Increased US Emergency Department Visits for Skin and Soft Tissue Infections, and Changes in Antibiotic Choices, During the Emergence of Community-Associated Methicillin-Resistant *Staphylococcus aureus*

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Study objective: Test the hypotheses that emergency department (ED) visits for skin and soft tissue infections became more frequent during the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA), and that antibiotics typically active against community-associated MRSA were chosen increasingly.

Methods: From merged National Hospital Ambulatory Medical Care Survey data for 1993–2005, we identified ED visits with diagnosis of cellulitis, abscess, felon, impetigo, hidradenitis, folliculitis, infective mastitis, nonpurulent mastitis, breast abscess, or carbuncle and furuncle. Main outcomes were change over time in rate of ED visits with such a diagnosis and proportion of antibiotic regimens including an agent typically active against community-associated MRSA. We report national estimates derived from sample weights. We tested trends with least squares linear regression.

Results: In 1993, infections of interest were diagnosed at 1.2 million visits (95% confidence interval [CI] 0.96 to 1.5 million) versus 3.4 million in 2005 (95% CI 2.8 to 4.1 million; *P* for trend $<.001$). As a proportion of all ED visits, such infections were diagnosed at 1.35% in 1993 (95% CI 1.07% to 1.64%) versus 2.98% in 2005 (95% CI 2.40% to 3.56%; *P* for trend $<.001$). When antibiotics were prescribed at such visits, an antibiotic typically active against community-associated MRSA was chosen rarely from 1993 to 2001 but increasingly thereafter, reaching 38% in 2005 (95% CI 30% to 45%; *P* for trend $<.001$). In 2005, trimethoprim-sulfamethoxazole was used in 51% of regimens active against community-associated MRSA.

Conclusion: US ED visits for skin and soft tissue infections increased markedly from 1993 to 2005, contemporaneously with the emergence of community-associated MRSA. ED clinicians prescribed more antibiotics typically active against community-associated MRSA, especially trimethoprim-sulfamethoxazole. Possible confounders are discussed, such as increasing diabetes or shifts in locus of care. [Ann Emerg Med. 2007;xx:xxx.]

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INTRODUCTION

Background

Staphylococcus aureus is a major cause of both abscesses and nonpurulent skin and soft tissue infections.[1,2] Strains resistant to β-lactams, known as methicillin-resistant *S aureus* (MRSA), emerged in the 1960s. These were found predominantly in patients exposed to health care facilities. This changed when new "community-associated" strains emerged in the mid-1990s, and community-associated MRSA is now the leading identifiable cause of skin and soft tissue infections in US

Editor's Capsule Summary

What is already known on this topic

Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as the predominant cause of skin and soft tissue infections in emergency department (ED) patients in the United States.

What question this study addressed

How did the number of ED visits for skin and soft tissue infections and the antibiotics prescribed for these infections change from 1993 to 2005?

What this study adds to our knowledge

Per the National Hospital Ambulatory Medical Care Survey, the number of ED visits for skin and soft tissue infections almost tripled, and use of drugs active against community-associated MRSA also increased.

How this might change clinical practice

This study demonstrates that the appearance of community-associated MRSA coincided with a marked increase in the number of ED visits for skin and soft tissue infection.

emergency department (ED) patients (though generally the cause is identifiable only when the infection is purulent).[1,2]

Importance

Recent studies have shown that cultures of ED patients' abscesses are likely to yield community-associated MRSA.[1] However, we still do not know whether abscesses and other infections commonly caused by *S aureus* are more common since the emergence of community-associated MRSA. Have ED visits for skin and soft tissue infections increased since community-associated MRSA was discovered? Or has this organism merely replaced others, with the underlying disease incidence remaining the same? Given the heterogenous patterns of antibiotic resistance exhibited by this organism, it is also important to monitor physician prescribing practices. Have prescribing practices changed in parallel to changes in disease incidence and cause?

Goals of This Investigation

We seek to determine whether the annual rate of ED visits for skin and soft tissue infections often caused by *S aureus* has changed since community-associated MRSA was first described in the mid-1990s. We hypothesized that from 1993 to 2005, there was a nationwide increase in ED visits attributable to such infections. We also hypothesized that US ED clinicians increased their use of antibiotics typically active against community-associated MRSA when prescribing antibiotics for such infections. To test these hypotheses, we sought data on ED utilization for relevant infections and prescribing practices for not only today but also the period before community-associated MRSA was described. Because it is not possible to initiate prospective surveillance after the fact (ie, after the new organism was described), we required a preexisting surveillance data set. Only 1 such data set exists for the US ED setting: the National Hospital Ambulatory Medical Care Survey (NHAMCS).[3]

MATERIALS AND METHODS

Study Design and Setting

We conducted a secondary analysis of NHAMCS data for 1993 to 2005. NHAMCS is a probability sample of ED visits in all 50 states and the District of Columbia, representing all US EDs, excluding federal, military, and Veterans Administration hospitals.[3] Trained staff collect data using standardized forms during randomly assigned 4-week periods. All collected forms are sent to the Constella Group (Durham, NC) and coded by using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). Medications are coded according to the National Drug Code Database and include those administered in the ED or prescribed at discharge.[4] For the purpose of this analysis, we pooled all data from 1993 to 2005.

Selection of Participants

We identified visits for skin and soft tissue infections commonly caused by *S aureus*, including cellulitis and abscess of finger (681.00), cellulitis and abscess of toe (681.10), other cellulitis and abscess (682, which includes head, neck, trunk, limbs, and buttocks), cellulitis digit not otherwise specified (681.90), felon (681.01), impetigo (684), hidradenitis (705.83), other specified diseases of the hair and hair follicle (ie, folliculitis, 704.8), neonatal infective mastitis (771.5), nonpurulent mastitis (675.2), breast abscess (675.1), or carbuncle and furuncle (680).[1,5] Below, we refer to this group of infections as "selected skin and soft tissue infections," or "infections of interest."

We did not include onychia, dental abscess, Bartholin's abscess, and pilonidal abscess, because these are less likely to be caused by *S aureus*.[6,7] We omitted paronychia (following previous studies[8]) because it typically occurs in the setting of nail biting or cuticle manipulation, rather than arising spontaneously; we assumed that any increased role for MRSA would represent ecologic substitution rather than an increase in disease incidence. This was confirmed in our data, as the proportion of all ED visits due to paronychia did not change significantly from 1993 to 2005 (data not shown).

We identified antibiotics used at each visit, categorizing a regimen as "containing an agent typically active against community-associated MRSA" if it included trimethoprim-sulfamethoxazole, tetracycline, doxycycline, clindamycin, rifampin, linezolid, or vancomycin.[1,5] It bears mentioning that resistance of community-associated MRSA to some of these agents does occur.[1]

Primary Data Analysis

Our main outcome measure is the annual number of ED visits (the visit rate) at which at least 1 of these infections was diagnosed. This visit rate quantifies the importance of such infections in absolute terms; we also describe the importance of such infections *relative* to all other conditions diagnosed among ED patients. Thus, in addition to analyzing changes in the visit *rate*, we analyze changes in visits for such infections as a *proportion* of all ED visits. In contrast to the rate, the proportion would not be affected by overall changes in ED utilization. For example, increases in the US population would lead to an increase in the rate of visits for any condition but should not cause an increase in the proportion of visits attributable to a particular condition. Similarly, increases in the number of US residents lacking health insurance, and therefore access to scheduled care, could cause ED visits to increase but should not cause the importance of one diagnosis to change relative to that of all others.

We used least squares linear regression to test for trends over time, generating *P* values for trend. Because many readers will not only be interested in whether a change occurred over time but also what the rates were for the beginning and end of the study period, we report rates and proportions for the first and last years of the study period and for the study period as a whole, with 95% confidence intervals (95% CI).

We also report the annual rate of ED visits for infections of interest per 100 US civilian population. This is presented as another way of observing the changing rate of these ED visits over time, with control for changes in population. This rate is calculated by dividing the annual number of visits by the midyear age, sex, race, ethnicity, region, and Metropolitan Statistical Area specific civilian population estimate from the US Census Bureau.

Our secondary outcome measure is the proportion of antibiotic regimens including an agent typically active against community-associated MRSA among visits of interest with an antibiotic prescription. Changes in this proportion over time are tested with least squares linear regression to generate *P* for trend, and we also report the proportion for the first and last years of the study period, with 95% CIs. The proportion of antibiotic regimens is used, rather than the raw number of prescriptions, because our specific question is whether clinicians increasingly perceived a need to treat for community-associated MRSA, given the decision to use antibiotics. We also examine changes in the likelihood of prescribing any antibiotic.

In addition to addressing our primary and secondary hypotheses, we report analyses of relevant predictors, using multivariate logistic regression to predict the odds of an ED patient having one of our diagnoses of interest. The independent variables included the following standard covariates: age, sex, race, Hispanic ethnicity, insurance status, and Metropolitan Statistical Area status of the hospital. We also included region (Northeast, Midwest, South and West), and season (December through February, March through May, June through August, September through November) because a predominance in the southern region and in summer has been reported previously.[8,9] We generated the season variable for each year by categorizing data from the month of visit variable into winter, spring, summer, and fall. Race categorization in the NHAMCS changed several times during the study period. To generate a consistent race variable, we categorized race as white, black, or other.

We also report the proportion of visits with fever (defined as temperature ≥38°C [100.4°F]). The fever variable first became available in 2001, and we took the denominator from the years during which the variable was available.

A potential confounder is that clinicians, knowing of the emergence of community-associated MRSA, might have become more likely to ask patients to return to the ED for follow-up reassessments, which would have led to a deceptive increase in the visit rate. NHAMCS distinguished first visits from follow-up visits for 2001 to 2005 only. For this period, we conducted our analysis of visit rates separately among first visits versus among follow-up visits. This allowed us to report the annual proportion of *initial* ED visits with diagnosis of an infection of interest and whether there was a change in the ratio of *initial* visits to *follow-up* visits.

Another potential confounder is that clinicians worried about community-associated MRSA may have become more likely to assign a diagnosis of an infection instead of a noninfectious inflammatory condition. To control for this possibility, we reviewed the *ICD-9-CM* categorization system for inflammatory diseases of the skin and identified 99 noninfectious inflammatory skin conditions. We examined whether the proportion of all ED visits with one of these diagnoses changed during the study period. If we observed a decrease in the number or proportion of ED visits with such noninfectious diagnoses, we would conclude that clinicians might indeed have begun to substitute infectious diagnoses for noninfectious inflammatory diagnoses. This would call into question a positive finding in our main outcome measure.

We used Stata 9.0 (StataCorp, College Station, TX) for analyses, and included design variables to estimate variance, accounting for the 4-stage sampling frame.[3] We tested trends over time using least squares linear regression and Stata's nptrend, a nonparametric test for trends based on the Wilcoxon-Mann-Whitney test. Though point estimates are reported only for the first and last years of the study period, *P* values for trend are generated using all data, 1993 to 2005. For point estimates, we report proportions with 95% CIs generated using NHAMCS sample weights. We report odds ratios from multivariate logistic regression to compare the odds of a diagnosis of interest among groups. NHAMCS sampling procedures make national estimates unstable when based on fewer than 30 observations, and therefore we avoid reporting such data.[3] We do so only in the following 2 instances: In Table 1, unstable annual estimates resulting from stratification into many small cells are displayed with an appropriate caveat; and

in the analysis of the change in antibiotic regimens, we include the small N for 1993 to 2001 in our test of trend for the entire study period and in the graphic display in the Figure.

RESULTS

From 1993 through 2005, the NHAMCS sampled 374,891 ED visits. Each year, 352 to 418 EDs participated.[10] An infection of interest was diagnosed at 6,628 of these visits. This allows us to estimate that there were 1.3 billion total ED visits in the United States during this period (95% CI 1.2 to 1.4 billion), with diagnosis of an infection of interest at 23 million (95% CI 21 to 25 million), or 1.7% of all ED visits (95% CI 1.6% to 1.8%). Patient age was younger than 18 years for 18% (95% CI 17% to 19%) of such visits. Fever was documented at 48% of such visits (95% CI 44% to 52%). Fourteen percent of such visits ended in hospital admission (95% CI 13% to 15%), with no change during the study period (data not shown).

In 1993, selected skin and soft tissue infections were diagnosed at 1.2 million ED visits (95% CI 0.96 to 1.5 million). In 2005, such infections were diagnosed at 3.4 million ED visits (95% CI 2.8 to 4.1 million; *P* for trend <.001), nearly a 3-fold increase. The results are depicted graphically in the Figure.

The proportion of all ED patients with an infection of interest also increased, by more than double, from 1.35% in 1993 (95% CI 1.07% to 1.64%), to 2.98% in 2005 (95% CI 2.40% to 3.56%; *P* for trend <.001). This indicates that not only did the absolute number of such infections increase but also that ED utilization for these infections increased relative to utilization for all other conditions.

Per 100 US residents, there were 0.48 ED visits with an infection of interest in 1993 (95% CI 0.38 to 0.58) versus 1.16 in 2005 (95% CI 0.94 to 1.39; *P* for trend <.001).

Table 1 provides a breakdown of visits by diagnosis and year. The fineness of stratification resulted in some cells having insufficient N for stable national estimates; such cells are indicated accordingly.

Table 2 stratifies the data by patient characteristics and provides 3 different results. First, the "Estimated Number" column shows the estimated number of visits for selected skin and soft tissue infections in US EDs during the study period. Second, the percentage column shows the proportion of all ED visits with a diagnosis of interest during the study period.

Neither of the above contains any control for confounders. Consider, for example, the data on insurance coverage, under Payer. The percentage column suggests that the probability of diagnosis of an infection of interest at an ED visit was similar for patients with private insurance (1.63%; 95% CI 1.53% to 1.72%) and those with Medicaid (1.70%; 95% CI 1.56% to 1.84%). This comparison does not consider the possibility that differing age, sex, race, geographic region, or other characteristics among Medicaid versus private insurance could have obscured a relationship between visit odds and insurance status.

Table 1. Estimated annual visits to US EDs for selected skin and soft tissue infections during the emergence of community-associated MRSA, 1993 to 2005.*

Diagnoses	*ICD-9-CM* Codes	Sample N	Estimated Annual Visits to US EDs (Thousands)												
			1993	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**
Other cellulitis and abscess (includes head, neck, trunk)	682	5,403	**935**	**1,016**	**1,021**	**855**	**984**	**1,070**	**1,211**	**1,308**	**1,431**	**1,652**	**2,001**	**2,356**	**2,950**
Cellulitis and abscess of finger, toe, or digit	681.00, 681.10, 681.9	477	**75**	**135**	109	80	100	93	95	**176**	**139**	**118**	**141**	**137**	**209**
Impetigo	684	364	**110**	**160**	114	80	103	105	116	81	85	82	51	**125**	**125**
Other diseases of the hair and hair follicle (ie, folliculitis)	704.8	237	45	55	36	62	48	55	42	28	42	**83**	**101**	72	**91**
Carbuncle and furuncle	680	178	48	31	55	54	27	45	37	17	45	73	32	116	72
Hidradenitis	705.83	57	9	4	2	14	22	3	2	28	16	18	12	26	20
Felon	681.01	16	10	6	8	0	1	0	0	0	5	7	1	0	8
Infective mastitis or nonpurulent mastitis	675.2, 771.50	3	0	0	0	0	0	0	0	0	3	3	7	0	0
Breast abscess	675.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total		6,735†	**1,222**	**1,385**	**1,331**	**1,128**	**1,278**	**1,352**	**1,459**	**1,625**	**1,745**	**1,995**	**2,315**	**2,755**	**3,426**

*Bolded numbers are robust estimates based on sample numbers sufficiently large for national estimation. Nonbolded numbers are estimates based on fewer than 30 observations because of fine stratification by condition and year. Such estimates are unstable. CIs are omitted because of space considerations.

†The number of sample visits reported in the article text (6,628) is smaller than the total here (6,735) because a few of the visits had more than 1 diagnosis. In all analyses of visit counts, each visit is counted only once.

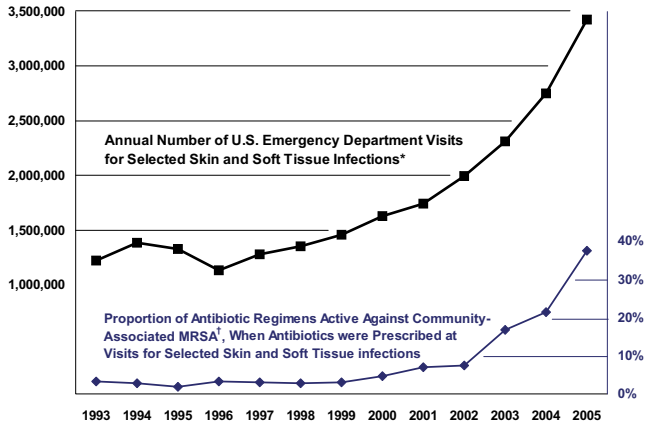

Figure. Annual visits to US EDs for selected skin and soft tissue infections, during the emergence of community-associated MRSA, 1993-2005.*

*Skin and soft-tissue infections commonly caused by *S aureus* were included in our case definition, and were defined by the *ICD9-CM* codes for: cellulitis and abscess of finger; cellulitis and abscess of toe; other cellulitis and abscess (which includes head, neck, trunk, limbs, and buttocks); cellulitis digit not otherwise specified; felon; impetigo; hidradenitis; other specified diseases of the hair and hair follicle (ie, folliculitis); infective mastitis; nonpurulent mastitis; breast abscess; or carbuncle and furuncle.

†An antibiotic regimen was considered "active against CA-MRSA" if it contained trimethoprim-sulfamethoxazole, tetracycline, doxycycline, clindamycin, rifampin, linezolid, or vancomycin, though resistance to some of these agents does occur.[1] Prior to 2002, too few prescriptions included an anti-CA-MRSA agent for robust estimates.

Third, in contrast, the "Odds Ratio" column does provide control for all of the covariates in the table because the odds ratios were calculated in a multivariate model. Returning to the example of insurance status, consider the odds ratio for Medicaid versus private insurance: 1.17 (95% CI 1.06 to 1.29). This odds ratio tells us that the odds of diagnosis of an infection of interest were 17% higher among Medicaid visits than among private visits after control for multiple confounders. In the "Estimated Number" and percentage columns, this relationship may have been obscured by confounding by age and race (eg, compared with adults, children are less likely to have skin and soft tissue infections and Medicaid; compared to whites, blacks are equally likely to have skin and soft tissue infections but more likely to have Medicaid).

The multivariate analysis suggests that likelihood of a visit for an infection of interest was associated with middle age, male sex, Southern and Western regions, Medicaid and self-insurance, warmer seasons, and diabetes. ED utilization for these infections was similar among whites and blacks but was significantly lower among those of other race. Because race categorization in the NHAMCS changed during the study period, we did not undertake further analysis of the other races. There was no significant variation by Hispanic ethnicity (data not shown).

We were concerned that the increases described above could have been due to an increase in the likelihood that clinicians planned follow-up visits, rather than an increase in visits for new disease. NHAMCS labeled visits as "initial" or "follow-up" for 2001 to 2005 only. During this period, 79% of visits with a diagnosis of interest were initial visits, 17% were follow-up visits, and 4% were of unknown episode. For this period, the rate of all *initial* ED visits with diagnosis of an infection of interest increased steadily from 1.4 million in 2001 (95% CI 1.1 to 1.7 million) to 2.8 million in 2005 (95% CI 2.3 to 3.3 million; *P* for trend <.001). Similarly, the *proportion* of initial visits with diagnosis of an infection of interest increased from 1.46% in 2001 (95% CI 1.27% to 1.65%) to 2.73% in 2005 (95% CI 2.44% to 3.02%; *P* for trend <.001). Among follow-up visits, the rate and proportion did not change (*P* for trend=.70; data not shown). The annual ratio of initial visits to follow-up visits was 5:1, with no change from 2001 to 2005 (*P*=.74; data not shown). Considering initial visits only, the above population figure (1.16 *total* ED visits per 100 US population in 2005) may be expressed as approximately 1 *initial* ED visit per 100 US population in 2005. The figures for ED visit rates and ED visit proportions may be adjusted similarly, but we have no reason to suspect that the degree of increase observed would be influenced by this.

Regarding the possibility of confounding due to substitution of infectious diagnoses for noninfectious inflammatory diagnoses (see Materials and Methods), our analysis did not suggest that this occurred. In fact, the 99 noninfectious inflammatory skin conditions included in our analysis of this potential confounder were diagnosed *more commonly* throughout the course of the study, increasing from 1.46% of all ED visits in 1993 to 1.64% in 2005 (*P* for trend .004). This provides evidence against the notion that clinicians examining patients with inflammatory skin conditions became more likely to diagnose an infection instead of a noninfectious inflammatory condition.

Prescription of any antibiotic increased slightly from 74% of ED visits for infections of interest in 1993 (95% CI 69% to 79%) to 78% in 2005 (95% CI 74% to 82%; *P* for trend <.001), with a mean of 75% for the study period.

Among visits for infections of interest, from 1993 to 2001, agents typically active against community-associated MRSA were included in antibiotic regimens too infrequently for generation of stable national estimates. In contrast, in 2005, 38% of regimens prescribed at these visits included an agent typically against community-associated MRSA (95% CI 30% to 45%). For 1993 to 2005, the increase in likelihood of choosing an agent typically active against community-associated MRSA was statistically significant (*P* for trend <.001). This is shown graphically in the Figure. Among such regimens, in 2005, trimethoprim-sulfamethoxazole was prescribed at 51% (95% CI 41% to 62%) and clindamycin at 42% (95% CI 32% to 53%).

For 1993 to 2005, among visits for infections of interest with an antibiotic prescription, cephalosporins were prescribed at 66% (95% CI 64% to 69%), penicillins 17% (95% CI 15% to 18%), quinolones 5.7% (95% CI 4.7% to 6.7%), clindamycin

Table 2. Predictors of diagnosis of a skin and soft tissue infection among US ED visits during the emergence of community-associated MRSA, 1993 to 2005.*

Variable	Stratum	Estimated Number of US ED Visits With a Diagnosis of Interest,* 1993 to 2005 (95% CI) (Thousands)	Percent of All US ED Visits With a Diagnosis of Interest,* 1993 to 2005 (95% CI)	Odds Ratio† for a Diagnosis of Interest* at a US ED Visit (95% CI)
Age, y	<10	2,744 (2,400–3,089)	1.19 (1.07–1.31)	Referent
	10–19	2,147 (1,860–2,434)	1.31 (1.16–1.47)	1.13 (0.99–1.30)
	20–29	4,068 (3,615–4,522)	1.82 (1.64–2.00)	1.59 (1.39–1.81)
	30–39	3,785 (3,396–4,174)	1.87 (1.71–2.03)	1.63 (1.44–1.84)
	40–49	3,749 (3,342–4,155)	2.25 (2.07–2.43)	1.96 (1.72–2.23)
	50–59	2,469 (2,175–2,763)	2.25 (2.03–2.47)	1.97 (1.70–2.28)
	60–69	1,689 (1,446–1,931)	2.08 (1.81–2.35)	1.81 (1.53–2.14)
	70–79	1,313 (1,141–1,458)	1.60 (1.42–1.78)	1.39 (1.16–1.66)
	80+	1,052 (883–1,221)	1.41 (1.20–1.62)	1.26 (1.03–1.54)
Sex	Female	11,000 (10,100–11,900)	1.55 (1.47–1.64)	Referent
	Male	12,000 (11,000–13,000)	1.92 (1.80–2.04)	1.28 (1.19–1.37)
Race	White	17,400 (16,00–18,800)	1.72 (1.63–1.81)	Referent
	Black American	5,121 (4,487–5,754)	1.81 (1.67–1.95)	1.01 (0.92–1.10)
	Other	486 (372–599)	1.30 (1.06–1.55)	0.71 (0.59–0.85)
Region	Northeast	3,951 (3,322–4,580)	1.50 (1.41–1.60)	Referent
	Midwest	5,164 (4,404–5,923)	1.53 (1.40–1.65)	1.05 (0.95–1.16)
	South	9,149 (7,864–10,400)	1.85 (1.67–2.03)	1.24 (1.10–1.39)
	West	4,752 (4,054–5,450)	1.98 (1.79–2.18)	1.37 (1.22–1.55)
Payer	Private	7,770 (7,065–8,475)	1.63 (1.53–1.72)	Referent
	Medicare	3,321 (2,955–3,687)	1.74 (1.59–1.89)	1.08 (0.95–1.23)
	Medicaid	4,660 (4,159–5,161)	1.70 (1.56–1.84)	1.17 (1.06–1.29)
	Self-pay	4,356 (3,828–4,833)	2.12 (1.91–2.32)	1.24 (1.12–1.37)
	Other	1,693 (1,147–1,968)	1.51 (1.32–1.70)	0.87 (0.76–0.99)
	Unknown/Missing	1,216 (975–1,456)	1.66 (1.39–1.94)	1.03 (0.87–1.22)
Season	Winter (Dec–Feb)	4,530 (4,033–5,026)	1.39 (1.28–1.51)	Referent
	Spring (March–May)	5,353 (4,749–5,957)	1.58 (1.46–1.70)	1.13 (1.02–1.25)
	Summer (June–Aug)	6,807 (6,050–7,564)	2.02 (1.87–2.17)	1.44 (1.30–1.60)
	Fall (Sept–Nov)	6,325 (5,621–7,028)	1.90 (1.75–2.06)	1.36 (1.23–1.51)
Diabetes	No Diabetes	22,600 (20,800–24,300)	1.71 (1.62–1.79)	Referent
	Diabetes	447 (351–544)	4.01 (3.23–4.80)	2.11 (1.73–2.57)
Total	All cases	23,000 (21,300–24,800)	1.7 (1.6–1.8)	n/a

*Skin infections commonly caused by *S aureus* were included, as indicated by the *ICD-9-CM* codes for cellulitis and abscess of finger, cellulitis and abscess of toe, other cellulitis and abscess (which includes head, neck, trunk, limbs, and buttocks), cellulitis digit not otherwise specified, felon, impetigo, hidradenitis, other specified diseases of the hair and hair follicle (ie, folliculitis), infective mastitis, nonpurulent mastitis, breast abscess, or carbuncle and furuncle.
†Odds ratios were calculated in a multivariate logistic regression model. The dependent variable was the logit of the odds of a diagnosis of interest at the visit. The independent variables were age, sex, race, Hispanic ethnicity, insurance status, Metropolitan Statistical Area status of the hospital, region, and season.

5.1% (95% CI 3.8% to 6.4%), macrolides 4.6% (95% CI 3.7% to 5.4%), tetracyclines 1.3% (95% CI 0.8% to 1.7%), and others too infrequently for national estimates.

In 1993, among such visits with an antibiotic prescription, cephalosporins were prescribed at 65% (95% CI 57% to 73%), macrolides 17% (95% CI 11% to 23%), penicillins 15% (95% CI 9.1% to 20%), and others too infrequently for national estimates.

In 2005, among such visits with an antibiotic prescription, cephalosporins were prescribed at 49% (95% CI 43% to 55%), trimethoprim-sulfamethoxazole 19% (95% CI 13% to 25%), clindamycin 16% (95% CI 11% to 21%), penicillins 15% (95% CI 11% to 19%), quinolones 7.2% (95% CI 4.6% to 9.8%), and others too infrequently for national estimates.

LIMITATIONS

An important unanswered question is whether community-associated MRSA plays a role in nonpurulent skin and soft tissue infections (eg, cellulitis), as well as purulent ones (abscess, folliculitis, etc). A flaw in the *ICD-9-CM* diagnostic categorization system is that cellulitis and abscess are lumped together. Therefore, we could not distinguish purulent from nonpurulent infections. We also could not identify visits with incision and drainage (which would obviously indicate suspicion for abscess), because our previous investigations have suggested that procedures are not captured reliably during NHAMCS data collection. It is possible that the increase we observed obscures an even more dramatic increase in purulent infections, with nonpurulent infections remaining stable.

Other limitations inherent in NHAMCS studies include lack of microbiological data and the fact that case ascertainment depends on entry of the correct *ICD-9-CM* code (though bias seems unlikely to have resulted from this). It is regrettable that visits before 2001 were not labeled as initial versus follow-up, with the result that we could compare the rate of initial versus follow-up visits only for 2001 to 2005. However, it is fortunate that the period for which these data were available coincided with the period during which we observed the steepest increase in rates. We think it unlikely that an increase in recommended follow-up visits would explain our observations.

With respect to our examination of prescribing practices, it bears mentioning that the antibiotics we deemed "typically active against community-associated MRSA" are not uniformly active against this organism.[1] It was not feasible to obtain antibiotic susceptibility data because NHAMCS is the only national ED data set that spanned the period of emergence of community-associated MRSA, and it lacks microbiological data.

Finally, our analysis did not control for the possibility that the increase in visit rates we observed resulted from a shift in care from physicians' offices and hospital outpatient departments to EDs. A previous study included not only ED visits but also visits to physicians' offices and outpatient departments and found that the rate of skin and soft tissue infections among physicians' office visits remained stable from 1992 to 1994, to 2001 to 2003, whereas the rate among outpatient and ED visits increased by 59% and 31%, respectively.[8] This suggests that the increases we observed were not likely due to a shift in locus of care, though it does suggest that the increases we observed in the ED setting might have been even more dramatic in outpatient departments and less dramatic in physicians' offices. Given the previous study, our only concern in this regard is that there may have been an abrupt shift in locus of care to the ED from other settings during 2004 to 2005, which seems unlikely. We plan to assess this in a future analysis.

DISCUSSION

We describe ED utilization and antibiotic choices during the period of emergence of community-associated MRSA, which is known to be important in purulent infections among ED patients.[1] Analyzing 13 years of data from a representative sample of US EDs, we categorized visits according to whether they involved a skin and soft tissue infection and whether an antibiotic typically active against community-associated MRSA was chosen.

The data are consistent with our 2 hypotheses. From 1993 to 2005, we observed nearly a 3-fold increase in the annual number of ED visits for skin and soft tissue infections, with 3.4 million such visits in 2005. This increase was also observed when skin and soft tissue infection visits were examined as a proportion of all visits: the proportion increased by more than double, reaching 2.98% in 2005. Emergency physicians' antibiotic choices changed as well. From 1993 to 2001, among antibiotic prescriptions at visits for infections of interest, agents typically active against community-associated MRSA were chosen infrequently. By 2005, 38% of such regimens included such an agent, trimethoprim-sulfamethoxazole in half of these and clindamycin in 42%. The choice of a cephalosporin decreased from 65% in 1993 to 49% in 2005. Considering that the probability of prescribing any antibiotic increased slightly, these results suggest that cephalosporins were used less because agents typically active against community-associated MRSA were chosen instead.

A previous study found a 31% increase in the rate of ED visits for skin and soft tissue infections from 1992 to 2003.[8] The discrepancy with our results is explained by the fact that the previous study's final time point was pooled from 2001 to 2003, and during this period and the next 2 years, the rate of infections of interest was increasing dramatically, as shown in our Figure. ED visits for diagnoses of interest were significantly more common in 2005 (2.98% of ED visits; 95% CI 2.40% to 3.56) than in 2001 (1.62% of ED visits; 95% CI 1.30% to 1.95). There were also minor differences in included *ICD-9-CM* codes. The previous study also examined changes in antibiotic prescribing practices, but its latest year was 2003, it did not categorize antibiotics according to their activity against community-associated MRSA, and it pooled ED and other ambulatory settings.[8] Its finding of a borderline increase in cephalosporin prescribing might suggest that non-ED clinicians increased their use of cephalosporins, whereas ED clinicians decreased it; also, in our data set, the decrease in cephalosporin prescribing was most marked during 2001 to 2005 (data not shown).

Another potential confounder is diabetes, which has increased in recent years, is known to be associated with skin and soft tissue infections, and was associated with ED utilization for skin and soft tissue infections in our own data set. However, the crude prevalence of diagnosed diabetes rose only 27% from 1988-1994 to 1999-2002 (longer than the period of our study), whereas undiagnosed diabetes remained stable.[11] Overweight and obesity also increased, by 18% from 1988 to 1994 to 2003 to 2004 (again, longer than our period of study).[12] However, obesity may be a risk factor for skin and soft tissue infection mostly through the adult-onset diabetes it causes, and many of the new cases of obesity would also be new cases of diabetes. The increase in diabetes and an additional small increase among nondiabetic patients with obesity seem unlikely to explain the increase in ED visit rates we observed, though they may explain part of it.

The probability of any antibiotic being prescribed at visits for infections of interest changed little, from 74% to 78%. When an ED patient with a purulent skin and soft tissue infection requires antibiotics, a regimen effective against community-associated MRSA is recommendable, but this does not imply that antibiotics are needed more frequently than before community-associated MRSA was discovered.[1,13] For uncomplicated abscesses treated surgically, antibiotics may be no more necessary than they were in the pre-community-

associated MRSA era.[13] For nonpurulent skin and soft tissue infections, little is known abot the role of community-associated MRSA, though *S aureus* is a common cause of cellulitis, along with streptococci.[2] Knowledge of the role of community-associated MRSA in nonpurulent skin and soft tissue infections will have to be inferred from response rates in antibiotic trials or from the low-yield techniques of microbiological diagnosis in cellulitis.[2]

We identified an increase in ED utilization for skin and soft tissue infections from 1993 to 2005. The annual rate of ED visits with such infections nearly tripled, and as a proportion of all ED visits, such visits increased by more than double. In 2005, about 1 initial ED visit for such infections occurred per 100 US residents. These changes were contemporaneous with the emergence of community-associated MRSA.[1] Although a causal relationship cannot be inferred, we are concerned about the possibility that community-associated MRSA may be causing more disease, rather than displacing other organisms from preexisting ecological niches. Even though we do not know the cause, our data provide good evidence that ED utilization for skin and soft tissue infections is increasing both in absolute terms and relative to all other conditions.

From 1993 to 2001, emergency physicians rarely treated skin and soft tissue infections with antibiotics active against community-associated MRSA. By 2005, they did so frequently, especially with trimethoprim-sulfamethoxazole and clindamycin. Clinical studies of the effectiveness and cost-effectiveness of these agents are needed, as is research on eradication regimens, novel vaccines, and methods of controlling the spread of community-associated MRSA. Clinicians should be aware of the local prevalence of MRSA, local patterns of antibiotic resistance, and the lack of data concerning the role of MRSA in nonpurulent skin and soft tissue infections.

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Editor's Capsule Summary *What is already known on this topic:* Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as the predominant cause of skin and soft tissue infections in emergency department (ED) patients in the United States. *What question this study addressed:* How did the number of ED visits for skin and soft tissue

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infections and the antibiotics prescribed for these infections change from 1993 to 2005? *What this study adds to our knowledge:* Per the National Hospital Ambulatory Medical Care Survey, the number of ED visits for skin and soft tissue infections almost tripled, and use of drugs active against community-associated MRSA also increased. *How this might change clinical practice:* This study demonstrates that the appearance of community-associated MRSA coincided with a marked increase in the number of ED visits for skin and soft tissue infection.