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BRIEF REPORT

Methicillin-Resistant and Methicillin-Sensitive *Staphylococcus aureus* Hospitalizations: National Inpatient Sample, 2016–2019

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Data from the National Inpatient Sample demonstrate that methicillin-resistant *Staphylococcus aureus* (MRSA)–related septicemia hospitalizations increased from 1.67 (95% CI, 1.63–1.72) to 1.94 (95% CI, 1.88–2.00; $P_{trend} < .001$) discharges per 1000 hospitalizations between 2016 and 2019. Regionally, the trends were similar. Rates of MSSA-related septicemia and pneumonia hospitalizations also increased significantly over this time period.

Keywords. antimicrobial stewardship; methicillin-resistant *Staphylococcus aureus*; methicillin-sensitive *Staphylococcus aureus*; MRSA; MSSA; National Inpatient Sample; NIS.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading cause of health care–associated infections in the United States [1]. After rapidly increasing in the early 2000s [1], MRSA-related hospitalizations and infections decreased from a peak in 2005 [2, 3]. However, after 2012, this decline appears to have slowed considerably [2, 3], and data are lacking in more recent years. Understanding trends in MRSA-related hospitalizations, stratified by type of infection, is important for understanding the population-level impact of prevention initiatives, setting national priorities, such as the National Action Plan Goals, and defining empiric treatment recommendations. Furthermore, because methicillin-susceptible *S. aureus* (MSSA) infections account for substantial morbidity and mortality, tracking trends in hospitalization for these infections is equally important to informing patient care [4]. This study updates estimates of the rate of MRSA- and MSSA-related hospitalizations in the United States from 2016 to 2019.

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METHODS

Hospitalization rates of MRSA-, MSSA-, and overall *S. aureus*–related hospitalizations from 2016 to 2019 were calculated using data from the National Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project of the Agency for Health Research and Quality, similar to prior reports [1, 4, 5]. The NIS includes >7 million inpatient records sampled from nonfederal hospitals in the United States each year. Each record is weighted to produce regional and national estimates of hospitalization and contains up to 30 discharge diagnoses in 2016 and 40 in 2017–2019, which are classified using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). All records containing ≥1 MSSA or MRSA infection code were included: septicemia (A410x), pneumonia (J1521x), cause of disease classified elsewhere (B956x), unspecified site (A490x), and carrier/suspected carriers (Z2232x). Records with multiple *S. aureus* infection codes were counted only once, with preference given to septicemia, followed by pneumonia and other classifications, unspecified sites, and carriers. Hospitalization rates were calculated by dividing the number of *S. aureus*– and MRSA/MSSA-related hospitalizations by the total number of hospitalizations. Regional estimates were calculated by using the subpopulation command under survey design. To account for the possibility that changes in the rates were due to changes in numbers of hospitalization, we also calculated the rate of MRSA-related discharges per capita using population data from the US Census.

To assess whether the epidemiology of MRSA-related skin and soft tissue infections (SSTIs) has changed, the primary diagnoses associated with patients who had a B9562, A4902, or Z22322 code, which are intended to be secondary codes, were evaluated. ICD-10-CM diagnosis codes of SSTIs are listed in Supplementary Table 1. Taylor series linearization was used to estimate standard errors. Logistic regression was used to determine whether the results for each diagnosis exhibited a trend over time. All analyses were performed using Stata MP 15.1 (StataCorp, College Station, TX, USA) and took into account the complex sampling design of the NIS.

RESULTS

While there was no difference between 2016 and 2017 in the overall rate of MRSA-related septicemia hospitalizations, there

Table 1. US Prevalence of MRSA-Related Hospitalizations, 2016–2019

Discharge Diagnosis	Discharges per 1000 Hospitalizations (95% CI)				P_{trend} [a]
	2016	2017	2018	2019	
MRSA septicemia	1.67 (1.63–1.72)	1.65 (1.60–1.70)	1.86 (1.80–1.91)	1.94 (1.88–2.00)	**<.001**
Northeast	1.33 (1.24–1.42)	1.32 (1.24–1.42)	1.49 (1.38–1.60)	1.53 (1.43–1.63)	**.001**
Midwest	1.53 (1.44–1.63)	1.54 (1.43–1.66)	1.75 (1.64–1.87)	1.88 (1.66–1.89)	**<.001**
South	1.90 (1.82–1.99)	1.83 (1.75–1.92)	2.08 (1.98–2.18)	2.21 (2.11–2.31)	**<.001**
West	1.71 (1.60–1.81)	1.71 (1.61–1.81)	1.87 (1.76–1.99)	1.96 (1.85–2.08)	**<.001**
MRSA pneumonia	1.27 (1.21–1.33)	1.25 (1.19–1.31)	1.25 (1.19–1.32)	1.10 (1.05–1.15)	**<.001**
Northeast	1.11 (0.93–1.32)	1.07 (0.87–1.31)	1.06 (0.84–1.33)	0.96 (0.80–1.17)	.322
Midwest	1.18 (1.08–1.29)	1.19 (1.09–1.29)	1.16 (1.05–1.27)	1.05 (0.96–1.15)	.066
South	1.46 (1.36–1.56)	1.43 (1.35–1.52)	1.45 (1.36–1.54)	1.26 (1.18–1.35)	**.010**
West	1.16 (1.08–1.25)	1.13 (1.05–1.22)	1.14 (1.04–1.25)	0.95 (0.88–1.03)	**.001**
SSTIs[b]	1.72 (1.67–1.77)	1.59 (1.54–1.64)	1.45 (1.41–1.50)	1.32 (1.28–1.36)	**<.001**
Northeast	1.51 (1.41–1.61)	1.45 (1.36–1.55)	1.31 (1.22–1.40)	1.19 (1.11–1.28)	**<.001**
Midwest	1.60 (1.51–1.69)	1.47 (1.38–1.56)	1.32 (1.24–1.40)	1.21 (1.13–1.29)	**<.001**
South	1.95 (1.86–2.04)	1.75 (1.67–1.84)	1.64 (1.57–1.72)	1.47 (1.40–1.54)	**<.001**
West	1.60 (1.49–1.71)	1.53 (1.43–1.64)	1.36(1.27–1.46)	1.27 (1.19–1.37)	**<.001**

Bolded *P*-values refer to those that are significant.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; SSTIs, skin and soft tissue infections.

[a] *P* values determined with logistic regression for trend from 2016 to 2019.

[b] SSTIs as determined based on the primary International Classification of Diseases, Ninth Revision, Clinical Modification code associated with the other *S. aureus* infection.

was an 18% increase from 2017 to 2019 as discharges per 1000 hospitalizations increased from 1.65 (95% CI, 1.60–1.70) to 1.94 (95% CI, 1.88–2.00). Overall, the increasing trend in septicemia hospitalizations was significant ($P_{trend} < .001$) (Table 1). Regionally, the trends were largely similar, except in the South, where MRSA-related septicemia hospitalizations decreased between 2016 and 2017 but increased 21% from 2017 to 2019. In 2019, the rate of MRSA-related septicemia hospitalizations was highest in the South (2.21; 95% CI, 2.11–2.31) and lowest in the Northeast (1.53; 95% CI, 1.43–1.63). Rates of MRSA-related pneumonia hospitalizations were also significantly higher in the South; however, between 2018 and 2019, rates decreased 12% nationally, due largely to reductions in the South (–13%) and West (–17%). Discharges per 100 000 population rather than per hospitalization showed similar trends (Supplementary Table 2).

The rate of SSTI hospitalizations that were likely MRSA-related decreased significantly and consistently during the study period, from 1.72 (95% CI, 1.67–1.77) hospitalizations per 1000 discharges in 2016 to 1.32 (95% CI, 1.28–1.36) in 2019 ($P_{trend} < .001$). Overall, the rate of SSTI hospitalizations decreased by 23%. Regionally, trends in reduction in SSTI-related MRSA hospitalizations were similar across regions, though the decreases were lowest in the Northeast and West. While the South had the highest rate in all years, rates in 2019 were more similar across regions than for MRSA-septicemia-related hospitalizations.

Table 2. US Prevalence of MSSA-Related Hospitalizations, 2016–2019

Discharge Diagnosis	Discharges per 1000 Hospitalizations (95% CI)				P_{trend} [a]
	2016	2017	2018	2019	
MSSA septicemia	1.68 (1.64–1.73)	1.83 (1.78–1.88)	2.01 (1.96–2.06)	2.16 (2.10–2.21)	**<.001**
Northeast	1.67 (1.57–1.77)	1.74 (1.64–1.84)	1.94 (1.82–2.06)	2.11 (1.99–2.24)	**<.001**
Midwest	1.69 (1.60–1.78)	1.90 (1.81–2.00)	1.97 (1.88–2.06)	2.18 (2.07–2.29)	**<.001**
South	1.50 (1.44–1.57)	1.63 (1.56–1.70)	1.78 (1.71–1.86)	1.91 (1.83–2.00)	**<.001**
West	2.05 (1.94–2.16)	2.22 (2.10–2.34)	2.55 (2.42–2.68)	2.66 (2.53–2.79)	**<.001**
MSSA pneumonia	0.73 (0.69–0.76)	0.77 (0.74–0.81)	0.79 (0.76–0.83)	0.73 (0.69–0.76)	.845
Northeast	0.68 (0.61–0.76)	0.74 (0.65–0.84)	0.83 (0.75–0.92)	0.73 (0.66–0.81)	.156
Midwest	0.73 (0.66–0.80)	0.77 (0.70–0.84)	0.79 (0.72–0.86)	0.74 (0.68–0.80)	.707
South	0.67 (0.61–0.72)	0.75 (0.70–0.81)	0.73 (0.68–0.78)	0.67 (0.62–0.73)	.920
West	0.89 (0.82–0.97)	0.85 (0.78–0.94)	0.88 (0.81–0.96)	0.82 (0.75–0.89)	.273

Bolded *P*-values refer to those that are significant.

Abbreviation: MSSA, methicillin-sensitive *Staphylococcus aureus*.

[a] *P* values determined with logistic regression for trend from 2016 to 2019.

MSSA-related septicemia hospitalizations increased ~10% per annum across the study period, from 1.68 (95% CI, 1.64–1.73) discharges per 1000 hospitalizations in 2016 to 2.16 (95% CI, 2.10–2.21) discharges per 1000 hospitalizations in 2019 (Table 2). Regionally, increases were most rapid in the West, which had the highest rate and had the largest increase between 2016 and 2018, but by 2019 rates across all regions had increased >25% compared with 2016. Unlike MRSA, the rate of MSSA-related septicemia hospitalizations was lowest in the South. Rates of MSSA-related pneumonia hospitalizations fluctuated but did not increase over the study period (P_{trend} = .845). In 2019, the rate of discharges per 1000 hospitalizations was 0.73 (95% CI, 0.69–0.76), the same rate as in 2016. Regionally, the largest fluctuations were in the Northeast, which increased from 0.68 (95% CI, 0.61–0.76) discharges per 1000 hospitalizations in 2016 to 0.83 (95% CI, 0.75–0.92) in 2018 (P_{trend} = .011), before falling to 0.73 (95% CI, 0.66–0.81) discharges per 1000 hospitalizations. No other region had a statistically significant change over the study period.

DISCUSSION

Using data from the National Inpatient Sample, the largest publicly available all-payer inpatient health care database, which provides regional and national estimates of inpatient hospitalizations, we found that MRSA-related septicemia hospitalizations increased between 2016 and 2019. Prior trends for MRSA-related septicemia hospitalizations showed non–statistically significant increases between 2010 and 2014 [5]. The current estimates from 2016 were only marginally higher than 2014, suggesting that rates have likely increased considerably since 2010. Several recent publications have shown declines in MRSA bloodstream infections between 2005 and 2017, although the rate of reduction had slowed in the latter years [2, 3]. The results here suggest that these trends may have turned around and started to increase again in 2018.

The drivers of increased MRSA-related septicemia hospitalizations are uncertain. While this may reflect flagging efforts to mitigate hospital-acquired transmission, it may also reflect increasing use of vascular devices outside of the hospital. Thus, there is a need for increased attention to approaches to reducing infections both inside and outside of the hospital. An additional consideration is the role of older individuals, who make up an ever-increasing share of the population, and who have higher rates of health care contact. Future studies should examine the role that an aging population may play in transmission and rates of MRSA and infection control policies, and goals need to account and adjust for this potential increase in risk.

While septicemia increased, MRSA-related SSTI hospitalization rates, which fell between 2010 and 2014 [5], continued to fall lower in the current analysis. As most SSTI infections are community-associated and rates are likely influenced by trends in antibiotic use in the community [6], falling rates of MRSA-related SSTIs suggest that efforts to reduce unnecessary antibiotic use may be playing a role in reducing transmission of MRSA in the community. As many patients seek care for cutaneous abscesses in the emergency department (ED) [7] and <5% are admitted [8], falling hospitalization rates could also be due to improved management of SSTIs in the emergency department.

While MRSA continues to be the focus of many antimicrobial stewardship programs and policies at the local and national levels, it is important to note that MSSA bloodstream infections continue to increase and may be more common in some areas than MRSA. As patients with MSSA treated with vancomycin rather than beta-lactam agents have been shown to have worse outcomes [9], excessive focus on MRSA could lead to inappropriate empirical treatment. Clinicians should be aware of local conditions and, where appropriate, utilize rapid molecular tests for MRSA to aid medication administration, particularly in urgent care settings where rapid initiation of the correct antibiotic is crucial.

Though the results are national in scope, the findings are subject to some of the inherent limitations of using large hospitalization databases. The results are based on diagnostic billing codes, which, though widely used, may reflect a bias in reporting and billing for MRSA infections [10, 11]. However, despite expansion of the MRSA codes available in moving from ICD-9 to ICD-10, the similarities in magnitude to prior reports using ICD-9 codes suggest that there has been no significant change in billing practices over time. In addition, recent estimates from the Centers for Disease Control and Prevention suggest that, while previously the relationship between invasive MRSA and ICD codes may not have always been aligned, in recent years they are relatively similar [12]. Finally, the NIS does not note which diagnoses are present on admission, so it is not possible to distinguish between hospital-acquired and community-associated infections.

Though the recent coronavirus disease 2019 pandemic has been a primary focus of policies and health care in general over the last 2 years, the more slow-moving antibiotic resistance crisis continues to slowly undermine the effectiveness of life-saving antibiotics. Tracking trends in these pathogens is crucial to maintaining momentum in controlling the spread of resistance.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Patient consent. The NIS database is a de-identified database that consists of a collection of billing and diagnostic codes used by participating hospitals with the goal of quality control, population monitoring, and tracking procedures. The NIS does not require institutional review board (IRB) approval or exempt determination.

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