BMC Infectious Diseases

RESEARCH

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Antibiotic adherence and treatment completion associated with partial oral therapy versus all intravenous therapy in patients with serious *Staphylococcus aureus* infections

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Abstract

Background Partial oral antibiotic therapy is a safe and effective alternative to all intravenous (IV) therapy for serious *Staphylococcus aureus* infections; however, antibiotic adherence and treatment completion rates associated with partial oral therapy outside of clinical trials are unknown.

Methods This was a retrospective study of adults hospitalized with *S. aureus* bacteremia, endocarditis, or bone or joint infection. Co-primary outcomes of antibiotic adherence and treatment completion were compared between patients who transitioned to oral antibiotics during treatment or received all IV therapy. Factors associated with lack of treatment completion were evaluated by logistic regression.

Results Of 249 patients, 148 (59%) and 101 (41%) were treated with partial oral or all IV therapy, respectively. Use of partial oral therapy was more common for bone or joint (73% of cases) than bloodstream infections (21% of cases). Antibiotic adherence was similar between the partial oral and all IV groups; 90% and 98% of patients completed the planned course, respectively ($p = 0.38$). By logistic regression, partial oral therapy was independently associated with lack of treatment completion (odds ratio 4.53 [95%CI 1.0–20.6]). Clinical failure occurred in 26% and 25% of patients who received partial oral and all IV therapy, respectively ($p = 0.87$).

Conclusions In clinical practice, a high proportion of patients treated with partial oral therapy for serious *S. aureus* infections completed treatment, but partial oral therapy was an independent risk factor for failure to complete treatment. These findings highlight the importance of identifying and addressing barriers to adherence when considering oral therapy.

Keywords Staphylococcus aureus, MSSA, MRSA, Deep-seated infection, Partial oral therapy, Adherence

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Background

Serious *Staphylococcus aureus* infections such as bacteremia, endocarditis, or other deep-seated infections are associated with substantial morbidity and mortality [1]. These infections typically require durations of therapy ranging from two to six weeks or longer [2]. Such prolonged treatment courses often pose logistical challenges to completion of therapy.

Due to potential barriers associated with prolonged courses of intravenous (IV) therapy, there has been increasing interest in use of oral therapy for serious *S. aureus* infections. In 2019, the landmark POET and OVIVA randomized trials demonstrated partial oral therapy to be non-inferior to all IV therapy for left-sided infective endocarditis and bone or joint infections, respectively [3, 4]. Furthermore, a recent systematic review and meta-analysis of randomized trials of patients with *S. aureus* bacteremia or endocarditis concluded that transitioning from intravenous to oral therapy is likely effective in selected patients [5].

In clinical practice, transitioning to oral therapy after clinical improvement on IV therapy in patients with serious *S. aureus* infections may pose several advantages over all IV regimens including avoidance of central venous catheter placement, the potential for fewer treatment-related adverse events, lower costs, and shorter length of stays [6–10]. In addition, patients with serious *S. aureus* infections often have concomitant substance use disorders, mental health disorders, or are experiencing homelessness which may preclude completion of an IV antibiotic course in the community. Such patients are therefore frequently kept in the hospital to complete an entire IV antibiotic course; however, these prolonged hospitalizations have potentially negative consequences for patients such as social isolation and inadequate inpatient substance use treatment. Among such patients, self-directed discharges (i.e., discharges against medical advice) are common and may further contribute to poor clinical outcomes [11].

Transitioning to oral antibiotic therapy once patients are medically stable for discharge is an attractive alternative to all IV therapy. However, the same factors that may preclude the safe administration of IV antibiotics in the community (e.g., substance use, mental health disorders, housing instability) may reduce the ability of patients to adhere to prescribed oral antibiotics, attend outpatient follow-up visits, and complete the recommended treatment course. Thus, in clinical practice – particularly in safety net institutions with a large proportion of vulnerable patients – it is not known whether partial oral therapy is truly an effective alternative to all IV therapy. The purpose of this study was to evaluate uptake of partial oral therapy for serious *S. aureus* infections in a public safety net institution and compare antibiotic adherence and treatment completion rates between patients treated with partial oral or all IV therapy.

Methods

Study setting

Denver Health is an academic, integrated health care system consisting of a 555-bed acute care hospital, 10 community health centers, three urgent care centers, an emergency department, and 18 school-based health clinics. It serves over 1 million people in Denver and surrounding metropolitan areas, a large proportion of whom are medically underserved. Denver Health Medical Center is the largest public safety-net hospital in Colorado.

Study design

This was a retrospective, observational cohort study. Adults 18 years and older hospitalized at Denver Health Medical Center between January 1, 2019 and June 30, 2021 with a blood, bone, synovial fluid, tissue, abscess, or other sterile site culture positive for *S. aureus* and who had an Infectious Diseases (ID) service consult were identified via our healthcare data warehouse. Of note, ID consultation is required for all patients with *S. aureus* bacteremia at Denver Health. The electronic health record of a random subset (identified by Microsoft Excel random number generator) of cases was screened to determine study eligibility. Patients were included if they had a diagnosis of bacteremia, infective endocarditis, osteomyelitis, or septic arthritis. Only the first episode of infection during the study period was included. Patients were excluded if they were not a candidate for oral antibiotics for medical reasons (e.g., impaired absorption of oral medications), left against medical advice before a treatment plan had been established, or were transferred from an outside hospital or discharged to receive ongoing care outside of Denver Health (i.e., incomplete records). For patients meeting study eligibility criteria, detailed electronic health record review was performed to extract clinical data, antibiotic treatment, and outcomes. A standardized data collection instrument was developed using a REDCap electronic database [12] hosted by the Rocky Mountain Drug and Poison Center. After two study authors (K.S. and A.C.) reviewed five pilot cases to establish an accurate and consistent data extraction process, a single reviewer (A.C.) extracted the following data from the electronic health record: demographics, clinical characteristics, microbiologic and diagnostic data, antibiotic therapy, and clinical visits within 6 months of the date of hospital admission.

In many cases, it cannot be determined retrospectively whether the initial intent of treating clinicians is to treat

exclusively with IV therapy or transition to oral therapy. In addition, treatment plans often evolve over the course of therapy. For these reasons, patients were categorized into partial oral and IV therapy groups based on what they actually received; those who received an oral antibiotic for any duration were categorized into the partial oral therapy group; whereas, the IV group received exclusively IV antibiotics (adjunctive oral rifampin allowed). For example, a patient who received four weeks of IV therapy in the hospital and was discharged to complete two weeks of oral therapy was categorized as having received partial oral therapy. Pre-specified clinical outcomes were assessed during a 6-month follow up period from the date of initial hospital admission. The study was approved by the Colorado Multiple Institutional Review Board with a waiver of informed consent. The study was conducted in accordance with the Declaration of Helsinki.

Outcome measures and definitions

The co-primary outcomes were the rate of antibiotic adherence and the proportion of patients who completed the planned antibiotic course. Antibiotic adherence was calculated as the proportion of the number of days of antibiotic taken (or received) out of the number of days planned by the ID service. Antibiotic days taken or received were estimated using inpatient medication administration records, fill records of outpatient prescriptions, and documentation at outpatient visits. Treatment completion was defined as provider documentation of completion of the planned antibiotic course in the electronic health record, or if such documentation was not available, confirmation of pick-up of the final antibiotic prescription. The planned antibiotic duration was based on the last ID note documenting a treatment plan. Patients who died prior to the planned end of therapy were excluded from the analysis of antibiotic adherence and treatment completion. The key secondary outcome of clinical failure was a composite of all-cause mortality, recurrent infection, new metastatic site of *S. aureus* infection identified more than 7 days after the initial positive culture, or requirement of an unplanned source control procedure within 6 months of the date of initial hospitalization [3, 4, 13]. An unplanned source control procedure was defined as any procedure that occurred more than 7 days after a presumed definitive source control procedure. Publicly available state vital records were used to identify deaths that occurred outside of Denver Health during the 6-month follow-up period.

Data analysis

The co-primary outcomes and pre-specified secondary outcomes were compared between the partial oral therapy and all IV groups for the overall cohort and stratified by the presence of substance use disorder, bone or joint infection, and bacteremia. Categorical and continuous variables were compared using the Chi-Square and Mann–Whitney U test, respectively. Multivariate logistic regression was conducted to model factors associated with failure to complete the treatment course. This model was developed using stepwise, best subset variable selection to maximize the Akaike information criterion. Because of the limited number of events, a maximum of two independent predictors were allowed into the model to reduce the likelihood of overfitting. As the primary explanatory variable, partial oral therapy (versus all IV) was included in the model. Inclusion of substance use disorder as the second variable provided the best model fit. A p value ≤ 0.05 was considered statistically significant.

Results

Nine hundred seventy-eight inpatients who had a positive *S. aureus* culture and ID consult during the pre-specified study period were identified. A random subset of 406 cases were reviewed, of which 249 met inclusion criteria as detailed in Fig. 1. Of these, 148 (59%) were treated with partial oral therapy and 101 (41%) received all IV therapy. Demographic characteristics and comorbid conditions were similar between the two groups (Table 1). Most patients were men (74% overall). Substance use disorders (50% overall) and homelessness (27% overall) were common among both groups. Notably, the proportion of patients who used injection drugs was similar between groups (18% vs 17%). More patients in the all IV group required an intensive care unit stay (33% vs 10%).

Eighty-six (35%) patients had an infection that involved bacteremia. Of these, 18 (21%) were treated with partial oral therapy while 68 (79%) received all IV therapy (Table 2). In contrast, of 188 patients with a bone or joint infection (with or without bacteremia), 138 (73%) were treated with partial oral therapy while 50 (36%) received all IV therapy. Use of partial oral therapy for complicated bacteremia and infective endocarditis was particularly uncommon. Vancomycin and cefazolin were the most common definitive IV antibiotic agents; clindamycin, levofloxacin, and linezolid (with or without rifampin) were the most common oral agents. Overall, the median treatment duration was 30 days (interquartile range [IQR] 14–42 days) and was similar between groups. In the partial oral therapy group, the median duration of IV therapy prior to oral transition was 4 days.

Of patients alive at the end of the planned treatment, rates of antibiotic adherence were similar among the two groups (Table 3). One hundred thirty-three (90%) who received partial oral therapy completed

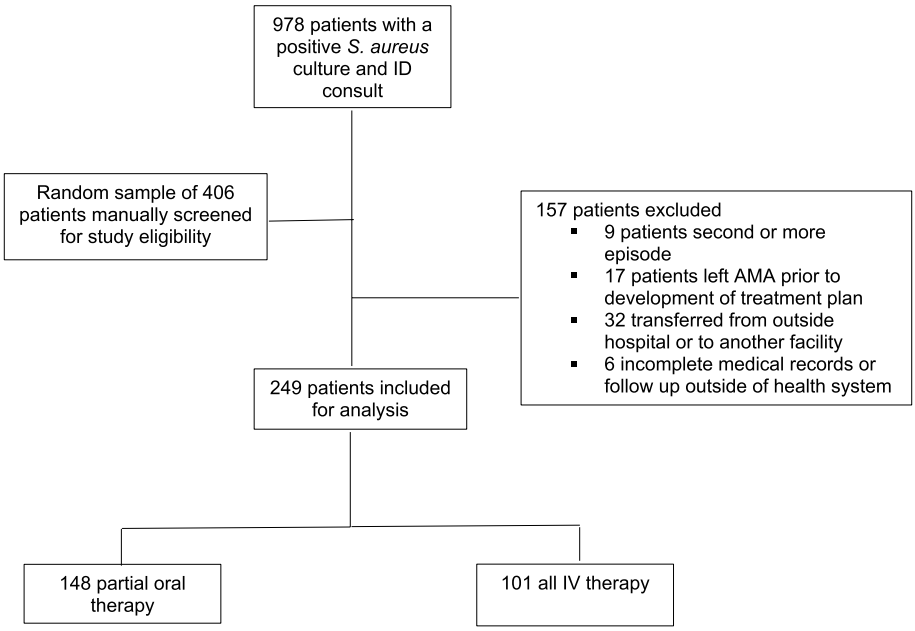

Fig. 1 Study flow diagram

their treatment course compared with 94 (98%) who received all IV therapy ($p = 0.38$). In the logistic regression model of factors associated with lack of treatment completion, both partial oral therapy (odds ratio 4.53 [95%CI 1.0–20.6]) and substance use disorder (OR 7.41 [95%CI 1.6–33.4]) were independently associated with failure to complete therapy.

The composite outcome of clinical failure occurred in 38 (26%) and 25 (25%) of patients in the partial oral and all IV therapy groups, respectively ($p = 0.87$). Similar proportions of patients in both groups required a change in antibiotic therapy or experienced an antibiotic-related adverse event. The median length of hospital stay was 6 (IQR 4–9) days and 12 (IQR 9–23) days in the partial oral and all IV therapy groups, respectively ($p = < 0.01$), and in the partial oral therapy group, a significantly larger proportion of the treatment course was completed in the outpatient setting (median 78% vs 50%, respectively, $p = < 0.01$). However, post-hospital discharge visits to an emergency department or urgent care center were more frequent in the partial oral therapy group (24% vs 9%, $p = < 0.01$).

In pre-specified subgroup analyses, patients with substance use disorder and bone or joint infection who were treated with partial oral therapy had significantly lower antibiotic adherence and treatment completion rates than those who received all IV therapy (Table 4).

Discussion

To our knowledge, this is the first study to compare antibiotic adherence and treatment completion rates with partial oral therapy versus all IV therapy for serious *S. aureus* infections in real world clinical practice. Clinical trials have previously established the safety and efficacy of partial oral therapy compared with IV therapy for invasive *S. aureus* infections [3–5, 14]. The purpose of this observational study was therefore to assess uptake of use of oral therapy and compare outcomes associated with the decision to use each strategy outside of the idealized clinical trial setting. The current study adds to the existing literature because differences in adherence or treatment completion rates with partial oral therapy as compared with IV therapy could be a leading indicator for poor clinical outcomes.

We demonstrated substantial uptake of partial oral therapy – used in about 60% of all cases – but observed markedly higher uptake for bone or joint infections (73% of cases) than for infections involving bacteremia (21% of cases), perhaps reflecting an increased comfort level with oral therapy for bone or joint infections than for bloodstream infections among ID clinicians at our institution. The fact that osteomyelitis and septic arthritis are more often amenable to definitive surgical source control than bacteremia or endocarditis may be one factor that in part explains this. Similarly, patients with bone or joint

Table 1 Demographic and baseline clinical characteristics[a]

	Partial Oral Therapy	All Intravenous Therapy	Total
Characteristic	(*n* = 148)	(*n* = 101)	(*N* = 249)
Age, median (IQR)	55 (42–62)	57 (48–65)	56 (44–63)
Male sex	115 (78)	70 (69)	185 (74)
Required intensive care unit stay[b]	14 (10)	33 (33)	47 (19)
Comorbid conditions			
HIV infection	2 (1)	5 (5)	7 (3)
Cardiovascular disease	64 (43)	51 (51)	115 (46)
Diabetes mellitus	68 (46)	38 (38)	106 (43)
Dialysis-dependent	5 (3)	11 (11)	16 (6)
Chronic liver disease	20 (14)	20 (20)	40 (16)
Antimicrobial prophylaxis prior to admission	3 (2)	1 (1)	4 (2)
Immunosuppression	2 (1)	4 (4)	6 (2)
Trauma within 30 days	1 (1)	2 (2)	3 (1)
Surgery within 30 days	12 (8)	10 (10)	22 (9)
Experiencing homelessness	42 (28)	25 (25)	67 (27)
Active substance use disorder[c]	82 (55)	43 (43)	125 (50)
Injection drug use[d]	26 (18)	17 (17)	43 (17)
Initiated or maintained on MOUD[e]	18 (12)	16 (16)	34 (14)
QSOFA score[f]			
0	99 (67)	46 (46)	145 (58)
1	46 (31)	37 (37)	83 (33)
2	2 (1)	13 (13)	15 (6)
3	1 (1)	5 (5)	6 (2)

[a] Data presented as *n* (%) unless noted otherwise

[b] At any point during hospitalization

[c] Medical record documentation of alcohol, opioid, or stimulant use disorder with use within the last year

[d] Medical record documentation of injection drug use within the last year

[e] MOUD, medication for opioid use disorder

[f] qSOFA- quick sequential organ failure assessment based on data collected 48 h after positive culture

infections may be perceived to be at lower risk for morbidity and mortality (e.g., septic shock, death) than bacteremia or endocarditis should the infection recur. Finally, the fact that IV therapy has historically been considered the standard of care for *S. aureus* bacteremia and endocarditis [15] may make ID clinicians less likely to recommend partial oral therapy despite data from randomized trials supporting this approach [3–5].

Another key factor that may influence the decision to use partial oral or all IV therapy for serious *S. aureus* infections is the likelihood that a patient will adhere to the prescribed treatment. Clinicians may perceive that the likelihood of completing therapy is higher with IV than oral antibiotic courses, and thus IV therapy is the "safer" choice. However, patients with substance use disorders, mental health illness, or experiencing homelessness may face barriers and challenges to completing either oral or IV antibiotic regimens. Similarly to Freling et al., we found that treatment completion rates were high overall (≥ 90%) and were similar between partial oral and all IV therapy [16]. However, after adjustment for confounders in the logistic regression model, partial oral therapy as compared with IV therapy was associated with more than four-fold odds of not completing therapy. It is also important to note that in the subgroup of patients with substance use disorder, treatment completion rates were significantly lower with partial oral therapy than with all IV therapy.

In aggregate, our findings suggest that most patients ultimately finish their antibiotic course regardless of route of therapy; however, partial oral therapy may indeed pose a small incremental risk for lack of treatment completion. Furthermore, 20% of patients in the partial oral therapy group were lost to follow up. This highlights several key points. First, it is important to assess the likelihood of antibiotic adherence and follow up when considering oral therapy for a given patient. Second, potential barriers should be discussed with patients and mitigated. Indeed, there have been recent updates in management of serious Staphylococcus infections that shift focus to shared

Table 2 Infection characteristics and treatment[a]

	Partial Oral Therapy	All Intravenous Therapy	Total
Characteristic	(*n* = 148)	(*n* = 101)	(*N* = 249)
Setting			
Community-onset	108 (73)	69 (68)	177 (71)
Hospital-onset	5 (3)	12 (12)	17 (7)
Healthcare-associated, community-onset	35 (24)	20 (20)	55 (22)
S. aureus susceptibility			
Methicillin-susceptible	101 (69)	67 (68)	168 (69)
Methicillin-resistant	43 (30)	31(31)	74 (30)
Unknown	2 (1)	1 (1)	3 (1)
Infection type			
Bacteremia	18 (12)	68 (67)	86 (35)
Uncomplicated bacteremia	3 (2)	15 (15)	18 (7)
Complicated bacteremia	5 (3)	21 (21)	26 (10)
Infective endocarditis	2 (1)	15 (15)	17 (7)
Osteomyelitis	6 (4)	15 (15)	21 (8)
Septic arthritis	2 (1)	2 (2)	4 (2)
Osteomyelitis without bacteremia	120 (81)	32 (32)	152 (61)
Septic arthritis without bacteremia[b]	10 (7)	1 (1)	11 (4)
Echocardiogram			
Transthoracic	29 (20)	73 (73)	102 (41)
Transesophageal	5 (3)	26 (26)	31 (12)
Definitive intravenous antibiotic[c]			
Vancomycin	75 (51)	34 (34)	109 (44)
Cefazolin	36 (24)	53 (53)	89 (36)
Dalbavancin	1 (1)	16 (16)	17 (7)
Other[d]	24 (16)	20 (20)	44 (18)
Definitive oral antibiotic(s)[c]			
Clindamycin	52 (35)	1 (1)	53 (21)
Levofloxacin	52 (35)	0	52 (21)
Linezolid	28 (19)	0	28 (11)
Rifampin	28 (19)	0	28 (11)
Trimethoprim-sulfamethoxazole	8 (5)	0	8 (3)
Amoxicillin-clavulanate	16 (11)	0	16 (6)
Doxycycline	12 (8)	0	12 (5)
Total duration of antibiotics, median (IQR)	30 (14–42)	31 (14–42)	30 (14–32)
Duration of IV antibiotics prior to oral transition, median (IQR)	4 (3–11)	-	-

[a] Data presented as *n* (%) unless otherwise noted

[b] 5 were prosthetic joint infections

[c] Definitive oral and intravenous therapy was defined as the final antibiotic planned by the ID consultant service for each respective group

[d] Piperacillin-tazobactam, ampicillin-sulbactam, levofloxacin, cefepime, ceftriaxone, ertapenem

decision making about treatment options in patients who are unable to complete inpatient therapy [14, 17]. Finally, systematic interventions to facilitate adherence to oral antibiotic courses and post-discharge follow up, such as those employed by Wildenthal and colleagues in a population with substance use disorder [18], should be disseminated.

Several prior observational studies comparing use of partial oral versus all IV therapy for serious *S. aureus* infections did not find significant differences in clinical outcomes such as clinical failure, microbiological failure, or hospital readmissions [8, 15, 18]. It is important to emphasize that comparisons of clinical outcomes in observational studies are subject to numerous confounders and should be interpreted in that context.

Table 3 Primary and secondary outcomes[a]

	Partial Oral Therapy	All Intravenous Therapy	Total	*P* value
	(*N* = 148)	(*N* = 101)	(*N* = 249)	
Co-primary outcomes				
Antibiotic therapy completed[b]	133 (90)	94/96 (98)	227 (93)	*0.38*
Antibiotic adherence[b]				*0.67*
< 50%	6 (4)	2/96 (2)	8 (3)	
50–75%	6 (4)	3/96 (3)	9 (4)	
76–90%	3 (2)	1/96 (1)	4 (2)	
> 90%	133 (90)	94/96 (98)	228 (92)	
Secondary outcomes				
Clinical failure	38 (26)	25 (25)	63 (25)	*0.87*
All-cause mortality	7 (5)	11 (11)	18 (7)	
Recurrent infection	4 (3)	7 (7)	11 (4)	
New metastatic site of infection	1 (1)	8 (8)	9 (4)	
Unplanned source control procedure	20 (14)	9 (9)	29 (12)	
Length of hospital stay, median (IQR)	6 (4–9)	12 (9–23)	9 (6–15)	*< 0.01*
Change in antibiotic therapy	49 (33)	32 (32)	81 (33)	*0.81*
Antibiotic toxicity	11 (7)	8 (8)	19 (8)	
Central venous catheter issue	1 (1)	1 (1)	2 (1)	
Clinical failure	6 (4)	6 (6)	12 (5)	
Patient preference	4 (3)	3 (3)	7 (3)	
Duration of therapy extended	17 (11)	16 (16)	33 (13)	
Percent of antibiotics received outpatient, median (IQR)	78 (60–90)	50 (0–83)	73 (35–88)	*< 0.01*
Loss to follow-up	30 (20)	13 (13)	43 (17)	*0.13*
Readmission related to original infection[c]	36 (24)	20 (20)	56 (22)	*0.40*
Post-discharge emergency or urgent care visit related to original infection[c]	35 (24)	9 (9)	44 (18)	*< 0.01*
Self-directed discharge[d]	4 (3)	2 (2)	6 (2)	*0.72*
Antibiotic-related adverse event	27 (18)	18 (18)	49 (20)	*0.93*
Gastrointestinal intolerance	17 (12)	8 (8)	25 (10)	
Rash	2 (1)	3 (3)	5 (2)	
Acute kidney injury	6 (4)	3 (3)	9 (4)	
Thrombocytopenia	3 (2)	1 (1)	4 (2)	
Liver function test elevation	0	2 (2)	2 (1)	

[a] Data presented as *n* (%) unless otherwise noted

[b] 5 patients who died early in the hospitalization were excluded from the antibiotic completion and adherence endpoints

[c] Within 6 months of date of initial hospital admission

[d] Documented as having left against medical advice

For example, in the present study, we observed important differences between the partial oral and all IV therapy groups in infection types (e.g., bacteremia vs bone or joint infections), certain clinical characteristics, and severity of illness. This important limitation notwithstanding, in accordance with prior studies [8, 18], we did not find substantive differences in clinical failure, unplanned changes in antibiotic therapy, hospital readmissions, and antibiotic-related adverse events. The substantially shorter length of hospital stay observed for the partial oral therapy group might be an expected finding (and potential benefit) of this treatment approach and has been observed in randomized trials, [3] however, this outcome measure is also subject to measured and unmeasured confounders. It is noteworthy that we also observed an increased frequency of post-discharge emergency department and urgent care visits in the partial oral therapy group. Although this outcome measure is also subject to confounding, the higher loss to follow up rate in the partial oral

Table 4 Antibiotic adherence, treatment completion, and clinical failure by key subgroups

Subgroup and outcomes	Partial Oral Therapy	All Intravenous Therapy	*P* value
Substance use disorder	*N* = 82	*N* = 41	
Antibiotic therapy completed	68 (83)	40 (98)	*0.02*
Antibiotic adherence			*0.03*
< 50%	5 (6)	1 (2)	
50–75%	6 (7)	0	
76–90%	3 (4)	0	
> 90%	68 (83)	40 (98)	
Clinical failure[a]	22 (27)	11 (26)	*0.88*
No substance use disorder	*N* = 66	*N* = 55	
Antibiotic therapy completed	65 (98)	54 (98)	*1.00*
Antibiotic adherence			*0.25*
< 50%	1 (2)	0	
50–75%	0	0	
76–90%	0	1 (2)	
> 90%	65 (98)	54 (98)	
Clinical failure[a]	16 (24)	14 (24)	*0.99*
Bone and Joint Infection	*N* = 138	*N* = 50	
Antibiotic therapy completed	124 (90)	50 (100)	*0.02*
Antibiotic adherence			*0.03*
< 50%	6 (4)	0	
51–75%	6 (4)	0	
76–90%	2 (1)	0	
> 90%	124 (90)	50 (100)	
Clinical failure	35 (25)	13 (26)	*0.93*
No Bone and Joint Infection	*N* = 10	*N* = 46	
Antibiotic therapy completed	9 (88)	44 (96)	*0.45*
Antibiotic adherence			*0.48*
< 50%	0	1 (2)	
50–75%	0	0	
76–90%	1 (10)	1 (2)	
> 90%	9 (90)	44 (96)	
Clinical failure	3 (30)	12 (26)	*0.70*
Presence of bacteremia	*N* = 18	*N* = 63	
Antibiotic therapy completed	16 (89)	60 (95)	*0.22*
Antibiotic adherence			*0.23*
< 50%	0	1 (2)	
50–75%	1 (5)	0	
76–90%	1 (5)	1 (2)	
> 90%	16 (89)	60 (95)	
Clinical failure[a]	5 (28)	18 (27)	*1.00*
No bacteremia	*N* = 130	*N* = 33	
Antibiotic therapy completed	117 (90)	33 (100)	*0.07*
Antibiotic adherence			*0.10*
< 50%	6 (5)	0	
50–75%	5 (4)	0	
76–90%	2 (2)	0	
> 90%	117 (90)	33 (100)	
Clinical failure	33 (25)	7 (21)	*0.62*

Table 4 (continued)

[a] Total *N* may vary due to inclusion of mortality patients

therapy group may reflect that this population is more likely to utilize emergency and urgent care services or may simply reflect the longer post-discharge time in the community for the partial oral as compared with all IV therapy group.

Previous studies have highlighted non-clinical benefits of partial oral therapy including decreased healthcare costs and resource utilization [19, 20]. For patients able to discharge on oral therapy, subsequent downstream effects may include increased hospital throughput, decreased chair time for infusion centers, and decreased utilization of home health nursing for antibiotic administration. Though our study did not evaluate cost associated with either treatment approach, the partial oral therapy group received a substantially higher proportion of their treatment course in the outpatient setting. This also highlights the potential benefit that partial oral therapy may allow patients to resume normal daily activities more quickly as compared with all IV therapy.

In addition to those already noted, this study has several additional limitations. First, the observed uptake of partial oral therapy represents the prescribing patterns of a single ID group during the care of patients hospitalized in a public safety-net hospital; thus, generalizability is limited. Second, like the clinical outcomes as discussed above, the comparison of antibiotic adherence and treatment completion between the two groups is subject to confounding and precludes definitive conclusions. We adjusted for potential measured confounders of treatment completion in our logistic regression model; however, this model was limited by the small numbers of cases where treatment was not completed and potential unmeasured confounders. Finally, we may have overestimated rates of antibiotic adherence and treatment completion, particularly in the oral therapy group, by inferring the last prescription that was picked up was taken.

Conclusions

In summary, use of partial oral therapy for serious *S. aureus* infections in a public safety-net hospital was common, with higher uptake for bone or joint infections than for bacteremia or endocarditis. Overall treatment completion and antibiotic adherence rates were relatively high and similar with partial oral and all IV therapy. However, partial oral therapy was independently associated with lack of treatment completion in an adjusted logistic regression model, and treatment completion rates were significantly lower with partial oral therapy

in patients with substance use disorders. These findings lend support to use of partial oral therapy but highlight the importance of evaluating and addressing potential barriers to adherence when considering this treatment approach.

Abbreviations

IV	Intravenous
ID	Infectious diseases
IQR	Interquartile range
OR	Odds ratio
AMA	Against medical advice
HIV	Human immunodeficiency virus
MOUD	Medication for opioid use disorder
QSOFA	Quick sequential related organ failure assessment

Acknowledgements
Not applicable.

Authors' contributions
AC- assisted in design of study, performed data collection and prepared initial manuscript draft including tables and figures. KS- assisted in design of study, reviewed manuscript. BK- performed data analysis, reviewed manuscript. WM- assisted in design of study, reviewed manuscript. HY- assisted in design of study, reviewed manuscript. DA- pulled initial data for screening, reviewed manuscript. TJ- assisted in design of study, reviewed manuscript, and assisted with data analysis interpretation.

Funding
This work was not funded.

Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Colorado Multiple Institutional Review Board (COMIRB) with a waiver of informed consent. COMIRB serves as the institutional review board for Denver Health and Hospital Authority. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 9 January 2025 Accepted: 8 May 2025
Published online: 17 May 2025

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