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Failure of Outpatient Antibiotics among Patients Hospitalized for Acute Bacterial Skin Infections: What is the Clinical Relevance?

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Abstract

Background—Infectious Diseases Society of America guidelines recommend that patients hospitalized for acute bacterial skin infections after failure of outpatient antibiotic therapy be managed as “severe” infections; however, the clinical relevance of apparent failure of outpatient therapy is not clear.

Methods—This was a secondary analysis of a multicenter, retrospective cohort of adults and children hospitalized for cellulitis, abscess, or wound infection. We compared clinical features, laboratory and microbiology findings, antibiotic treatment, and outcomes among patients who received outpatient antibiotics prior to admission and those who did not.

Results—Of 533 patients, 179 (34%) received outpatient antibiotics prior to admission. Compared with those who did not, patients who received antibiotics prior to admission less frequently had fever (18% vs. 26%, $p = .04$) and leukocytosis (33% vs. 51%, $p < .001$). In the 202 cases where a microorganism was identified, *S. aureus* was more common among those who received antibiotics prior to admission (75% vs. 58%, $p = .02$), particularly methicillin-resistant *S.*

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aureus (MRSA) (41% vs. 27%, $p = .049$), whereas aerobic gram-negative bacilli were less common (3% vs. 13%, $p = .03$). After hospitalization, clinical failure occurred with similar frequency between the two groups (12% vs. 11%, $p = .73$).

Conclusions—Patients hospitalized with skin infections after apparently failing outpatient therapy had clinical features suggestive of less severe infection and similar outcomes compared with patients who did not receive antibiotics prior to admission. Our results suggest that inpatient treatment of patients not responding to outpatient therapy should focus on MRSA, not gram-negative pathogens.

Keywords

Acute bacterial skin and skin structure infection; ABSSSI; skin and soft tissue infection; cellulitis; cutaneous abscess

1. Introduction

Acute bacterial skin infections result in approximately 14 million ambulatory care visits [1] and 900,000 hospitalizations [2] per year and are among the leading indications for antibiotic use in hospitals [3]. In prior cohorts of patients requiring hospitalization for acute bacterial skin infections, 28 – 51% had failed an initial attempt at outpatient antibiotic therapy [4, 5]. However, the determination of whether a patient is responding to outpatient therapy can be challenging for Emergency Department providers, particularly in cases of cellulitis, given that the skin may remain inflamed despite eradication of the causative pathogen. Whether failure of outpatient therapy as judged by clinicians is associated with an increased breadth of microbial pathogens or affects clinical outcomes has not been previously studied.

Current Infectious Diseases Society of America guidelines for the management of skin infections stratify treatment recommendations based on a clinical classification of mild, moderate, or severe infection [6]. Patients who have failed outpatient antibiotic therapy, have systemic signs of infection, are immunosuppressed, or have clinical signs suggestive of necrotizing infection are classified as having “severe” infection. In the case of “severe” non-purulent cellulitis, an antibiotic regimen with a broad spectrum of gram-positive and gram-negative activity is recommended (e.g., vancomycin plus piperacillin-tazobactam). Given the frequency of failure of outpatient therapy, adherence to this suggested treatment approach would lead ED providers to start broad-spectrum antibiotics in a sizeable proportion of cases. It is thus important to gain a better understanding of the clinical relevance of failure of outpatient therapy as judged by clinicians. We utilized a large cohort of patients requiring hospitalization for treatment of an acute bacterial skin infection to determine whether an initial attempt at outpatient therapy prior to admission impacted the microbiology, treatment, and clinical outcomes.

2. Methods

2.1 Study Design

We previously described a multicenter, retrospective cohort of patients requiring hospitalization for acute bacterial skin infection between June 1, 2010 and May 31, 2012 [7]. Using this cohort, we performed a secondary analysis comparing patients who were initially attempted to be treated with outpatient antibiotic therapy prior to admission with those who were not.

2.2 Study Setting and Population

The study was performed in seven Colorado hospitals including a Veteran's Affairs hospital, tertiary referral center, public safety-net hospital, children's specialty hospital, and three private community hospitals. Detailed study entry criteria have been described previously [7]. Briefly, adults and children with a principal discharge diagnosis of cellulitis, cutaneous abscess, or wound infection were identified through *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes (680.*, 681.*, 682.*, 686, 035). Cases were manually reviewed to confirm eligibility. The main exclusion criteria were infections with deep tissue involvement (e.g., necrotizing fasciitis, osteomyelitis, myositis) and clinical scenarios that require specialized management, including: infected ulcers, surgical site infection, periorbital or perineal infection, infected human or animal bites, healthcare-associated infections, and hidradenitis suppurativa. At each hospital, for cases meeting study entry criteria, a clinician with experience in the management of skin infections abstracted clinical and pharmacy data from the medical record using a standardized data collection form. Each clinician underwent training to standardize data collection across sites. The study was approved by each hospital's institutional review board.

2.3 Definitions and Study Outcomes

Outpatient antibiotic therapy prior to admission was defined as the receipt of one or more systemic antibiotic for the current episode of skin infection leading up to hospitalization, as documented in the medical record (Figure 1, Panel A). Both parenteral and oral antibiotics prescribed at ambulatory care visits prior to admission were included in this definition; this information was obtained from provider documentation and pharmacy fill data. When it was specifically noted in the medical record that a patient was prescribed an antibiotic but either did not fill the prescription or did not take any doses of the antibiotic, this was not classified as antibiotic therapy prior to admission. Antibiotic courses for a previous, distinct episode of skin infection were also not classified as antibiotic therapy prior to admission. The specific antibiotics received leading up to hospital admission were recorded; however, the number of days of therapy and the timing in relation to admission were not collected as this information was frequently not available in the medical record.

Fever and leukocytosis were defined as a core body temperature of $\geq 38.0^{\circ}\text{C}$ and a serum white blood cell count $>10,000$ cells/mm³, respectively. The Charlson-age comorbidity index (a measure of the presence of underlying medical conditions) and Laboratory Risk Index for Necrotizing Fasciitis (LRINEC) scores were calculated as previously defined [8, 9]. Vancomycin, daptomycin, linezolid, clindamycin, trimethoprim-sulfamethoxazole, and

doxycycline were classified as antibiotics with activity against methicillin-resistant *Staphylococcus aureus* (MRSA). β -lactam/ β -lactamase inhibitor combinations, 2nd- through 5th-generation cephalosporins, fluoroquinolones, carbapenems, tigecycline, aminoglycosides, and colistin were classified as antibiotics with a broad spectrum of gram-negative activity. From the time of hospitalization to 45 days after admission (i.e., excluding the period prior to admission), clinical failure was defined as a composite endpoint of any of the following: 1) treatment failure, defined as a change in antibiotic therapy or unplanned drainage procedure due to inadequate clinical response more than 5 days after hospital admission; 2) recurrence, defined as re-initiation of antibiotics for skin infection after completion of the initial treatment course; or 3) re-hospitalization due to skin infection [10].

2.4 Statistical Analysis

Cases were stratified by the presence or absence of outpatient antibiotic therapy prior to admission. For the analysis of clinical characteristics, laboratory and microbiology data, in-hospital and discharge antibiotic therapy, and clinical outcomes, comparisons were performed using the Chi-square test of association or Fisher's exact test where appropriate for categorical variables and the Wilcoxon non-parametric rank-sum test for continuous variables. Key analyses were stratified by adult (>18 years old) versus pediatric cases. A *P* value of <.05 was considered significant. We used SAS Version 9.3 (SAS Institute, Cary, NC) for data analysis.

3. Results

Of the 533 patients included in the cohort who were hospitalized for management of an acute bacterial skin infection, 179 (34%) received outpatient antibiotic therapy prior to admission while the remaining 354 (66%) did not (Figure 1). The proportion of cases involving outpatient antibiotic therapy prior to admission was similar among adults and children (Supplemental Table 1). For the entire cohort, the demographic characteristics, types of skin infections, risk factors, and anatomic location of infection were largely similar between those who received outpatient antibiotic therapy prior to admission and those who did not (Table 1). Those who received prior antibiotics had lower Charlson age-comorbidity index scores (median 1 [interquartile range (IQR) 0–3] vs. 2 [IQR 0–4], *p* = .03) and less frequently had fever (18% vs. 26%, *p* = .04) and leukocytosis (33% vs. 51%, *p* < .001). C-reactive protein (CRP) levels were performed in similar proportions in each group (52% vs. 57%, *p* = .32). Mean CRP levels (24.5 mg/dL vs. 43.4 mg/dL, *p* = .15) and LRINEC scores (*p* = .06) were lower in the group that received outpatient antibiotic therapy prior to admission; however, these comparisons did not reach statistical significance. In addition, those who received antibiotics prior to admission were more frequently admitted from outpatient clinics (16% vs. 7%) and less frequently admitted from the emergency department (79% vs. 87%) (*p* = .002).

3.1 Microbiology

Microbiological cultures were less likely to be obtained in patients who received outpatient antibiotics prior to admission (77% vs. 85%, *p* = .02), primarily due to less frequent use of blood cultures (55% vs. 69%, *p* < .001) (Table 2). At least one microorganism was identified

in a similar proportion of cases in the two groups (35% vs. 39%, $p = .36$). Of the 202 cases in which a microorganism was identified, *S. aureus* was more common among those who received outpatient antibiotics prior to admission (75% vs. 58%, $p = .02$), particularly MRSA (41% vs. 27%, $p = .049$). In contrast, β -hemolytic streptococci (10 vs. 22%, $p = .03$) and aerobic gram-negative organisms (3% vs. 13%, $p = .03$) were identified less frequently among those who received antibiotics prior to admission. The microbiological findings were similar when the analysis was stratified by adult versus pediatric cases (Supplemental Table 1) and when limited to cases involving purulent infections (Supplemental Table 2).

3.2 Outpatient Antibiotic Therapy Prior to Admission

Of the 179 patients who received outpatient antibiotic therapy prior to admission, 142 (79%) had received oral antibiotics alone while 37 (21%) received at least one dose of a parenteral agent (Table 3). Seventy-five (42%) received more than one antibiotic prior to admission. The outpatient antibiotic regimen lacked an MRSA-active agent in 67 (37%) cases, including 19 of 60 (32%) cases involving a cutaneous abscess.

3.3 Antibiotic Therapy after Hospital Admission

Once hospitalized, patients who received outpatient antibiotic therapy prior to admission were more likely to be started on an MRSA-active agent (92% vs. 85%, $p = .04$) – most commonly vancomycin – by the provider assuming care for the patient in the hospital (Table 4). Of the 67 patients who received antibiotics that lacked MRSA activity prior to admission, 58 (87%) were started on MRSA-active therapy in the hospital. Patients who received antibiotics prior to admission were somewhat more likely to be prescribed combination antibiotic therapy upon hospitalization (41% vs. 33%, $p = .06$). Use of antibiotics with broad gram-negative activity upon hospitalization were similar between the groups (38% vs. 32%, $p = .18$). At the time of hospital discharge, more patients who had received outpatient antibiotic therapy prior to admission were prescribed an MRSA-active agent (79% vs. 67%, $p = .003$) and combination therapy (22% vs. 15%, $p = .049$).

3.4 Clinical Outcomes after Hospitalization

From the time of hospitalization to the end of the 45-day follow-up period, there were no significant differences in the composite endpoint of clinical failure (12% vs. 11%, $p = .73$) nor the individual components of this endpoint between the two groups (Table 5). For patients who received outpatient antibiotic therapy prior to admission, the median length of hospital stay was shorter (3 [IQR 3 – 5] vs. 4 [IQR 3 – 5] days, $p = .07$), although this difference did not reach statistical significance.

4. Discussion

Similar to previous studies [4, 5], in this multicenter cohort, we found that approximately one-third of patients requiring hospitalization for acute bacterial skin infections had been attempted to be treated as outpatients prior to admission. To our knowledge, this is the first study to evaluate the clinical relevance of what is frequently referred to as “failure of outpatient therapy” by evaluating the effects of outpatient antibiotic therapy prior to admission on the microbiology, treatment, and clinical outcomes. We found that compared

with patients who were not attempted to be treated with outpatient antibiotics prior to admission, those who appeared to have failed outpatient therapy had features of less severe illness: they had less frequent fever and leukocytosis, a trend toward lower CRP levels and LRINEC scores, and fewer comorbidities. *S. aureus* was more likely to be isolated from those who received outpatient therapy prior to admission, but aerobic gram-negative or anaerobic pathogens were not. Initiation of antibiotic therapy with MRSA activity in the hospital and prescription of an MRSA-active agent at hospital discharge were more common among those who received outpatient therapy prior to admission. Clinical outcomes between the two groups were similar.

There are a number of reasons why patients with acute bacterial skin infections may not appear to have an appropriate clinical response to initial outpatient antibiotic therapy (Figure 1). Among such reasons are failure to drain abscesses, insufficient antibiotic levels at the site of infection, antimicrobial-resistant pathogens, patient non-adherence to antibiotic therapy, ongoing inflammation despite eradication of the infecting pathogen, or incorrect diagnosis. Although the lack of clear improvement in signs and symptoms of infection after the initiation of outpatient antibiotics is often considered by clinicians to represent “failure of outpatient therapy” and is referred to as such in IDSA guidelines, our results raise the question of whether the lack of response is due to a true failure of antibiotic therapy or a process that mimics ongoing infection. One might expect that patients who truly fail outpatient antibiotic therapy are more likely to have underlying comorbid conditions or severe infection that reduce the probability of initial treatment success; the findings from this study are therefore notable. First, compared to patients who did not receive outpatient antibiotics prior to admission, those with apparent failure of outpatient therapy actually had lower Charlson comorbidity scores, fewer comorbidities that might delay the clinical response to antibiotics such as lower extremity vascular impairment and immunosuppression, less frequent fever and leukocytosis, and a trend toward lower CRP levels and LRINEC scores. In addition, they were more likely to have presented to an outpatient clinic and had a trend toward shorter hospital stays.

Taken together, these findings suggest that the group of patients with apparent failure of outpatient therapy had milder, less complicated infections. One logical explanation for this is that patients who were hospitalized *without* receiving antibiotics prior to admission had associated comorbid conditions or severe infections that compelled ED providers to hospitalize immediately rather than attempt outpatient treatment. However, an alternative explanation is that the patients with apparent failure of outpatient therapy had evidence of less severe infection because the outpatient antibiotics were effective to some degree. That is, the outpatient antibiotics had at least partially treated the infection by the time of hospitalization despite the clinical findings that prompted hospitalization. This is plausible since residual inflammation (erythema) of the skin after eradication of the infecting pathogen can be difficult to distinguish from active infection. This underscores the potential importance of research to identify biomarkers that correlate with treatment response that could be used as a tool to augment the clinical evaluation of the response to therapy.

The differences in the microbiology between the two groups have potentially important treatment implications. First, as discussed previously, current IDSA guidelines suggest that

failure of outpatient therapy should prompt the classification of “severe” infection, and, in the case of non-purulent cellulitis, treatment with broad-spectrum antibiotic regimens [6]. In our cohort, patients who had apparently failed outpatient therapy had a significantly lower frequency of gram-negative pathogen involvement and similar frequency of anaerobic involvement. In addition, *S. aureus*, particularly MRSA, was actually more common among those who failed outpatient therapy. Although the findings from this study must be interpreted cautiously, the clinical and microbiological data suggest that in patients with skin infections who require hospitalization due to an inadequate response to outpatient antibiotic therapy, expanding therapy to include gram-negative and anaerobic activity is not likely to be beneficial, and thus is not routinely indicated. Furthermore, these data suggest that in the IDSA guideline, grouping failure of outpatient therapy with clinical factors such as immunosuppression and evidence of necrotizing infection as criteria for “severe” infection may not be appropriate. Additional studies are needed to confirm these preliminary findings and to investigate the underlying reasons for apparent lack of clinical response to outpatient therapy. Furthermore, in future revisions to national guidelines, treatment recommendations for this common clinical scenario should be re-evaluated.

The fact that *S. aureus* was isolated more commonly in cases that involved apparent failure of outpatient therapy warrants additional discussion. There are several potential explanations for this finding. First, skin infections caused by *S. aureus* may be more difficult to treat or may be slower to clinically respond compared with those caused by streptococci and other pathogens (e.g., due to increased virulence, antimicrobial resistance). Therefore, among patients not responding to outpatient antibiotic therapy who require hospitalization, this could result in a disproportionate number of cases involving *S. aureus* compared with those who are hospitalized without an attempt at outpatient treatment. Second, in our cohort, the outpatient antibiotic regimen lacked MRSA activity in over 30% of cases, including in cutaneous abscesses where MRSA is known to be the most common pathogen [10, 11]. This frequent lack of MRSA-active antibiotic therapy may have contributed to the disproportionate identification of MRSA among patients who failed outpatient therapy as compared with those who did not receive antibiotics prior to admission. It is also important to note that of patients with a cutaneous abscess who failed outpatient therapy, approximately half had not undergone incision and drainage. Since drainage is the mainstay of therapy for abscesses, this may explain the lack of clinical response to antibiotic therapy in such cases. These findings suggest that ensuring primary drainage of skin abscesses and prescription of antibiotics with MRSA activity (when the decision is made to prescribe adjunctive antibiotics) are opportunities to improve the initial management of acute bacterial skin infections that may potentially reduce the need for hospitalizations.

5. Limitations

This study has a number of limitations. First, as a secondary analysis with multiple comparisons, there is the risk of Type 1 error. We did not adjust for multiple comparisons since this was an exploratory analysis that was intended to raise questions for the field about a common clinical scenario. Second, since the data were collected retrospectively, the exposure variable of receipt of outpatient antibiotic therapy prior to admission (failure of outpatient therapy) was subject to misclassification. The most likely misclassification is that

antibiotics were taken prior to admission but not reported by the patient or not documented by the provider in the medical record; however, this would have biased the comparison between the two groups toward the null. In addition, the specific rationale for the decision to hospitalize patients who were receiving outpatient antibiotic therapy prior to admission was not known. Since this study was limited to cases where the skin infection was the primary reason for admission (i.e., the principal diagnosis), it is likely that most cases were judged by providers not to be responding adequately to the outpatient antibiotic therapy; however, there may have been alternative reasons for admission in a subset of cases. Third, we were not able to evaluate the underlying reasons for the apparent lack of response to outpatient therapy with this study design. Fourth, the study included only patients who were hospitalized for treatment. It would have also been of interest to have a comparison group of patients who were treated as outpatients and responded appropriately to therapy. Fifth, due to the observational nature of the study, the comparisons made were subject to confounding, and thus, the observed differences between the groups may have been due to factors other than the receipt of outpatient antibiotic therapy prior to admission. Sixth, we did not have data on the dose, duration, and adherence to antibiotics prescribed prior to admission and thus cannot make inferences about their effects. Finally, since the infecting pathogen is uncommonly identified in patients with cellulitis, the inferences from the microbiological data may not be able to be extrapolated to cellulitis.

6. Conclusions

This study highlights that among patients requiring hospitalization for acute bacterial skin infection, an apparent lack of clinical response to initial outpatient therapy was very common. Compared with patients who did not receive antibiotics prior to admission, those who appeared to fail outpatient therapy had fewer comorbidities, clinical features of less severe illness, and similar outcomes. These findings have potential implications for ED providers, raising the question of whether such cases could represent partially treated infection rather than true failure of therapy. In our cohort, the key interventions among patients who had received prior antibiotic therapy were to assure coverage for MRSA and identify drainable pus. Additional research is needed to better understand the reasons for the frequent apparent lack of clinical response to outpatient therapy and to develop tools to augment clinical judgment when evaluating response to therapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Conceptual framework of the process of care for patients requiring hospitalization for treatment of acute bacterial skin infections. Panel A represents patients who appear to fail an initial attempt at outpatient antibiotic therapy and lists potential reasons for the lack of response to therapy. Panel B represents patients hospitalized for initial treatment with no attempt at outpatient antibiotic therapy. Ambulatory care refers to emergency departments, urgent care, and outpatient clinics.

Table 1

Demographic and clinical characteristics

	Outpatient antibiotic therapy prior to admission N=179	No antibiotics prior to admission N=354	<i>P</i>
Type of infection			.20
Non-purulent cellulitis	98 (55)	222 (63)	
Wound infection or purulent cellulitis	21 (12)	23 (7)	
Cutaneous abscess	60 (34)	109 (31)	
Age, mean (SD)	42 (23)	46 (25)	.08
Male	101 (56)	216 (61)	.31
Comorbid conditions/risk factors			
Diabetes mellitus	39 (22)	68 (19)	.48
Injection drug use	11 (6)	25 (7)	.70
HIV infection	3 (2)	9 (3)	.76
Dialysis dependence	4 (2)	3 (1)	.23
Cirrhosis	3 (2)	18 (5)	.06
Lower extremity vascular impairment ^a	25 (14)	71 (20)	.08
Prior skin infection	51 (28)	94 (27)	.63
Prior MRSA infection or colonization	18 (10)	42 (12)	.53
Immunosuppressing medication or condition	17 (10)	52 (15)	.09
Charlson age-comorbidity index, median (IQR)	1 (0–3)	2 (0–4)	.03
Anatomical location			
Head and neck	23 (13)	31 (9)	.14
Upper extremity	27 (15)	75 (21)	.09
Trunk	13 (7)	25 (7)	.93
Buttock, inguinal, or groin	13 (7)	27 (8)	.88
Lower extremity	107 (60)	218 (62)	.69
Site from which admitted to hospital			.002
Emergency department	141 (79)	309 (87)	
Urgent care center	9 (5)	20 (6)	
Outpatient clinic	29 (16)	25 (7)	
Core body temperature, °C, mean (SD)	37.1 (0.9)	37.4 (0.9)	.002
Fever ^b	32 (18)	91 (26)	.04
Serum WBC count, cells/mm ³ , mean (SD)	9.7 (4.2)	11.6 (6.4)	<.001
Leukocytosis ^c	59 (33)	182 (51)	<.001
Fever or leukocytosis	76 (42)	215 (61)	<.001
CRP obtained	93 (52)	200 (57)	.32
CRP, mg/dL, mean (SD)	24.5 (35.3)	43.4 (59.4)	.15

	Outpatient antibiotic therapy prior to admission N=179	No antibiotics prior to admission N=354	<i>P</i>
LRINEC score	N=69	N=126	.06
0–5	68 (99)	116 (92)	
6–7	1 (1)	8 (6)	
8	0	2 (2)	

Note: Data presented as n (%) unless otherwise noted

SD, standard deviation; IQR, interquartile range; WBC, white blood cell; CRP, C-reactive protein; LRINEC, laboratory risk indicator for necrotizing fasciitis

^a chronic venous stasis, lymphedema, peripheral arterial disease, saphenous vein harvest

^b core body temperature 38.0° Celsius

^c serum WBC >10,000 cells/mm³

Table 2

Microbiology

	Outpatient antibiotic therapy prior to admission N=179	No antibiotics prior to admission N=354	P
Any microbiological culture obtained	138 (77)	302 (85)	.02
Surface culture	30 (17)	52 (15)	.53
Abscess material	47 (26)	91 (26)	.89
Tissue culture	10 (6)	25 (7)	.52
Blood culture	98 (55)	246 (69)	<.001
Any microorganism identified	63 (35)	139 (39)	.36
Any gram-positive organism	61 (97)	129 (93)	.35
<i>Staphylococcus aureus</i>	47 (75)	80 (58)	.02
Methicillin-susceptible	20 (32)	38 (27)	.52
Methicillin-resistant	26 (41)	38 (27)	.049
Susceptibility not performed	1 (2)	4 (93)	1.00
Streptococcal species	16 (25)	43 (31)	.42
<i>S. anginosus</i> group	5 (8)	10 (7)	1.00
β -hemolytic streptococcus	6 (10)	31 (22)	.03
Other alpha-hemolytic streptococcus	4 (6)	4 (3)	.26
Other	1 (2)	1 (1)	.53
<i>S. aureus</i> or streptococci	57 (90)	114 (82)	.12
Coagulase-negative staphylococcus	11 (17)	22 (16)	.77
Aerobic gram-negative	2 (3)	18 (13)	.03
Anaerobic organism(s)	4 (6)	13 (9)	.48
Enterococcus species	0	2 (1)	1.00
Other	4 (6)	6 (4)	.51

Note: Data presented as n (%)

Table 3

Antibiotics administered or prescribed at ambulatory care visits for the 179 patients who received outpatient antibiotic therapy prior to admission.

	Non-purulent cellulitis N=98	Purulent cellulitis or wound infection N=21	Cutaneous abscess N=60	Total N=179
Received parenteral antibiotic	20 (20)	7 (33)	10 (17)	37 (21)
Received oral antibiotic(s) only	79 (80)	14 (67)	50 (83)	142 (79)
Received two or more antibiotics	41 (42)	12 (57)	22 (37)	75 (42)
Any MRSA-active agent	56 (57)	15 (71)	41 (68)	112 (63)
Trimethoprim-sulfamethoxazole	35 (36)	14 (67)	29 (48)	78 (44)
Clindamycin	11 (11)	0	6 (10)	17 (10)
Doxycycline	6 (6)	2 (10)	5 (8)	13 (7)
Linezolid	2 (2)	0	0	2 (1)
Parenteral MRSA-active agent ^a	10 (10)	4 (19)	8 (13)	22 (12)
Any β -lactam	68 (69)	15 (71)	35 (58)	118 (66)
Cephalexin	41 (42)	12 (57)	26 (43)	79 (44)
Amoxicillin-clavulanate	16 (16)	1 (5)	3 (5)	20 (11)
Other oral β -lactam	8 (8)	2 (10)	3 (5)	13 (7)
Parenteral β -lactam ^b	12 (12)	4 (19)	5 (8)	21 (12)
Fluoroquinolone	5 (5)	0	3 (5)	8 (4)
Other or unknown	4 (4)	1 (5)	2 (3)	7 (4)
Drainage procedure prior to presentation	4 (4)	4 (19)	29 (48)	37 (21)

Note: Data presented as n (%)

^aParenteral vancomycin (17) or daptomycin (5)

^bParenteral cephalosporin (17), ertapenem (3), or ampicillin-sulbactam (1)

Table 4

Antibiotic therapy after hospital admission.

	Outpatient antibiotic therapy prior to admission N=179	No antibiotics prior to admission N=354	P
<i>Antibiotics initiated by the hospital provider assuming care for patient</i>			
MRSA-active agent	164 (92)	302 (85)	.04
Agent with broad gram-negative activity	68 (38)	114 (32)	.18
Combination therapy ^a	74 (41)	117 (33)	.06
Vancomycin	128 (72)	224 (63)	.06
Clindamycin	39 (22)	82 (23)	.72
β-lactam/ β-lactamase inhibitor combination	34 (19)	62 (18)	.67
Higher generation cephalosporins	14 (8)	29 (8)	.88
Cefazolin	7 (4)	27 (8)	.10
Carbapenem	12 (7)	12 (3)	.08
Other ^b	26 (15)	45 (13)	.56
<i>Antibiotics prescribed at hospital discharge</i>			
MRSA-active agent	142 (79)	237 (67)	.003
Agent with broad gram-negative activity	37 (21)	85 (24)	.39
Combination therapy	39 (22)	53 (15)	.049
Clindamycin	43 (24)	99 (28)	.33
Trimethoprim-sulfamethoxazole	51 (28)	67 (19)	.01
Cephalexin	17 (10)	49 (14)	.15
Amoxicillin-clavulanate	17 (10)	47 (13)	.20
Doxycycline	26 (15)	42 (12)	.38
Fluoroquinolone	14 (8)	27 (8)	.94
Linezolid	13 (7)	14 (4)	.10
Vancomycin or daptomycin	17 (9)	18 (5)	.052
Other ^c	12 (7)	30 (8)	.47
Total duration of therapy, median (IQR)	12 (10–15)	12 (10–15)	.59
Duration of inpatient therapy, median (IQR)	3 (3–4)	4 (3–5)	.16
Duration of therapy after discharge, median (IQR)	9 (7–10)	8 (7–10)	.58

Note: Data presented as n (%) unless otherwise noted

IQR, interquartile range

^a defined as receipt of two or more antibiotics concurrently^b Includes fluoroquinolone (23), daptomycin (18), nafcillin (7), linezolid (7), trimethoprim-sulfamethoxazole (9), doxycycline (3), other β-lactam (5), other (9)^c Includes nafcillin (1), ertapenem (5), meropenem (1), ceftriaxone (4), rifampin (1), cefuroxime (1), cefdinir (2), ceftaroline (1), amoxicillin (5), dicloxacillin (14), penicillin VK (1), metronidazole (1), erythromycin (1)

Table 5

Clinical outcomes after hospitalization.

	Outpatient antibiotic therapy prior to admission N=179	No antibiotics prior to admission N=354	P
Survived to discharge	179 (100)	353 (99.7)	1.00
Clinical failure	21 (12)	38 (11)	.73
Treatment failure	8 (4)	22 (6)	.40
Recurrence	12 (7)	15 (4)	.22
Rehospitalization due to skin infection	11 (6)	21 (6)	.92
Rehospitalization for reason other than skin infection	9 (5)	22 (6)	.58
Length of stay, median days (IQR)	3 (3–5)	4 (3–5)	.07

Note: Data presented as n (%) unless otherwise noted

IQR, interquartile range