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Danielle Palms

Date

Risk Factors Associated with Thirty-Day Readmission among Patients Receiving
Outpatient Parenteral Antimicrobial Therapy

By

Danielle Palms

Degree to be awarded: Master of Public Health
Epidemiology

Jesse T. Jacob, MD
Committee Chair

Risk Factors Associated with Thirty-Day Readmission among Patients Receiving
Outpatient Parenteral Antimicrobial Therapy

By

Danielle Palms
B.A., Brown University, 2014

Thesis Committee Chair: Jesse T. Jacob, MD

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Abstract

Risk Factors Associated with Thirty-Day Readmission among Patients Receiving Outpatient Parenteral Antimicrobial Therapy By Danielle Palms

Outpatient parenteral antimicrobial therapy (OPAT) programs allow patients who are otherwise ready to be discharged from the hospital to receive intravenous treatment in an outpatient setting. These programs have become more popular as health policies incentivize shifting care to the outpatient setting. In this study we developed a predictive model of thirty-day readmission among hospitalized patients discharged with OPAT from two academic medical centers with a dedicated OPAT clinic for management. We used logistic regression to assess OPAT and other outpatient clinic follow-up in conjunction with age, sex, pathogen, diagnosis, discharge medication, planned length of therapy, and comorbidities using the modified Charlson score. We hypothesized that at least one follow-up visit at the Emory OPAT clinic would reduce the risk for hospital readmission within 30 days. Of the 755 eligible individuals, 137 (18%) patients were readmitted within 30 days. Most patients (73%) received some type of follow-up care at Emory Healthcare within 30 days of discharge or prior to readmission, including 52% of patients visiting the Emory OPAT clinic. The final predictive model contains type of follow-up (no visit, OPAT visit, or non-OPAT visit only), enterococci, Charlson score (≥ 3 vs. 0-2), discharge location (rehabilitation facility vs. home), home county (inside vs. outside metropolitan Atlanta), gastrointestinal infection, polymicrobial infection, and interaction between gastrointestinal and polymicrobial infection. This final model indicated that having an OPAT visit was associated with a 90% reduction in odds of readmission compared to those who had no follow-up visit at all, adjusted for all other variables in the model (OR 0.10, 95% CI 0.06-0.17). In a pre-specified sensitivity analysis excluding patients discharged to a rehabilitation facility or living outside metropolitan Atlanta, the odds ratio for readmission was consistent (OR 0.06, 95% CI 0.03-0.13). These results can be used as a guide to develop interventions to prevent readmissions and to study how to improve the outcomes of patients who have factors potentially putting them at increased odds of readmission.

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Introduction

Over the last several decades, policies and changing reimbursements combined with new technology have incentivized hospitals to reduce unnecessary inpatient days by shifting care to the outpatient setting. One such population is those that require intravenous antimicrobials but are otherwise ready to be discharged from the hospital. Recent medical advances including catheters and intravenous delivery systems enable patients to be discharged safely with intravenous antimicrobials as part of an outpatient parenteral antimicrobial therapy (OPAT) program. OPAT can avoid unnecessary inpatient days as well as the potential for complications and expenses associated with the inpatient setting, by providing an option for patients to receive antimicrobial treatment in their own home or to be treated as an outpatient.(1) Potential benefits of OPAT compared to inpatient treatment include higher patient satisfaction, shorter inpatient stays, and improved cost-effectiveness.(2, 3)

OPAT was first introduced in the United States in 1974 and is now part of standard medical practice across the world.(1) There are two main models for OPAT delivery. The self-administration model requires a patient, family member, or designated person to infuse the antimicrobial in the patient's home, work, or other convenient location, while the supervised infusion model requires the patient to travel to a clinic or a physician's office.(1) As OPAT becomes a more widely used treatment option, it is important to understand its benefits and risks, particularly focusing on quality of treatment and prevention of hospital readmission. The Agency for Healthcare Research and Quality estimated that 30-day all-cause readmissions occurred in 13.8% of patients, and were associated with hospital costs totaling \$41.3 billion in 2011.(4) The diagnoses with the highest rates of 30-day readmissions among U.S. hospitals in 2010 were congestive heart failure (24.7%), schizophrenia (22.3%), and acute renal failure (21.7%).(5) Readmissions are a key factor addressed in healthcare policies focused on quality improvement and healthcare cost reduction and identifying risk factors for readmission of OPAT patients is an important step to optimize use and improve quality of care.

Background

OPAT programs have demonstrated success in treating a wide variety of infections, and report high clinical cure rates, high patient satisfaction, improved quality of life during treatment, program sustainability over time, and low rates of healthcare-associated infections.(6-11) Several studies have also demonstrated the cost-effectiveness of OPAT compared to inpatient care or care in a rehabilitation facility.(2, 12-14) The total cost for patients treated with OPAT can be markedly reduced compared to treatment as an inpatient.(2) Another study found that OPAT may be associated with significantly lower treatment costs per day compared to inpatient care.(13)

Outcomes of patients discharged with OPAT demonstrate a high rate of treatment success for a wide variety of infections. Multiple studies assessing treatment success with OPAT for skin and soft tissue infections indicate high success rates, bed days saved, and economic benefits.(15, 16) High success rates (>85%) have been demonstrated in bone and joint infections as well as diabetic foot infections.(17, 18) These studies also identified potential risks including high rates of relapse, suggesting the need for close monitoring.(18, 19) Several studies show that in carefully selected situations, OPAT has been successful for patients with infective endocarditis, a particularly high risk population for adverse outcomes, though many studies recommend more careful observation in these patients.(20-26)

Several studies have assessed factors associated with adverse events and treatment failure in particular populations. Effectiveness has been shown for osteomyelitis treatment, though one study suggests that recurrence was associated with risk factors including peripheral vascular disease, diabetes, and treatment with vancomycin.(27-29) Another study suggested that infection with *Pseudomonas aeruginosa* increased risk of recurrence in patients.(30) Female sex, diabetes, and teicoplanin treatment were independently associated with treatment failure, including readmission, in a study of OPAT for skin and soft tissue infection.(15) Additionally, one study of OPAT for bone and joint infections found older age (>80 years), methicillin-resistant *Staphylococcus aureus* (MRSA) infection, and diabetic foot or stump osteomyelitis were all

associated with both early and long-term failure in multivariate analyses.(17) Another study of OPAT failure specifically in patients with infective endocarditis suggested from a multivariate analysis that cardiac or renal comorbidities as well as treatment with teicoplanin were associated with treatment failure.(31) In a Veterans' Administration OPAT program assessing all clinical conditions, patients with diabetes were associated with clinical failure 90 days after treatment in a multivariate analysis, but this study did not assess readmission.(32) Overall, many risk factors have been associated with treatment failure for particular conditions including sex, age, comorbidities, pathogen, and antimicrobial. While OPAT has proven effective for a wide range of infections, the risks for hospital readmission are not well understood for most OPAT recipients.

Few studies have focused on the risk factors for adverse events in all patients receiving OPAT. Readmission trends have not been well-defined in OPAT patients, and one survey found that among physicians directing an OPAT program, only 28% monitored readmission rates for quality measures.(33) However, one recent study has developed a predictive model for 30-day readmission since the patient's first hospitalization in which they were discharged on OPAT. These authors found age, aminoglycoside use, history of resistant organism, and number of previous hospitalizations without OPAT discharge independently predicted hospital readmission.(34)

While there is a paucity of existing data, we hypothesized that patients who follow up in the OPAT clinic have fewer readmissions. We sought to assess OPAT follow-up in conjunction with age, sex, infecting organism, diagnosis, discharge medication, planned length of therapy, and comorbidities. We predict at least one follow-up visit with an infectious disease physician will reduce the risk for thirty-day readmission. Defining the risk factors among patients discharged on OPAT can be used to inform prevention interventions in this at-risk population in order to effectively treat infections while aiming to avoid unnecessary adverse events.

Methods

Setting

The OPAT clinic at Emory Healthcare serves two 500-bed teaching hospitals, Emory University Hospital and Emory University Hospital Midtown. All patients considered for OPAT are evaluated by the infectious diseases consultation service in the hospital and have an electronic OPAT order filled out which includes diagnosis, pathogen(s), a brief narrative, antimicrobial(s), including an anticipated stop date, and follow-up plans. Generally, the inpatient consultation service recommends interim visits with an advance practice provider every two weeks per the OPAT guidelines, followed by an end of treatment visit with an infectious diseases physician. Urgent visits are usually with the advance practice provider, and some patients (particularly self-pay patients) have weekly visits with the registered nurse for central line checks and labs.

Patient Selection

A retrospective chart review using patient records from the clinical data warehouse at Emory Healthcare was performed. Adults (age ≥ 18 years) hospitalized at Emory University Hospital (including the Emory University Orthopedic and Spine Hospital) or Emory University Hospital Midtown that were discharged with OPAT orders between January 1, 2014 and July 31, 2015 were included. Three separate databases were merged, one containing OPAT orders, one containing all hospital admissions (encounters) for all patients, and one containing all Emory Healthcare clinic visits for all patients. Only patients with follow up listed at the Emory OPAT clinic were included and the first (index) admission in which a patient was discharged on OPAT was included in the analysis. Patients who had antibiotics managed outside OPAT including transplant recipients (International Classification of Diseases (ICD-9) codes 996.8, V42) or cystic fibrosis patients (CF, ICD9 code 277.0), without an antimicrobial agent documented on the OPAT order (rarely used for non-antimicrobial infusions), with a medication stop date before discharge date or less than 7 days after discharge (indicating that follow up in OPAT clinic was not necessarily indicated), or not in the encounters database (OPAT started in clinic) were

excluded. Patients discharged to hospice, other short-term hospital, Veterans Administration (VA) hospital, long-term acute care hospital, or other non-rehabilitation facility were also excluded, as these patients were determined to be not likely to follow up at Emory OPAT clinic or be readmitted to a hospital within Emory Healthcare. Finally, patients with a documented readmission in which they were readmitted on the same date as their index discharge date were excluded because these represented hospital transfers.

Variable Selection

Variables extracted from the medical record included date of birth, sex, address elements (county and state), hospital, admission and discharge dates, primary insurance type, discharge location, microbiology, antimicrobial(s), planned duration of outpatient treatment, comorbidities included in the Charlson comorbidity index, and dates and type of follow-up visits at Emory OPAT clinic and non-OPAT Emory Healthcare clinics. Age was calculated as the difference between discharge date and date of birth. Length of stay was calculated as the difference between discharge date and admission date documented on the OPAT order. Primary insurance was extracted from the OPAT order form and categorized as private, Medicare, Medicaid, self-pay, and other (including Tricare, Veterans Administration, workers compensation, and insurance coded on the order form as “miscellaneous”). Discharge location was taken from administrative data from the index encounter and categorized as either home or rehabilitation facility. Resident home county was dichotomized as inside or outside metropolitan Atlanta (using health district 3 for Atlanta: Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, and Rockdale counties).

Pathogen was identified from the OPAT order form and supplemented using microbiology results and physician notes. For analysis, organisms were grouped into several categories including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-sensitive *Staphylococcus aureus* (MSSA), other staphylococci, streptococci, enterococci, *Klebsiella* spp., *Escherichia coli*, other Enterobacteriaceae, *Pseudomonas* spp., anaerobes, candida, mold, culture-

negative, and all other organisms (Supplementary Table 1). Infections were then classified as polymicrobial if more than one organism was documented or if the patient was treated for an empiric polymicrobial infection. Infections were considered antibiotic resistant if an individual was infected with MRSA, carbapenem-resistant Enterobacteriaceae (CRE), or vancomycin-resistant enterococci (VRE).

Antimicrobials were extracted from the OPAT order form and grouped into categories by class. Medications were classified as aminoglycoside, antifungal (subcategorized as fluconazole, micafungin, and other antifungals), carbapenems, cephalosporins, daptomycin, fluoroquinolones, penicillins, vancomycin, and all other antimicrobial agents (Supplementary Table 2). These categories are not mutually exclusive, since patients could be treated with more than one medication. Outpatient treatment duration was calculated using the difference between the stop date documented on the OPAT order and discharge date. If more than one stop date was indicated in the OPAT order, the longest duration among all discharge antimicrobials was used in the analysis.

Charlson comorbidities were extracted from administrative ICD-9 codes from the index admission. Comorbidities were defined using the enhanced ICD-9-CM coding algorithm⁽³⁵⁾ and updated weights were used to calculate a score for each individual⁽³⁶⁾. If patients had ICD-9 codes for both diabetes without complications and diabetes with complications, they were categorized as having diabetes with complications since “downcoding” for complications of diabetes is common. Patients were categorized as having mild liver disease if they had diagnosis codes for mild liver disease as well as moderate or severe liver disease (effect of “downcoding” not clear), and categorized as having metastatic solid tumor if they had diagnosis codes for both any malignancy and metastatic solid tumor. Diagnoses were determined by reviewing the narrative text in the OPAT order and categorized into clinical diagnosis groups (Supplementary Table 3).

Readmission was determined by searching the medical records for any inpatient encounters with an admission day thirty days or less from an individual's index discharge date. Lastly, we determined if the patient had a follow-up visit at Emory OPAT clinic or non-OPAT visit in Emory Healthcare within thirty days of their index discharge date or, for those readmitted, if the patient had a follow-up visit before their date of readmission. Only completed visits were considered in this analysis in order to exclude scheduled visits in which the patient did not attend. Patients with no clinic visits (either OPAT or non-OPAT) were categorized as having no follow-up within 30 days of discharge or before readmission and patients with at least one visit to an Emory clinic during this time period were categorized as having "any visit" in Table 1. Individuals with "any visit" were further subcategorized as having an OPAT visit if they visited the OPAT clinic at least once during the follow-up period or as having non-OPAT only visits if their follow-up visit(s) did not include a visit to the OPAT clinic. Finally, individuals with an OPAT visit were further categorized as having a nurse visit, a visit with a nurse practitioner or physician's assistant, or a visit with a physician. Visits in which a provider was not recorded were excluded because this represented a dummy encounter for data entry. For provider, patients with more than one type of provider visit were categorized only in the highest level of care they received (i.e. patients with a nurse visit and physician visit were included in the physician visit analytic group).

Univariate Analysis

We used frequencies for categorical variables and medians and quartiles for continuous variables (after assessing for normality) to describe the population, then conducted a univariate analysis to determine factors independently associated with the outcome thirty-day readmission. Age and length of stay were treated as continuous variables and a Wilcoxon rank-sum test was used to measure their association with readmission. Univariate associations for all other variables were analyzed using logistic regression. Since each patient could have more than one organism and medication documented, each of the organism and medication responses were treated as

unique binary variables in the analysis. Duration was analyzed as a categorical variable using clinically significant cutoffs (by week, starting with day 7 since shorter duration of therapy would typically not necessitate an outpatient follow-up visit). Type of follow-up visit was analyzed first by comparing any follow-up to no follow-up and further analyzed comparing no follow-up, follow-up at OPAT clinic, and non-OPAT only follow-up, using no follow-up as the referent group. Type of provider OPAT follow-up visit and insurance were treated as categorical variables using no OPAT follow-up visit and private insurance as the referent groups, respectively.

Multivariate Analysis

A multivariate analysis was performed using logistic regression to develop a predictive model for thirty-day readmission among our OPAT patient population. The main exposure is defined as type of follow-up visit within thirty days of discharge, categorized as no follow-up, OPAT clinic visit(s), or non-OPAT visit(s) only. We decided a priori to include in the initial multivariate model all variables with a P value of 0.25 or less in univariate analysis. Additionally, we included all two-way interactions between the primary exposure and secondary exposures included in the initial multivariable model, as well as all product terms between healthcare facility and all other secondary exposures included in the initial model, and all product terms between polymicrobial and other pathogen terms included in the initial model. Any product terms that caused quasi-separation of data were removed from the initial model.

After assessing collinearity, model selection was performed using automatic forward, backward, and stepwise selection methods in the logistic regression procedure in SAS 9.4. The performance of the models from each method were compared using c-statistics and Hosmer-Lemeshow fit statistics. The final model was selected on the basis of goodness of fit, simplicity, and biologic plausibility. Finally, since our main population of interest is outpatients discharged on OPAT who would be likely to return to Emory Healthcare if readmitted, we conducted a pre-specified sensitivity analysis by running the potential final models on the population excluding

individuals discharged to rehabilitation facilities as well as those residing outside metropolitan Atlanta.

Spatial Analysis

A spatial analysis was conducted using ArcGIS software. Restricting the spatial analysis to Georgia, we analyzed the spatial distribution of home counties among the final study population, individuals with an OPAT clinic visit, and individuals readmitted within thirty days.

This study was approved by Emory University Institutional Review Board. All analyses were conducted using Microsoft Excel 2013, SAS 9.4, and ArcGIS 10.3.1.

Results

The overall study population included 1,365 patients with a combined total of 1,710 admissions producing an OPAT order. Most patients (83%) had only one visit in which they were discharged on OPAT (median: 1, range 1-8). After initial exclusion, the study population consisted of 865 patients intending to follow-up at Emory OPAT clinic including CF and transplant patients that indicated OPAT clinic follow-up on the order form (Table 1). For all further analyses we excluded patients with CF and transplant recipients, for a final population of 755 individuals. (Figure 1) Most patients (57%) were male, with a median age of 58 years, a median length of initial hospital stay of 8 days, and a median planned outpatient treatment duration of 30 days (Table 1a). Over sixty percent of patients were infected with a gram-positive cocci, with 21% of all patients infected with MSSA. Additionally, 18% of patients had a polymicrobial infection and 45% of patients were diagnosed with a bone or joint infection. The most common medications prescribed were cephalosporins (32%), vancomycin (31%), penicillins (22%), and carbapenems (17%). One third of patients had an updated Charlson comorbidity score of 0, 1-2, and ≥ 3 . (Table 1a) The most common Charlson comorbidities included chronic pulmonary disease (21%), congestive heart failure (22%), diabetes without complications (21%), and renal disease (20%). (Table 1b) A total of 137 patients were readmitted within 30 days, for a readmission rate of 18%, and approximately half of readmitted patients were readmitted within ten days of discharge (Figure 2).

The majority of patients (73%) received some type of follow-up care at Emory Healthcare within 30 days of discharge or prior to readmission, including 52% of patients visiting the Emory OPAT clinic. Most of the individuals visiting the OPAT clinic within this time period had a visit with an advanced practice provider or physician (92%, Table 1a). A larger proportion of non-readmitted patients had at least one OPAT visit than among readmitted patients as well as a larger proportion having multiple OPAT visits. (Figure 3) Readmitted patients had a shorter time to non-OPAT visits than OPAT visits. (Figure 4)

In univariate analyses there was a strong protective association between having a follow-up visit and being readmitted within thirty days. Any follow-up visit at Emory Healthcare within thirty days of discharge or before readmission was associated with an 84% reduction in the odds of readmission compared to those who did not have any follow-up (OR 0.16, 95% CI 0.11-0.24). A visit at the OPAT clinic increased this association to a 93% reduction in the odds of readmission among individuals without a bone/joint infection (OR 0.07, 95% CI 0.04-0.14) and a 77% reduction in the odds of readmission among individuals with a bone/joint infection (OR 0.23, 95% CI 0.11-0.47).

Additionally, while a protective association was identified between readmission and having a nurse visit only at the OPAT clinic compared to not visiting the OPAT clinic, the strength and statistical significance of this association increased for visits with an advanced practice provider or physician. Enterococci, *E. coli*, and candida infections were strongly associated with an increased odds of readmission, while a culture-negative infection had a statistically significant protective association. Treatment with antifungals, including fluconazole or micafungin, was strongly associated with increased odds of readmission. Length of stay was also independently associated with readmission in our study ($P = 0.005$). Compared to individuals with 7-13 days of planned outpatient treatment duration, the odds of readmission decreased with increased duration of planned outpatient treatment. Additionally, polymicrobial infection increased the odds of readmission among individuals with a GI infection, but had no effect on those without GI infection ($P = 0.005$ and 0.68, respectively). Compared to individuals with a Charlson score of 0, those with a Charlson score of 3 or more were two times more likely to be readmitted (OR 2.07, 95% CI 1.31-3.25). Finally, the odds of being readmitted within 30 days was 1.7 times higher among individuals living within metropolitan Atlanta compared to individuals living outside metropolitan Atlanta (OR 1.67, 95% 1.13-2.47. (Table 2)

The initial multivariable model included 21 variables meeting the inclusion criteria of a P value less than 0.25 from univariate analysis. Variables initially eligible for inclusion were length

of stay, healthcare facility, insurance, enterococci, *E. coli*, candida, culture-negative infection, polymicrobial infection, treatment with antifungal, fluoroquinolones, and vancomycin treatment, planned duration of outpatient treatment, Charlson comorbidity score, discharge location, home county, type of follow-up visit, and the diagnoses bone or joint infection, bloodstream infection, central nervous system infection, gastrointestinal, and skin or soft tissue infection. Duration and Charlson scores were included as binary variables in the final model based on clinically significant cutoffs (categorized as 7-27 days and ≥ 28 days, and a score of ≥ 3 and < 3 , respectively). Although age did not meet the P value inclusion criteria, we pre-specified including it in the initial model based on the biological plausibility and the established association between age and readmission. Additionally, we included all product terms between the main exposure, type of follow-up visit, and all other terms in the model, product terms between healthcare facility and all other terms in the model, and product terms between polymicrobial infection and other pathogen terms in the model. After removing terms that caused quasi-separation of data and concluding that no major collinearity issues existed (although the largest condition index was > 30 , only one variance decomposition proportion was > 0.5), the automated forward, backward, and stepwise procedures in the logistic regression procedure in SAS resulted in two potential models. (Table 3) Both models demonstrated good discrimination and had no evidence of lack of fit based on the c-statistic and Hosmer-Lemeshow Goodness-of-Fit test.

Both potential final models include type of follow-up visit, enterococci, gastrointestinal (GI) diagnosis, Charlson score, discharge location, and home county. One potential model indicated two significant interaction terms. First, the interaction between clinic follow-up (no follow-up, OPAT follow-up, and non-OPAT follow-up only) and bone/joint infection was significant for OPAT visits but non-significant for non-OPAT visits ($P = 0.02$ and 0.09 , respectively). The second interaction term, between healthcare facility and bloodstream infection, had a P value of 0.006 in this model (model 2 in Table 3). Although these two interaction terms were significant in the model identified through backwards elimination, it was decided that these

terms would not be included in the final model due to desired simplicity and ease of interpretation of the final predictive model. Based on known differences between the patient populations at the two hospitals, we also tested the addition of prosthetic joint infection, healthcare facility, and the product term between prosthetic joint infection and healthcare facility to the most parsimonious potential model, although none of these terms remained significant. Additionally, we tested the addition of polymicrobial, the interaction between polymicrobial and GI infection, and the interaction between enterococci infection and GI infection. The interaction term between enterococci infection and GI infection was not significant, and all other terms were retained to make up the final predictive model (model 3 in Table 3). The final model has no collinearity, no evidence of lack of fit, and has good discrimination (c -statistic = 0.81). This final model indicates that having an OPAT visit was associated with a 90% reduction in odds of readmission compared to those who had no follow-up visit at all, adjusted for all other variables in the model including enterococci infection, Charlson comorbidity score, discharge location, home county, and polymicrobial infection (OR 0.10, 95% CI 0.06-0.17). Individuals who had non-OPAT follow-up within Emory Healthcare after discharge also had a significantly decreased odds of readmission compared to those who had no follow-up visit, although the magnitude was not as large as for those who had an OPAT visit (OR 0.31, 95% CI 0.18-0.55). Additionally, enterococcal infection, living in metropolitan Atlanta and a Charlson score of 3 or more were independently associated with increased odds of readmission, while discharge to a rehabilitation facility was independently associated with a decreased odds of readmission compared to those that were discharged home. Since enterococcal infection was significant in the final model, we assessed the characteristics of these infections. Among 55 patients with enterococci infections, there were 17 diagnoses of bone/joint infections, 14 cardiovascular infections, and 10 GI infections. The majority of patients (28/55) patients received penicillin-based therapy including 11 combined with either an aminoglycoside (5) or cephalosporin (6). Another 16 received daptomycin and 5 vancomycin, none with the addition of aminoglycosides. Additionally, having a polymicrobial infection

significantly increased the odds of readmission among individuals with a GI infection, adjusted for all other variables in the model, although this estimate lacked precision. Polymicrobial infection did not have an effect among those that did not have a GI infection. (Table 4)

Finally, the pre-specified sensitivity analysis of these three potential models on a restricted population of individuals who were discharged home and live in metropolitan Atlanta demonstrated that all models had good discrimination and did not have any evidence of lack of fit based on the c-statistic and Hosmer-Lemeshow Goodness-of-Fit test. (Table 3) Similar to the final model in the whole population, the final model in the sensitivity analysis indicated that a visit to the OPAT clinic in the restricted population was associated with a 94% reduction in readmission compared to having no follow-up visits, adjusted for all other variables in the model (OR 0.06, 95% CI 0.03-0.13). In this population, individuals who had a non-OPAT visit only also had a significantly decreased odds of readmission than those who did not have any follow-up visit, although the effect was smaller than the effect of an OPAT clinic visit (OR 0.24, 95% CI 0.11-0.53). (Table 4)

Spatial analysis was conducted on only Georgia patients, which made up 718 (95%) of the final analysis population. The map of the distribution of all Georgia patients demonstrates that most patients live in metropolitan Atlanta or surrounding counties. (Figure 5) Additionally, most of the patients with at least one follow-up visit lived in metropolitan Atlanta and surrounding counties, while most of the counties where no patients visited the clinic were located further from metropolitan Atlanta. (Figure 6) Lastly, many of the readmitted patients resided in metropolitan Atlanta, which agrees with our univariate analysis results. (Figure 7).

Discussion

For patients discharged on IV antibiotic therapy from a large academic system, follow-up at Emory OPAT clinic significantly prevented readmission in multivariate analysis. Additionally, we found that a non-OPAT follow-up visit at Emory Healthcare was also a protective factor of readmission. However, while any follow-up with a healthcare provider after discharge protected against readmission within thirty days, our results clearly show that in our population, a visit at the OPAT clinic was more protective than non-OPAT visits. Additionally, we were able to further examine the OPAT visits and determine in univariate analysis that compared to individuals with no OPAT visits, those individuals who saw any provider at an OPAT clinic had a decreased odds of readmission; however the association was stronger for individuals who saw an advanced practice provider or physician at their OPAT visit. These results all demonstrate the effectiveness of follow-up visits in preventing readmission among OPAT patients, potentially due to these visits allowing for early detection and intervention for any complications during treatment. While OPAT guidelines do recommend routine follow-up for OPAT patients, this protective association had not previously been well-defined in the literature.

The thirty-day readmission rate of 18% in our study was comparable to the literature, ranging from 3% to 26% but higher than the average of 13.8% reported by AHRQ. (2, 4, 9, 11, 15, 21, 25, 31, 34) However, this readmission rate may have been underestimated for patients living outside of Atlanta since we could only determine readmission of those admitted to a hospital within Emory Healthcare. Since we had a geographically diverse population, it is possible that we also did not capture all of the readmissions if patients discharged home were readmitted to a more local hospital outside of Emory Healthcare. In the sensitivity analysis where we included only patients that were discharged home and reside in metropolitan Atlanta (366 total patients), the readmission rate was 22%, which is likely a more appropriate estimate of the readmission rate among true OPAT patients in our population. We included all-cause readmission, whether planned or unplanned, and may have overestimated the readmission rate. In

contrast, several previous studies have included only unplanned readmissions or readmissions due to OPAT, but this was not feasible in our study. Since all-cause readmission represents more heterogeneity and the magnitude of the effect was large, many of these admissions may be preventable, though some may reflect the underlying acute disease or chronic illness of some patients.

In the univariate results, the finding that there was an increased odds of readmission among individuals living in metropolitan Atlanta compared to those living outside metropolitan Atlanta was unexpected. We had hypothesized that geography would affect an individual's ability to attend the OPAT clinic, which is located in metropolitan Atlanta. Based on the spatial analysis, it does appear that most patients who were able to visit the OPAT clinic resided around metropolitan Atlanta and the counties where no patients were able to visit the clinic were located further from metropolitan Atlanta. However, we were only able to track readmissions for individuals who were readmitted to Emory Healthcare, with a potential for misclassification bias of those living outside metropolitan Atlanta. Individuals living in counties further from Emory may be more likely to be readmitted to a local hospital. We believe that the association between metropolitan Atlanta residence and readmission is likely a result of the feasibility of tracking readmissions among those located outside of metropolitan Atlanta rather than a true difference in readmission trends. Additionally, our results suggested that individuals discharged to rehabilitation centers were less likely to be readmitted than patients discharged home. This could be due to the fact that individuals discharged to rehabilitation are not truly outpatients since they are already in a healthcare facility, and may be treated there for adverse events rather than returning to the hospital.

To address this issue, we pre-specified a sensitivity analysis restricted to patients discharged home and residing in metropolitan Atlanta, which may more accurately reflect the population of interest. Comparing the final models from the original analysis and the sensitivity analysis, a Charlson comorbidity score greater or equal to 3 increased the odds of readmission

compared to a score of 0-2 in the whole population and this relationship was no longer significant in the sensitivity analysis. One potential explanation is that individuals who were discharged to rehabilitation centers were sicker, and thus had higher Charlson scores, which may explain why Charlson score was no longer significant in the sensitivity analysis.

Univariate analysis also suggested a stepwise relationship between planned duration of outpatient treatment and odds of readmission. Compared to outpatient treatment of 7-13 days, the odds of readmission decreased for each increase in one week of planned outpatient treatment duration. One potential explanation is that individuals in the referent group, with planned duration 7-13 days, were healthier individuals with less serious infections. Additionally, patients that are sicker with many comorbidities may be more likely to have a longer inpatient length of stay, thus receiving less of their treatment as an outpatient. This could explain why we observed higher odds of readmission among individuals with shorter planned duration of outpatient treatment. Future analyses could compare the length of stay among these individuals and further investigate this relationship.

Our results also showed a strong independent association between increased odds of readmission and enterococci infections in both univariate and multivariate analyses. Regardless of follow-up status, our results demonstrated that individuals with these types of infections had a significantly increased odds of readmission compared to individuals not infected with enterococci spp. Many (31/41) of these patients had difficult to treat infections, including bone/joint and cardiovascular infections. Additionally enterococci, while not particularly virulent, can be challenging to treat because no agents are clearly very bactericidal. Few patients received combination therapy to achieve bactericidal effect, which may increase risk of failure or relapse, and only 11 received a beta-lactam based dual therapy. Taken together, these factors provide an explanation for why enterococci may be associated with clinical failure and readmission. Additionally, the final model suggests that a GI infection modified the effect of a polymicrobial infection on the odds of readmission. Although the small number of observations makes this

estimate imprecise, these results indicate that a polymicrobial infection is more difficult to treat when it involves a GI infection. Most of these GI diagnoses (24/58) were intra-abdominal abscesses. Since these infections are difficult to treat, the large proportion of intra-abdominal abscesses could explain why polymicrobial infections, which are also difficult to treat, increase the odds of readmission among these individuals. The finding that the crude and adjusted analyses both demonstrate the effect of these infections on increased odds of readmission may indicate a need for more intensive follow-up and physician monitoring in order to improve outcomes among these specific patient populations.

Strengths & Limitations

A strength of this study is the large sample size. The final analysis was conducted on 755 individuals and although the sensitivity analysis was restricted to about half of those patients, the resulting final predictive models were similar between the two populations and we believe the estimates from the sensitivity analysis may more accurately reflect the effect of these factors in a true OPAT population. Additionally, extracting data from patient medical records allowed us to analyze the relationships of a large number of patient variables. Access to physician narratives in the medical record enabled us supplement data missing from the variable fields in the OPAT order.

One limitation of this analysis is that only planned duration of outpatient treatment could be determined, which may not be an accurate representation of completed duration of outpatient treatment. In addition, if patients had more than one medication stop date listed, we considered their treatment duration in the analysis as the maximum of these two durations. While one stop date may have correlated to an intravenous antibiotic while another correlated to an oral medication or a non-antimicrobial medication, we included only the longest duration to approximate the duration of interest. We believe this strategy was appropriate based on the reasonable assumption that an individual discharged on multiple medications would receive the intravenous antimicrobial agent for the longest duration. As previously mentioned, our analysis

includes all readmissions since we could not determine if admissions were planned or unplanned, which may be an overestimate of the actual number of unplanned readmissions due to adverse events related to OPAT. Additionally, we could only capture readmissions and follow-up visits within Emory Healthcare, presenting potential for misclassification bias for individuals that sought care outside of the Emory Healthcare system. Lastly, our patient population must be taken into account in interpreting these results and considering the generalizability of the conclusions. The most common diagnoses of our patients included osteomyelitis, bacteremia, and prosthetic joint infections (196, 145, 95, respectively, Supplementary Table 3). Therefore, the two facilities in our study see a large number of bone and joint patients, which may not represent the patient population of many hospitals. We did not assess compliance with OPAT guidelines, including monitoring, and did not assess other adverse outcomes from OPAT including complications from central access or adverse drug reactions.

Future Directions

Future studies should continue to investigate this protective association between follow-up visits, particularly at an infectious disease clinic, and readmissions among OPAT patients. A closer assessment of preventable, unplanned readmissions is also warranted. Based on our analysis, follow-up visits appear to be a strong protective factor of readmissions. Therefore, it may be helpful to consider future interventions that enable individuals to have easier access to these follow-up visits and study other variables that may affect access to follow-up visits, including socioeconomic status. One potential intervention could be linking patients with transportation options to the clinic. Since this factor is the most significant predictor in our final models, future studies should focus on strategies to increase participation in outpatient follow-up visits in order to ultimately decrease readmissions in patients discharged home on intravenous antimicrobials. Possible other interventions include home visits, since the concept of the medical home has emerged. Transitions of care from the inpatient to outpatient should also be critically examined, since most readmissions occurred in patients with a shorter anticipated duration of

therapy, including the role of a clinical navigator to help patients through the complex healthcare system. In addition, emphasis should be placed on the factors that were associated with increased odds of readmission since these patients may require enhanced follow-up or physician monitoring.

Conclusion

The recent focus in the healthcare field to improve cost-effective practices has emphasized reducing unnecessary inpatient days and searching for alternative treatment options. This study focuses on one patient population that will be impacted by these practices, since a major reason for continued inpatient stay would be to receive intravenous antibiotics. OPAT provides an alternative treatment to receive this service at home or in an outpatient setting and may be more cost-effective to the healthcare system, but patient safety and the risk for adverse events must also be considered. By developing a predictive model for readmission in one OPAT patient population, we were able to consider a large number of patient factors and determine which factors independently predict the odds of thirty-day readmission. These results can be used as a guide to develop interventions to prevent readmissions and to study how to improve the outcomes of patients who have factors potentially putting them at increased odds of readmission.

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Table 1. Characteristics of patients intending to follow-up at Emory Outpatient Parenteral Antimicrobial Therapy (OPAT) clinic by readmission status (N=865)

Characteristic	All Patients (N=865)	Readmitted (N=153)	Not Readmitted (N=712)
Age (years), median (Q1, Q3)	57 (44, 67)	57 (45, 69)	57 (43, 66.5)
Male, n (%)	497 (57.5)	95 (62.1)	402 (56.5)
Length of Stay (days), median (Q1, Q3)	7 (5, 12)	8 (6, 15)	7 (5, 12)
Index Admission Location, n (%)			
Emory University Hospital	520 (60.1)	99 (64.7)	421 (59.1)
Emory University Hospital Midtown	345 (39.9)	54 (35.3)	291 (40.9)
Primary Insurance, n (%)			
Private	417 (48.2)	76 (49.7)	341 (47.9)
Medicare	281 (32.5)	45 (29.4)	236 (33.1)
Medicaid	98 (11.3)	20 (13.1)	78 (11.0)
No insurance	38 (4.4)	7 (4.6)	31 (4.4)
Other insurance	31 (3.6)	5 (3.3)	26 (3.7)
Organism, n (%)			
Gram Positive Cocci	536 (62.0)	98 (64.1)	438 (61.5)
Methicillin-resistant <i>S. aureus</i>	154 (17.8)	23 (15.0)	131 (18.4)
Methicillin-sensitive <i>S. aureus</i>	173 (20.0)	26 (17.0)	147 (20.6)
Other staphylococci	82 (9.5)	17 (11.1)	65 (9.1)
Streptococci	96 (11.1)	19 (12.4)	77 (10.8)
Enterococci	62 (7.2)	22 (14.4)	40 (5.6)
Gram Negative Rods	188 (21.7)	38 (24.8)	150 (21.1)
<i>Klebsiella</i> spp.	18 (2.1)	4 (2.6)	14 (2.0)
<i>Escherichia coli</i>	71 (8.2)	24 (15.7)	47 (6.6)
Other Enterobacteriaceae	47 (5.4)	5 (3.3)	42 (5.9)
<i>Pseudomonas</i> spp.	72 (8.3)	13 (8.5)	59 (8.3)
Anaerobes	23 (2.7)	6 (3.9)	17 (2.4)
Fungi	28 (3.2)	15 (9.8)	13 (1.8)
Candida	26 (3.0)	14 (9.2)	12 (1.7)
Molds	2 (0.2)	1 (0.7)	1 (0.1)
Other organism	84 (9.7)	17 (11.1)	67 (9.4)
Culture Negative	92 (10.6)	8 (5.2)	84 (11.8)
Infection Type			
Polymicrobial Infection	160 (18.5)	41 (26.8)	119 (16.7)
Resistant Infection	157 (18.2)	24 (15.7)	133 (18.7)
Diagnosis¹			
Bone/Joint Infection	347 (41.0)	53 (35.8)	294 (42.1)
Bloodstream Infection	194 (22.9)	39 (26.4)	155 (22.2)
Central Nervous System	47 (5.5)	5 (3.4)	42 (6.0)
Cardiovascular	101 (11.9)	17 (11.5)	84 (12.0)
Ear, Nose, Throat	12 (1.4)	2 (1.4)	10 (1.4)
Gastrointestinal	65 (7.8)	24 (16.2)	41 (5.9)
Genitourinary	46 (5.4)	8 (5.4)	38 (5.4)
Lung	72 (8.5)	11 (7.4)	61 (8.7)
Skin and soft tissue infection	29 (3.4)	3 (2.0)	26 (3.7)
Other diagnosis	49 (5.8)	7 (4.7)	42 (6.0)

Table 1 continued

Discharge Medication Class, n (%)			
Aminoglycosides	30 (3.5)	4 (2.6)	26 (3.7)
Antifungals	40 (4.6)	20 (13.1)	20 (2.8)
Fluconazole	16 (1.8)	9 (5.9)	7 (1.0)
Micafungin	18 (2.1)	9 (5.9)	9 (1.3)
Other Antifungals	6 (0.7)	2 (1.3)	4 (0.6)
Carbapenems	154 (17.8)	30 (19.6)	124 (17.4)
Cephalosporins	289 (33.4)	48 (31.4)	241 (33.8)
Daptomycin	68 (7.9)	13 (8.5)	55 (7.7)
Fluoroquinolones	49 (5.7)	4 (2.6)	45 (6.3)
Penicillins	177 (20.5)	36 (23.5)	141 (19.8)
Vancomycin	260 (30.1)	40 (26.1)	220 (30.9)
Other antimicrobial	106 (12.3)	15 (9.8)	91 (12.8)
Outpatient Treatment Duration (days), median (Q1, Q3)²	28 (16, 36)	24 (15, 35)	30 (16, 37)
Outpatient Treatment Duration, n (%)²			
7-13 days	169 (20.5)	26 (17.8)	143 (21.1)
14-20 days	113 (13.7)	29 (19.9)	84 (12.4)
21-27 days	130 (15.8)	33 (22.6)	97 (14.3)
28-34 days	120 (14.5)	20 (13.7)	100 (14.7)
≥ 35 days	293 (35.5)	38 (26.0)	255 (37.6)
Charlson Score, median (Q1, Q3)	2 (0, 3)	2 (1, 4)	1 (0, 3)
Charlson Score, n (%)			
0	257 (29.7)	37 (24.2)	220 (30.9)
1	168 (19.4)	16 (10.5)	152 (21.3)
2	159 (18.4)	30 (19.6)	129 (18.1)
≥ 3	281 (32.5)	70 (45.8)	211 (29.6)
Type of Follow-up Visit, n (%)			
No follow-up	225 (26.0)	89 (58.2)	136 (19.1)
Any follow-up at Emory Healthcare	640 (74.0)	64 (41.8)	576 (80.9)
OPAT clinic	432 (49.9)	30 (19.6)	402 (56.5)
Non-OPAT clinic only	208 (24.0)	34 (22.2)	174 (24.4)
Type of OPAT Follow-up Visit, n (%)			
No OPAT follow-up	433 (50.1)	123 (80.4)	310 (43.5)
Nurse visit only (no NP/PA or physician visit)	41 (4.7)	6 (3.9)	35 (4.9)
NP/PA visit only (no physician visit)	220 (25.4)	17 (11.1)	203 (28.5)
Physician visit	171 (19.8)	7 (4.6)	164 (23.0)
Discharge Location, n (%)			
Home	743 (85.9)	136 (88.9)	607 (85.3)
Rehabilitation facility	122 (14.1)	17 (11.1)	105 (14.7)
Home County^{3,4}			
Outside Metro Atlanta	368 (42.6)	52 (34.0)	316 (44.4)
Metro Atlanta	496 (57.4)	101 (66.0)	395 (55.6)

¹ 18 of all patients missing diagnosis (% of 847); 5 of readmitted patients missing diagnosis (% of 148); 13 of patients not readmitted missing diagnosis (% of 699)

² 40 of all patients missing duration (% of 825); 7 of readmitted patients missing duration (% of 146); 33 of patients not readmitted missing duration (% of 679)

³ 1 of all patients missing home county (% of 864); 1 of patients not readmitted missing home county (% of 711)

⁴ Metro Atlanta includes Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, & Rockdale

Table 1a. Characteristics of final analysis population: All non-CF and non-transplant patients intending to follow-up at Emory Outpatient Parenteral Antimicrobial Therapy (OPAT) clinic by readmission status (N=755)

Characteristic	All Patients (N=755)	Readmitted (N=137)	Not Readmitted (N=618)
Age (years), median (Q1, Q3)	58 (45, 67)	57 (45, 69)	58 (45, 67)
Male, n (%)	433 (57.4)	84 (61.3)	349 (56.5)
Length of Stay (days), median (Q1, Q3)	8 (5, 13)	9 (6, 15)	7 (5, 12)
Index Admission Location, n (%)			
Emory University Hospital	423 (56.0)	85 (62.0)	338 (54.7)
Emory University Hospital Midtown	332 (44.0)	52 (38.0)	280 (45.3)
Primary Insurance, n (%)			
Private	363 (48.1)	71 (51.8)	292 (47.2)
Medicare	243 (32.2)	37 (27.0)	206 (33.3)
Medicaid	88 (11.7)	18 (13.1)	70 (11.3)
No insurance	34 (4.5)	7 (5.1)	27 (4.4)
Other insurance	27 (3.6)	4 (2.9)	23 (3.7)
Organism, n (%)			
Gram Positive Cocci	476 (63.0)	92 (67.2)	384 (62.1)
Methicillin-resistant <i>S. aureus</i>	126 (16.7)	19 (13.9)	107 (17.3)
Methicillin-sensitive <i>S. aureus</i>	160 (21.2)	26 (19.0)	134 (21.7)
Other staphylococci	77 (10.2)	17 (12.4)	60 (9.7)
Streptococci	88 (11.7)	17 (12.4)	71 (11.5)
Enterococci	55 (7.3)	21 (15.3)	34 (5.5)
Gram Negative Rods	142 (18.8)	33 (24.1)	109 (17.6)
<i>Klebsiella</i> spp.	16 (2.1)	4 (2.9)	12 (1.9)
<i>Escherichia coli</i>	64 (8.5)	24 (17.5)	40 (6.5)
Other Enterobacteriaceae	42 (5.6)	5 (3.6)	37 (6.0)
<i>Pseudomonas</i> spp.	37 (4.9)	8 (5.8)	29 (4.7)
Anaerobes	23 (3.0)	6 (4.4)	17 (2.8)
Fungi	26 (3.4)	13 (9.5)	13 (2.1)
Candida	25 (3.3)	13 (9.5)	12 (1.9)
Mold	1 (0.1)	0 (0.0)	1 (0.2)
Other organism	68 (9.0)	15 (10.9)	53 (8.6)
Culture Negative	89 (11.8)	8 (5.8)	81 (13.1)
Infection Type, n (%)			
Polymicrobial Infection	136 (18.0)	39 (28.5)	97 (15.7)
Resistant Infection	128 (17.0)	20 (14.6)	108 (17.5)
Diagnosis, n (%)¹			
Bone/Joint Infection	331 (44.7)	50 (37.6)	281 (46.3)
Bloodstream Infection	172 (23.2)	36 (27.1)	136 (22.4)
Central Nervous System	47 (6.4)	5 (3.8)	42 (6.9)
Cardiovascular	89 (12.0)	16 (12.0)	73 (12.0)
Ear, Nose, Throat	11 (1.5)	2 (1.5)	9 (1.5)
Gastrointestinal	58 (7.8)	22 (16.5)	36 (5.9)
Genitourinary	40 (5.4)	7 (5.3)	33 (5.4)
Lung	27 (3.6)	6 (4.5)	21 (3.5)
Skin & Soft Tissue Infection	25 (3.4)	2 (1.5)	23 (3.8)
Other diagnosis	47 (6.4)	7 (5.3)	40 (6.6)

Table 1a continued

Discharge Medication Class, n (%)			
Aminoglycosides	11 (1.5)	2 (1.5)	9 (1.5)
Antifungals	33 (4.4)	17 (12.4)	16 (2.6)
Fluconazole	16 (2.1)	9 (6.6)	7 (1.1)
Micafungin	15 (2.0)	8 (5.8)	7 (1.1)
Voriconazole	2 (0.3)	0 (0.0)	2 (0.3)
Carbapenems	126 (16.7)	27 (19.7)	99 (16.0)
Cephalosporins	242 (32.1)	44 (32.1)	198 (32.0)
Daptomycin	66 (8.7)	13 (9.5)	53 (8.6)
Fluoroquinolones	45 (6.0)	4 (2.9)	41 (6.6)
Penicillins	167 (22.1)	35 (25.5)	132 (21.4)
Vancomycin	236 (31.3)	36 (26.3)	200 (32.4)
Other antimicrobial	83 (11.0)	13 (9.5)	70 (11.3)
Outpatient Treatment Duration (days), median (Q1, Q3)²	30 (18, 37)	26 (16, 35)	32 (18, 37)
Outpatient Treatment Duration, n (%)²			
7-13 days	126 (17.6)	20 (15.4)	106 (18.1)
14-20 days	92 (12.8)	25 (19.2)	67 (11.4)
21-27 days	111 (15.5)	29 (22.3)	82 (14.0)
28-34 days	112 (15.6)	20 (15.4)	92 (15.7)
≥ 35 days	276 (38.5)	36 (27.7)	240 (40.9)
Charlson Score, median (Q1, Q3)	2 (0, 3)	2 (0, 4)	1 (0, 3)
Charlson Score, n (%)			
0	252 (33.4)	36 (26.3)	216 (35.0)
1	117 (15.5)	13 (9.5)	104 (16.8)
2	136 (18.0)	24 (17.5)	112 (18.1)
≥ 3	250 (33.1)	64 (46.7)	186 (30.1)
Type of Follow-up Visit, n (%)			
No follow-up	207 (27.4)	83 (60.6)	124 (20.1)
Any follow-up at Emory Healthcare	548 (72.6)	54 (39.4)	494 (79.9)
OPAT clinic	391 (51.8)	27 (19.7)	364 (58.9)
Non-OPAT clinic only	157 (20.8)	27 (19.7)	130 (21.0)
Type of OPAT Follow-up Visit, n (%)			
No OPAT follow-up	364 (48.2)	110 (80.3)	254 (41.1)
Nurse visit only (no NP/PA or physician visit)	30 (4.0)	4 (2.9)	26 (4.2)
NP/PA visit only (no physician visit)	216 (28.6)	17 (12.4)	199 (32.2)
Physician visit	145 (19.2)	6 (4.4)	139 (22.5)
Discharge Location, n (%)			
Home	636 (84.2)	120 (87.6)	516 (83.5)
Rehabilitation facility	119 (15.8)	17 (12.4)	102 (16.5)
Home County, n (%)^{3, 4}			
Outside Metro Atlanta	316 (41.9)	44 (32.1)	272 (44.1)
Metro Atlanta	438 (58.1)	93 (67.9)	345 (55.9)

¹ 15 of all patients missing diagnosis (% of 740); 4 readmitted patients missing diagnosis (% of 133); 11 of patients not readmitted missing diagnosis (% of 607)

² 38 of all patients missing duration (% of 717); 7 readmitted patients missing duration (% of 130); 31 of patients not readmitted missing duration (% of 587)

³ 1 of all patients missing home county (% of 754); 1 of patients not readmitted missing home county (% of 617)

⁴ Metro Atlanta includes Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton & Rockdale

Table 1b. Charlson comorbidities among non-CF and non-transplant patients intending to follow-up at Emory Outpatient Parenteral Antimicrobial Therapy (OPAT) clinic (N=755)

Charlson Comorbidities ¹	All Patients (N=755) n (%)	Readmitted (N=137) n (%)	Not Readmitted (N=618) n (%)
AIDS/HIV	31 (4.1)	9 (6.6)	22 (3.6)
Cerebrovascular disease	78 (10.3)	17 (12.4)	61 (9.9)
Chronic pulmonary disease	161 (21.3)	31 (22.6)	130 (21.0)
Congestive heart failure	167 (22.1)	45 (32.8)	122 (19.7)
Dementia	14 (1.9)	4 (2.9)	10 (1.6)
Diabetes with chronic complications	45 (6.0)	6 (4.4)	39 (6.3)
Diabetes without chronic complications	155 (20.5)	31 (22.6)	124 (20.1)
Hemiplegia or paraplegia	29 (3.8)	2 (1.5)	27 (4.4)
Malignancy	74 (9.8)	18 (13.1)	56 (9.1)
Metastatic solid tumor	43 (5.7)	10 (7.3)	33 (5.3)
Mild liver disease	89 (11.8)	22 (16.1)	67 (10.8)
Moderate/severe liver disease	1 (0.1)	1 (0.7)	0 (0.0)
Myocardial infarction	65 (8.6)	15 (10.9)	50 (8.1)
Peptic ulcer disease	13 (1.7)	4 (2.9)	9 (1.5)
Peripheral vascular disease	63 (8.3)	13 (9.5)	50 (8.1)
Renal disease	151 (20.0)	37 (27.0)	114 (18.4)
Rheumatic disease	45 (6.0)	7 (5.1)	38 (6.1)

¹ Charlson Scores in Table 1a calculated using updated weights described in Quan, et al., 2011(36):

0 points: myocardial infarction, peripheral vascular disease, cerebrovascular disease, peptic ulcer disease, diabetes without chronic complications

1 point: chronic pulmonary disease, rheumatic disease, diabetes with chronic complications, renal disease

2 points: congestive heart failure, dementia, mild liver disease, hemiplegia/paraplegia, any malignancy

4 points: moderate/severe liver disease, AIDS/HIV

6 points: metastatic solid tumor

Table 1c. Characteristics of final analysis population: All non-CF and non-transplant patients intending to follow-up at Emory Outpatient Parenteral Antimicrobial Therapy (OPAT) clinic by healthcare facility (Emory University Hospital (EUH) Midtown (EUHM) vs. EUH). (N=755)

Characteristic	All Patients (N=755)	EUHM (N=332)	EUH (N=423)
Age (years), median (Q1, Q3)	58 (45, 67)	59 (45, 68)	57 (46, 66)
Male, n (%)	433 (57.4)	189 (56.9)	244 (57.7)
Length of Stay (days), median (Q1, Q3)	8 (5, 13)	9 (6, 13)	7 (5, 12)
Readmission Status, n (%)			
Readmitted within 30 days	137 (18.1)	52 (15.7)	85 (20.1)
Not readmitted within 30 days	618 (81.9)	280 (84.3)	338 (79.9)
Primary Insurance, n (%)			
Private	363 (48.1)	147 (44.3)	216 (51.1)
Medicare	243 (32.2)	111 (33.4)	132 (31.2)
Medicaid	88 (11.7)	49 (14.8)	39 (9.2)
No insurance	34 (4.5)	15 (4.5)	19 (4.5)
Other insurance	27 (3.6)	10 (3.0)	17 (4.0)
Organism, n (%)			
Gram Positive Cocci	476 (63.0)	204 (61.4)	272 (64.3)
Methicillin-resistant <i>S. aureus</i>	126 (16.7)	54 (16.3)	72 (17.0)
Methicillin-sensitive <i>S. aureus</i>	160 (21.2)	65 (19.6)	95 (22.5)
Other staphylococci	77 (10.2)	35 (10.5)	42 (9.9)
Streptococci	88 (11.7)	38 (11.4)	50 (11.8)
Enterococci	55 (7.3)	24 (7.2)	31 (7.3)
Gram Negative Rods	142 (18.8)	63 (19.0)	79 (18.7)
<i>Klebsiella</i> spp.	16 (2.1)	5 (1.5)	11 (2.6)
<i>Escherichia coli</i>	64 (8.5)	25 (7.5)	39 (9.2)
Other Enterobacteriaceae	42 (5.6)	20 (6.0)	22 (5.2)
<i>Pseudomonas</i> spp.	37 (4.9)	17 (5.1)	20 (4.7)
Anaerobes	23 (3.0)	16 (4.8)	7 (1.7)
Fungi	26 (3.4)	6 (1.8)	20 (4.7)
Candida	25 (3.3)	6 (1.8)	19 (4.5)
Mold	1 (0.1)	0 (0.0)	1 (0.2)
Other organism	68 (9.0)	17 (5.1)	51 (12.1)
Culture Negative	89 (11.8)	60 (18.1)	29 (6.9)
Infection Type, n (%)			
Polymicrobial Infection	136 (18.0)	53 (16.0)	83 (19.6)
Resistant Infection	128 (17.0)	54 (16.3)	74 (17.5)
Diagnosis, n (%)¹			
Bone/Joint Infection	331 (44.7)	169 (51.4)	162 (39.4)
Bloodstream Infection	172 (23.2)	68 (20.7)	104 (25.3)
Central Nervous System	47 (6.4)	20 (6.1)	27 (6.6)
Cardiovascular	89 (12.0)	40 (12.2)	49 (11.9)
Ear, Nose, Throat	11 (1.5)	10 (3.0)	1 (0.2)
Gastrointestinal	58 (7.8)	20 (6.1)	38 (9.2)
Genitourinary	40 (5.4)	23 (7.0)	17 (4.1)
Lung	27 (3.6)	10 (3.0)	17 (4.1)
Skin & Soft Tissue Infection	25 (3.4)	13 (4.0)	12 (2.9)
Other diagnosis	47 (6.4)	13 (4.0)	34 (8.3)

Table 1c continued

Discharge Medication Class, n (%)			
Aminoglycosides	11 (1.5)	5 (1.5)	6 (1.4)
Antifungals	33 (4.4)	6 (1.8)	27 (6.4)
Fluconazole	16 (2.1)	5 (1.5)	11 (2.6)
Micafungin	15 (2.0)	1 (0.3)	14 (3.3)
Voriconazole	2 (0.3)	0 (0.0)	2 (0.5)
Carbapenems	126 (16.7)	68 (20.5)	58 (13.7)
Cephalosporins	242 (32.1)	97 (29.2)	145 (34.3)
Daptomycin	66 (8.7)	31 (9.3)	35 (8.3)
Fluoroquinolones	45 (6.0)	20 (6.0)	25 (5.9)
Penicillins	167 (22.1)	72 (21.7)	95 (22.5)
Vancomycin	236 (31.3)	114 (34.3)	122 (28.8)
Other antimicrobial	83 (11.0)	34 (10.2)	49 (11.6)
Outpatient Treatment Duration (days), median (Q1, Q3)²	30 (18, 37)	32 (17, 36)	29 (18, 37)
Outpatient Treatment Duration, n (%)²			
7-13 days	126 (17.6)	56 (17.9)	70 (17.3)
14-20 days	92 (12.8)	36 (11.5)	56 (13.8)
21-27 days	111 (15.5)	41 (13.1)	70 (17.3)
28-34 days	112 (15.6)	56 (17.9)	56 (13.8)
≥ 35 days	276 (38.5)	123 (39.4)	153 (37.8)
Charlson Score, median (Q1, Q3)	2 (0, 3)	2 (0, 4)	1 (0, 3)
Charlson Score, n (%)			
0	252 (33.4)	108 (32.5)	144 (34.0)
1	117 (15.5)	47 (14.2)	70 (16.5)
2	136 (18.0)	55 (16.6)	81 (19.1)
≥ 3	250 (33.1)	122 (36.7)	128 (30.3)
Type of Follow-up Visit, n (%)			
No follow-up	207 (27.4)	94 (28.3)	113 (26.7)
Any follow-up at Emory Healthcare	548 (72.6)	238 (71.7)	310 (73.3)
OPAT clinic	391 (51.8)	181 (54.5)	210 (49.6)
Non-OPAT clinic only	157 (20.8)	57 (17.2)	100 (23.6)
Type of OPAT Follow-up Visit, n (%)			
No OPAT follow-up	364 (48.2)	151 (45.5)	213 (50.4)
Nurse visit only (no NP/PA or physician visit)	30 (4.0)	14 (4.2)	16 (3.8)
NP/PA visit only (no physician visit)	216 (28.6)	107 (32.2)	109 (25.8)
Physician visit	145 (19.2)	60 (18.1)	85 (20.1)
Discharge Location, n (%)			
Home	636 (84.2)	268 (80.7)	368 (87.0)
Rehabilitation facility	119 (15.8)	64 (19.3)	55 (13.0)
Home County, n (%)^{3, 4}			
Outside Metro Atlanta	316 (41.9)	121 (36.4)	195 (46.2)
Metro Atlanta	438 (58.1)	211 (63.6)	227 (53.8)

¹ 15 of all patients missing diagnosis (% of 740); 3 EUH Midtown patients missing diagnosis (% of 329); 12 EUH patients missing diagnosis (% of 411)

² 38 of all patients missing duration (% of 717); 20 EUH Midtown patients missing duration (% of 312); 18 EUH patients missing duration (% of 405)

³ 1 of all patients missing home county (% of 754); 1 EUH patient missing home county (% of 422)

⁴ Metro Atlanta includes Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton & Rockdale

Table 2. Univariate logistic regression for readmission among non-CF and non-transplant patients intending to follow-up at Emory Outpatient Parenteral Antimicrobial Therapy (OPAT) clinic (N=755)

Characteristic	Odds Ratio [95% Confidence Interval]	Test Statistic	P value
Age (years, continuous)		0.59 ¹	0.55 ¹
Male [Ref=Female]	1.22 [0.84, 1.78]		0.30
Length of Stay (days, continuous)		2.84 ¹	0.005 ¹
Primary Insurance			
Private	Ref.		
Medicare	0.74 [0.48, 1.14]		0.17
Medicaid	1.06 [0.59, 1.89]		0.85
No insurance	1.07 [0.45, 2.55]		0.89
Other insurance	0.72 [0.24, 2.13]		0.55
Organism			
Gram Positive Cocci	1.25 [0.84, 1.84]		0.27
Methicillin-resistant <i>S. aureus</i>	0.77 [0.45, 1.30]		0.33
Methicillin-sensitive <i>S. aureus</i>	0.85 [0.53, 1.35]		0.48
Other staphylococci	1.32 [0.74, 2.34]		0.35
Streptococci	1.09 [0.62, 1.92]		0.76
Enterococci	3.11 [1.74, 5.55]		0.0001
Gram Negative Rods	1.48 [0.95, 2.31]		0.08
<i>Klebsiella</i> spp.	1.52 [0.48, 4.79]		0.47
<i>Escherichia coli</i>	3.07 [1.78, 5.29]		< .0001
Other Enterobacteriaceae	0.60 [0.23, 1.54]		0.29
<i>Pseudomonas</i> spp.	1.26 [0.56, 2.82]		0.57
Anaerobes	1.62 [0.63, 4.19]		0.32
Fungi	4.88 [2.21, 10.78]		< .0001
Candida	5.29 [2.36, 11.88]		< .0001
Mold	N/A		N/A
Other organism	1.31 [0.72, 2.40]		0.38
Culture Negative	0.41 [0.19, 0.87]		0.02
Infection Type			
Polymicrobial Infection ²			
GI Infection	10.00 [2.03, 49.21]		0.005
No GI Infection	1.13 [0.64, 1.99]		0.68
Resistant Infection	0.81 [0.48, 1.36]		0.42
Diagnosis²			
Bloodstream Infection			
EUH	0.88 [0.50, 1.56]		0.67
EUHM	2.15 [1.12, 4.14]		0.02
Central Nervous System	0.53 [0.20, 1.36]		0.18
Cardiovascular	1.00 [0.56, 1.78]		1.00
Ear, Nose, Throat	1.01 [0.22, 4.75]		0.99
Genitourinary	0.97 [0.42, 2.24]		0.94
Lung	1.32 [0.52, 3.33]		0.56
Skin & Soft Tissue Infection	0.39 [0.09, 1.67]		0.20
Other diagnosis	0.79 [0.35, 1.80]		0.57

Table 2 continued

Discharge Medication Class		
Aminoglycosides	1.00 [0.21, 4.69]	1.00
Antifungals	5.33 [2.62, 10.84]	< .0001
Fluconazole	6.13 [2.24, 16.77]	0.0004
Micafungin	5.41 [1.93, 15.19]	0.001
Voriconazole	N/A	N/A
Carbapenems	1.29 [0.80, 2.06]	0.30
Cephalosporins	1.00 [0.68, 1.49]	0.99
Daptomycin	1.12 [0.59, 2.11]	0.73
Fluoroquinolones	0.42 [0.15, 1.20]	0.11
Penicillins	1.26 [0.82, 1.94]	0.29
Vancomycin	0.75 [0.49, 1.13]	0.17
Other antimicrobial	0.82 [0.44, 1.53]	0.53
Outpatient Treatment Duration (days)³		
7-13 days	Ref.	
14-20 days	1.98 [1.02, 3.84]	0.04
21-27 days	1.87 [0.99, 3.55]	0.05
28-34 days	1.15 [0.58, 2.27]	0.68
≥ 35 days	0.80 [0.44, 1.44]	0.45
Charlson Score		
0	Ref.	
1	0.75 [0.38, 1.47]	0.40
2	1.29 [0.73, 2.26]	0.38
≥ 3	2.07 [1.31, 3.25]	0.002
Type of Follow-up Visit		
No follow-up	Ref.	
Any follow-up at Emory Healthcare	0.16 [0.11, 0.24]	< .0001
OPAT clinic ²		
Bone/Joint Infection	0.23 [0.11, 0.47]	< .0001
No Bone/Joint Infection	0.07 [0.04, 0.14]	< .0001
Non-OPAT clinic only ²		
Bone/Joint Infection	0.52 [0.24, 1.15]	0.11
No Bone/Joint Infection	0.25 [0.13, 0.48]	< .0001
Type of OPAT Follow-up Visit		
No OPAT follow-up	Ref.	
Nurse visit only (no NP/PA or physician visits)	0.36 [0.12, 1.04]	0.06
NP/PA visit only (no physician visits)	0.20 [0.12, 0.34]	< .0001
Physician visit	0.10 [0.04, 0.23]	< .0001
Discharge Location		
Home	Ref.	
Rehabilitation facility	0.72 [0.41, 1.24]	0.24
Home County^{4,5}		
Outside Metro Atlanta	Ref.	
Metro Atlanta	1.67 [1.13, 2.47]	0.01

¹ Normal approximation Z score and two-sided P value used for Wilcoxon rank-sum test results² 15 patients missing diagnosis³ 38 patients missing medication⁴ 1 patient missing home county⁵ Metro Atlanta includes Clayton, Cobb, DeKalb, Douglas, Fulton, Gwinnett, Newton, & Rockdale

Table 3. Potential final models and performance statistics based on multiple selection procedures.

Model Number	Final Model Selections ¹	C-statistic	Hosmer-Lemeshow		Notes
			Goodness of Fit	Test P value	
Original Population (N=702) ²					
1	Follow-up, enterococci, Charlson score, rehab, metro Atlanta, GI	0.80	0.63		Forward, Stepwise selection procedures
2	Follow-up, midtown, enterococci, Charlson score, rehab, metro Atlanta, bone/joint, BSI, GI, bone/joint*Follow-up interaction, midtown*BSI interaction	0.83	0.63		Backward selection procedure
3	Follow-up, enterococci, Charlson score, rehab, metro Atlanta, GI, polymicrobial, polymicrobial*GI interaction	0.81	0.73		Final model
Sensitivity Analysis (N=344) ³					
1a	Follow-up, enterococci, Charlson score, GI	0.83	1.00		
2a	Follow-up, midtown, enterococci, Charlson score, bone/joint, BSI, GI, bone/joint*Follow-up interaction, midtown*BSI interaction	0.85	0.92		
3a	Follow-up, enterococci, Charlson score, GI, polymicrobial, polymicrobial*GI interaction	0.83	1.00		Final model

¹ Follow-up: No follow-up visits (ref.), OPAT visit, non-OPAT visit only; Charlson Score: 0-2 (ref.), ≥ 3 ; enterococci infection, discharge to rehabilitation facility (vs. home), midtown (vs. EUH), metro Atlanta (vs. outside), bone/joint infection, bloodstream infection (BSI), & polymicrobial are all yes/no variables

² Model based on 702 individuals (out of 755) due to missing data

³ Sensitivity analysis performed only on individuals residing in metro Atlanta and discharged home. Model based on 344 individuals (of 366) due to missing data

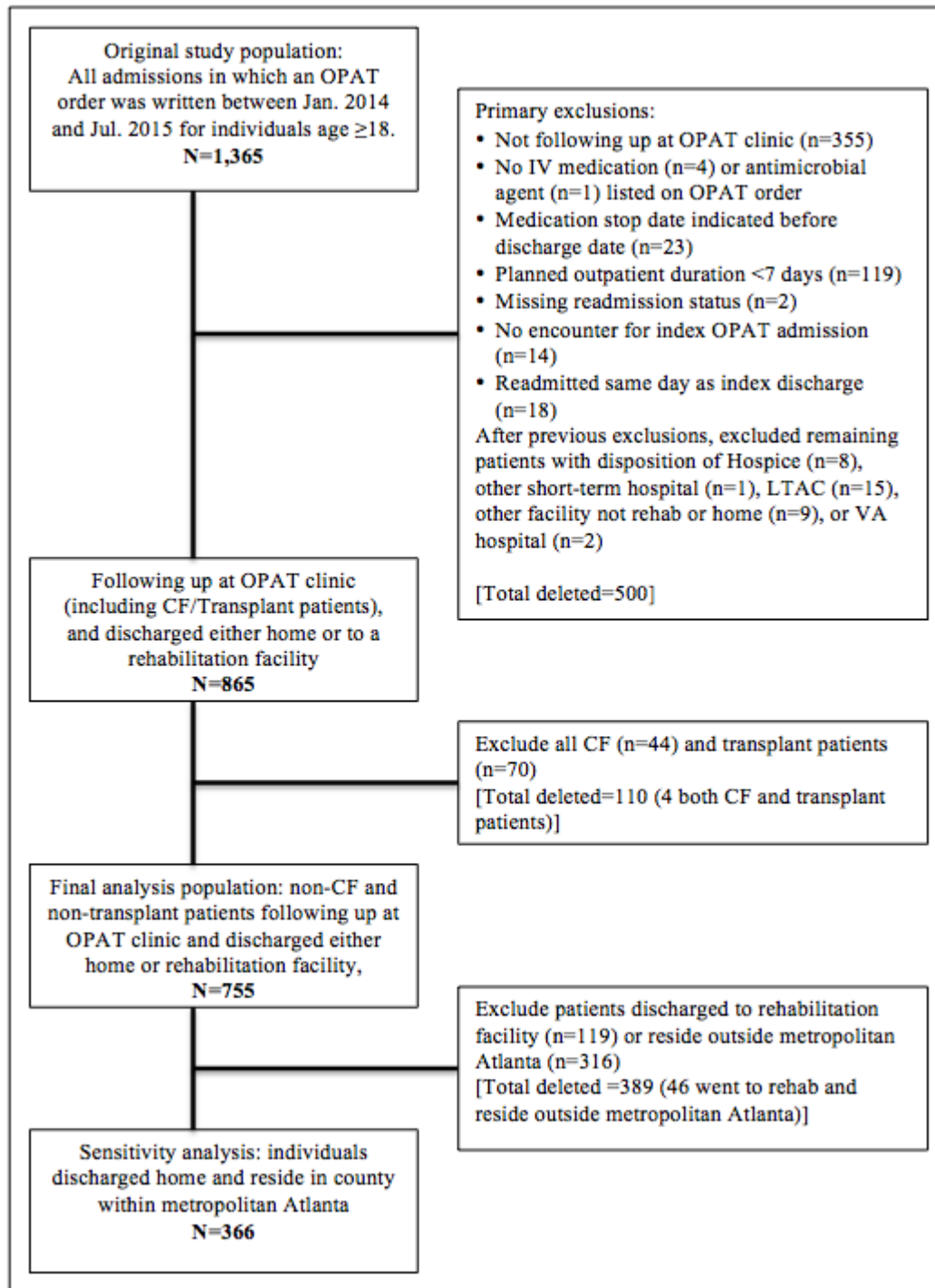
Table 4. Final predictive modeling results.

Characteristic	Odds Ratio [95% Confidence Interval]	P-value
Final Model from Original Population (N=702)¹		
Type of Follow-up Visit		
No follow-up	Ref.	
OPAT clinic	0.10 [0.06, 0.17]	< .0001
Non-OPAT clinic only	0.31 [0.18, 0.55]	<.0001
Enterococci Infection	4.20 [2.00, 8.84]	0.0002
Charlson Score		
0-2	Ref.	
≥ 3	2.08 [1.33, 3.26]	0.001
Rehabilitation Facility (vs. Home)	0.43 [0.23, 0.81]	0.01
Metro Atlanta Residence (vs. Outside)	1.95 [1.22, 3.12]	0.005
Polymicrobial		
GI Infection	11.89 [1.97, 71.80]	0.007
No GI Infection	0.98 [0.51, 1.90]	0.95
Final Model from Sensitivity Analysis (N=344)²		
Type of Follow-up Visit		
No follow-up	Ref.	
OPAT clinic	0.06 [0.03, 0.13]	< .0001
Non-OPAT clinic only	0.24 [0.11, 0.53]	0.0004
Enterococci Infection	7.79 [2.37, 25.64]	0.0007
Charlson Score		
0-2	Ref.	
≥ 3	1.60 [0.85, 2.98]	0.14
Polymicrobial		
GI Infection	13.12 [1.00, 172.0]	0.05
No GI Infection	0.48 [0.17, 1.35]	0.17

¹Model based on 702 individuals (of 755) due to missing data

²Sensitivity analysis performed only on individuals residing in metro Atlanta and discharged home. Model based on 344 individuals (of 366) due to missing data

Figure 1. Flow chart of patient selection for analysis.



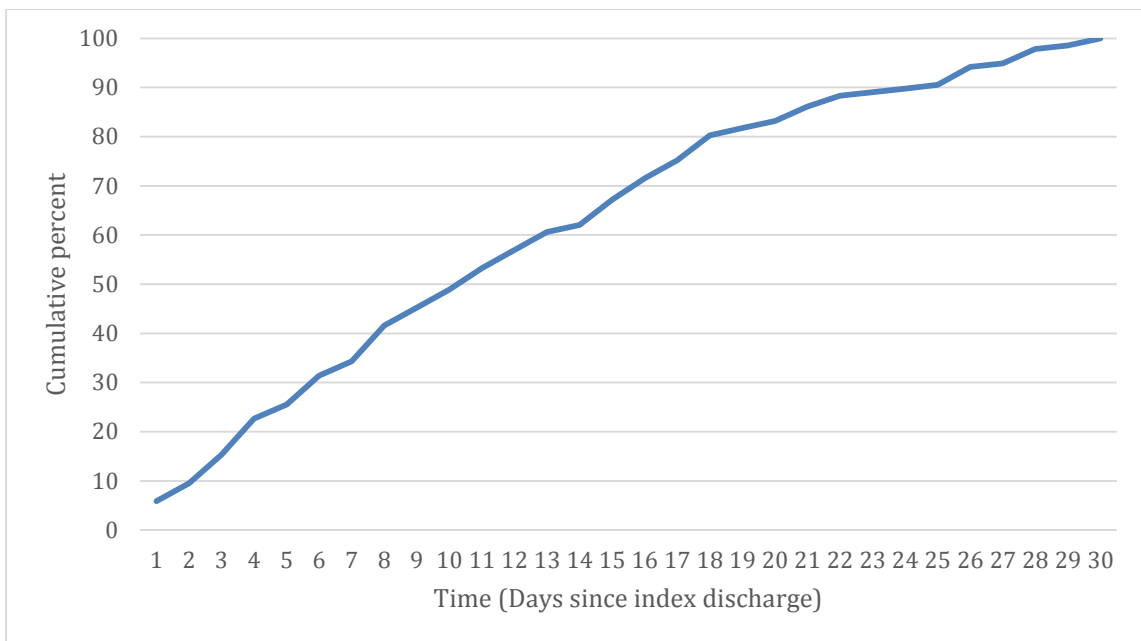


Figure 2. Cumulative thirty-day readmission rate (N=137 readmitted patients).

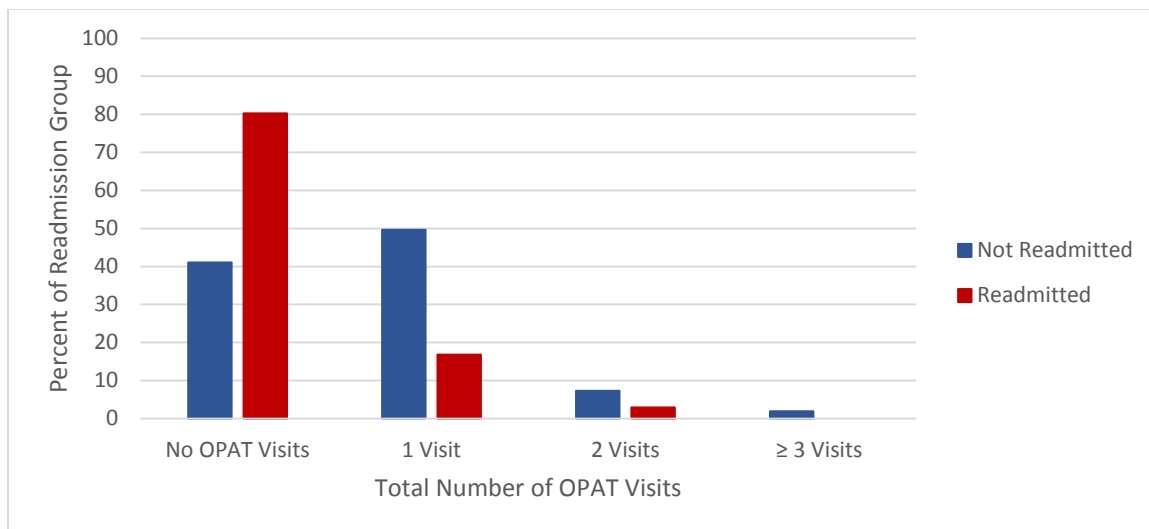


Figure 3. Total number of OPAT visits within thirty days by readmission status (N=755)

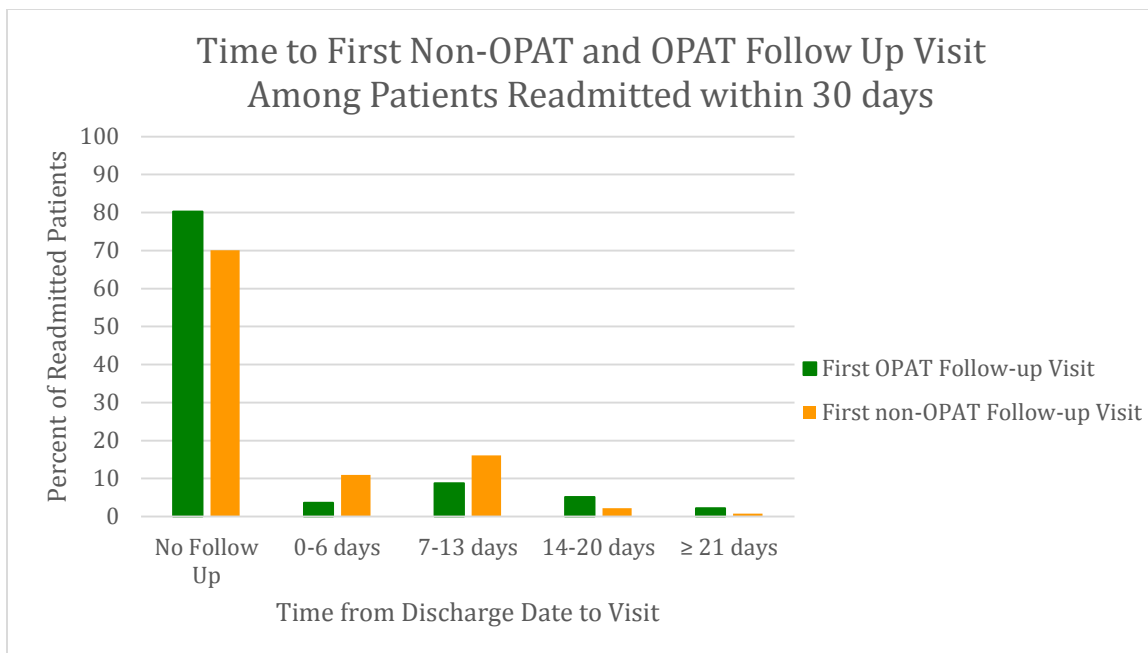


Figure 4. Time to first follow-up visit by visit type among readmitted patients (N=137)

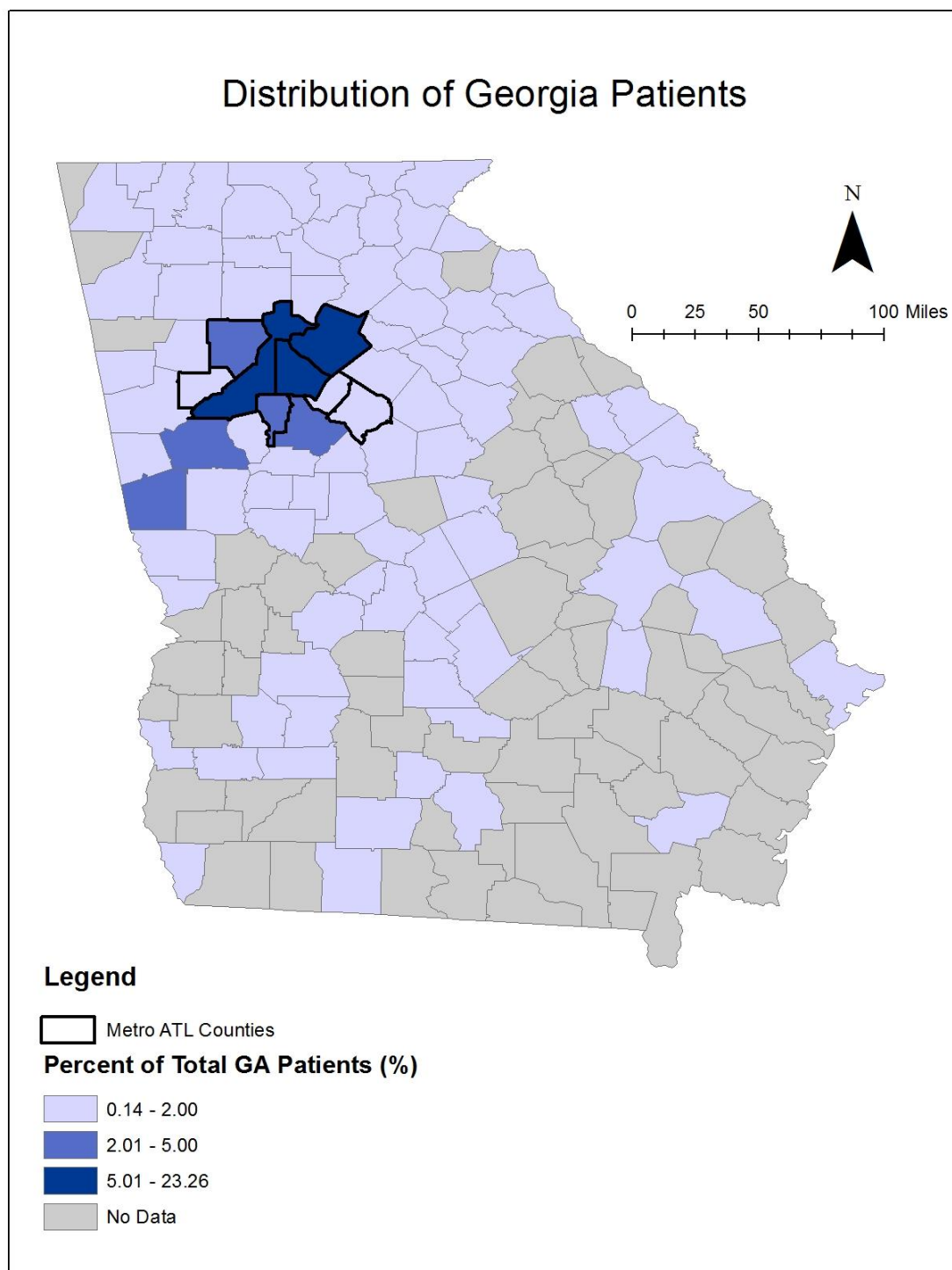


Figure 5. Percent of Georgia patients in the final analysis population residing in each county (N=718)

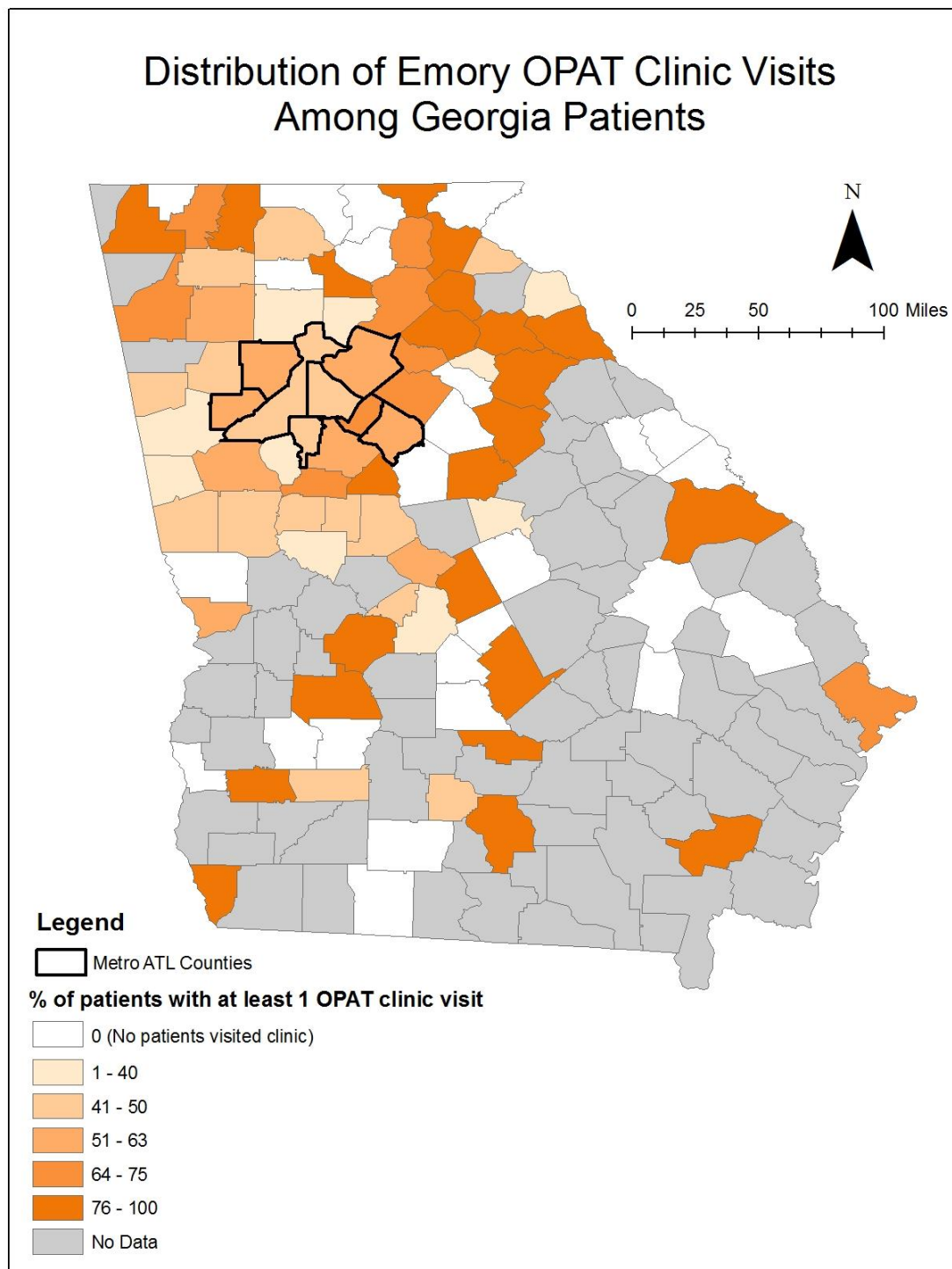


Figure 6. Percent of patients in each Georgia county that attended at least one visit at the Emory OPAT clinic.

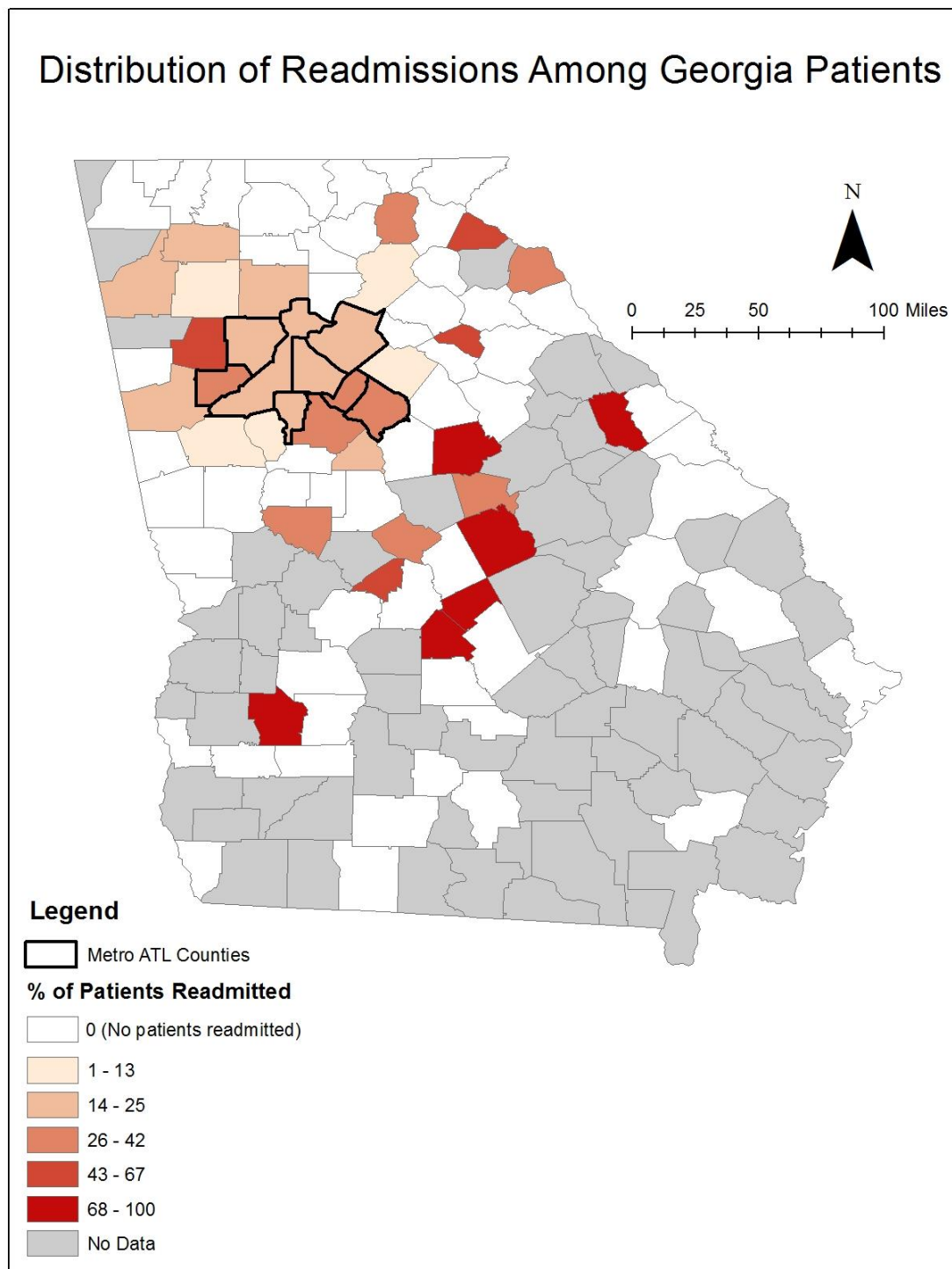


Figure 7. Percent of patients in each Georgia county that were readmitted within thirty days of their index discharge date.

Appendix

Supplementary Table 1. Counts of pathogens in final population (N=755)

Pathogen		N	
Gram Positive Cocci Species	Methicillin-resistant <i>S. aureus</i>		126
	Methicillin-sensitive <i>S. aureus</i>		160
	Other Staphylococci	Coagulase-negative staphylococci/ <i>S. lugdunensis</i>	77
		<i>S. intermedius</i>	1
	Streptococci	Alpha hemolytic streptococci	7
		Beta hemolytic streptococci	1
		Group A streptococci/ <i>S. pyogenes</i>	5
		Group C streptococci	1
		Group G streptococci	4
		Non-hemolytic streptococci	2
		Other streptococci	4
		<i>S. agalactiae</i> /group B streptococci	24
		<i>S. anginosus</i>	19
		<i>S. gordonii</i>	1
		<i>S. intermedius</i>	1
		<i>S. mitis/oralis</i>	7
		<i>S. mutans</i>	2
		<i>S. pneumoniae</i>	7
	<i>S. sanguinis</i>	1	
	Viridans streptococci	3	
Enterococci	<i>E. avium</i>	2	
	<i>E. faecalis</i>	41	
	<i>E. faecium</i>	8	
	Other	4	
Gram Negative Rods	Klebsiella	<i>Klebsiella pneumoniae</i>	11
		<i>Klebsiella oxytoca</i>	4
		Other	1
	<i>E. coli</i>		64
	Enterobacteriaceae	<i>Citrobacter freundii</i>	4
		<i>Citrobacter koseri</i>	2
		<i>Enterobacter aerogenes</i>	5
		<i>Enterobacter cloacae</i>	6
		<i>Enterobacter</i> spp.	1
		<i>Morganella morganii</i>	1
		<i>Morganella</i> spp.	1
		<i>Pantoea agglomerans</i>	1
		<i>Pantoea</i> spp.	1
		<i>Proteus mirabilis</i>	5
		<i>Proteus vulgaris</i>	1
		<i>Proteus</i> spp.	2
		<i>Providencia rettgeri</i>	1
<i>Providencia stuartii</i>		1	
<i>Providencia</i> spp.	2		
<i>Salmonella</i> serotype Enteritidis	1		
<i>Salmonella</i> spp.	2		

Gram Negative Rods (cont.)	Enterobacteriaceae (cont.)	<i>Serratia marcescens</i>	6
		<i>Serratia</i> spp.	2
	Pseudomonas	<i>Pseudomonas aeruginosa</i>	30
<i>Pseudomonas putida</i>		1	
<i>Pseudomonas</i> spp.		6	
Anaerobes	<i>Actinomyces</i>	1	
	<i>Bacteroides fragilis</i>	1	
	<i>Bacteroides thetaiotaomicron</i>	1	
	<i>Bacteroides</i> spp.	3	
	<i>Fingoldia magna</i>	2	
	<i>Fusobacterium</i>	2	
	<i>Peptostreptococcus</i>	2	
	<i>Prevotella</i>	4	
Other	10		
Fungi	Candida	<i>Candida albicans</i>	11
		<i>Candida glabrata</i>	7
		<i>Candida krusei</i>	2
		<i>Candida parapsilosis</i>	5
		<i>Candida tropicalis</i>	2
		<i>Candida</i> spp.	1
	Mold	<i>Aspergillus</i>	1
Other	<i>Achrombacter xylosoxidans</i>	1	
	<i>Acinetobacter haemolyticus</i>	1	
	<i>Acinetobacter</i> spp.	2	
	<i>Aeromonas hydrophila</i>	1	
	<i>Aggregatibacter actinomycetemcomitans</i>	3	
	<i>Borrelia burgdorferi</i>	1	
	<i>Burkholderia cepacia</i>	1	
	<i>Campylobacter gracilis</i>	1	
	<i>Cardiobacterium hominis</i>	1	
	<i>Clostridium perfringens</i>	1	
	<i>Corynebacterium jeikeium</i>	1	
	<i>Corynebacterium striatum/amycolatum</i>	1	
	<i>Corynebacterium</i> (unspecified)	9	
	Coryneform bacteria	3	
	Cytomegalovirus (CMV)	1	
	Empiric gram positive	6	
	Gram negative (not further identified)	1	
	<i>Haemophilus influenzae</i>	1	
	Herpes simplex virus	3	
	<i>Kodamaea ohmeri</i>	1	
	<i>Lactobacillus</i>	2	
	<i>Micrococcus</i>	1	
	<i>Moraxella</i>	1	
	<i>Mycobacterium abscessus</i>	1	
	<i>Mycobacterium avium</i>	2	
	<i>Pasteurella</i>	1	
	<i>Propionibacterium acnes</i>	8	
<i>Rhodococcus</i>	1		

Other (cont.)	<i>Steonotrophomonas maltophilia</i>	1
	<i>Stenotrophomonas</i> spp.	3
	<i>Treponema pallidum</i>	7
	<i>Vibrio vulnificus</i>	1

Supplementary Table 2. Counts of antimicrobials among final population (N=755)

Medication		N
Aminoglycosides	Amikacin	2
	Gentamicin	8
	Tobramycin	1
Antifungal	Fluconazole	16
	Micafungin	15
	Voriconazole	2
Carbapenems	Ertapenem	100
	Meropenem	27
Cephalosporins	Cefazolin	70
	Ceftazidime	27
	Cefepime	13
	Cefoxitin	1
	Ceftaroline	20
	Ceftriaxone	118
	Cephalexin	1
Daptomycin		66
Fluoroquinolone	Ciprofloxacin	7
	Levofloxacin	36
	Moxifloxacin	2
Penicillins	Ampicillin	20
	Ampicillin-sulbactam	9
	Amoxicillin-clavulanate	1
	Nafcillin	93
	Penicillin	30
	Piperacillin-tazobactam	14
	Ticarcillin	1
Vancomycin		241
Other	Acyclovir	3
	Azithromycin	3
	Aztreonam	3
	Bactrim	2
	Clindamycin	1
	Colistin	1
	Doxycycline	1
	Ethambutol	2
	Metronidazole	29
	Ganciclovir	1
	Isoniazid	1
	Linezolid	1
	Minocycline	1
	Pyrazinamide	1
	Rifampin	38
	Tigecycline	4
	Valacyclovir	2
Valganciclovir	1	

Supplementary Table 3. Counts of diagnoses among final population (N=755)

	Diagnosis	N
Bone/Joint Infection	Bone/joint infection	2
	Epidural abscess	24
	Mediastinitis	3
	Orthopedic hardware infection	3
	Osteomyelitis	196
	Prosthetic joint infection	95
	Septic arthritis	21
Bloodstream infection (BSI)	Bacteremia	145
	Central Line-Associated BSI (CLABSI)	23
	Fungemia	3
	Viremia	1
Central Nervous System (CNS)	Brain abscess	17
	Encephalitis	3
	Endophthalmitis	1
	Infected neurosurgical device	10
	Meningitis	18
Cardiovascular	Cardiac-device associated infection	23
	Endocarditis	43
	Infected vascular device	6
	Mycotic aneurysm	3
	Prosthetic valve	2
	Septic emboli	9
	Septic thrombophlebitis	6
	Thrombophlebitis	2
	Vascular infection with prosthetic material	4
Ear, Nose, & Throat	Malignant otitis externa	3
	Neck abscess	5
	Pharyngitis	1
	Sinusitis	3
Gastrointestinal (GI)	Abdominal abscess	3
	Biliary infection	3
	Cholangitis	2
	Diverticular abscess	1
	Diverticulitis	2
	Intra-abdominal abscess	24
	Intra-abdominal infection	3
	Liver abscess	13
	Liver infection	1
	Peritonitis	9
Genitourinary (GU)	Endometritis	1
	Epididymitis	1
	Perinephric abscess	1
	Prostate abscess	1
	Prostatitis	1
	Pyelonephritis	27
	Renal abscess	1

Genitourinary (GU) (cont.)	Tubo-ovarian abscess	1
	Urinary tract infection	7
Lung	Bronchiectasis	2
	Empyema	11
	Lung abscess	3
	Lung, mycobacterial	1
	Pneumonia	11
Skin and soft tissue infection (SSTI)	Cellulitis	10
	Psoas abscess	1
	Skin abscess	2
	Soft tissue infection	10
	SSTI	1
	Thigh abscess	1
Other	Actinomycosis	1
	Gastritis due to CMV	1
	Lyme disease	1
	Neurosyphilis	7
	Pericarditis	3
	Pulmonary actinomycosis	1
	Pyomyositis	12
	Retroperitoneal abscess	2
	Surgical site infection	19