The Effect of Insurance on Appropriate Hospital Discharge Antibiotics for Patients With \textit{Staphylococcus aureus} Bacteremia

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\begin{abstract}
Inappropriate antimicrobial therapy of \textit{Staphylococcus aureus} bacteremia (SAB) is associated with worsened outcomes. The impact of insurance coverage on appropriate selection of antibiotics at discharge is poorly understood.

\textbf{Methods.} We used a retrospective cohort design to evaluate whether patients with SAB at a large academic medical center over 2 years were more likely to receive inappropriate discharge antibiotics, depending on their category of insurance. Insurance was classified as Medicare, Medicaid, commercial, and none. Logistic regression was used to determine the odds of being prescribed inappropriate discharge therapy.

\textbf{Results.} A total of 273 SAB patients met inclusion criteria, with 14.3\% receiving inappropriate discharge therapy. In the unadjusted model, there was 2-fold increased odds of being prescribed inappropriate therapy for Medicare, Medicaid, and no insurance, compared with commercial insurance, respectively (odds ratio [OR], 2.08; 95\% CI, 1.39–3.13). After controlling for discharge with nursing assistance and infectious diseases (ID) consult, there were 1.6-fold increased odds (OR, 1.57; 95\% CI, 0.998–2.53; \(P = .064\)) of being prescribed inappropriate therapy for Medicare, Medicaid, and no insurance, compared with commercial insurance, respectively. We found that being discharged home without nursing assistance resulted in 4-fold increased odds of being prescribed inappropriate therapy (OR, 4.16; 95\% CI, 1.77–9.77; \(P < .01\)), and failing to consult an ID team resulted in 59-fold increased odds of being prescribed inappropriate therapy (OR, 59.2; 95\% CI, 11.4–306.9; \(P < .001\)).

\textbf{Conclusions.} We found strong evidence that noncommercial insurance, discharging without nursing assistance, and failure to consult ID are risk factors for being prescribed inappropriate antimicrobial therapy for SAB upon hospital discharge.

\textbf{Keywords.} \textit{Staphylococcus aureus}; bacteremia; uninsured/underinsured; antimicrobial therapy.
\end{abstract}

Antibiotics are ubiquitously used in clinical practice and have revolutionized modern medicine. However, misuse of antibiotic therapy is associated with development of resistance both in individual patients and in community populations \cite{1}. The clinical and social features that influence the use of antibiotics are complex, including factors such as clinical presentation, comorbidities, hospital admission, race, provider specialty, geography, and socioeconomic status \cite{2–8}. While medical factors certainly influence antibiotic prescribing, the social and economic factors influencing prescribing as patients transition from the hospital to the ambulatory arena are poorly described. In our own experience of managing patients in the hospital with infectious diseases, we are often asked to alter our original recommendations for discharge antibiotics in order to accommodate restraints forced upon the patient by cost, discharge location, nursing support, or payer preferences. As far as we are aware, this issue has not been addressed in the literature.

Given the consequential societal implications of antimicrobial resistance and the vital need for high-quality patient care, we sought to study the impact of insurance on appropriateness of discharge antimicrobial therapy. We chose \textit{Staphylococcus aureus} bacteremia (SAB) as a model for a complicated infection with high morbidity rates associated with inappropriate treatment \cite{9}. In addition, the list of what would generally be considered “appropriate therapy choices” is relatively limited. This research is an important addition to the body of evidence that nonclinical factors affect the quality of patient care. Specifically, we hypothesized that not having health insurance would lead to more inappropriate antibiotic selection on discharge from the hospital.

\textbf{METHODS}

\textbf{Study Design}

We evaluated the appropriateness of discharge SAB therapy in a historical cohort of patients admitted to a 519-bed academic hospital.
hospital between 2015 and 2016 who were found to have SAB and were prescribed antimicrobial therapy upon discharge to treat SAB. SAB was defined as having at least 1 blood culture during the hospital stay that was positive for S. aureus. Exclusion criteria included age <19 years, completed antibiotic therapy for SAB during hospitalization, death during hospitalization, transferred to another hospital, or discharged to hospice. Using chart review, we collected the following information: age, sex, race, home zip code, infectious disease team consulted, source of infection, type of insurance, 30-day readmission, and 30-day mortality after discharge. Patient home poverty level was estimated by identifying the percentage of people living below the federal poverty level in the patient’s home zip code using the American Fact Finder webpage [10]. The discharge antibiotic and planned duration of therapy for SAB were identified from the discharge summary, but the actual duration and method of antibiotic administration were not measured. The total length of therapy was calculated by adding the in-patient treatment duration (measured from the date of first active antibiotic started after first positive blood culture to discharge) to the planned duration of outpatient therapy. The type of nursing care patients received at their discharge location was defined as no nursing service or any nursing service (including home with service or any level of nursing facility). We assumed that patients discharged home on intravenous (IV) antibiotics with no health service were returning to an infusion center. The insurance status of each patient at the time of SAB hospitalization was categorized as (i) no insurance, (ii) Medicaid, (iii) Medicare, and (iv) commercial. Patients who had Medicare alone or Medicare with any other insurance were included in the “Medicare” category. For example, a patient with Medicare and Medicaid or Medicare and commercial insurance would still be included in the Medicare category. In addition, patients with Veterans Administration (VA) insurance were included in the “Medicare” category. Any patient with Medicaid was included in the “Medicaid” category, unless they also had Medicare. The “commercial” category consisted of those patients who had coverage exclusively from a commercial insurance company. The “no insurance” category consisted of those without any insurance coverage.

Outcome Variable
The primary outcome was receipt of inappropriate therapy for SAB. Therapy was classified as appropriate or inappropriate based on an assessment of the agent, route, and duration of therapy planned upon discharge. While the Infectious Diseases Society of America (IDSA) guidelines suggest defining SAB as complicated or uncomplicated, we did not perform detailed chart reviews and so were unable to classify patients in this manner. Therefore, we used the strictest definition of appropriate length of therapy and considered treatment courses of <14 days inappropriate. Treatment was considered appropriate for methicillin-sensitive S. aureus (MSSA) if a beta-lactam with antistaphylococcal activity was used but inappropriate if the patient was treated with vancomycin without evidence of a beta-lactam allergy. Methicillin-resistant S. aureus (MRSA) not treated with vancomycin or daptomycin was considered inappropriate, and all oral therapy was considered inappropriate.

Statistical Analysis
Parameter space was limited to 4, due to the relatively small number of outcomes in the inappropriate category. Forward modeling was used to identify potential confounders. The most parsimonious model was treatment category as the outcome and insurance as the exposure. Using this method, we determined that adding ID consult team and discharge location to the model caused changes in the effect estimate of >10%, and thus these factors were potential confounders.

A logistic regression model was used to evaluate the relationship between the outcome and exposure and to control for potential confounders. The crude model included treatment category as the outcome and insurance category as the exposure. For the purposes of analysis, we treated insurance as an ordinal variable with 4 increasing levels: commercial, Medicare, Medicaid, no insurance. We compared a model treating insurance as a linear vs factor variable, but we failed to find evidence that the model was more complicated than linear. It would be possible to create a model where each level was considered independently with an independent odds ratio, but this model would be too noisy given our sparsity of data. It is also not necessary, as we have shown that the model is not more complex than linear. Consequently, the OR calculated for the insurance variable demonstrates a linear association applying to each level of insurance.

In an alternative approach, we separated insurance into 4 binary variables comparing each level described above with a composite of all other types of insurance (see Supplementary Text 1 for details). The strength of evidence was evaluated using P values from a likelihood ratio test (LRT). All statistical analysis was done using the statistical program Stata (version 13.0; StataCorp, College Station, TX, USA).

RESULTS
Of the 439 patients who were diagnosed with SAB between January 1, 2015, and December 31, 2016, 166 were excluded. Of the 166 excluded from the study, 35 were excluded for completing therapy during admission. Of these 35, 11 were uninsured, 4 had Medicaid, 10 had Medicare, and 9 had commercial insurance; 31.4% of those excluded were uninsured. Among the 273 patients included in the study, 16 (5.9%) were uninsured.

The majority were white males, with 65.6% male and 79.5% Caucasian, with nearly 40% living in a zip code with a poverty
level of 15% or greater (Table 1). The population tended to be older, with one-third being >65 and 19% <40. The ID team was consulted in 95% of cases. The hospital was served by both academic and private practice physicians; the ID team consulted during the hospital stay was academic for 69.6% of patients and private for 25.3% of patients, and no team was consulted for 5.13% of patients (Table 1). Nearly two-thirds of patients were discharged with some form of nursing service (nursing facility or home nursing service), while one-third were discharged home without service. Readmission rates were high, with nearly one-fourth of patients readmitted to the hospital within 30 days of discharge, and 4% died within 30 days of discharge (Table 1).

In unadjusted models, the lack of an ID consult team was associated with inappropriate therapy (reference group: academic; private: OR, 1.43; 95% CI, 0.61–3.36; not consulted: OR, 57.3; 95% CI, 11.9–276.6; LRT P < .001) (Table 1). The lack of nursing service after discharge was associated with inappropriate treatment (reference group: nursing assistance; home without assistance: OR, 3.68; 95% CI, 1.82–7.44; LRT P < .001) (Table 1).

A linear relationship between insurance category and inappropriate therapy was observed. A 2-fold increased odds of being prescribed inappropriate antibiotics (reference group: commercial: OR, 2.08; 95% CI, 1.39–3.13; LRT P < .001) (Table 1) was noted with decreasing level of insurance coverage (commercial > Medicare > Medicaid > no insurance).

After adjusting for the variables ID consult team and nursing service, we found weak evidence that not having insurance was associated with about 1.6 times the odds of being prescribed inappropriate antimicrobial therapy for each decreasing unit of insurance (reference group: commercial: OR, 1.57; 95% CI, 0.98–2.53; LRT P = .0644) (Table 2).

We additionally assessed if the receipt of nursing services was an independent risk factor for being prescribed inappropriate antimicrobial therapy. After adjusting for type of insurance, we still found strong evidence that being discharged home without any nursing assistance was associated with 4-fold increased odds of being prescribed inappropriate therapy (reference group: nursing assistance; no assistance: OR, 4.16; 95% CI, 1.79–9.77; LRT P < .001) (Table 3).

We also assessed whether failing to consult an ID consult team was an independent risk factor for being prescribed inappropriate antimicrobial therapy. We found very strong evidence that, after adjusting for nursing service and type of insurance, there was still a 59-fold increased odds of being prescribed inappropriate antibiotics in the group without an ID consult (reference group: academic or private ID consult: OR, 59.2; 95% CI, 11.4–306.9; LRT P < .001) (Table 4).

| Table 1. Patient Characteristics, Frequency Distribution, and Unadjusted Odds Ratio for Being Prescribed Inappropriate Antimicrobial Therapy Upon Discharge From the Hospital |
|-------------------------|-------------------|-----------------|------------------|
|                        | Univariate OR (95% CI) | LRT P Value |
| **Cases, n/N (%)**     |                   |                |
| **Total**              | 39/273 (14.3)     | -              |
| **Sex**                |                    |                |
| Male                   | 22/179 (12.3)     | 1.00           |
| Female                 | 17/94 (18.1)      | 1.58 (0.79–3.14) |
| **Age**                |                    |                |
| <40 y                  | 9/52 (17.3)       | 1.00           |
| 41–55 y                | 11/66 (16.7)      | 0.96 (0.36–2.51) |
| 56–65 y                | 8/64 (12.5)       | 0.69 (0.24–1.92) |
| 66+ y                  | 11/91 (12.1)      | 0.66 (0.25–1.71) |
| **Race**               |                    |                |
| Caucasian              | 34/218 (15.6)     | 1.00           |
| African American       | 5/40 (12.5)       | 0.52 (0.22–1.2) |
| Other                  | 0/40 (15.0)       | -              |
| **Percent poverty home county** |                |                |
| <15%                   | 24/153 (15.7)     | 1.00           |
| >15%                   | 13/100 (13.0)     | 0.80 (0.39–1.66) |
| **Source of infection** |                    |                |
| SSTI/Bone/joint        | 15/105 (14.3)     | 1.00           |
| Pulmonary/CVC/endocarditis/primary | 24/168 (14.3) | 1.00 (0.50–2.02) |
| **Resistance pattern** |                    |                |
| Methicillin-sensitive S. aureus | 19/155 (10.9) | 1.00           |
| Methicillin-resistant S. aureus | 7/92 (7.0)  | 0.621 (0.251–1.53) |
| **ID treatment team** |                    |                |
| Academic               | 18/190 (9.5)      | 1.00           |
| Private                | 9/69 (13.0)       | 1.43 (0.61–3.36) |
| Not consulted          | 12/14 (85.7)      | 57.3 (11.9–276.6) |
| **Nursing services**  |                    |                |
| Nursing service (home or LTCF) | 15/179 (8.4) | 1.00           |
| Home without service   | 24/94 (25.3)      | 3.75 (1.86–7.57) |
| **30-d readmission**  |                    |                |
| No                     | 31/206 (8.7)      | 1.00           |
| Yes                    | 8/67 (9.0)        | 0.77 (0.33–1.76) |
| **30-d mortality**    |                    |                |
| No                     | 38/259 (9.8)      | 1.00           |
| Yes                    | 1/14 (7.1)        | 0.45 (0.06–3.52) |
| **Insurance status**  |                    |                |
| Commercial             | 4/76 (5.3)        | 1.00           |
| Noncommercial*         | 35/197 (17.8)     | 2.08 (1.39–3.13) |
| Medicare               | 23/155 (14.8)     |                |
| Medicaid               | 6/26 (23.1)       |                |
| No insurance           | 6/16 (37.5)       |                |

**Abbreviations:** CVC, central venous catheter; ID, infectious diseases; LRT, likelihood ratio test; LTCF, long-term care facility; SSTI, skin and soft tissue infection.

**Table 2. Multivariate Logistic Regression for the Odds of Being Prescribed Inappropriate Therapy, Controlled for Nursing Service and ID Consult**

|                        | Odds Ratio | 95% CI     | LRT P Value |
|------------------------|------------|------------|-------------|
| **Commercial**         | 1.0        | -          | .644        |
| **Noncommercial**      | 1.57       | 0.98–2.53  |             |

**Abbreviations:** ID, infectious diseases; LRT, likelihood ratio test.
When we performed an alternative analysis comparing each insurance category with a composite of all other types of insurance (Supplementary Text 1), we also found that patients with no insurance had 4 times the odds of being prescribed inappropriate therapy in univariate analysis (reference group: all other insurance: OR, 4.07; 95% CI, 1.29–12.0; LRT P = .0167) (Supplementary Table 1), while patients with commercial insurance had 0.26 times the odds of being prescribed inappropriate therapy (reference group: all other insurance: OR, 0.26; 95% CI, 0.09–0.75; LRT P = .004) (Supplementary Table 1).

After controlling for ID consult and discharge nursing services, having commercial insurance still had 0.31 times the odds of being prescribed inappropriate therapy (reference group: all other insurance: OR, 0.31; 95% CI, 0.10–0.97; LRT P = .0254) (Supplementary Table 2). The other types of insurance no longer had a strong association in the multivariate model (Supplementary Table 2).

**DISCUSSION**

In our population of patients, who were usually seen by infectious disease physicians, receipt of inappropriate therapy was infrequent. When inappropriate therapy did occur, it was associated with failure to consult an ID team, discharge without nursing service, and lack of insurance. While this observational study is not comprehensive enough to establish causal relationships, it does demonstrate clear trends that underline the importance of expert consultation and adequate health care resources at the individual level in providing high-quality care.

In our univariate model, we found a 2-fold increased risk of being prescribed inappropriate antimicrobial therapy for each level of insurance. This evidence demonstrates that patients with commercial insurance receive more appropriate SAB management than patients with what might be considered lesser levels of insurance coverage. After adjusting for discharge nursing service and lack of an ID treatment team, the evidence for this effect persisted. While the sparsity of the outcomes was associated with wide confidence intervals, the trends were consistent even when controlling for confounders. It is unlikely that ID consultation was associated with insurance type, as this information is not generally known or considered when primary teams consult an ID service. While failing to consult ID was an independent risk factor for inappropriate therapy, it most likely does not confound the relationship between insurance type and therapy. Taken together, this body of evidence provides a strong argument that patients with commercial insurance may receive a higher quality of care on hospital discharge compared with those with governmental insurance or no insurance. It also suggests that patients without insurance receive the lowest quality of care.

Numerous studies have demonstrated the importance of an ID consult in the management of SAB [11–17]. These studies clearly demonstrate that patients who are managed in consultation with an ID team have lower mortality and are more likely to be managed with certain quality-of-care metrics, such as obtaining follow-up blood cultures to assess clearance of SAB, obtaining an echocardiogram, removing infected foci, and adequate duration of therapy [11–17]. Our study emphasizes that ID consultation is an essential aspect of management of a patient with SAB, as we found very strong evidence that failure to consult an ID team was associated with inappropriate therapy.

When evaluating the influence of nursing service receipt as an independent risk factor for inappropriate therapy, insurance status is likely to be a confounder as it is associated with both discharge location and type of therapy selected. After adjusting for insurance and ID consultation, we still found strong evidence that lack of nursing service was an independent risk factor for inappropriate therapy. This effect may be biased because we combined services from long-term care facilities (LTCFs) with home nursing services. Nursing services at LTCFs are often limited, and thus antibiotic choices may become constrained to agents that are administered once or twice per day, thus eliminating many beta-lactam agents. Conversely, patients with home nursing services may be more likely to receive appropriate therapy as they do not have this limitation. Nursing services are rarely available to patients without insurance unless done on a charity basis, which is unusual.

Our methodology was limited by the fact that we did not distinguish between complicated and uncomplicated SAB. While the evidence to guide the clinical management of *S. aureus* bacteremia is weak, as detailed by Tong et al., it is generally accepted that patients should be classified into complicated and uncomplicated SAB [9]. To account for this limitation and avoid bias toward the hypothesis, we used an inclusive definition of appropriate therapy as it relates to duration (receiving at least 14 days of intravenous therapy). This may have resulted in bias toward the null hypothesis by categorizing those with complicated SAB as appropriate even when they were treated for <28 days. While this may have also reduced our statistical power by decreasing

### Table 3. Multivariate Logistic Regression of Nursing Service, Adjusted for ID Consult Team and Type of Insurance

|                | Adjusted Odds Ratio | 95% CI    | LRT P Value |
|----------------|---------------------|-----------|-------------|
| Nursing assistance | 1.00 | - | <.001 |
| Home without assistance | 4.16 | 1.77–9.77 | |

Abbreviations: ID, infectious diseases; LRT, likelihood ratio test.

### Table 4. Multivariate Logistic Regression of ID Consult Team, Adjusted for Nursing Service and Type of Insurance

|                | Adjusted Odds Ratio | 95% CI   | LRT P Value |
|----------------|---------------------|----------|-------------|
| ID team consulted | 1.00 | - | <.001 |
| No ID team consulted | 59.2 | 11.4–306.9 | |

Abbreviations: ID, infectious diseases; LRT, likelihood ratio test.
the outcome of interest, we wanted to avoid bias toward finding a difference when one was not present.

Our definition of appropriate therapy agent and the route of antibiotic therapy may also have been limitations. The route of antibiotic therapy for SAB has not been adequately studied, and in certain situations, oral therapy for SAB may be adequate. For example, a patient adherent to oral therapy with a well-drained skin and soft tissue infection due to an isolate sensitive to highly bioavailable antibiotics may be transitioned to oral therapy appropriately. While the choice of a beta-lactam over vancomycin in MSSA is very clear, which beta-lactam is preferred for treating SAB based on the source of infection is much more difficult to define. Rather than attempt to define this for every type of infection, we chose an inclusive definition of appropriate therapy to ensure that the definition of inappropriate therapy would not be debatable. Additionally, we may have limited our findings by only including patients who were discharged on therapy. This may have disproportionally excluded patients with no insurance who, due to financial restraints, often spend their entire treatment duration in the hospital. This is strongly suggested by the findings that among the 35 patients excluded due to completion of therapy while still hospitalized 11 (31%) lacked insurance coverage, compared with 5.9% of the 273 patients who were discharged on antimicrobial therapy.

In the United States, lack of health insurance has been linked to poorer health outcomes in a multitude of studies [18]. In 2003, a report by Hadley, commissioned by the Kaiser Family Foundation (KFF), reviewed 25 years of research and provided a comprehensive review of the studies that assessed the link between health insurance and health outcomes [18]. While quantitative measures were not widely agreed upon and difficult to assess individually given the varied methodological flaws, there were clear trends [18]. For example, patients without insurance had a 4%–25% increase in mortality compared with those with insurance [18]. The uninsured also tended to be diagnosed at a later stage of disease process and receive fewer interventional treatments [18]. Our research adds to this body of evidence by clearly showing that there is an association between the type of insurance a patient has and the risk of receiving inappropriate SAB therapy.

An important finding in our study was the gradation of influence that insurance status had, with commercial insurance being “better” than Medicare and Medicaid and those insurance programs being “better” than no insurance at all. We have demonstrated that lack of insurance coverage for IV antibiotics and nursing care may negatively affect patients. Coverage for these services is highly variable in Medicare and Medicaid. The ID community should advocate to policy-makers on behalf of patients to support therapies that will improve patient outcomes.

Our study is limited in that it focuses on a single infectious condition that is highly complex in its management. Despite that, the factors identified in our study likely impact the treatment of other serious infectious conditions such as endocarditis and bone and joint infections, which often require lengthy courses of antibiotics. Our experience has been that the issues identified in the treatment of patients with SAB occur in other conditions where ID experts are asked to choose less-than-ideal agents based on lack of insurance support.

Other limitations were that our study was a retrospective single-center analysis and our patient population was predominantly white and male. The insurance mix at our facility may also vary from other regions. Still, the hospital is a tertiary care center serving a large geographic area providing a similar level of care and social services and is most likely comparable to many other academic medical centers in the United States. Additionally, we did not specifically evaluate whether patients left against medical advice, which may predispose them to receiving inadequate treatment regimens.

The principles of medical practice demand delivering the highest quality medicine to all patients, regardless of socioeconomic status. While our data are insufficient to prove a causal relationship between not having insurance and inappropriate antimicrobial therapy, they do suggest that this is an area that requires vigorous research. The findings in this paper identify ongoing barriers to quality of care that have not been adequately addressed. All patients have a right to high-quality care, and we should increase our patient advocacy in areas such as SAB, which is associated with dire consequences when not treated appropriately. The barriers identified here could be overcome with feasible interventions, such as mandatory ID consultation (or another method to ensure adequate clinical treatment) for SAB and ensuring that patients are discharged with appropriate support services for the duration of their intravenous antibiotic course.

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

Acknowledgments
The authors would like to thank Guy Mollett and Joseph Timothy of the London School of Hygiene and Tropical Medicine and Elizabeth Lyden of the University of Nebraska Medical Center for input on the epidemiological and statistical approach to this work.

Financial support. No funding source was used.

Potential conflicts of interest. The authors declare that they have no potential conflicts of interest related to the subject matter of this paper. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Availability of data and materials. The raw data and all tables produced from the data are held by Trevor Van Schooneveld.

Human consent. The study was approved by our Institutional Review Board as a waived consent study.
**Author contributions.** T.M. and T.V. conceived of the original study design. T.M., T.V., M.R., J.M., and J.G. contributed to the planning, strategy, ethical approval, and design of the study. T.M. collected data from medical records. T.M. did the primary analysis, and T.V. and M.R. contributed critical feedback on the analysis approach. T.M. wrote the first and successive drafts of the manuscript. All authors have contributed important intellectual content and have read and approved the manuscript.

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