National Trends in Ambulatory Visits and Antibiotic Prescribing for Skin and Soft-Tissue Infections

Adam L. Hersh, MD, PhD; Henry F. Chambers, MD; Judith H. Maselli, MSPH; Ralph Gonzales, MD, MSPH

Background: Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) has emerged as a common cause of skin and soft-tissue infections (SSTIs) in the United States. It is unknown whether this development has affected the national rate of visits to primary care practices and emergency departments (EDs) and whether changes in antibiotic prescribing have occurred.

Methods: We examined visits by patients with SSTIs to physician offices, hospital outpatient departments, and EDs using the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey from 1997 to 2005. We estimated annual visit rates for all SSTIs and a subset classified as abscess/cellulitis. For abscess/cellulitis visits, we examined trends in characteristics of patients and clinical settings and in antibiotic prescribing.

Results: Overall rate of visits for SSTIs increased from 32.1 to 48.1 visits per 1000 population (50%; \( P = .003 \) for trend), reaching 14.2 million by 2005. More than 95% of this change was attributable to visits for abscess/cellulitis, which increased from 17.3 to 32.5 visits per 1000 population (88% increase; \( P < .001 \) for trend). The largest relative increases occurred in EDs (especially in high safety-net-status EDs and in the South), among black patients, and among patients younger than 18 years. Use of antibiotics recommended for CA-MRSA increased from 7% to 28% of visits (\( P < .001 \)) during the study period. Independent predictors of treatment with these antibiotics included being younger than 45 years, living in the South, and an ED setting.

Conclusions: The incidence of SSTIs has rapidly increased nationwide in the CA-MRSA era and appears to disproportionately affect certain populations. Although physicians are beginning to modify antibiotic prescribing practices, opportunities for improvement exist, targeting physicians caring for patients who are at high risk.

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TYPHOLOCoccus Aureus is the most commonly identified cause of purulent skin and soft-tissue infections (SSTIs) in the United States.\(^1\,\,^2\) When cellulitis is a dominant feature, Streptococcus pyogenes is also a common cause.\(^3\) During the past several years, community-acquired methicillin-resistant \( S \) \( aureus \) (CA-MRSA) has rapidly emerged as a major pathogen among the SSTIs.\(^2\,\,^4\,\,^8\) In recent studies among ambulatory patients, the proportion of SSTIs caused by CA-MRSA ranges from 45% to 75%.\(^2\,\,^5\,\,^7\,\,^9\)

Studies from single centers or cities have reported that CA-MRSA appears to contribute to an increased incidence of SSTIs, especially purulent abscesses.\(^3\,\,^7\,\,^9\,\,^12\) Increased visit rates were not evident in a study that reported on national trends in ambulatory visits for SSTIs through 2003.\(^13\) However, the impact of CA-MRSA on SSTIs may not have been evident at the national level because this study occurred relatively early in the CA-MRSA epidemic.

Before the emergence of CA-MRSA, empirical therapy with \( \beta \)-lactam antibiotics such as cephalaxin was appropriate for most SSTIs requiring antibiotic therapy because these agents are effective for methicillin-sensitive \( S \) \( aureus \) and \( S \) \( pyogenes \). Now that CA-MRSA accounts for most SSTIs in many communities throughout the country, \( \beta \)-lactam antibiotics may not be appropriate, especially when incision and drainage cannot be performed.\(^3\,\,^14\) In 2006, the Centers for Disease Control and Prevention issued guidelines for empirical antibiotic therapy for suspected CA-MRSA. This therapy includes clindamycin, a combination of trimethoprim and sulfamethoxazole, and tetracyclines.\(^15\)

In this study, we examined the clinical epidemiology of office and emergency department (ED) visits for SSTIs from 1997 through 2005 and further examined whether physicians' antibiotic prescribing practices have been modified in response to the emergence of CA-MRSA.

METHODS

DATA SOURCE

We analyzed public use data from the National Ambulatory Medical Care Survey...
(NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 1997 to 2005. These surveys are conducted annually by the National Center for Health Statistics on a nationally representative sample of patient visits to ambulatory physicians (http://www.cdc.gov/nchs/about/major/ahcd/ahcill.htm). Both surveys include information about the patient’s chief reason for the visit, up to 3 diagnoses based on the International Classification of Diseases, Clinical Modification, Ninth Revision (ICD-9-CM), up to 8 medications prescribed, and patient demographic characteristics.

The NAMCS consists of a probability sample of patient visits to nonfederal, office-based physician practices. The NHAMCS consists of patient visits to hospital-affiliated outpatient departments and EDs. For both surveys, the National Center for Health Statistics weights each patient visit to enable extrapolation to national estimates for all data elements contained in the survey.

STUDY POPULATION

Visits to physicians for SSTIs were identified from 1997 to 2005 from the NAMCS and NHAMCS based on the following ICD-9-CM codes: erysipelas (035), carbuncle/furuncle (680.x), cellulitis/abscess (681.x and 682.x), acute lymphadenitis (683), impetigo (684), skin/subcutaneous infection (686.x), folliculitis (704.8), myositis (728.0), mastitis (611.0 and 771.5), and necrotizing fasciitis (728.86). For inclusion, the visit needed 1 of these diagnoses in any of the 3 diagnosis fields. These conditions were selected on the basis of guideline review and consensus by two of us (A.L.H. and R.G.).

ANALYSIS OF VISITS FOR SSTI

We examined visits for SSTIs in the following 3 categories: (1) all SSTIs, encompassing all of the ICD-9-CM codes identified in the “Study Population” subsection; (2) abscess cellulitis, consisting of codes 681.x and 682.x; and (3) other SSTIs, consisting of the remainder. The abscess cellulitis subcategory was examined independently because we hypothesized that this would account for most of the visits for SSTI; abscess is a commonly recognized clinical manifestation of CA-MRSA. This represents a more discrete population for conducting detailed analysis of trends and practice patterns, thereby enhancing validity. To account for background secular trends in acute ambulatory visits that would be less affected by CA-MRSA, we compared trends in visits for abscess cellulitis with trends in visits for other SSTIs and urinary tract infections as a nondependent equivalent variable.

To estimate the annual number of visits in all ambulatory settings, we combined data from both databases (NAMCS and NHAMCS). We calculated annual visit rates per 1000 population by using estimates of the US population provided by the US Census Bureau. Visit rates were then stratified according to the patient age categories (<18, 18-44, and ≥45 years). We compared visits for abscess cellulitis in 2004 to 2005 with those in 1997 to 1998 in terms of patient demographics, including sex, age, race, ethnicity, US census region, and standardized metropolitan statistical area (SMSA) as a proxy for urban location in office settings vs EDs. The SMSA designation is determined by the US Census Bureau to represent an urban area of at least 50 000 inhabitants and surrounding communities. We combined 2 years at the beginning and end of the study period to increase the sample size for analysis. For visits to EDs, we compared the proportion of visits requiring hospitalization and the proportion that represented a return within 72 hours. In addition, we rated the safety-net status of the ED or the hospital based on the proportion of overall visits where the expected source of payment was Medicaid, self-pay, or no charge or charity as previously applied with the NHAMCS.17,18 High safety-net status was defined as EDs rated in the top 2 quintiles of all EDs; low safety-net status was defined as EDs rated in the bottom 3 quintiles of all EDs.

ANTIBIOTIC PRESCRIBING

To examine temporal patterns of antibiotic prescribing associated with the emergence of CA-MRSA, we measured antibiotic prescription rates specifically for visits concerning abscess cellulitis. To most accurately link the intended purpose of an antibiotic prescription to the SSTI (as opposed to another medical problem), we restricted our sample of visits to those where abscess cellulitis (ICD-9-CM codes 681.x and 682.x) was listed as the principal (first) diagnosis. Furthermore, we excluded visits with conditions that could have potentially influenced the decision to prescribe an antibiotic or influenced the selection of antibiotic (eg, pneumonia, sinusitis, urinary tract infection). To accomplish this, two of us (A.L.H. and R.G.) conducted a manual review of all second and third diagnosis fields. This reduced the sample by 25%. For each year, we measured the proportion of visits where any antibiotic was prescribed and calculated the percentage of antibiotics prescribed in the following classes: penicillins, cephalosporins, fluoroquinolones, tetracyclines, clindamycin, and a combination of trimethoprim and sulfamethoxazole. We excluded antifungals, antivirals, and all topical or ophthalmic formulations. We clustered certain antibiotic classes into the categories of β-lactams, consisting of penicillins and cephalosporins, and antibiotics recommended for CA-MRSA (ARFs), consisting of tetracyclines, clindamycin, a combination of trimethoprim and sulfamethoxazole, vancomycin, and linezolid.19 Because some patients may have been prescribed multiple antibiotics in a single visit, these percentages may sum to greater than 100%.

STATISTICAL ANALYSIS

For each estimate, we calculated 95% confidence intervals (CIs) using commercially available statistical software (SAS, version 9.1 [SAS Institute Inc., Cary, North Carolina], and SUDAAN, version 9.0 [RTI, Research Triangle Park, North Carolina]) to account for the stratified sampling design of the NAMCS and NHAMCS. To assess the significance of changes in visit rates and prescribing patterns over time, we used a weighted linear regression model.19 We evaluated categorical variables with the χ² test. We created a multivariable logistic regression model to identify independent predictors of antibiotic prescribing with ARFs in 2004 to 2005, including patient age, race, setting (ie, ED vs office, SMSA), and geographic region. Variables were included in the multivariate model based on association with ARFs at P < .20. We used only the most recent years of analysis to enhance the model’s ability to reflect predictors of prescribing for CA-MRSA during an era when it was clearly established as a leading cause of SSTIs.

RESULTS

TRENDS IN VISIT RATES

The total number and incidence (visit rate) of SSTI-related visits to ambulatory physicians increased from 1997 to 2005 (Figure 1). Total visits increased from 8.6 (95% CI, 7.0-10.2) million in 1997 to 14.2 million (95% CI, 11.7 million to 16.8 million) in 2005 (a 65% increase), whereas the visit rate increased from 32.1 (95% CI, 26.1-38.1) visits per 1000 population in 1997 to 48.1


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(95% CI, 39.4-56.7) visits per 1000 population in 2005 (a 50% increase; \( P = .003 \) for trend, Figure 1). A substantial increase in overall SSTI visit rates occurred from 2001 to 2004 and appears to have flattened in 2005 (Figure 1).

The large increase in visits for SSTI was primarily attributable to visits for abscess/cellulitis, which accounted for 95% of this increase, whereas other types of SSTIs did not show significant changes (\( P = .38 \) for trend) during this period (Figure 1). Annual visits for abscess/cellulitis increased from 4.6 million (95% CI, 3.6 million to 5.7 million) in 1997 to 9.6 million (95% CI, 7.8 million to 11.5 million) in 2005 (a 109% increase), whereas the visit rate increased from 17.3 (95% CI, 13.4-21.2) visits per 1000 population in 1997 to 32.5 (95% CI, 26.2-38.8) visits per 1000 population in 2005 (an 88% increase; \( P < .001 \) for trend) (Figure 1).

The trend in visits for abscess/cellulitis occurred among all age groups, with the largest rate change among patients younger than 18 years (173%), increasing from 10.1 (95% CI, 5.9-14.3) to 27.6 (95% CI, 17.0-38.2) visits per 1000 population during the study period (\( P < .001 \) for trend) (Figure 2A). Visit rates among patients aged 18 to 44 years more than doubled (13.1 to 27.1 per 1000 population; \( P = .002 \) for trend), whereas the increase among patients 45 years or older was less than 50% (27.9 to 41.3 per 1000 population; \( P = .003 \) for trend) although still a significant change (Figure 2A). Office practices provided care to the largest number of patients each year. Although visit rates increased in office practices and EDs, EDs experienced the largest rate of increase in visits, rising 156% from 4.3 (95% CI, 3.3-5.2) to 11.0 (95% CI, 8.8-13.1) visits per 1000 population for abscess/cellulitis (65%-69%), and the frequency did not change from 1997 to 2005 (\( P = .38 \) for trend) (Figure 2B). The proportion of ambulatory visits for abscess/cellulitis that took place in EDs increased from 24% to 34% during this period (\( P = .02 \)).

**TRENDS IN VISIT CHARACTERISTICS**

To identify patient and environmental factors associated with the increased rate of visits for abscess/cellulitis, we compared the changes in the distribution of these factors within and between office-based and ED practice settings (Table 1). When compared with visits for abscess/cellulitis in 1997 to 1998, there was a significant increase in the proportion of office visits by male patients (from 40% to 54%; \( P = .03 \)) and a trend toward an increased proportion of visits by patients younger than 18 years (from 14% to 22%; \( P = .11 \)) in 2004 to 2005 (Table 1). In EDs, when compared with visits in 1997 to 1998, there was an increase in the proportion of ED visits by patients aged 18 to 44 years (from 39% to 50%; \( P = .001 \)), by patients in the South (from 33% to 47%; \( P = .07 \)), and by black patients (from 17% to 25%; \( P = .10 \)). This corresponded to a 3-fold increase in the visit rate for black patients (5.9 to 18.4 visits per 1000 population) and patients in the South (4.1 to 12.8 visits per 1000 population). Although the largest relative increase occurred in the South, visit rates increased in all regions of the United States to offices and EDs.

Because a disproportionate share of visits by black patients occurs among safety-net hospitals, we further examined changes in visits to hospitals stratified by high and low safety-net status. The proportion of ED visits that occurred in high safety-net–status hospitals increased from 30% to 50% during the study period (\( P < .001 \)). This corresponded to a nearly 4-fold increased visit rate. Although overall ED visits by black patients increased during this period, we found no differences in the distribution of race among the highest safety-net–status hospitals between the periods from 1997 to 1998 and 2004 to 2005 (\( P = .22 \)).

Return visits and hospitalization rates were calculated as measures of disease severity for ED visits. There was no significant change in the proportion of ED visits that represented return visits within 72 hours of the index visit. Although the rate of hospitalizations increased from 0.7 to 1.2 per 1000 population (accounting for approximately 320 000 additional hospitalizations from EDs alone in 2004 to 2005 compared with 1997 to 1998), there was a trend toward decreased hospitalization (Table 2).

**TRENDS IN ANTIBIOTIC USE FOR ABSCESS/CELLULITIS**

Antibiotics were prescribed for most of the patients who made visits for abscess/cellulitis (65%-69%), and the frequency did not change from 1997 to 2005 (\( P = .43 \)). The leading antibiotic category was β-lactams (73% cephalosporins), which accounted for most of the prescribing in all of the study years (Figure 3). The proportion of ARFM prescriptions increased significantly from 7% of visits where an antibiotic was used in 1997 to 28% in 2005 (\( P < .001 \)), with much of the increase occurring since 2004.
A combination of trimethoprim and sulfamethoxazole was the leading drug in the ARFM class (59%) prescribed in 2005. A single antibiotic was prescribed during most of the visits (77%-86% annually).

Using multivariate regression analysis, we examined patient, geographic, and health care setting characteristics associated with the prescribing of ARFMs in 2005. Independent predictors included younger age (odds ratio [OR], 2.67 [95% CI, 1.09-6.58] for ≤18 years; OR, 2.76 [95% CI, 1.23-5.59] for 18-44 years) compared with those 45 years or older, US census region (OR, 4.58 [95% CI, 1.99-10.50] for the South; OR, 0.34 [95% CI, 0.13-0.89] for the Northeast) compared with the Midwest, SMSA region (OR, 2.99 [95% CI, 1.44-6.22]) compared with non-SMSA regions, and delivery setting in the ED (OR, 2.31 [95% CI, 1.44-4.66]) compared with an office setting (Table 2). Although patients presenting to offices and black patients experienced large increases in visit rates, neither of these variables was independently associated with prescribing ARFMs.

COMMENT

Rates of ambulatory visits for abscess/cellulitis have rapidly increased in recent years. From 1997 to 2005, visit rates nearly doubled overall, nearly tripled among children and in EDs, and increased nearly 4-fold among high safety-net–status EDs. A substantial portion of these changes has occurred since 2003, coincident with ecologic evidence that CA-MRSA was becoming a common organism cultured from SSTIs. Although outbreaks of CA-MRSA were reported in 1998, followed by larger community-based studies after 2000, limited data exist addressing the national impact of CA-MRSA on SSTIs over time. To our knowledge, this is the first study to assess nationally representative longitudinal trends in ambulatory care for SSTIs coincident with the emergence of CA-MRSA. These data provide compelling evidence of a US epidemic of SSTIs, one that is not confined to urban EDs and hospitals, but that appears to have a major impact in pediatric and adult office-based practices as well.

Although we do not have microbiological data in our study to confirm the etiology, several observations suggest that CA-MRSA is driving this epidemic. First, CA-MRSA is primarily associated with purulent SSTIs, and we found that visit rates increased among purulent forms (abscess/cellulitis), whereas rates remained stable among nonpurulent forms (eg, impetigo and erysipelas). Because the same ICD-9-CM code is used for abscess and cellulitis, we were not able to further distinguish between these 2 conditions. Second, the inflection point for the increase in visit rates appears to have occurred in 2003, consistent with timing from local studies showing increased CA-MRSA in SSTIs. Third, the largest relative increase in visit rates occurred among EDs, especially those with high safety-net status, a setting that previous research studies have shown serves populations at high risk for CA-MRSA. A previous study of SSTIs using the NHAMCS and NAMCS surveys reported no changes in visit rates when 1992 to 1994 was compared with 2001 to 2003. This is likely because CA-MRSA was only beginning to have an impact in communities on a national scale in 2003.

Our study suggests that the current SSTI epidemic is disproportionately affecting certain populations, includ-
ing children and young adults, black patients, and communities served by high safety-net–status hospitals. These patient characteristics may reflect previously identified CA-MRSA risk factors, including injected drug use, human immunodeficiency virus infection, incarceration, athletic team participation, public housing, and lower socioeconomic status.8,10,12,14,24 The differential increase in ED visits for SSTIs suggests that CA-MRSA may cause more rapid and severe symptom onset. Alternatively, the ED may be the only source of health care for some patients who are at increased risk of CA-MRSA. This possibility is supported by our finding of a differential increase in visits to EDs affiliated with high safety-net–status hospitals. However, among these hospitals, we found no temporal changes by race or payment type among visits for abscess/cellulitis. This finding suggests that the SSTI epidemic may be more strongly influenced by factors related to the community (eg, housing and sanitation) rather than individual demographic characteristics.

Previous studies have suggested that CA-MRSA may be more virulent than other strains of S aureus, leading to more severe disease that requires hospitalization.20,25 Although we detected an increased number of hospitalizations for SSTIs coincident with the emergence of CA-MRSA, the proportion of ED visits for SSTIs that required hospitalization was not different from 1997 to 2005. This suggests that severe infections associated with CA-MRSA may in part be a consequence of increasing case numbers rather than increased strain virulence. Alternatively, systematic changes in the patterns of ED care trending toward lower rates of hospitalization or recent improvements in the quality of care may have masked increases in severity.

Our analyses do not indicate that the increased rate of visits for SSTIs was related to increased use of ambulatory care or represented multiple episodes of care for the same infection. The US rate of ambulatory visits increased by only 20% and 7% to primary care offices and EDs, respectively, during the study period.26 We found increased visit rates only among patients with abscess/cellulitis. The stable rate of visits for other SSTIs and urinary tract infections indicates that the increase in abscess/cellulitis does not reflect an underlying trend of an increased rate of visits for acute illnesses. Some of the increased visits noted for abscess/cellulitis may reflect increased awareness of CA-MRSA, leading to an increased propensity to assign the code for abscess rather than another SSTI code. However, this possibility seems un-

| Table 1. Characteristics of Visits for Abscess/Cellulitis in Offices and EDs
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Abbreviations: ED, emergency department; SMSA, standardized metropolitan statistical area.

a Based on codes 681.x and 682.x from the International Classification of Diseases, Clinical Modification, Ninth Revision. Unless otherwise indicated, data are expressed as percentage of visits (reflecting weighted estimates). Percentages have been rounded and may not total 100.

b Years of comparison are 2001 to 2002 vs 2004 to 2005.

c Indicates a proxy for urban location.
likely because the code represents a clinical diagnosis and other SSTIs should have decreased correspondingly. As with hospitalization, improvements in the quality of care provided for patients with SSTIs, such as ARFM use, may have blunted increases in the percentage of SSTIs requiring multiple episodes of care.

Increased prescribing of ARFMs suggests that awareness of CA-MRSA has grown in certain settings and patient populations. Our analysis of antibiotic prescribing showed that many, but not all, patient characteristics that were associated with increasing visit rates were predictors of ARFM use. Notable exceptions include black patients, who appear disproportionately affected in relative terms, and patients in office settings, who accounted for the largest absolute increase in visits. This suggests that opportunities exist for continued improvement in care through education and awareness campaigns targeting office-based physicians and those caring for black patients.

Although antibiotic prescribing for SSTIs has shifted toward ARFMs, our estimate of 28% remains significantly lower than the estimated prevalence of CA-MRSA in national studies of SSTIs. In studies at single centers, a similar change in prescribing practice has been observed, as have the results of a recent survey. Because CA-MRSA is known to have a propensity for purulent abscess formation, we believed that many of these infections would be recorded with an ICD-9-CM code using this word. Indeed, the temporal changes we observed in SSTIs were almost entirely attributable to the abscess/cellulitis codes, suggesting that physicians were using these codes appropriately. Another limitation is ensuring that the intended purpose of the antibiotic prescription was treatment of the SSTI and not another problem. We restricted our analysis to visits for abscess/cellulitis where this was the principal diagnosis, and we excluded other potentially confounding diagnoses to enhance the internal validity of the study population. The lack of microbiological data limits our ability to definitively conclude that the increased number of visits is attributable to CA-MRSA. Alternative explanations for the changes in visit rates include an increased propensity to seek ambulatory care among patients in general (which does not appear to have occurred to this extent), demographic changes in the patients included in the sample that might have overrepresented patients with risk factors for SSTIs such as homelessness, and increased awareness among physicians of CA-MRSA, leading to an increased propensity to assign the code for abscess to a visit.

There are several limitations to our study. First, the nature of the NAMCS and NHAMCS data sets we used relied on ICD-9-CM codes for SSTIs that have not been prospectively validated, although the staff members of the National Center for Health Statistics conduct training, provide technical support to all study sites, and perform periodic validation of their survey methods. Because CA-MRSA is known to have a propensity for purulent abscess formation, we believed that many of these infections would be recorded with an ICD-9-CM code using this word. Indeed, the temporal changes we observed in SSTIs were almost entirely attributable to the abscess/cellulitis codes, suggesting that physicians were using these codes appropriately. Another limitation is ensuring that the intended purpose of the antibiotic prescription was treatment of the SSTI and not another problem. We restricted our analysis to visits for abscess/cellulitis where this was the principal diagnosis, and we excluded other potentially confounding diagnoses to enhance the internal validity of the study population. The lack of microbiological data limits our ability to definitively conclude that the increased number of visits is attributable to CA-MRSA. Alternative explanations for the changes in visit rates include an increased propensity to seek ambulatory care among patients in general (which does not appear to have occurred to this extent), demographic changes in the patients included in the sample that might have overrepresented patients with risk factors for SSTIs such as homelessness, and increased awareness among physicians of CA-MRSA, leading to an increased propensity to assign the code for abscess to a visit.

Furthermore, because data are available only through 2005, it is unknown whether the trends we observed in
visit rates and antibiotic prescribing have persisted or stabilized.

In summary, we found that the medical burden of SSTIs has almost doubled nationwide since the emergence of CA-MRSA, suggesting that CA-MRSA is contributing to this epidemic. The shift in antibiotic prescribing for SSTIs that we observed may reflect information dissemination about an emerging infection, occurring even before the publication of clinical guidelines. Nonetheless, opportunities for improvement exist in terms of increasing awareness of local epidemiology and resistance patterns to assist physicians in making informed decisions regarding antibiotic prescribing. Special attention should be paid to populations at high risk, including younger patients, and to raising awareness among office-based physicians. Further surveillance of trends in visit rates and prescribing patterns will be necessary to evaluate ongoing efforts to control the impact of CA-MRSA.

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Correspondence: Adam L. Hersh, MD, PhD, Department of Pediatrics, University of California, San Francisco, 3333 California St, San Francisco, CA 94118-0936 (hershad@peds.ucsf.edu).

Author Contributions: Dr Hersh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hersh, Chambers, and Gonzales.

Acquisition of data: Hersh and Gonzales.

Analysis and interpretation of data: Hersh, Chambers, Maselli, and Gonzales.

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