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A population-based study of the epidemiology and clinical features of methicillin-resistant *Staphylococcus aureus* infection in Pennsylvania, 2001–2010

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SUMMARY

No U.S. general population-based study has characterized the epidemiology and risk factors, including skin and soft tissue infection (SSTI), for healthcare-associated (HA) and community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA). We estimated the incidence of HA- and CA-MRSA and SSTI over a 9-year period using electronic health record data from the Geisinger Clinic in Pennsylvania. MRSA cases were frequency-matched to SSTI cases and controls in a nested case-control analysis. Logistic regression was used to assess risk factors, while accounting for antibiotic administration. We identified 1713 incident CA- and 1506 HA-MRSA cases and 78 216 SSTI cases. On average, from 2005 to 2009, the annual incidence of CA-MRSA increased by 34%, HA-MRSA by 7%, and SSTI by 4%. Age, season, community socioeconomic deprivation, obesity, smoking, previous SSTI, and antibiotic administration were identified as independent risk factors for CA-MRSA.

Key words: Epidemiology, incidence, methicillin-resistant *S. aureus* (MRSA), skin infections.

INTRODUCTION

Until the late 1990s methicillin-resistant *Staphylococcus aureus* (MRSA) was primarily a healthcare-associated (HA) pathogen. Thereafter, in the USA, younger, healthier individuals with none or few traditional healthcare risk factors began acquiring community-associated MRSA (CA-MRSA), which often presents as skin and soft tissue infections (SSTIs) [1, 2]. Data describing trends in the annual incidence of and the risk factors for HA- and CA-MRSA in a general population sample over the past decade are not available. Limitations in existing US research include study of: only invasive infection [3–7]; restricted populations (e.g. military, inmate, athlete) [6–16]; patients from hospital-based surveillance that could bias ascertainment towards HA- rather than CA-MRSA [16–19]; and limited time windows [16, 20]. Among those studies, only two [11, 20] applied rigorous case definitions to separate CA- and HA-MRSA; others used location of onset as a surrogate or categorized using antibiotic-resistance profiles. Furthermore, trends in SSTI incidence in the

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general population are important because these infections could represent a source of undiagnosed MRSA, but have not been well described. No previous studies have included both MRSA and a range of SSTIs.

Since no longitudinal U.S. population-based study has been conducted including both HA- and CA-MRSA for all clinical indications in a large contiguous geography, little is known about healthcare and non-healthcare risk factors for HA- and CA-MRSA and SSTIs in the general US population. We characterized the epidemiology of MRSA using 10 years of medical data from the electronic health record (EHR) of the Geisinger Health System in Pennsylvania. The EHR includes data on over 440 000 primary-care patients of all ages that live in both urban and rural areas. We evaluated individual, community, and clinical risk factors for CA- and HA-MRSA patients and SSTI patients, compared to controls. Our goals were to: (1) estimate the incidence of HA- and CA-MRSA and SSTIs over a 10-year period; and (2) examine clinical and non-healthcare risk factors for HA- and CA-MRSA and SSTIs, with and without consideration of antibiotic use.

METHODS

Study overview

We first determined MRSA and SSTI incidence rates from 2001 to 2009 (in incident cases per 100 000 person-years). Any patient with an inpatient or outpatient encounter in a given calendar year contributed 1 person-year to the denominator. We next selected cases and controls to perform a nested case-control analysis. The study was approved by Institutional Review Boards at the Johns Hopkins Bloomberg School of Public Health and the Geisinger Health System.

Study population and design

Data were obtained on 446 480 patients with a Geisinger Clinic primary-care provider, from outpatient encounter records from 1 January 2001 to 9 February 2010 and from inpatient encounter records from 1 July 2003 to 9 February 2010. The system provides primary-care services in 41 community practice clinics and four hospitals in a 31-county region of central and northeastern Pennsylvania. We utilized only the primary-care population because health data are more complete and because it is representative of the general population in the region. Patients were geocoded using ArcGIS as described previously [21].

Data sources

Data in 157 106 929 records consisted of demographics, inpatient, outpatient, and emergency department encounters, laboratory data, medication orders, and procedures. All orders and encounters were accompanied by International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9) codes or Geisinger system (EP) codes for diagnoses, and Current Procedural Terminology (CPT) codes for encounters, laboratory tests and procedures. Specific ICD-9 codes for MRSA only became available after 2007, but the Geisinger Clinic began using a system code for MRSA (EP884) in 2003.

Identification of MRSA cases, SSTI cases and controls

Incident MRSA was defined as: (1) a culture positive for MRSA; (2) an ICD-9 or EP code for MRSA; or (3) an ICD-9 code for *S. aureus* infection with an ICD-9 code for penicillin resistance (the clinical microbiology laboratory method to encode MRSA before 2007) (Fig. 1). The year of onset was defined as the first diagnosis of MRSA infection. No recurrent MRSA infections were included. We identified community-onset SSTI (CO-SSTI) cases (using 29 ICD-9 codes) using outpatient records; an incident CO-SSTI was defined as the first occurrence in any 6-month period. For the case-control analysis, SSTIs who never had a MRSA diagnosis were randomly selected and frequency-matched to the MRSA cases on age, sex, and year of diagnosis. Controls were also randomly selected and frequency-matched to MRSA cases on age, sex and an outpatient encounter in the same year as MRSA diagnosis. If SSTI cases or controls had multiple SSTI diagnoses or visits, respectively, during the matched year of MRSA diagnosis a single visit was randomly selected as the match visit.

Assignment to HA- or CA-MRSA

Assignment required inpatient records from the year preceding diagnosis; so all cases diagnosed before 2005 were excluded from this categorization ($n=854$, primarily hospital-onset MRSA). MRSA

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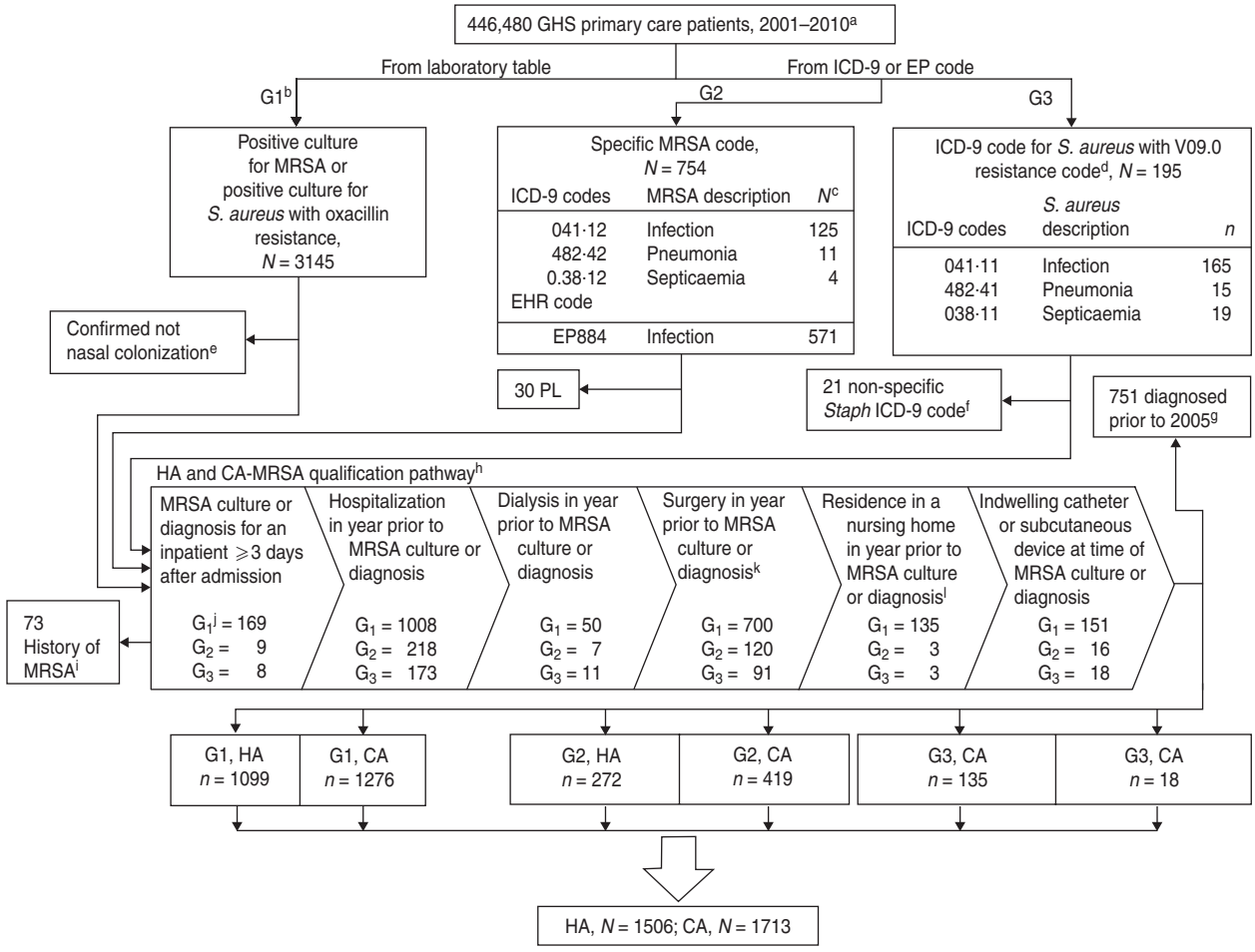

Fig. 1. Flow chart depicting MRSA case selection and diagnosis location. GHS, Geisinger Health System; G1, Group 1; G2, Group 2; G3, Group 3; ICD-9, International Classification of Diseases, 9th Revision, Clinical Modification; EP, Geisinger Clinic generated electronic health record code; PL, problem list table; HA-MRSA, healthcare-associated methicillin-resistant *Staphylococcus aureus*; CA-MRSA, community associated MRSA; *S. aureus*, *Staphylococcus aureus*. [a] Geisinger Health System, outpatient data was available 2001–2010, and inpatient data 2004–2010. [b] G1, G2 and G3 indicate the method by which MRSA cases were identified. The numbered hierarchy was used when a case was identified by multiple methods on the same day, otherwise the case was linked to the method that identified the earliest MRSA diagnosis. [c] These numbers are not mutually exclusive. [d] Before 2007 there was no MRSA-specific ICD-9 code and MRSA was identified at GHS by the analogous MSSA code plus a V09.0 code, indicating infection with microorganisms resistant to penicillins. [e] Checked for PCR indicating MRSA colonization. [f] Cases originally selected with codes 041·10 (*Staphylococcus* infection, unspecified) and 038·10 (*Staphylococcus* septicaemia, unspecified) were excluded. [g] Due to the lack of inpatient data before 2004, cases could not be categorized as CA- or HA-MRSA before 2005. [h] If a patient met any of the six criteria they were classified as HA-MRSA. [i] V12.04, the ICD-9 code for history of MRSA infection in record. [j] Patients were disqualified from the CA-MRSA category if their procedures file contained a surgery or their inpatient, outpatient or emergency department file contained a post-operative visit in the 330 days before MRSA infection. [k] n_1, n_2, n_3 correspond to the numbered hierarchy and represent the total number of patients with each characteristic by group (i.e. these numbers are not mutually exclusive). [l] Patients were disqualified from the CA-MRSA category if their address matched an address of a nursing home facility in Pennsylvania listed on the Nursing Home Compare database website provided by the U.S. Department of Health and Human Services.

was classified as CA based on the case definition of the Centers for Disease Control and Prevention (CDC); all other cases were categorized as HA [20, 22]. Antibiotic susceptibility of isolates and the site of infection were assessed in the subset of cases identified by culture.

Statistical analysis

Using data from 2005 to 2010, HA-MRSA, CA-MRSA, and SSTI cases were compared to controls on demographics, body mass index (BMI), season of infection, community socioeconomic deprivation

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(CSD), residential community (representing the macro-environment of the patient, defined by census tracts in cities, moderate to high density boroughs, and suburban and rural townships), SSTI diagnosis in varying time windows in the year before MRSA diagnosis, antibiotic prescriptions, and selected acute and chronic health conditions [23]. We determined antibiotic administration in the 30–365 days preceding diagnosis to avoid protopathic bias [24].

Multinomial logistic regression was used to compare HA- and CA-MRSA cases to controls and a separate logistic regression model was used to compare SSTI cases to controls. We first present crude odds ratios (ORs) [with 95% confidence intervals (CIs)]. We then adjusted for the following potential confounders: age (grouped to balance sample size and life stage considerations), sex, race/ethnicity and smoking status (ever *vs.* never). Health condition ORs were determined with and without adjustment for any antibiotic administration in the previous 2 years. We also assessed associations for antibiotic administration for specific indications and subsequent MRSA or SSTI infection.

All analysis was performed using Stata version 11.2 (StataCorp, USA) and R version 12.2.2 software (www.r-project.org). A multilevel multinomial logistic model (Stata gllamm with random intercept) was used to assess the association between case status and residential communities, as well as CSD [23].

RESULTS

Incidence of MRSA infection and SSTIs

From 2001–2009 an annual mean of 211 102 (S.D. = 29301) unique patients had an inpatient or outpatient encounter. A total of 4094 MRSA cases and 78216 SSTI cases were identified between 1 January 2001 and 9 February 2010. After 1 January 2005, we were able to categorize 1506 as HA- and 1713 as CA-MRSA cases. MRSA cases, selected SSTI cases and controls had a mean of 38 (S.D. = 32) outpatient visits over the follow-up period and 6 (S.D. = 3) years of follow-up time between their first and last outpatient encounter in the EHR, providing strong evidence that these patients were longitudinally followed. The mean annual incidence rate from 2001–2009 for all MRSA cases was 195 (95% CI 189–201) cases/100 000 person-years, compared to 4008 (95% CI 3980–4037) SSTI cases/100 000 person-years. The mean percent annual increase in MRSA incidence over the 9 years was 23% (range −15% to 51%), compared to 3·6% (range 1–8%) for SSTI cases. The average annual percent increase in HA-MRSA incidence was 7% (range −13% to 23%). In contrast, the average annual increase in CA-MRSA incidence was 34% (range 6–94%) from 2005 to 2009, with the largest percent and absolute increase during 2005–2006 (Fig. 2). For CA-MRSA, no rate exceeded 100/100 000 person-years in patients aged >46 years, but several age- and sex-specific rates exceeded 300/100 000 person-years including girls aged <14 years, the group that saw the most impressive increases incidence. SSTI incidence increased reasonably monotonically as a whole and in age and sex subgroups. The percent of total MRSA cases classified as CA rose from 38% in 2005 to 59% in 2009.

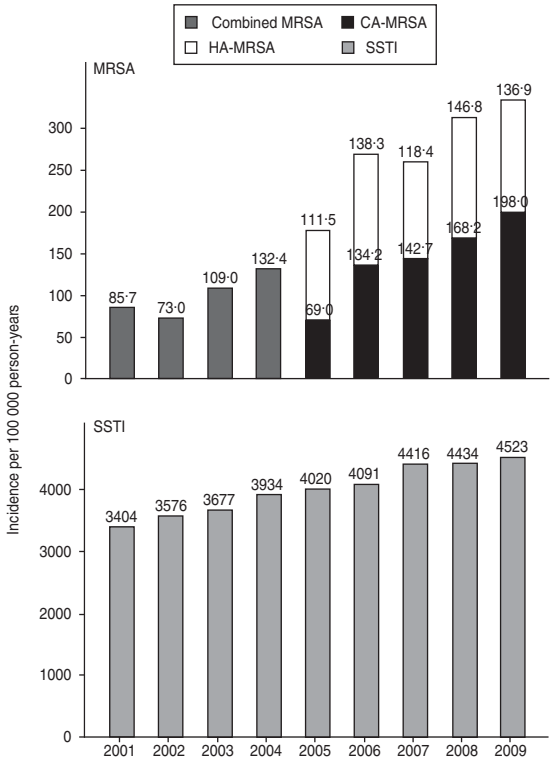

Fig. 2. Incidence of MRSA infection and SSTI per 100 000 person-years among the Geisinger Clinic's primary-care patients, 2001–2009 (MRSA cases are combined before 2005 because lack of inpatient data did not allow for assignment to HA- and CA-MRSA groups). CA-MRSA, Community-associated MRSA; HA-MRSA, healthcare-associated MRSA; SSTI, skin and soft tissue infection.

Demographic and clinical comparisons of HA-MRSA, CA-MRSA, SSTIs and controls

The majority (77·5%) of MRSA cases were identified by laboratory culture (many also had ICD-9 codes),

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followed by specific ICD-9 codes only (17·6%) and combined ICD-9 codes only (4·9%). Patient characteristics did not differ by method of identification (data not shown), and a subgroup analysis using only cases with both a positive culture and a MRSA ICD-9 code on the same day ($n=824$) did not reveal any substantive change in associations; therefore, all MRSA cases were combined in subsequent analyses. Among SSTI cases the three most common diagnoses were cellulitis (62%), carbuncle (17%), and impetigo (12%). Only 8·5% of SSTI cases had a culture taken, and *S. aureus* was by far the most common organism identified, followed by *Pseudomonas aeruginosa* and *Escherichia coli*.

HA-MRSA cases were substantially older and less likely to be a race/ethnic minority than CA-MRSA cases (Table 1). For each identification method, HA cases had more outpatient encounters per year, compared to CA cases, SSTI cases and controls. HA isolates had higher odds of being resistant to two or more antibiotic classes than CA isolates (OR 6·47, 95% CI 4·92–8·60). Specimen descriptions were available for 954 HA- and 1088 CA-MRSA cases; of these the most common sources for HA-MRSA were skin and soft tissue (50·3%), respiratory (16·0%), urine (15·9%) and blood (8·0%), and for CA-MRSA were skin and soft tissue (86·4%), other (7·1%), urine (5·2%) and respiratory (0·6%).

Associations of non-healthcare risk factors with case status

Obesity, ever smoking and summer and autumn seasons were associated in both unadjusted and adjusted analyses with HA- and CA-MRSA and SSTI compared to controls (Table 2). There were no substantive changes in point estimates when CSD was added to the model (data not shown). An urban living environment was associated with both HA- and CA-MRSA, but not with SSTI. More deprived places (i.e. higher CSD) were also associated with higher odds of HA- and CA-MRSA (OR 1·2 and 1·1 per quartile, respectively), but not SSTI.

Associations of antibiotic administration with case status

MRSA and SSTI cases were significantly more likely than controls to have an antibiotic order in the 2 years before diagnosis (Table 1). Four or more antibiotic orders was associated with nearly a tenfold increase in the odds of HA-MRSA and a fourfold increase in the odds of CA-MRSA compared to those who received no antibiotics (Table 2). In particular, the more antibiotics prescribed in the 30–365 days before diagnosis of CA-MRSA, the higher the odds of CA-MRSA in both unadjusted and adjusted analyses. Most classes of antibiotics commonly prescribed in the outpatient setting, with the exception of macrolides, were independently associated with increased risk of CA-MRSA. The associations between antibiotic prescribing and CA-MRSA remained when antibiotic prescriptions were assessed in the 90–365 days before diagnosis, suggesting the association is not only due to protopathic bias from antibiotics for undiagnosed CA-MRSA infection (data not shown).

Associations of previous SSTIs with case status

On the day of diagnosis, the majority of CA-MRSA cases presented with a SSTI ($n=1028$, 60%), compared to a quarter of HA-MRSA cases ($n=429$), all SSTI cases (by definition) and less than 2% of controls. In the year before MRSA or SSTI diagnosis or visit date, SSTI diagnosis in all time windows was strongly associated with case status (Fig. 3). Previous SSTI was a risk factor for subsequent SSTI with a linear decline in odds as time from diagnosis increased. In contrast, the associations of previous SSTI with subsequent diagnosis of both HA and CA-MRSA were nonlinear and stronger than these were for subsequent diagnosis of SSTI.

Associations of selected healthcare risk factors with case status

In unadjusted analysis, in the 2 years preceding diagnosis, a visit for most respiratory tract, cardiac, and skin conditions was associated with HA- and CA-MRSA and SSTI case status (Table 3). After adjustment for antibiotic administration, only SSTI visit remained associated in all three comparisons. Asthma and chronic obstructive pulmonary disease (COPD) remained associated with both HA-MRSA and SSTI after adjustment. Hypertension, diabetes, heart disease, and kidney disease were each risk factors for HA-MRSA and SSTIs, but not for CA-MRSA, suggesting that CA-MRSA cases were healthier than HA-MRSA cases, SSTIs and controls. In adjusted analysis, antibiotic orders in the previous 2 years for several acute respiratory tract conditions and SSTIs were strongly associated with MRSA and

Table 1. *Patient demographic and clinical characteristics*

Characteristic	HA-MRSA ($n=1506$)	CA-MRSA ($n=1713$)	SSTI ($n=3336$)	Control ($n=3336$)
Male sex	766 (51)	803 (47)	1626 (49)	1626 (49)
Age in years at infection or visit				
Median	61·1	24·0	42·0	42·0
<7	139 (9)	319 (19)	475 (14)	475 (14)
7 to <19	72 (5)	407 (24)	495 (15)	497 (15)
19 to <46	246 (16)	545 (32)	820 (25)	816 (25)
46 to <62	313 (21)	247 (14)	583 (18)	583 (18)
62 to <75	289 (19)	111 (6)	423 (13)	487 (14)
⩾75	447 (30)	84 (5)	540 (16)	498 (15)
Race/ethnicity				
White[a]	1463 (96)	1611 (94)	3199 (96)	3165 (95)
Black	28 (2)	53 (3)	51 (2)	64 (2)
Hispanic	15 (1)	35 (2)	59 (2)	64 (2)
Other	11 (1)	13 (1)	27 (1)	42 (1)
Unknown	4 (0)	1 (0)	0	3 (0)
Adult BMI[b]	($n=1306$)	($n=1023$)	($n=2418$)	($n=2418$)
Normal	329 (25)	222 (22)	601 (25)	523 (22)
Overweight	284 (22)	247 (24)	1012 (42)	697 (29)
Obese	527 (40)	398 (39)	372 (15)	819 (34)
Missing	167 (13)	156 (15)	372 (15)	379 (16)
Child BMI[c]	($n=101$)	($n=578$)	($n=805$)	($n=918$)
Normal	49 (49)	236 (41)	352 (44)	488 (53)
Overweight	14 (14)	109 (19)	128 (16)	107 (12)
Obese	28 (28)	103 (18)	124 (15)	95 (10)
Missing	10 (10)	130 (23)	201 (25)	228 (25)
Smoking[d]				
Never	1075 (71)	1426 (83)	1540 (90)	3025 (91)
Season[e]				
Winter	371 (24)	384 (22)	769 (23)	891 (27)
Spring	338 (22)	306 (18)	753 (23)	815 (24)
Summer	397 (26)	462 (27)	953 (29)	783 (24)
Autumn	415 (27)	561 (33)	861 (26)	847 (25)
Community type[f]				
City	240 (16)	255 (15)	376 (11)	327 (10)
Borough	386 (26)	542 (32)	840 (25)	854 (26)
Township	700 (46)	732 (43)	1774 (53)	1802 (55)
Missing[g]	180 (12)	183 (11)	414 (14)	353 (11)
Socioeconomic deprivation[h]				
Median	−4·1	−4·3	−5·0	−5·0
Any antibiotic prescription in previous 2 years	1176 (76)	1246 (73)	2341 (70)	1720 (52)
Antibacterial prescriptions[i]				
No prescription	582 (39)	810 (47)	1712 (51)	2228 (67)
Carbapenems	8 (1)	0	2 (<1)	0
Cephalosporins	394 (26)	315 (18)	502 (15)	220 (7)
Clindaymycin	67 (4)	34 (2)	64 (2)	20 (1)
Linezolid	7 (<1)	0	1 (<1)	1 (<1)
Macrolides	220 (14)	237 (14)	460 (14)	215 (9)
Penicillins	358 (24)	442 (26)	741 (22)	531 (16)
Penicillin	12 (1)	12 (1)	26 (1)	22 (1)
Amino	216 (14)	347 (20)	553 (17)	404 (12)
Anti-staphylococcal	8 (1)	2 (<1)	4 (<1)	2 (<1)
β-lactam/β-lactamase inhibitors	176 (12)	159 (9)	267 (8)	153 (5)

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Table 1 (*cont.*)

Characteristic	HA-MRSA ($n=1506$)	CA-MRSA ($n=1713$)	SSTI ($n=3336$)	Control ($n=3336$)
		112 (7)		
Quinolones	337 (22)		242 (7)	167 (5)
Tetracyclines	85 (6)	79 (5)	157 (5)	84 (3)
TMP/SMX	171 (11)	174 (10)	225 (7)	136 (4)
Vancomycin	73 (5)	2 (<1)	19 (1)	9 (<1)
Antibacterial drug prescriptions[j]				
0	582 (39)	810 (47)	1705 (51)	2228 (67)
1	289 (19)	396 (23)	783 (23)	639 (19)
2–3	331 (22)	344 (20)	613 (18)	349 (10)
⩾4	304 (20)	163 (10)	235 (7)	120 (4)

Data are no. (%) of patients, unless otherwise indicated.

BMI, Body mass index; CA-MRSA, community-associated methicillin-resistant *S. aureus*; HA-MRSA, healthcare-associated MRSA; SSTI, skin and soft tissue infection; TMP/SMX, trimethoprim/sulfamethoxzole.

[a] White, non-Hispanic.

[b] Body mass index was categorized as normal (<25 kg/m²), overweight (25–29·9 kg/m²) and obese (⩾30 kg/m²) for persons aged 18–59·9 years the most recent height and a weight within 2 years of the encounter/visit were used; for persons aged ⩾60 years the most recent height and weight within 1 year of encounter/visit were used. Missing either due to the absolute value of the *z* score being >5 or if a height and weight were not recorded in the vitals table within the 3 months before the diagnosis or visit.

[c] Body mass index *z* scores for children aged 2–18 years were calculated using the 2000 CDC Growth Reference by implementing the zanthro function in Stata version 11 (normal, *z* score <85th percentile; overweight, 85th percentile ⩽*z* score <95th percentile; obese, *z* score ⩾95th percentile).

[d] Based on presence of ICD-9 codes 305.1 (tobacco use disorder), V15.82 (history of tobacco use), 649.0 (tobacco use complicating pregnancy) or CPT codes 99 406 or 99 407 (smoking cessation counselling).

[e] Season of onset: spring (March–May), summer (June–August), autumn (September–November), winter (December–February).

[f] Census tracts were assigned to patients in cities due to the large geographical area and heterogeneous community of some cities.

[g] The overall geocoding rate was 88·6%, non-geocoding patients could not be assigned a community type or a community socioeconomic deprivation score and thus were omitted from multilevel analysis.

[h] Community socioeconomic deprivation was assigned at the township, borough or census tract-level and is based on six indicators (all percentages) derived from US Census 2000 data: combined less than high school education, not in the labour force, in poverty, on public assistance, civilian unemployment, and does not own a car; a higher score represents a more deprived community.

[i] Order for an antimicrobial prescription in the 30–365 days before infection or visit.

[j] Count of antimicrobial prescription order in the 30–365 days before infection or visit.

SSTI (Table 4). The number of previous healthcare visits also increased the odds of HA (OR 1·10, 95% CI 1·10–1·12) and, to a lesser extent, CA-MRSA (OR 1·01, 95% CI 1·0–1·02).

DISCUSSION

This study revealed a substantial increase in CA-MRSA, a stabilization of HA-MRSA, and a modest increase in SSTI incidence over a 10-year period in a large general population-based sample in the USA. The 2009 CA-MRSA incidence of 198/100 000 person-years in our combined urban and rural cohort is similar to previous estimates, which were derived mainly from urban areas [8, 11, 15, 16, 25], suggesting that the incidence CA-MRSA in rural areas may be greater than currently appreciated. The incidence of CO-SSTI was consistently 25 times higher than that of CA-MRSA. Previous work on MRSA infection has not included a SSTI comparison group and has generally used only one method to identify MRSA cases, while we used two methods to enhance case detection [8, 10, 14, 16, 17, 25–29]. We confirmed previous reported, and identified new risk factors for CA-MRSA. Obesity, smoking and use of antibiotics conferred particular risk. The finding that SSTI as long as 1 year before was an independent risk factor for subsequent MRSA diagnosis suggests either that

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Table 2. *Associations of demographic and clinical characteristics with MRSA and SSTI case status compared to controls, in multinomial and binomial logistic regression models, respectively*[a]

	HA-MRSA		CA-MRSA		SSTI	
Characteristic	Crude OR (95% CI)	Adjusted OR[b] (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Male sex	1·1 (1·0–1·2)	1·0 (0·9–1·2)	0·9 (0·8–1·0)	0·9 (0·8–1·0)	1·0 (0·9–1·1)	1·0 (0·9–1·1)
Age in years at infection or visit						
<7	0·5 (0·4–0·7)	0·8 (0·6–1·0)	1·6 (1·3–1·9)	1·9 (1·6–2·4)	1·0 (0·8–1·2)	1·3 (1·1–1·5)
7 to <19	0·3 (0·2–0·4)	0·4 (0·3–0·5)	1·9 (1·6–2·4)	2·3 (1·9–2·8)	1·0 (0·8–1·2)	1·2 (1·0–1·5)
19 to <46	0·6 (0·5–0·7)	0·6 (0·5–0·7)	1·6 (1·3–1·9)	1·6 (1·3–1·9)	1·0 (0·9–1·2)	1·0 (0·9–1·2)
46 to <62	Reference	Reference	Reference	Reference	Reference	Reference
62 to <75	1·2 (0·9–1·4)	1·2 (1·0–1·5)	0·6 (0·4–0·7)	0·6 (0·4–0·7)	0·9 (0·8–1·1)	1·0 (0·8–1·2)
⩾75	1·7 (1·4–2·0)	2·0 (1·7–2·4)	0·4 (0·3–0·5)	0·4 (0·3–0·6)	1·1 (0·9–1·3)	1·2 (1·0–1·5)
Race/ethnicity						
White[c]	Reference	Reference	Reference	Reference	Reference	Reference
Black	0·9 (0·6–1·5)	1·4 (0·9–2·2)	1·6 (1·1–2·4)	1·3 (0·9–1·8)	0·8 (0·5–1·1)	0·8 (0·5–1·1)
Hispanic	0·5 (0·3–0·9)	0·8 (0·4–1·4)	1·1 (0·7–1·7)	0·8 (0·5–1·3)	0·9 (0·7–1·4)	1·0 (0·7–1·4)
Other	0·6 (0·3–1·1)	0·9 (0·5–1·8)	0·6 (0·3–1·1)	0·5 (0·3–1·0)	0·6 (0·4–1·0)	0·7 (0·4–1·1)
Adult BMI[d]						
Normal	Reference	Reference	Reference	Reference	Reference	Reference
Overweight	0·6 (0·5–0·8)	0·6 (0·5–0·8)	0·8 (0·6–0·9)	1·0 (0·8–1·2)	1·7 (1·2–2·2)	1·5 (1·1–2·1)
Obese	1·3 (1·1–1·5)	1·1 (0·9–1·3)	1·3 (1·1–1·5)	1·3 (1·1–1·6)	1·8 (1·3–2·4)	1·7 (1·2–2·3)
Child BMI[e]						
Normal	Reference	Reference	Reference	Reference	Reference	Reference
Overweight	0·8 (0·4–1·4)	1·0 (0·5–1·8)	1·4 (1·0–1·9)	1·5 (1·1–2·1)	1·2 (0·9–1·6)	1·2 (0·9–1·7)
Obese	2·2 (1·3–3·6)	2·2 (1·3–3·8)	1·5 (1·1–2·0)	1·6 (1·2–2·3)	1·4 (1·0–1·8)	1·4 (1·0–1·9)
Smoking						
Ever	4·0 (3·4–4·7)	3·9 (3·3–3·6)	2·0 (1·6–2·3)	2·4 (2·0–2·8)	2·4 (2·0–2·7)	2·4 (2·2–3·0)
Season[f]						
Winter	Reference	Reference	Reference	Reference	Reference	Reference
Spring	1·0 (0·8–1·2)	1·0 (0·8–1·2)	0·9 (0·7–1·0)	0·9 (0·7–1·1)	1·1 (0·9–1·2)	1·1 (0·9–1·2)
Summer	1·2 (1·0–1·4)	1·3 (1·1–1·5)	1·4 (1·2–1·6)	1·3 (1·1–1·6)	1·4 (1·2–1·6)	1·4 (1·2–1·6)
Autumn	1·2 (1·0–1·4)	1·2 (1·0–1·4)	1·5 (1·3–1·8)	1·5 (1·3–1·8)	1·2 (1·0–1·3)	1·2 (1·0–1·3)
Community type[g]						
Township	Reference	Reference	Reference	Reference	Reference	Reference
Borough	1·2 (1·0–1·4)	1·2 (1·0–4·0)	1·6 (1·3–1·9)	1·5 (1·2–1·8)	1·1 (1·0–1·2)	1·1 (0·9–1·2)
City[h]	2·0 (1·6–2·5)	2·1 (1·6–2·6)	2·1 (1·6–2·6)	1·8 (1·4–2·3)	1·2 (1·0–1·5)	1·2 (1·0–1·4)
Socioeconomic deprivation, per quartile[i]	1·2 (1·1–1·3)	1·2 (1·1–1·3)	1·2 (1·1–1·3)	1·1 (1·1–1·2)	1·1 (1·0–1·1)	1·1 (1·0–1·1)
Any antibiotic prescription in previous 2 years	3·0 (2·7–3·5)	2·9 (2·6–3·4)	2·5 (2·2–2·8)	2·4 (2·1–2·8)	2·2 (2·0–2·4)	2·1 (1·9–2·3)

Table 2 (*cont.*)

Characteristic	HA-MRSA		CA-MRSA		SSTI	
	Crude OR (95% CI)	Adjusted OR[b] (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Antibiotic prescription[j]						
No prescription	Reference	Reference	Reference	Reference	Reference	Reference
Cephalosporins	6·9 (5·7–8·3)	3·4 (2·8–4·2)	3·9 (3·3–4·8)	2·8 (2·3–3·4)	2·9 (2·5–3·5)	2·1 (1·8–2·5)
Clindamycin	12·8 (7·7–21·3)	4·2 (2·4–7·4)	4·7 (2·7–8·2)	2·6 (1·4–4·6)	4·2 (2·5–6·9)	2·3 (1·4–3·9)
Macrolides	2·7 (2·2–3·3)	1·1 (0·9–1·4)	2·1 (1·7–2·5)	1·2 (1·0–1·4)	1·9 (1·6–2·2)	1·2 (1·0–1·4)
Penicillins	2·6 (2·3–3·0)	1·4 (1·2–1·7)	2·3 (2·0–2·7)	1·3 (1·1–1·5)	1·8 (1·6–2·1)	1·4 (1·2–1·6)
Penicillin	2·1 (1·0–4·2)	1·8 (0·8–3·9)	1·5 (0·8–3·0)	0·7 (0·3–1·4)	1·6 (0·9–2·9)	0·9 (0·5–1·7)
Amino	2·0 (1·7–2·5)	1·2 (1·0–1·5)	2·4 (2·0–2·8)	1·3 (1·1–1·6)	1·8 (1·5–2·0)	1·3 (1·1–1·5)
Antistaphylococcal	15·3 (3·4–72·4)	3·2 (0·6–18·6)	2·8 (0·4–19·6)	1·1 (0·1–8·8)	2·6 (0·5–14·2)	1·1 (0·2–7·0)
β-lactam/β-lactamase inhibitors	4·4 (3·5–5·6)	1·7 (1·3–2·2)	2·9 (2·3–3·6)	1·3 (1·0–1·7)	2·3 (1·9–2·9)	1·5 (1·2–1·8)
Quinolones	7·7 (6·3–9·5)	2·4 (1·9–3·0)	1·8 (1·4–2·4)	1·5 (1·1–2·2)	1·9 (1·5–2·3)	1·1 (0·9–1·4)
Tetracyclines	3·9 (2·8–5·3)	1·5 (1·1–2·2)	2·6 (1·9–3·6)	1·6 (1·1–2·2)	2·4 (1·8–3·2)	1·7 (1·3–2·2)
TMP/SMX	4·8 (3·8–6·1)	1·7 (1·3–2·2)	3·5 (2·8–4·5)	2·1 (1·6–2·7)	2·2 (1·7–2·7)	1·4 (1·1–1·7)
Vancomycin	31·1 (15·5–63)	3·3 (1·5–7·2)	0·6 (0·1–2·8)	0·2 (0·04–1·0)	2·7 (1·2–6·1)	1·1 (0·5–2·6)
Antibiotic prescription[k]						
0	Reference	Reference	Reference	Reference	Reference	Reference
1	1·7 (1·5–2·0)	1·7 (1·4–2·0)	1·7 (1·5–2·0)	1·7 (1·4–2·0)	1·6 (1·4–1·8)	1·5 (1·4–1·7)
2–3	3·6 (3·0–4·3)	3·6 (3·0–4·4)	2·7 (2·3–3·2)	2·5 (2·0–3·0)	2·2 (1·9–2·6)	2·1 (1·8–2·5)
$\geqslant$4	9·7 (7·7–12·2)	9·0 (7·1–11·4)	3·7 (2·9–4·8)	3·7 (2·9–4·8)	2·6 (2·1–3·3)	2·4 (1·9–3·1)

Data are no. (%) of patients, unless otherwise indicated.

BMI, Body mass index; CI, confidence interval; CA-MRSA; community-associated methicillin-resistant *S. aureus*; HA-MRSA; healthcare-associated MRSA; OR, odds ratio; SSTI, skin and soft tissue infection; TMP/SMX, trimethoprim/sulfamethoxzole.

[a] SSTI cases and controls were frequency-matched to MRSA cases on age, sex, and year of diagnosis or outpatient encounter.

[b] Adjusted for category [$<$7, 7 to $<$19, 19 to $<$45, 46 to $<$62 (ref.), 62 to $<$75 and $\geqslant$75 years), sex, race/ethnicity, ever-smoking status.

[c] White, non-Hispanic.

[d] Body mass index was categorized as normal ($<$25 kg/m^2), overweight (25–29·9 kg/m^2) and obese ($\geqslant$30 kg/m^2) for persons aged 18–59·9 years the most recent height and a weight within 2 years of the encounter/visit were used; for persons aged $\geqslant$60 years the most recent height and weight within 1 year of encounter/visit were used. Missing either due to the absolute value of the *z* score being $>$5 or if height and weight were not recorded in the vitals table within the 3 months before the diagnosis or visit.

[e] Body mass index *z* scores for children aged 2–18 years were calculated using the 2000 CDC Growth Reference by implementing the zanthro function in Stata version 11 (normal, *z* score $<$85th percentile; overweight, 85th percentile $\leqslant$*z* score $<$95th percentile; obese, *z* score $\geqslant$95th percentile.

[f] Season of onset: spring (March–May), summer (June–August), autumn (September–November), winter (December–February).

[g] The overall geocoding rate was 88·6%, non-geocoding patients could not be assigned a community type or a community socioeconomic deprivation score and thus were omitted from multilevel analysis.

[h] Census tracts were assigned to patients in cities due to the large geographical area and heterogeneous community of some cities.

[i] ORs for socioeconomic deprivation are quartile increase in level; a higher quartile represents a more deprived community.

[j] Order for an antimicrobial prescription in the 30–365 days before infection or visit, these are additionally adjusted for all other antibiotic classes in the table. Data on linezolid is not presented due to small cell sizes.

[k] Count of antimicrobial prescription order in the 30–365 days before infection or visit.

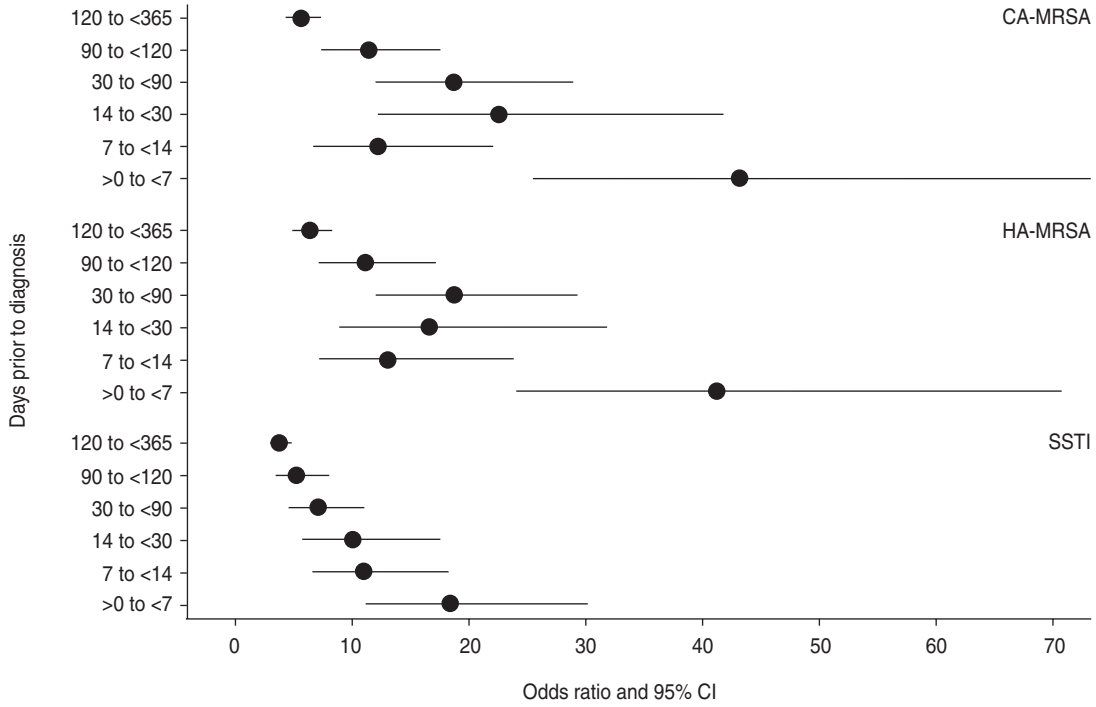

Fig. 3. Adjusted odds ratios for skin and soft tissue infection in the year preceding diagnosis, comparing CA- and HA-MRSA and SSTI cases to controls. SSTIs include: cellulitis and abscess, carbuncle and furuncle, erysipelas, impetigo, and unspecified local infection of skin and subcutaneous tissue. CA-MRSA, Community-associated MRSA; CI, confidence interval; HA-MRSA, healthcare-associated MRSA; SSTI, skin and soft tissue infection.

MRSA goes undiagnosed for an extended time or that compromised skin is a long-term risk factor for MRSA.

The results suggest that CA-MRSA cases were healthier than the other two infection groups and even controls, which could be due, in part, to the stringent CA-MRSA definition based on that of the CDC. For example, chronic kidney disease, diabetes, and some cardiac conditions were risk factors for HA-MRSA and SSTIs, but protective factors for CA-MRSA. This result may indicate that the CDC case definition for CA-MRSA may be too restrictive, leading to the study of a highly selected, very healthy group of patients due to misclassification of CA-MRSA as HA-MRSA cases. This misclassification may lead to underestimation of the burden of CA-MRSA infection.

Considering non-healthcare risk factors, obesity was a risk factor in paediatric patients for both HA- and CA-MRSA, which to our knowledge has not been previously reported. Obesity was also associated with CA-MRSA infection in adults [30–32]. The literature is inconsistent regarding smoking as a risk for MRSA infection [20, 29, 30, 32]. Herein, cigarette smoking was identified as an independent risk factor for both HA- and CA-MRSA, even after adjustment for comorbidities and antibiotics. Summer and autumn were associated with increased odds of HA- and CA-MRSA consistent with previous studies [4, 11, 33]. CSD was associated with both HA-MRSA [34] and CA-MRSA infection. Residence in a city has been associated with MRSA infection [3, 15], attributed to injecting drug use (IDU) [25], crowding, and lower individual-level socioeconomic status [2]. Few previous studies have included non-urban areas [3, 4, 29]; their inclusion in the current study allowed us to identify increased risk in small towns compared to rural areas.

Consistent with previous studies, the majority of our CA-MRSA cases [9, 11, 16, 20, 26, 35] and many HA-MRSA cases presented with SSTIs, but HA-MRSA also presented with pneumonia, bacteraemia, endocarditis, and SSTIs, especially chronic skin ulcers and wound infections [6, 16, 25, 29, 35]. We also identified evidence of previous SSTI as a risk factor for subsequent MRSA infection, even controlling for antibiotic use. In the 30 days before diagnosis, this is probably due to the use of SSTI as a preliminary diagnosis in patients subsequently diagnosed with MRSA; however, as discussed

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Table 3. *Associations of acute and chronic conditions in the 2 years preceding MRSA and SSTI with MRSA and SSTI case status compared to controls, in multinomial and binomial logistic regression models, respectively*[a]

	Unadjusted analysis[b]						Adjusted analysis[c]					
	HA-MRSA		CA-MRSA		SSTI		HA-MRSA		CA-MRSA		SSTI	
Condition	Crude OR (95% CI)	*P*	Crude OR (95% CI)	*P*	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Respiratory tract												
Acute												
Bronchitis	1·9 (1·7–2·3)	<0·001	1·4 (1·2–1·6)	<0·001	1·4 (1·3–1·6)	<0·001	1·1 (1·0–1·4)	0·14	1·1 (0·9–1·3)	0·52	1·0 (0·9–1·2)	0·96
Otitis media	0·9 (0·7–1·2)	0·53	1·9 (1·5–2·3)	<0·001	1·3 (1·0–1·5)	0·01	1·0 (0·7–1·3)	0·88	1·0 (0·8–1·3)	0·97	0·9 (0·8–1·1)	0·50
Pharyngitis	0·6 (0·5–0·8)	<0·001	1·5 (1·3–1·8)	<0·001	1·3 (1·2–1·5)	<0·001	0·7 (0·6–0·9)	0·01	0·8 (0·7–1·0)	0·01	1·0 (0·9–1·2)	0·60
Rhinosinusitis	0·9 (0·7–1·0)	0·08	1·5 (1·3–1·7)	<0·001	1·4 (1·3–1·6)	<0·001	0·6 (0·5–0·7)	<0·001	0·8 (0·7–1·0)	0·01	0·9 (0·8–1·1)	0·40
Streptococcal sore throat	0·7 (0·4–1·0)	0·07	1·8 (1·3–2·5)	<0·001	1·4 (1·0–1·8)	0·03	0·9 (0·6–1·5)	0·81	0·9 (0·7–1·3)	0·71	1·1 (0·8–1·4)	0·72
Upper respiratory infection	1·1 (0·9–1·2)	0·54	1·6 (1·3–1·8)	<0·001	1·3 (1·2–1·5)	<0·001	1·1 (0·9–1·3)	0·54	1·0 (0·8–1·2)	0·92	1·1 (1·0–1·3)	0·15
Chronic												
Asthma	2·1 (1·8–2·6)	<0·001	1·6 (1·3–1·9)	<0·001	1·5 (1·3–1·8)	<0·001	1·8 (1·5–2·2)	<0·001	1·1 (0·9–1·4)	0·21	1·2 (1·0–1·4)	0·04
COPD	4·0 (3·5–4·6)	<0·001	1·1 (1·0–1·3)	0·20	1·5 (1·4–1·7)	<0·001	2·7 (2·3–3·1)	<0·001	1·0 (0·8–1·1)	0·57	1·2 (1·1–1·4)	0·002
Lung diseases	13·7 (11·2–16·8)	<0·001	0·7 (0·5–1·0)	0·05	1·6 (1·3–2·0)	<0·001	8·5 (6·8–10·5)	<0·001	0·9 (0·6–1·3)	0·52	1·2 (0·9–1·5)	0·22
Rhinosinusitis	3·2 (2·4–4·4)	<0·001	1·3 (0·9–1·9)	0·19	1·6 (1·2–2·2)	0·002	2·2 (1·6–3·0)	<0·001	1·0 (0·6–1·4)	0·80	1·2 (0·9–1·6)	0·24
Cardiac												
Heart diseases	5·6 (4·8–6·5)	<0·001	0·4 (0·3–0·5)	<0·001	1·3 (1·1–1·5)	<0·001	3·9 (3·2–4·6)	<0·001	0·7 (0·5–0·9)	0·01	1·2 (1·0–1·4)	0·08
Hypertension	2·7 (2·4–3·1)	<0·001	0·4 (0·4–0·5)	<0·001	1·1 (1·0–1·3)	0·01	1·5 (1·3–1·8)	<0·001	0·7 (0·6–0·9)	<0·001	1·1 (1·0–1·3)	0·11
Lipid disorders	1·9 (1·7–2·2)	<0·001	0·5 (0·4–0·6)	<0·001	1·2 (1·1–1·3)	<0·001	0·9 (0·8–1·1)	0·27	0·7 (0·6–0·9)	<0·001	1·2 (1·1–1·4)	0·002
Skin and soft tissue												
Carbuncle/furuncle[d]	5·9 (4·0–8·8)	<0·001	10·1 (7·0–14·6)	<0·001	3·8 (2·6–5·6)	<0·001	4·7 (3·1–7·0)	<0·001	6·8 (4·7–10·0)	<0·001	2·5 (2·1–3·0)	<0·001
Cellulitis/abscess[d]	5·6 (4·6–6·8)	<0·001	3·4 (2·8–4·2)	<0·001	3·1 (2·6–3·8)	<0·001	3·5 (2·8–4·3)	<0·001	3·0 (2·4–3·7)	<0·001	2·7 (1·8–3·9)	<0·001
Chronic ulcer of skin	42·3 (26·5–68)	<0·001	4·4 (2·5–7·6)	<0·001	2·9 (1·7–4·9)	<0·001	26·9 (16·7–43·4)	<0·001	6·7 (2·1–2·7)	<0·001	2·1 (1·3–3·7)	0·01
Other												
Chronic kidney disease	6·3 (5·0–8·0)	<0·001	0·2 (0·1–0·4)	<0·001	1·6 (1·3–2·1)	<0·001	4·1 (3·1–5·3)	<0·001	0·4 (0·2–0·8)	0·01	1·5 (1·1–1·9)	0·01
Diabetes	4·0 (3·4–4·6)	<0·001	0·6 (0·5–0·8)	<0·001	1·6 (1·4–1·9)	<0·001	2·6 (2·2–3·1)	<0·001	1·0 (0·8–1·3)	0·82	1·5 (1·3–1·8)	<0·001

CA-MRSA, Community-associated methicillin-resistant *S. aureus*; COPD, chronic obstructive pulmonary disease; CI, confidence interval; HA-MRSA; healthcare-associated MRSA; OR, odds ratio; SSTI, skin and soft tissue infection.

[a] SSTI cases and controls were frequency-matched to MRSA cases on age, sex, and year of diagnosis or outpatient encounter.

[b] Models the association between the condition identified in inpatient, outpatient, or emergency department encounters, or on problem list or in medications table (excluding antibiotic prescriptions) in the 2 years preceding diagnosis or visit and case status.

[c] Adjusted for age category [<7, 7 to <19, 19 to <45, 46 to <62 (ref.), 62 to <75 and ⩾75 years], sex, race/ethnicity, ever-smoking status, and any antibiotic order in the previous 2 years.

[d] The 30 days preceding infection or visit were excluded for carbuncle, furuncle, cellulitis or abscess to avoid protopathic bias.

Table 4. *Adjusted associations of antibiotic orders for acute and chronic conditions in the 2 years preceding MRSA and SSTI, compared to controls, in multinomial and binomial logistic regression models, respectively*

	HA-MRSA		CA-MRSA		SSTI	
Condition	Adjusted OR[a] (95% CI)	*P*	Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Respiratory tract						
Acute						
Bronchitis	1·3 (1·1–1·6)	0·003	1·3 (1·1–1·6)	0·004	1·3 (1·1–1·5)	<0·001
Otitis media	1·4 (1·0–2·0)	0·03	1·4 (1·1–1·8)	0·004	1·3 (1·0–1·6)	0·06
Pharyngitis	1·2 (0·9–1·7)	0·28	1·0 (0·7–1·3)	0·83	1·0 (0·8–1·3)	0·71
Rhinosinusitis	1·0 (0·8–1·1)	0·66	1·3 (1·1–1·5)	<0·001	1·4 (1·2–1·5)	<0·001
Streptococcal sore throat	1·1 (0·7–1·9)	0·70	1·2 (0·9–1·7)	0·29	1·5 (1·1–2·0)	0·01
Upper respiratory infection	1·7 (1·2–2·4)	0·002	1·1 (0·8–1·6)	0·54	1·4 (1·0–1·8)	0·01
Chronic						
Asthma	4·3 (2·2–8·2)	<0·001	1·4 (0·6–3·1)	0·39	2·1 (1·2–4·0)	0·01
COPD	3·2 (2·2–4·6)	<0·001	1·6 (1·1–2·4)	0·02	1·5 (1·1–2·2)	0·01
Lung diseases	2·6 (1·6–4·4)	<0·001	1·7 (0·9–3·6)	0·12	1·1 (0·6–1·9)	0·18
Rhinosinusitis	1·5 (0·9–2·7)	0·13	1·1 (0·6–2·0)	0·65	1·1 (0·6–1·7)	0·63
Skin and soft tissue						
Carbuncle/furuncle[b]	8·9 (5·7–14·0)	<0·001	17·9 (11·8–27)	<0·001	4·7 (3·0–7·2)	<0·001
Cellulitis/abscess[b]	5·2 (4·2–6·6)	<0·001	6·7 (5·4–8·3)	<0·001	4·2 (3·4–5·2)	<0·001
Chronic ulcer of skin	16·6 (7·1–38·8)	<0·001	6·5 (2·4–17·4)	<0·001	3·4 (1·4–8·4)	0·003

CA-MRSA, Community-associated methicillin-resistant *S. aureus*; COPD, chronic obstructive pulmonary disease; CI, confidence interval; HA-MRSA; healthcare-associated MRSA; OR, odds ratio; SSTI, skin and soft tissue infection.

[a] Models the association between any antibiotic order for the condition in the 2 years preceding diagnosis or visit and case status; adjusted for age category (<7, 7 to <19, 19 to <45, 46 to <62 (ref.), 62 to <75 and ⩾75 years], sex, race/ethnicity, ever-smoking status.

[b] The 30 days preceding infection or visit were excluded for carbuncle, furuncle, cellulitis or abscess to avoid protopathic bias.

previously, the association remained strong in all earlier time windows out to 1 year before MRSA diagnosis.

Our data suggest that previous antibiotic use is a risk factor for MRSA in both sexes and across the age range. Although often assumed, this relationship has rarely been rigorously assessed [36, 37]. In accord with two English studies, the relationship between antibiotic use and MRSA varied by antibiotic class and number of times ordered [14, 30]. No conditions, other than SSTI, were significantly associated with CA-MRSA after accounting for antibiotic administration. There were many antibiotics administered for conditions that are usually caused by viruses (e.g. bronchitis, rhinosinusitis, otitis media) and there was risk of MRSA associated with antibiotic prescriptions for those conditions, providing additional evidence supporting more judicious antibiotic use in the outpatient setting.

MRSA infection may go undiagnosed since previous studies have suggested that empirical treatment or incision and drainage is often sufficient to treat CA-MRSA SSTI [38, 39]. We included a SSTI case group to assess this possibility. As anticipated, similar associations were observed in the SSTI and CA-MRSA groups. We also found COPD, diabetes and skin conditions associated with SSTI, consistent with known risk factors for SSTI [40]. Examination of the similarities and differences in risk factor associations with HA-MRSA, CA-MRSA and SSTIs may support the conclusion that there is undiagnosed MRSA in the SSTI cases.

The strengths of this study include the wealth of longitudinal clinical data available for both paediatric and adult patients. We used two methods to identify MRSA cases with high sensitivity and subgroup analysis that required MRSA cases to have both a positive culture and an ICD-9 code confirming the reported associations. The EHR allowed the careful application of criteria for CA-MRSA classification, identification of patients with SSTIs that might represent undiagnosed MRSA cases, as well as

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comprehensive adjusted analysis, including consideration of antibiotic administration.

This study also had limitations. Molecular typing of isolates was not completed and culture data was not available for every MRSA case, consistent with practice in the community. The EHR did not have information on individual-level socioeconomic status and other CA-MRSA risk factors, such as crowded living conditions, incarceration, IDU, and athlete [1, 2, 27, 41]. It should be noted that adjustment for place-level CSD did not lead to substantive changes in associations.

This study has several important implications. CA-MRSA incidence in a general US population continues to rise, as does SSTI incidence, but less markedly. We identified several opportunities for intervention by identifying modifiable risk factors for CA-MRSA including avoidance of unnecessary antimicrobial prescribing particularly in the setting of upper respiratory tract infection. Finally, the study demonstrates the utility of EHR data for epidemiological research, a practice likely to increase in the future due to incentives provided by the Patient Protection and Affordable Healthcare Act.

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DECLARATION OF INTEREST

None.

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