Reduction of Inappropriate Antibiotic Use and Improved Outcomes by Implementation of an Algorithm-Based Clinical Guideline for Nonpurulent Skin and Soft Tissue Infections

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Study objective: Clinicians currently do not reliably adhere to antibiotic treatment guidelines, resulting in unnecessary patient exposure to broad-spectrum antimicrobials. Our objective is to determine whether a treatment intervention for the management of nonpurulent skin and soft tissue infections increases clinician adherence and improves patient outcomes.

Methods: Between January 1 and December 31, 2017, patients presenting to 2 emergency departments (EDs) and who had received a diagnosis of a nonpurulent skin and soft tissue infection were enrolled and assigned to a pre- or postintervention cohort with a treatment intervention implemented on June 1. Primary outcomes were percentage of ED providers following the guidelines and percentage of patients admitted to the hospital. Secondary outcomes were patient self-reported treatment failure and hospital readmission.

Results: There were 1,360 patients, 665 in the preintervention and 695 in the postintervention cohorts. After algorithm implementation, guideline adherence increased (43.0% versus 55.1%; $P<.001$) and number of patients admitted to the hospital declined (36.5% versus 12.0%; $P<.001$). In addition, patients reported fewer treatment failures (26.8% versus 16.5%; $P=.02$) and fewer readmissions (22.3% versus 12.7%; $P=.013$). After multivariate adjustment, guideline adherence increased by 22% (adjusted relative risk [RR] 1.22; 95% confidence interval [CI] 1.10 to 1.37), whereas hospital admissions were reduced by 26% (adjusted RR 0.74; 95% CI 0.64 to 0.87). In addition, the risks of treatment failure and readmission were reduced by 46% (adjusted RR 0.64; 95% CI 0.43 to 0.97) and 45% (adjusted RR 0.55; 95% CI 0.34 to 0.87), respectively.

Conclusion: Among patients with a nonpurulent skin and soft tissue infection, implementing an easy-to-follow treatment algorithm can reduce unnecessary antibiotic exposure by increasing clinician guideline adherence while reducing patient treatment failure rates. [Ann Emerg Med. 2020;■:1-11.]

Please see page XX for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

During the past decade, the prevalence and economic costs of skin and soft tissue infections (SSTIs) in the United States have significantly increased.[1] Annual US visits for SSTIs doubled in the early 2000s, with the largest increase occurring in emergency departments (EDs).[2,3] Currently, SSTIs are the second most common infection leading to hospitalization.[4,5]

Nonpurulent SSTIs are without purulent drainage or abscess,[6] and have high treatment failure and hospital admission rates. One in 5 patients fails initial treatment,[7] and one third of ED patients are admitted to hospital services.[6] According to laboratory markers and clinical response to β-lactam antimicrobials,[8] nonpurulent SSTIs are largely due to infection with β-hemolytic streptococci. As such, narrow-spectrum β-lactam antibiotics are the drugs of choice.[8] *Staphylococcus aureus* is a less common cause of nonpurulent SSTI and, when present, is most likely due to methicillin-sensitive *S aureus*.[9] Despite this, the use of antibiotics effective against methicillin-resistant *S aureus* (MRSA) is increasing.[10]

Vancomycin and other agents active against MRSA are not recommended for routine use in hemodynamically stable patients with nonpurulent

Editor's Capsule Summary

What is already known on this topic

Published guidelines for treatment of nonpurulent skin infections recommend narrow-spectrum β-lactam antibiotics, but emergency physicians commonly use antibiotics such as vancomycin.

What question this study addressed

A treatment algorithm was initiated in 2 emergency departments, with feedback to clinicians who did not follow the guideline. Management was compared for 665 patients before and 695 after the intervention for guideline adherence and outcomes.

What this study adds to our knowledge

After the intervention, guideline adherence increased by 22%, and hospital admissions were reduced by 26%, with treatment failures and readmissions reduced by 46% and 45%.

How this is relevant to clinical practice

A locally developed treatment algorithm with clinician feedback can improve adherence to antibiotic guidelines for nonpurulent skin infections and improve outcomes.

cellulitis owing to additional monitoring criteria and their overly broad-spectrum coverage.[9] Current vancomycin guidelines for therapy of SSTI call for a steady-state vancomycin trough of 10 to 15 μg/mL,[11] which is achieved after 4 to 5 doses of therapy. Therefore, administering one dose in the ED before discharging a patient with oral therapy is unlikely to have a significant clinical influence[11,12] and inpatient use is suboptimal, given increased risk of adverse events and the need for monitoring.[8]

Importance

The Infectious Diseases Society of America (IDSA) published guidelines for the management of SSTIs, recommending the use of antimicrobials active against MRSA only for severe infections.[9] Unfortunately, clinicians' adherence to these guidelines is suboptimal. Previous studies indicate ED providers are in concordance with the guidelines less than half of the time.[13-15] Inappropriate broad-spectrum antibiotic selection, including MRSA coverage, is typically the most common cause of deviation from guidelines.[14,16] Unnecessary MRSA coverage likely does more harm than good, given the adverse events associated with these antimicrobials.[17-19]

Goals of This Investigation

The purpose of our clinical intervention was to adapt the 2014 IDSA guidelines into an easy-to-follow treatment algorithm guide presented to clinicians with education and individualized feedback to reduce the use of MRSA-targeting antimicrobial therapies for nonpurulent SSTIs, with a specific focus on decreasing the use of vancomycin, concentrating instead on using first-generation cephalosporins; better align ED clinician prescribing practices with IDSA guidelines for nonpurulent SSTIs; and improve disposition decisionmaking in the ED. The objective of this investigation was to determine whether the treatment algorithm intervention based on IDSA guidelines for the management of nonpurulent SSTIs increased clinician adherence, reduced unnecessary antibiotic use, and reduced the number of patients admitted to the hospital from the ED. Secondary outcomes were patient self-reported treatment failure and hospital readmission.

MATERIALS AND METHODS

Study Design and Setting

We conducted a multicenter, prospective cohort intervention study. Patients aged 18 years and older who presented for treatment of a nonpurulent SSTI between January and December 2017 at one urban tertiary care academic center (annual ED census=93,000 visits) or one community ED (annual ED census=42,000 visits) were included. Nonpurulent SSTI was defined by manual review of the ED registry. This study was approved by the institutional review board.

Selection of Participants

Patients were eligible if they had an admission or discharge diagnosis of nonpurulent SSTI in the electronic medical record. They were excluded if they underwent an incision and drainage with expression of purulent material or if they had been treated for the same SSTI in 1 of the 2 EDs within 4 weeks.

Treatment of nonpurulent SSTIs with MRSA-targeting antimicrobial therapies was identified as a common cause of inappropriate use as determined by stewardship review. In 2016, the ED partnered with the antimicrobial stewardship team, led by an infectious disease physician and infectious disease pharmacist, to design an algorithm based on IDSA guidelines for treatment of SSTIs, the Centers for Disease Control and

Prevention's recommendations for antibiotic therapy, and primary literature about antimicrobial therapy of SSTIs.[9,18,20-22] The algorithm was printed on a 5×8-inch card that fit easily into providers' pockets and on 8×10-inch poster boards for display (Figure 1). This algorithm differed from the IDSA guidelines primarily by dividing severe infections into conditions that should be treated with vancomycin and others that could be treated with first-generation cephalosporin according to recent treatment evidence,[18] and by including recommended dispositions in the algorithm.

Interventions

Education was initiated at the first ED faculty meetings and included a presentation about the treatment algorithm, evidence-based data used to develop it, and data about previous departmentwide vancomycin usage. Each provider was given a treatment algorithm card and confidential, personalized vancomycin prescribing data (Figure E1, available online at http://www.annemergmed.com). ED providers who did not attend the staff meeting were individually provided with the algorithm and their personal prescribing data in print and electronic form so that all ED providers were reached. The treatment algorithm was posted at physician workstations in the ED. For 1 month after intervention initiation, any use of vancomycin to treat a nonpurulent SSTI was reviewed, and the ED treatment provider was contacted for detailed feedback in regard to any deviations from the algorithm. This process was performed for both the academic and community sites and for residents who worked at the academic site. Finally, a brief review of the algorithm and study progress was presented monthly at faculty meetings for 4 months. We began data collection 2 weeks after the initial faculty meeting to ensure all providers had received the intervention material. More detail of the intervention is provided in the template for intervention description and replication checklist[23] (Table E1, available online at http://www.annemergmed.com).

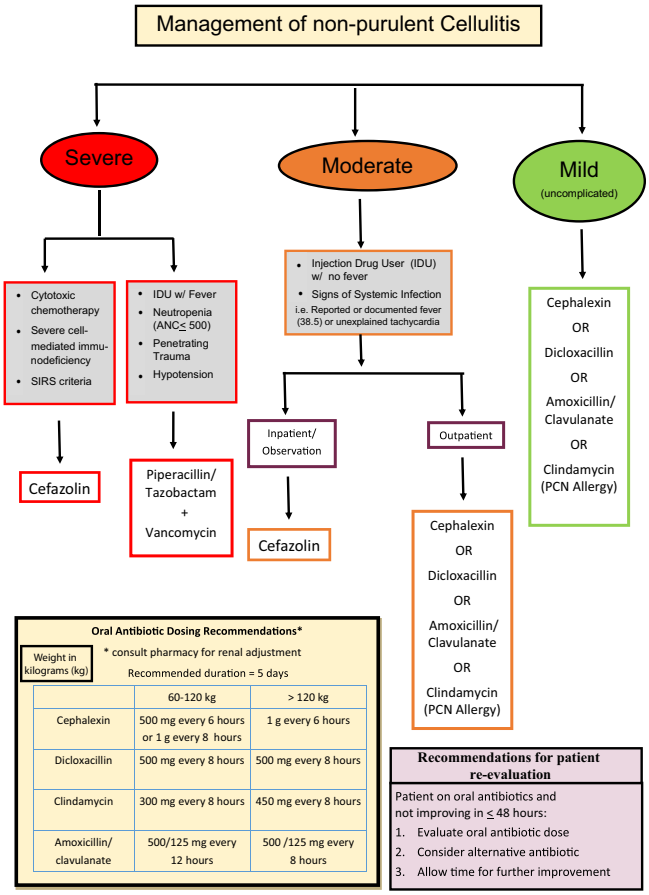

Figure 1. Management of nonpurulent cellulitis.

Methods of Measurement

Patients were eligible for an opt-out telephone survey if they were treated 3 months before or after the intervention for a nonpurulent SSTI, were discharged home from either the ED or the inpatient service, were English speaking, and had a working telephone number. Patients were identified through the electronic medical record and contacted 2 to 6 weeks after discharge. This contact window was selected to reflect the time during which readmission to the hospital or clinical cure would have already occurred, while minimizing recall bias.[14,24] After the patient agreed to enrollment, a structured interview was conducted in which treatment failure and readmission for the SSTI they were treated for on the index visit within 14 days was asked about.

To reduce the potential for systematic error and to mitigate bias, we followed protocols for the optimal conduct of chart review studies.[25] Before data abstraction activities, we a priori defined relevant variables to be collected in a standardized manner. Abstractors were research assistants who were uniformly trained by the investigators and were unaware of treatment algorithm adherence at data abstraction. Abstractors confirmed nonpurulent SSTI status and pulled data from the initial ED visit, including demographic and clinical data. We used the Charlson comorbidity index to categorize patients' medical comorbidities.[26,27] Abstractors met regularly with the investigators to review the coding rules. An interrater reliability assessment was performed on a 10% random sample of charts.

Outcome Measures

Our primary outcomes established in the study design phase were the percentage of ED providers following the guidelines as presented in the treatment algorithm, the frequency with which vancomycin was prescribed, and the percentage of patients admitted to the hospital from the ED. Given the multifaceted approaches to SSTI treatment, we chose to use multiple-measure endpoints.[28] To determine guideline adherence, ED clinician investigators compared the ED treatments rendered with the infection severity class (Figure 1). Accordingly, each patient received a clinical score of 1 for mild, 2 for moderate, and 3 for severe with respect to their nonpurulent SSTI at the initial ED visit and a second score with respect to the treatments rendered according to the algorithm. For example, any patient receiving oral antibiotics alone was classified as having antimicrobial treatments matching the mild category (score 1). After scoring, we compared the clinical presentation and treatment scores of each patient to determine whether the observed treatment matched the guideline-appropriate treatment class or whether the patient was over- or undertreated. This scoring system is similar to ones used previously to assess IDSA guideline adherence.[14,29] Our main secondary outcomes were the percentage of patients with treatment failure and hospital readmission by patient self-report.

Primary Data Analysis

We used χ^2 tests to compare categoric variables and the Student's t test for continuous variables to compare patients in the pre- and postintervention cohorts. We also used χ^2 tests to compare the primary and secondary outcomes between the pre- and postintervention cohorts and then conducted multivariable logistic regression analyses to test whether these outcomes were associated with the intervention period. To select the set of covariates for the multivariable models, we included any covariates with a $P<.10$ from the unadjusted bivariate analyses (age continuous, sex, race, hand location, and Charlson comorbidity index score) and included whether treatment followed the guidelines in the patient follow-up model. None of the assumptions for multivariable logistic regression were violated (ie, homoscedasticity assumption). To analyze the effect of patients lost to telephone follow-up, we performed a sensitivity analysis using best- and worst-case scenarios. We first computed the models assuming none of the patients lost to follow-up had been readmitted to the hospital (best case) and then again assuming all had been readmitted (worst case). We used Stata (version 13.1; StataCorp, College Station, TX) for all analyses.

The available sample sizes were sufficient to detect at least a 7% difference in proportions for the primary outcomes with $\alpha=.05$ and 80% power. For the secondary outcomes, the available sample sizes were sufficient to detect at least an 11% difference with $\alpha=.05$ and 80% power. All sample size calculations were made before the study conduct.

RESULTS

Characteristics of Study Subjects

During the 12-month study period at the 2 ED clinical sites, there were a total of 1,524 patients treated who had an ED or admitting diagnosis of a nonpurulent SSTI, of whom 129 (8.4%) had repeated visits in less than 4 weeks. An additional 35 patients (2.3%) were excluded on secondary chart review because an incision and drainage was performed, thus making the infection type

Table 1. Characteristics of study patients.*

	Preintervention (n=665)		Postintervention (n=695)	
Demographics	**No.**	**%**	**No.**	**%**
Age (IQR)	51.9	(28.0)	49.9	(28.0)
≥65 y	166	(25.0)	145	(20.9)
Women	291	(43.8)	336	(48.3)
White	516	(77.6)	514	(74.0)
Hispanic	42	(6.3)	70	(10.1)
Black	31	(4.7)	38	(5.5)
Asian	14	(2.1)	7	(1.0)
Medical history				
CCI score (SD)	0.82	(1.30)	1.04	(1.44)
IVDA	47	(7.1)	43	(6.2)
Currently receiving any Abx	145	(21.8)	148	(21.3)
Infection characteristics				
Location				
Face	90	(13.5)	106	(15.3)
Trunk	65	(9.8)	73	(10.5)
Hand	78	(11.7)	59	(8.5)
Extremity, not hand	405	(60.9)	435	(62.6)
Buttocks	14	(2.1)	15	(2.2)
Genitals	13	(2.0)	15	(2.2)
Infection severity				
Mild	454	(68.3)	482	(69.4)
Moderate	99	(14.9)	111	(16.0)
Severe	112	(16.8)	102	(14.7)

IQR, Interquartile range; *CCI*, Charlson comorbidity index; *IVDA*, current intravenous drug abuse; *Abx*, antibiotics.
*Data are presented as No. (%) unless otherwise indicated.

purulent. This resulted in a total of 1,360 patients, with 665 in the preintervention and 695 in the postintervention periods.

The final study sample had an average age of 50.8 years (SD 18.2 years) and was 46.1% women. Approximately half of all patients were treated at the academic site (54.3%). The majority of patients were discharged home from the ED (69.3%), whereas 30.7% were admitted to the hospital and 12.0% were admitted to the ED observation unit. Most patient characteristics were the same in the pre- and postintervention periods, with the exception of a higher percentage of blacks, and patients with higher Charlson comorbidity index scores presenting in the postintervention period (Table 1). Charlson comorbidity index scores were low on average in both study periods.

There was a significant increase in guideline adherence in the EDs between the pre- and postintervention periods (Figure 2 and Table 2). Guideline adherence increased from 56.6% to 63.5% of patients treated and discharged home from the ED. Adherence was lower among patients admitted, although an increase from a baseline of 19.3% to 29.9% did occur in this group. In the preintervention period, 50% of ED patients received overly broad therapy as defined by the IDSA guidelines. After the intervention, overtreatment was reduced to 1 in 3 ED patients (Table 2). The percentage of clinicians adherent to SSTI guidelines increased to more than 50%, whereas the percentage of patients who were undertreated was unaffected. ED discharge rates increased from 63.5% to 75.0% after implementation of the treatment algorithm, reflecting a decrease in the number of patients admitted or treated in the ED observation unit. There were no statistically significant differences in primary outcomes between the academic and community sites (Table E2, available online at http://www.annemergmed.com). In a multivariable model, guideline adherence increased by 22% (adjusted RR 1.22; 95% confidence interval [CI] 1.10 to 1.37) between the pre- and postintervention periods after adjusting for age, sex, race, hand location, and Charlson comorbidity index score.

Table 2. Patients treated according to recommended guidelines by study period.*

	Preintervention (n=665)		Postintervention (n=695)	
Type	**No.**	**%**	**No.**	**%**
Guideline adherence				
Followed guidelines	286	(43.0)	383	(55.1)
Undertreated	67	(10.1)	86	(12.4)
Overtreated	312	(46.9)	226	(32.5)
Antibiotic use				
IV ED Abx	367	(55.2)	316	(45.5)
Vancomycin	222	(33.4)	89	(12.8)
Cefazolin	44	(6.6)	134	(19.3)
MRSA coverage	327	(49.2)	247	(35.5)
Patient disposition				
Admitted	243	(36.5)	174	(25.0)
ED observation	90	(13.5)	73	(10.5)

IV, Intravenous.
*Data are presented as No. (%) unless otherwise indicated.

Main Results

There were significant changes in both antibiotics prescribed in the ED and for home between the pre- and

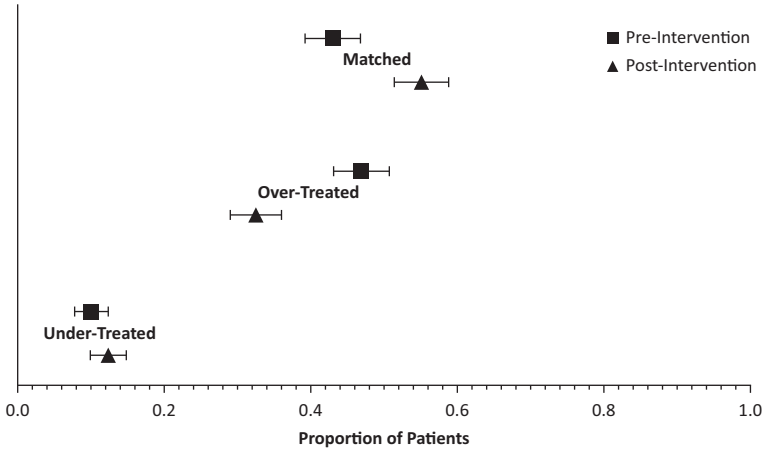

Figure 2. Patients treated in each study period.

postintervention periods (Figure 3). Intravenous vancomycin administration in patients discharged home from the ED decreased from 16.3% in the preintervention period to 3.5% postintervention. Among patients admitted to the hospital, vancomycin prescribing similarly decreased, from 63.0% preintervention to 40.8% postintervention, and patients treated in the ED observation unit decreased from 42.2% to 16.4%. Other specific antibiotic classes prescribed postdischarge did not change between intervention periods (Table E3, available online at http://www.annemergmed.com); however, there was a significant reduction in the use of combined antibiotic classes to include potential MRSA infection (55.9% preintervention to 34.4% postintervention).

In multivariable models, vancomycin usage and hospital admission were reduced by 59% (adjusted RR 0.41; 95% CI 0.32 to 0.51) and 26% (adjusted RR 0.74; 95% CI 0.64 to 0.87), respectively, between the pre- and postintervention periods after adjusting for age, sex, race, hand location, and Charlson comorbidity index score. The area under the receiver operating characteristic (ROC) curve was 0.70 (95% CI 0.67 to 0.73) for vancomycin usage and 0.70 (95% CI 0.66 to 0.73) for hospital admission.

A total of 839 patients were treated in the 3-month window before and after intervention implementation. Of these, 228 patients (27.2%) did not have contact information or were unable to communicate in English. Of the remaining 611 eligible patients, 452 (80.0%) consented and completed the survey, whereas 79 (12.9%) refused and 80 (13.1%) could not be reached. The percentage of patients reached and who provided consent was similar in both the pre- and postintervention periods, with 197 and 255 patients completing the survey, respectively. We noted similar trends in our primary outcomes among the patients contacted for follow-up (Table E4, available online at

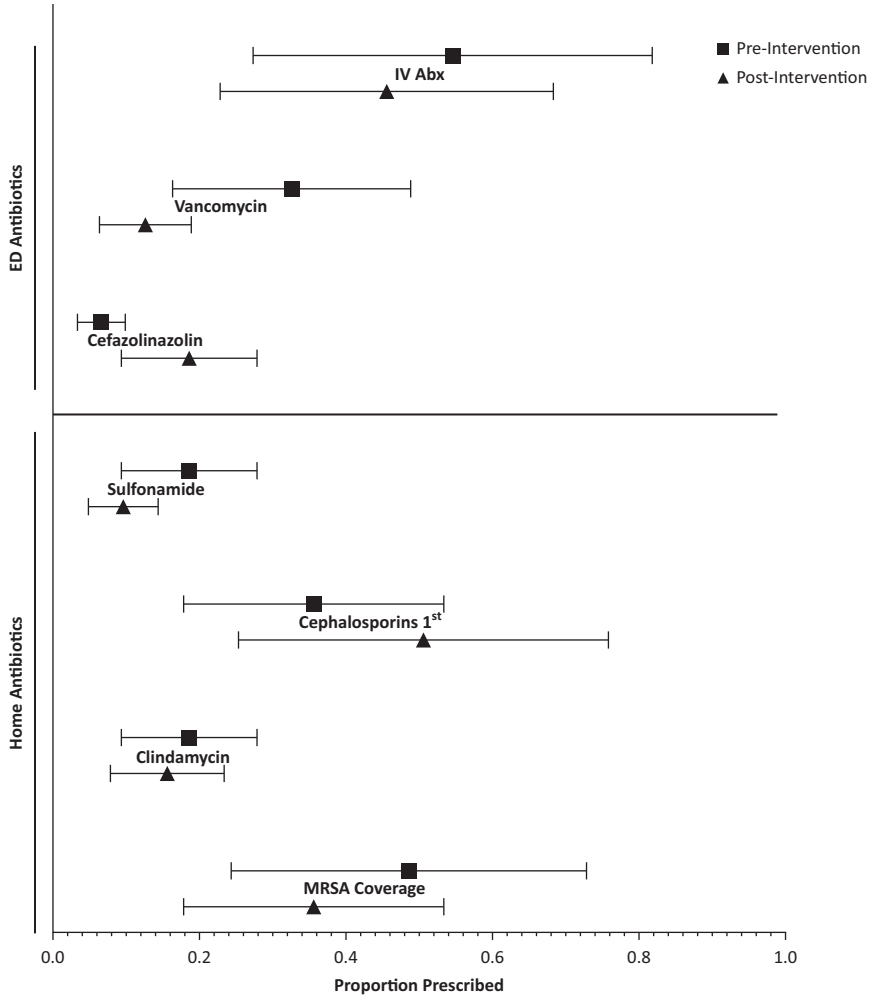

Figure 3. Antibiotics characteristics in each study phase.

http://www.annemergmed.com) as well as in the characteristics of these study patients (Table E5, available online at http://www.annemergmed.com). Among patients who completed the survey, there was a significant reduction in the percentage of those who reported both treatment failure and need for readmission between the pre- and postintervention periods (Figure 4). The reduction in treatment failure and readmission occurred among patients with both mild and moderate infection types (Figure 5). In the postintervention period, the percentage of patients failing treatment or being readmitted was lower only in the intravenous antibiotic group (Figure 6*A* and *B*) but was lower among patients either receiving MRSA coverage or not (Figure 6*C* and *D*). We also conducted a secondary sensitivity analysis rerunning the multivariable model for guideline adherence between the pre- and postintervention periods after adjusting for age, sex, race, hand location, and Charlson comorbidity index score for patients lost to follow-up, using best- and worst-case scenarios (in which all patients lost to follow-up were coded as either all failed/readmitted or not), which did not change our model findings.

In multivariable models, the risk of treatment failure was reduced by 45% (adjusted RR 0.65; 95% CI 0.44 to 0.98) and the risk of readmission was reduced by 43% (adjusted RR 0.57; 95% CI 0.36 to 0.90) between the pre- and postintervention periods after adjusting for following guidelines, age, sex, race, hand location, and Charlson comorbidity index score. The area under the ROC curve was 0.60 (95% CI 0.53 to 0.67) for treatment failure and 0.63 (95% CI 0.56 to 0.71) for readmission. Following the guidelines had nonsignificant reductions of treatment failure that were 30% (adjusted RR 0.70; 95% CI 0.46 to 1.06) and 31% (adjusted RR 0.69; 95% CI 0.43 to 1.10), respectively.

LIMITATIONS

Our study has some limitations. First, we noted differences in patients' demographics between the pre- and postintervention periods. The postintervention group was younger, included more men and blacks, and had higher average Charlson comorbidity index scores. Because we believe these differences were not clinically relevant, we used multivariable logistic regression models to demonstrate that our outcomes remained significant after adjustment for these demographic and clinical covariates. Our study is also limited by loss to follow-up for the telephone survey. This was mainly due to a lack of means to contact patients after hospital discharge. To account for this fact, we conducted additional sensitivity analyses demonstrating that patients lost to follow-up did not significantly alter the risk for treatment failure or readmission through best- and worst-case analysis. Another possible limitation is the use of univariate screening for model variable selection. Given the hospital administrations' increased awareness of inappropriate antibiotic use in nonpurulent SSTIs,[14] we designed this 12-month study to collect preintervention data prospectively while the algorithm was under development and then timed our postintervention cohort enrollment to coincide with algorithm approval for clinical use.

DISCUSSION

In this prospective, multicenter cohort study of pre- and postintervention patients with nonpurulent SSTI who presented to the ED, we improved clinician adherence to IDSA guidelines and reduced unnecessary antibiotic use by 14.4% and hospital admissions by 11.5%. This was associated with a nearly 50% relative reduction in the risk of both treatment failure and readmission to the hospital.

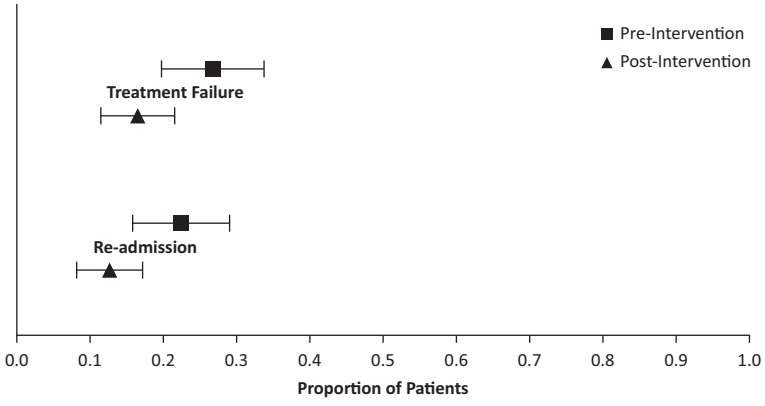

Figure 4. Treatment failure and admissions by patient report.

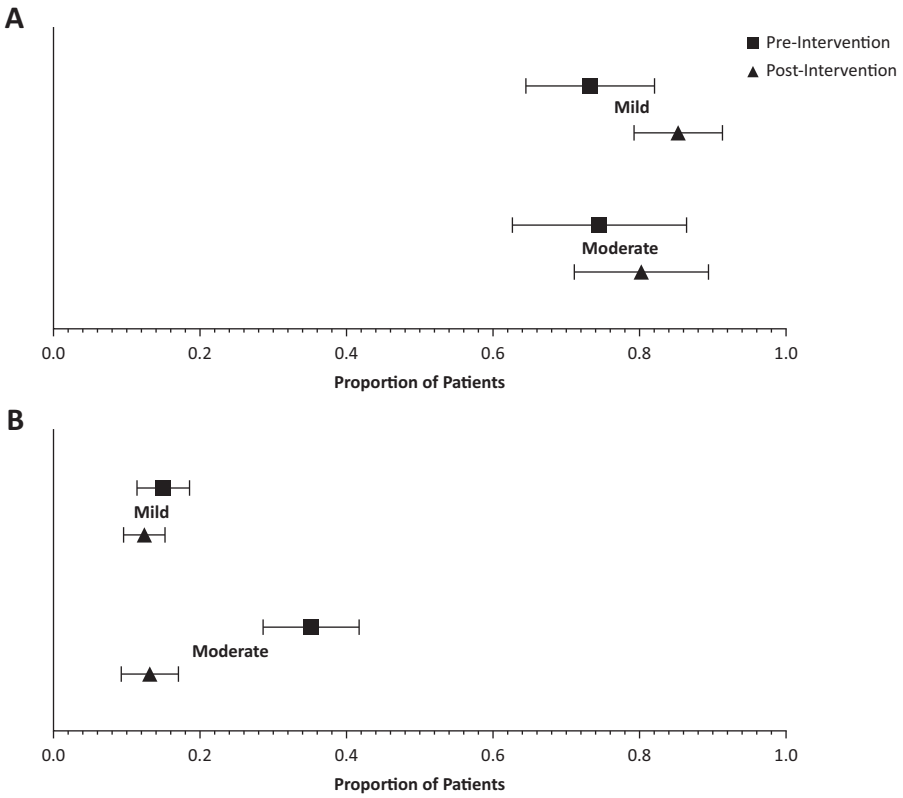

Figure 5. Secondary outcomes by study period and infection severity.

The effect of this intervention was similar at both the academic and community sites.

ED clinician treatment guideline adherence increased by 12.1%. Despite this increase, the compliance rate for guideline adherence remained just greater than 50% for all ED patients treated and 64% of the subset of patients discharged home from the ED. This is consistent with a documented history of low levels of clinicians' adopting published guidelines. In the United States, poor clinician treatment concordance rates for both SSTI types, purulent and nonpurulent, range from 20% to 40%.[13-15]

Among patients admitted to the hospital, our intervention was able to increase guideline adherence to only 30%. This low increase was mainly due to the practice of treating admitted patients with vancomycin; however, the percentage of patients discharged home from the ED after receiving vancomycin decreased to less than 3% after the intervention. Our preintervention percentage of ED ambulatory patients receiving vancomycin is similar to that of previous reports, in which 1 in 5 patients has been shown to receive vancomycin before ED discharge.[14,30] The reduced usage of vancomycin does make positive stewardship strides in reducing vancomycin-resistant enterococci.

Another notable benefit of the implementation of our treatment algorithm was the reduction in hospital admissions. One of the most common reasons for hospital admission from the ED is need for intravenous antibiotics.[31] This often leads to administration of unnecessary broad-spectrum antibiotics and prolonged treatment courses.[32] By focusing our treatment algorithm on the distinction between patients who should receive oral antibiotics alone and those who need hospital admission, we were able to significantly reduce the hospital admission rates and, in so doing, achieve an important antimicrobial stewardship goal.

To our knowledge, this is the first ED-based investigation to implement IDSA guidelines into clinical practice to improve antibiotic prescribing while reducing treatment failure. Our patient-reported failure rate is consistent with clinical trial data failure rates of 15% to 20%.[7,33,34] We observed a similar difference (which did not reach statistical significance) in guideline adherence among the patients followed up; however, vancomycin use was significantly reduced. This may be due simply to sample size or other aspects of the intervention (ie, patient evaluation, disposition decisions). ED-based studies have found that approximately 1 in 5 patients with nonpurulent SSTI and prescribed antibiotics fails treatment.[35,36] This current investigation strengthens the body of literature and gives hospitals and clinicians the tools necessary to improve targeted therapy.

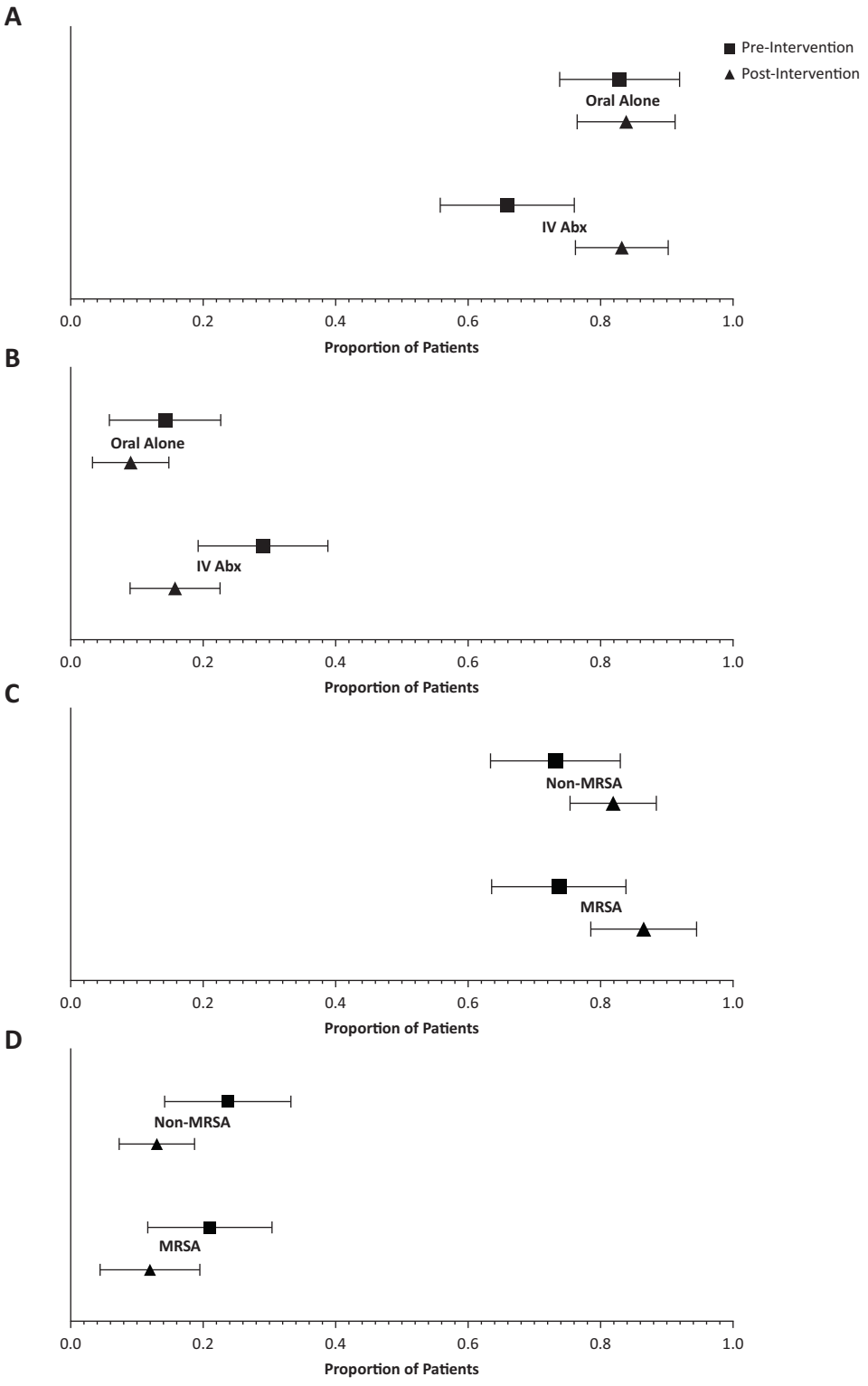

Figure 6. Secondary outcomes by antibiotic route and class.

We demonstrated that an evidence-based treatment intervention for patients with nonpurulent SSTIs can reduce both unnecessary antibiotic exposure and hospital admissions. Our intervention not only made strides in antimicrobial stewardship but also reduced patient-reported outcomes of treatment failure and hospital readmission. Implementing these guidelines may provide a means to reduce antibiotic resistance and improve

patient outcomes for a disease process in which guideline adherence is low and treatment failure rates are high.

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Author contributions: JPH, MC, GS, and MAC conceived the study, designed the trial, and obtained research funding. JPH, AC, RG, AD, and EM supervised the conduct of the trial and data collection. JPH, MG, and AC managed the data, including quality control. MAC provided statistical advice on study design and analyzed the data. JPH drafted the article, and all authors contributed substantially to its revision. JPH takes responsibility for the paper as a whole.

All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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