891 (31)	122 (14)	0	1013 (21)	...[g]
No	2021 (69)	746 (86)	966 (100)	3859 (79)	
Underlying conditions: MRSA risk factors					
Abscess/boil	89 (3)	35 (4)	86 (9)	216 (4)	<.001
Current smoker	456 (16)	162 (19)	294 (30)	933 (19)	<.001
Decubitus/pressure ulcer	394 (14)	81 (9)	52 (5)	536 (11)	<.001
Diabetes	1355 (47)	331 (38)	276 (29)	1999 (41)	<.001
Intravenous drug use	99 (3)	30 (3)	133 (14)	272 (6)	<.001
Metastatic solid tumor	126 (4)	34 (4)	14 (1)	176 (4)	<.001
Obesity	372 (13)	117 (13)	77 (8)	569 (12)	<.001
Solid organ malignancy	256 (9)	99 (11)	43 (4)	402 (8)	<.001
Other underlying conditions					
Charlson Index, median (range)	3 (0-12)	2 (0-13)	0 (0-12)	2 (0-13)	...[d,f]
Chronic liver disease	123 (4)	58 (7)	41 (4)	223 (5)	.008
Chronic pulmonary disease	719 (25)	211 (24)	182 (19)	1145 (24)	.001
Chronic renal insufficiency	1260 (43)	247 (28)	83 (9)	1604 (33)	<.001
Chronic skin breakdown	359 (12)	108 (12)	95 (10)	572 (12)	.09
Congestive heart failure	689 (24)	202 (23)	69 (7)	985 (20)	<.001
Stroke (not TIA)	430 (15)	93 (11)	47 (5)	577 (12)	<.001
Dementia	388 (13)	77 (9)	44 (5)	525 (11)	<.001
HIV/AIDS	134 (5)	32 (4)	60 (6)	227 (5)	.03
Myocardial infarction	236 (8)	69 (8)	30 (3)	336 (7)	<.001
Unknown	20 (1)	2 (0)	3 (0)	47 (1)	.21
Other	857 (29)	254 (29)	152 (16)	1282 (26)	<.001
Health care					
Hospitalization in the past 1 year[h]	2291 (79)	501 (58)	0	2792 (57)	...[g]
Surgery within 1 year prior to culture	1164 (40)	333 (38)	0	1497 (31)	...[i]
Long-term care facility within 1 year	1057 (36)	182 (21)	0	1239 (25)	...[g]
Central venous catheter within 2 days	790 (27)	303 (35)	0	1093 (22)	...[g]

Abbreviations: HIV/AIDS, human immunodeficiency virus/acquired immunodeficiency syndrome; MRSA, methicillin-resistant *Staphylococcus aureus*; TIA, transient ischemic attack.

[a] Defined as MRSA isolated from a normally sterile site.

[b] Twenty-six additional cases with unknown epidemiological category included in total.

[c] χ² Test (or Fisher exact test if values ≤5) comparing all epidemiologic categories.

[d] HACO significantly different from non-HACO (P < .001).

[e] HO significantly different from non-HO (P < .01).

[f] CA significantly different from non-CA (P < .001).

[g] HACO and HO significantly different (P < .001).

[h] For infants younger than 12 months, hospitalization for a normal delivery was not counted as a hospitalization.

[i] HACO and HO not significantly different (P = .40).

Table 2. Hospitalization Characteristics of Health Care–Associated Community-Onset (HACO), Hospital-Onset (HO), and Community-Associated (CA) MRSA Infection[a] Reported to the Emerging Infections Program–Active Bacterial Core Surveillance, United States, 2011

Characteristic	Infections, No. (%)				P Value[c]
	HACO	HO	CA	Total[b]	
Total	2912 (100)	868 (100)	966 (100)	4872 (100)	
Hospitalized	2590 (89)	868 (100)	876 (91)	4416 (91)	<.001
Location prior to date of initial culture					
Incarcerated	16 (1)	5 (1)	12 (1)	33 (1)	.07
Homeless	32 (1)	17 (2)	25 (3)	79 (2)	.003
Long-term acute care hospital	50 (3)	7 (1)	0	64 (0)	.053
Long-term care facility	876 (30)	139 (16)	0	1046 (21)	<.001
Private residence	1812 (62)	646 (74)	910 (94)	3428 (70)	<.001
Transferred from hospital/acute care facility	52 (2)	29 (3)	0	83 (2)	<.001
Unknown	59 (2)	14 (2)	18 (2)	104 (2)	.73
Other	12 (0)	11 (1)	0	31 (1)	<.001
Location of culture collection					
Emergency department	1692 (58)	35 (4)	584 (60)	2368 (49)	<.001
Inpatient unit, nonintensive care	389 (13)	427 (49)	133 (14)	962 (20)	<.001
Intensive care unit	118 (4)	224 (26)	59 (6)	412 (8)	<.001
Long-term acute care hospital	57 (2)	3 (0)	0	64 (1)	<.001
Long-term care facility	52 (2)	2 (0)	0	57 (1)	<.001
Outpatient	299 (10)	7 (1)	54 (6)	380 (8)	<.001
Surgery/operating room	206 (7)	127 (15)	101 (10)	439 (9)	<.001
Unknown	34 (1)	19 (2)	25 (3)	89 (2)	.004
Other	65 (2)	24 (3)	10 (1)	101 (2)	.02
MRSA infections diagnosis type (multiple categories possible for each case)[d]					
Any BSI	2452 (84)	619 (71)	738 (76)	3907 (80)	<.001
With CVC exit site or AV fistula infection	160 (7)	21 (3)	0	182 (5)	…[e]
BSI with uncertain focus	996 (41)	312 (50)	226 (31)	1572 (40)	<.001
Presence of CVC in prior 2 days	377 (15)	137 (22)	0	514 (13)	…[e]
No CVC documented	619 (25)	175 (28)	226 (31)	1058 (27)	.21
BSI with other infection focus	1296 (53)	286 (46)	512 (69)	2153 (55)	<.001
Skin infection (cellulitis, abscess, ulceration)	656 (27)	162 (26)	241 (33)	1082 (22)	.005
Pneumonia	441 (15)	146 (17)	154 (16)	760 (16)	.47
Confirmed lower respiratory tract infection	127 (29)	58 (40)	51 (33)	239 (31)	.02
Osteomyelitis	346 (12)	123 (14)	139 (14)	629 (13)	.054
Arthritis, joint infection, or bursitis	227 (8)	48 (6)	157 (16)	440 (9)	<.001
Abscess (not skin)	180 (6)	52 (6)	133 (14)	370 (8)	<.001
Endocarditis	150 (5)	48 (6)	73 (8)	277 (6)	.02
Urinary tract infection	191 (7)	33 (4)	56 (6)	285 (6)	.009
Surgical site infection	119 (4)	15 (2)	11 (1)	146 (3)	<.001
Other	328 (11)	109 (13)	165 (17)	610 (13)	<.001
Patient outcomes					
Death (all causes)	350 (12)	182 (21)	94 (10)	650 (13)	<.001
Death within 7 days of culture (all causes)	213 (7)	103 (12)	59 (6)	393 (8)	.53

Abbreviations: BSI, bloodstream infection; CVC, central vascular catheter; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Defined as MRSA isolated from a normally sterile site.

[b] One hundred twenty-six additional cases with unknown epidemiological category included in total.

[c] χ² Test (or Fisher exact test if values ≤5) comparing all epidemiologic categories.

[d] Based on physician documentation in admission or discharge summary and/or sterile sites where MRSA was isolated. A single case could have multiple infection types within a 30-day period.

[e] HACO and HO significantly different (P < .05).

all-cause mortality rate (10%) compared with other epidemiologic categories.

National Estimated Incidence and All-Cause Mortality
An estimated 80 461 (95% CI, 69 516-93 914) invasive MRSA infections occurred nationally in 2011 (compared with an esti-

mated 111 261 in 2005) (Table 3); of these, 48 353 (95% CI, 40 195-58 642) were HACO, 14 156 (95% CI, 10 096-20 440) were hospital onset, and 16 560 (95% CI, 12 806-21 811) were community associated.

National estimated incidence rates from 2005 through 2011 are illustrated in Figure 2. Compared with 6 years earlier (2005),

Figure 1. Distribution of Weeks Between Previous Hospitalization and Current Admission Date, Stratified by Long-term Care Facility Residence
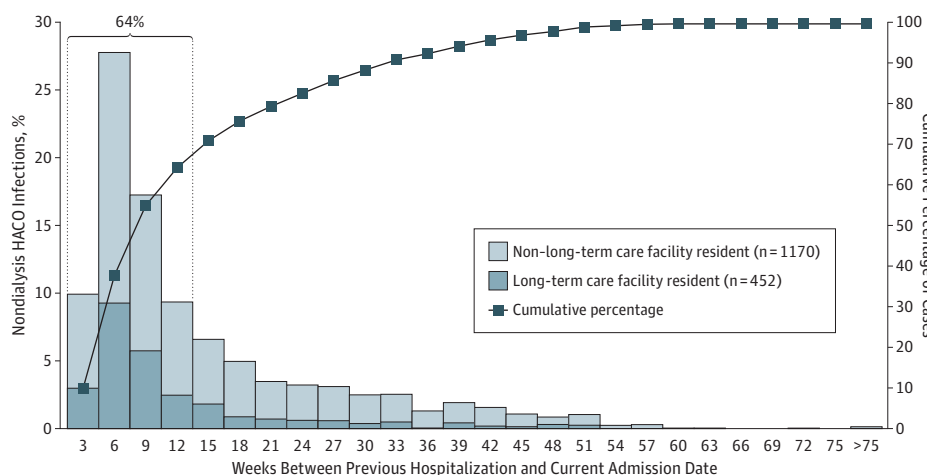
Data are given for nondialysis cases of health care–associated community-onset (HACO) invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infection[a] with hospitalization in the prior year in 2011 (n = 1622[b]).
[a] Defined as MRSA isolated from a normally sterile source.
[b] A total of 399 cases of HACO infections in nondialysis patients who had no prior hospitalization date in the prior year are not represented in this figure.

Table 3. National Estimated Incidence and Mortality of Invasive MRSA Infections,[a] United States, 2005 and 2011

Epidemiologic Category	Year	Surveil-lance Population	Incidence				Mortality[b]			
			Case Incidence	Crude Rate[c]	Adjusted National Rate[c] (95% CI)	Estimated National Incidence (95% CI)	Case Deaths	Crude Rate[c]	Adjusted National Rate[c] (95% CI)	Estimated National Deaths (95% CI)
HACO	2005	16 489 254	3463	21.00	21.46 (18.06-25.72)	63 598 (5531-76 237)	559	3.39	3.69 (2.58-5.35)	10 934 (7647-15 858)
	2011	19 393 677	2912	15.02	15.52 (12.90-18.82)	48 353 (40 195-58 642)	350	1.80	1.95 (1.26-3.12)	6071 (3926-9722)
HO	2005	16 489 254	1601	9.71	9.91 (7.75-12.91)	29 373 (22 972-38 267)	418	2.53	2.71 (1.77-4.36)	8042 (5246-12 924)
	2011	19 393 677	868	4.48	4.54 (3.24-6.56)	14 156 (10 096-20 440)	182	0.94	1.00 (0.51-2.06)	3126 (1589-6419)
CA	2005	16 489 254	966	5.86	5.59 (4.31-7.33)	16 566 (12 775-21 726)	105	0.64	0.64 (0.31-1.25)	1905 (919-3705)
	2011	19 393 677	1010	5.21	5.31 (4.11-7.00)	16 560 (12 806-21 811)	100	0.52	0.57 (0.30-1.04)	1764 (935-3241)
Overall	2005	16 489 254	6134	37.20	37.54 (32.93-43.06)	111 261 (97 608-127 634)	1098	6.66	7.13 (5.47-9.52)	21 138 (16 214-28 218)
	2011	19 393 677	4872	25.12	25.82 (22.31-30.14)	80 461 (69 516-93 914)	650	3.35	3.62 (2.58-5.31)	11 285 (8039-16 545)

Abbreviations: CA, community-associated; HACO, health care–associated community-onset; HO, hospital-onset; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Defined as MRSA isolated from a normally sterile site.

[b] Mortality due to all causes during hospitalization where invasive MRSA infection was diagnosed.

[c] Rate per 100 000 persons.

the estimated national rate of invasive MRSA has decreased by 31.2%. Although this rate decrease was most precipitous among hospital-onset infections, at 54.2%, rate decreases were evident among other categories as well: health care–associated community-onset by 27.7% and community-associated infections by 5.0%.

An estimated 11 285 (95% CI, 8039-16 545) persons with invasive MRSA infections died of all causes during their hospitalizations in 2011 (Table 3); of these estimated deaths, 6071 (95% CI, 3926-9722) had health care–associated community-onset, 3126 (95% CI, 1589-6419) had hospital-onset, and 1764 (95% CI, 935-3241) had community-associated infections.

Discussion

In 2011, we estimated the overall number of invasive MRSA infections was 80 461; 31% lower than when estimates were first available in 2005. Also, for the first time since the CDC began tracking invasive MRSA infections nationally, the estimated incidence of invasive hospital-onset infections is lower than that among persons residing in the community without significant health care contact. However, the largest burden of disease remains among patients with infection onset outside of acute care hospitals but with recent or ongoing exposure to

Figure 2. National Estimated Incidence Rates of Invasive MRSA
Infections, Stratified by Epidemiologic Category[a]
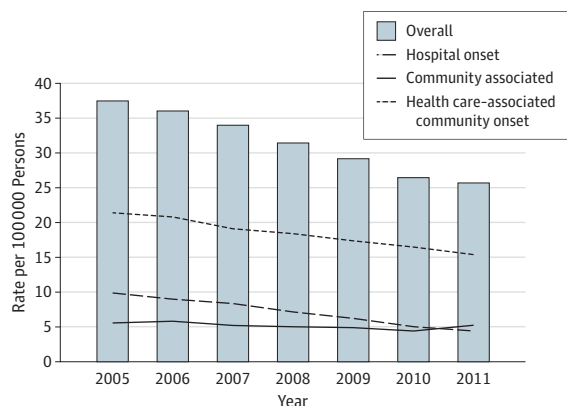
Data are given for methicillin-resistant *Staphylococcus aureus* (MRSA) infections
reported to the Emerging Infections Program–Active Bacterial Core surveillance
(United States, 2005-2011).
[a]Defined as MSRA isolated from a normally sterile source.

health care services, such as recent discharge from acute care
hospitals. In these patients, infection rates only decreased mod-
erately. Overall, these estimates indicate the United States is
on track to meet the Department of Health and Human Ser-
vices 2013 target of reducing health care–associated MRSA in-
vasive infections by 50%.[11] However, little progress has been
made in reducing invasive community-associated MRSA in-
fections during this time.

Our findings strongly support those from other studies that
have documented decreasing incidence of invasive MRSA in-
fections among health care-related infections since 2005.[2,9]
While prior studies focused on invasive MRSA incidence for a
specific population or region,[9,20] our study used data from the
largest US population surveillance system for invasive MRSA
to provide robust national burden estimates of this disease. The
methodology in this study was improved from our prior
methods[3] (and applied to historical 2005 data) by (1) includ-
ing all cases, both recurrent infections in the same patient (at
least 30 days apart) and new infections, (2) adjusting national
estimates for the receipt of dialysis, a critical risk factor for in-
vasive MRSA,[10] and (3) including confidence intervals of na-
tional estimates.

The large decrease (54%) in hospital-onset invasive MRSA
infections between 2005 and 2011 is highly encouraging and
may be attributable to increased awareness and implementa-
tion of local and nationwide infection prevention measures in
many health care settings, including those targeting intravas-
cular catheter-related infections[21,22] and health care transmis-
sion of multidrug-resistant organisms.[23] National survey data
suggest that the number of hospitalizations and the average
length of stay were stable between 2007 and 2010,[24,25] mak-
ing it unlikely that the reductions in hospital-onset MRSA we
observed could be attributable to reductions in length of hos-
pital stays.

It is notable that the incidence of community-associated
invasive MRSA infections, although relatively stable, has not

increased over this time, despite increases in hospitaliza-
tions related to MRSA skin and soft-tissue infections (ie, mostly
noninvasive infections) documented in discharge data.[7] Prog-
ress in reducing infections among this population is likely to
be most challenging due to a lack of clearly effective strate-
gies to control endemic MRSA transmission in the commu-
nity setting. While guidance exists for the prevention of trans-
mission in some institutions such as schools, athletic facilities,
and correctional facilities,[26] prevention of community-
associated MRSA transmission outside of these settings is not
well described. Changes in this setting may related to trans-
mission in households, prevention of invasive disease from im-
proved early treatment of noninvasive infections,[27] or the natu-
ral evolution of this pathogen.

Approximately 78% of all invasive MRSA infections in 2011
had onset in the outpatient or community setting (health care-
associated community-onset and community-associated in-
fections), an increase from 72% in 2005. Of these infections,
77% were classified as HACO, which comprised mostly re-
cently discharged patients, long-term care residents, and di-
alysis patients. The moderate decrease of these infections could
be attributable to decreased transmission in hospital settings
or prevention efforts outside of the acute care hospital. Among
nondialysis cases with prior hospitalization, nearly two-
thirds developed their infections within 3 months of hospital
discharge. This suggests a higher risk of invasive MRSA in the
weeks following hospitalization. Invasive devices that re-
main placed during the postdischarge period, progression from
colonization to clinical infection, and breakdowns in host de-
fense and skin integrity during hospitalization may account for
this increased risk. Further research is needed to understand
(1) risk factors for progression of colonization and noninva-
sive infection to invasive infections and (2) transmission dy-
namics within health care settings after discharge from acute
care hospitals. Significant progress in preventing invasive MRSA
infections in the dialysis and postdischarge settings is needed
to substantially reduce the overall burden of invasive MRSA
infections.

There are several limitations to this study. First, although
this program operates in several metropolitan areas with di-
verse populations, these specific areas were not randomly se-
lected to be representative; however, when calculating na-
tional estimates, we adjusted for regional differences in sex,
age, race, and use of dialysis to produce estimates that more
accurately represent the entire US population. In addition, this
surveillance system does not track MRSA colonization or non-
invasive MRSA infections, such as skin and soft-tissue infec-
tions. Therefore, we cannot draw any conclusions about the
relatedness between MRSA colonization or prior noninvasive
infection and invasive infection. However, this system was de-
signed to create national estimates capturing infections in both
inpatient and outpatient settings and therefore delivers a more
comprehensive assessment of invasive MRSA than systems fo-
cused predominantly on acute care facility-specific perfor-
mance measures, including NHSN.

In conclusion, a substantial decrease in the national bur-
den of invasive MRSA infections has been observed in the
United States between 2005 and 2011, with the largest de-

creases among hospital-onset infections and the smallest among community-associated infections. Despite these decreases, invasive MRSA infections with onset in the community or outpatient setting remain problematic and represent the majority of invasive MRSA infections. Future research is needed to understand the progression of colonization and non-invasive MRSA infection to invasive infection in outpatient settings. Future prevention efforts should target both community and health care transmission, especially among patients with recent hospitalization.

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Invited Commentary

Methicillin-Resistant *Staphylococcus aureus*
Where Is It Coming From and Where Is It Going?

Franklin D. Lowy, MD

Despite the availability of effective preventative and therapeutic strategies, methicillin-resistant *Staphylococcus aureus* (MRSA) remains a major cause of health care–associated and, more recently, community-acquired infections. Since the introduction of methicillin in 1959, epidemics due to different clones of MRSA have occurred in diverse geographic regions.[1] The result has been the persistence of MRSA as an important pathogen worldwide.

In the United States, the most recent MRSA epidemic has been due to the clone USA300. USA300 has been responsible for the majority of community and health care–associated outbreaks since the early 1990s.[1] Until recently, the number of infections has continued to rise, especially in urban centers. While the majority of these have been skin and soft-tissue infections (SSTIs), a notable minority have been invasive and life-threatening.[1] Two articles in this issue of *JAMA Internal Medicine* provide additional insight into both the incidence and the risks associated with development of MRSA infections. Dantes et al[2] provide evidence that the overall incidence of invasive MRSA infections nationally is declining. Casey et al[3] perform an ecological investigation; they find that individuals living near high-density farming operations (ie, farms having an animal density of 2 animals or 1000-lbs live weight per acre) or near crop fields using manure exported from the high-density livestock farms are at increased risk of developing MRSA or other bacterial SSTIs. Both studies raise questions that warrant further investigation.

Dantes et al[2] used data from the Active Bacterial Core Surveillance Program (ABCSP) to compare the national incidence rate of invasive MRSA infections for the years 2005 through 2011. The findings are of special importance because of the survey methods that are used and the size of the sample population (approximately 15 million). The ABCSP is an active surveillance program that is population based and includes a review of medical records. It serves as a model for this type of surveillance. The results show that the incidence of health care–associated community-onset and hospital-onset invasive MRSA infections have declined by 27.7% and 54.2%, respectively. The findings are consistent with several earlier reports including one from the same group. This impressive decline may well be due to the implementation of infection control efforts at the hospital level; however, it is also possible that the epidemic MRSA strains circulating in the health care setting have evolved, becoming less virulent. In contrast to the decline in health care–associated MRSA, the estimated reduction in incidence of community-associated infections was a modest 5%.

In addition to the evidence that the incidence of MRSA infections is declining, the study highlights 2 important points. The first is the observation that there is an increased risk of recurrent infection among recently hospitalized patients with health care–associated community-onset infections. These patients had a 64% risk of infection at 3 months or less following discharge. Others have also reported a high risk of reinfection in discharged patients either infected or colonized with MRSA.[4] Possible explanations for the patients' increased risk include underlying medical comorbidities, persistent colonization or recolonization with MRSA, or exposure to similar risks of MRSA infection following discharge. This subset of patients would appear to be candidates for studies directed at reducing their high risk of recurrent infection. The second finding is the limited change in the incidence of community-associated infections. This is in marked contrast with the reduction in the incidence of health care–associated infections. As noted by the authors, the study highlights the need for a greater understanding of how these epidemic MRSA strains spread and initiate infection within the community.

Risks identified in the health care setting do not necessarily translate to those in the community. While households appear to be an important reservoir for MRSA in the community, other sites or modes of spread remain to be identified.

Casey et al[3] provide a new wrinkle regarding MRSA spread in the community. The authors investigated whether living close to high-density livestock farms or to crop farms using large quantities of manure transported from the high-density livestock farms contribute to the local incidence of MRSA infections. Eighty percent of antibiotics currently used in the United States are used for growth enhancement of livestock raised on these high-density farms; the bulk of these antibiotics are excreted in manure.[3] Many of the antibiotics used on these farms are from the same antibiotic families that are used to treat human infections. Extensive use of these antibiotics for livestock growth enhancement can potentially result in the selection of antimicrobial-resistant bacteria that may spread to humans, ultimately causing infections that are difficult to treat. These strains may spread by direct animal contact, which occurred with farmers in the Netherlands who developed SSTIs caused by the livestock-associated MRSA clone ST398.[5] Alternatively, spread may occur by exposure to meats introduced into the food chain. Kluytmans et al[6] recently identified extended spectrum β-lactamase–containing *Escherichia coli* in chicken meats that were similar to strains found in humans. Manure obtained from farms that use antibiotics is yet another potential reservoir for antibiotic-resistant bacteria. Several studies have demonstrated that genes conferring antimicrobial resistance are readily found in sewage, soil, and, relevant to the current study, manure.[7]

A particular strength of the study by Casey et al[3] is the novel approach used to demonstrate the potential contribution of the livestock intense farms and the redistributed antibiotic-exposed manure to MRSA infections. They accomplished this by accessing a combination of medical, agricultural, and geographic sources. They obtained data regarding farming practices in Pennsylvania including information on livestock operations and tonnage of manure applied to crop fields. In addition, the medical records of primary care patients in the Geisinger Health system were screened to identify those with MRSA or SSTIs and those without infections. Finally, the authors performed a spatial analysis using, among other strategies, Google Earth, to map the home addresses of cases and controls, the locations of the livestock operations, and the farms that used exported manure. This allowed them to calculate the proximity of the homes of the cases and controls to the different farms.

The results demonstrated that patients with MRSA and SSTIs lived closer to farm fields containing the largest amounts of swine manure than controls. A similar trend was observed for subjects living closer to the high-density livestock operations. The authors estimate that approximately 11% of these infections may be related to this exposure. The spatial relationship was preserved when other confounders that might increase the risk of MRSA infection were considered.

This study is the first to demonstrate an association between MRSA infections and proximity to high-density livestock farms or to antibiotic-exposed manure. The authors speculate that aerosols of bacteria from the manure-containing fields might account for the spread and ultimately for the infections of those living close to the fields. Alternatively, it is possible that there are as yet unrecognized risks of infection for those living nearest the farms. Strains classically associated with livestock-associated infections or colonization were not found among the human infection isolates. Future studies that would strengthen the identified association include (1) determining the types and concentrations of antibiotics in manure; (2) determining the prevalence of genes mediating antimicrobial resistance found in the manure; and (3) comparing human infection isolates with those in the manure. Even without these additional studies, this investigation provides yet another reason to be concerned regarding the use of antibiotics as growth enhancers in animal feed and argues for legislation that restricts the use of antibiotics in this setting.

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