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An Investigation of the Attributable Outcomes of Carbapenem-Resistant *Acinetobacter baumannii* (CRAB) Among Hospitalized Patients with Urinary Tract Infections or Bloodstream Infections

By

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Master of Public Health

Epidemiology

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By

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Bachelor of Science/Bachelor of Arts

North Carolina State University

2020

Thesis Committee Chair: Scott Fridkin, MD

An abstract of

A thesis submitted to the Faculty of the

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## ABSTRACT

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Antibiotic resistance bacteria are an increasing area of concern due to poor outcomes attributable to these infections, resulting in morbidity and mortality. Carbapenem-resistance *Acinetobacter baumannii* (CRAB) has been deemed an "urgent" threat by CDC due to increasing resistance to this class of antibiotics. CRAB presents an extraordinary challenge for healthcare facilities, as infected or colonized patients can spread the bacteria when appropriate infection prevention and control procedures are inadequately executed. Patients with CRAB infections are usually very ill to begin with and estimates of attributable outcomes of CRAB infections may be imprecise due to biased selection of uninfected controls with lower likelihood for poor outcomes. This study explored if individuals with CRAB experience more severe outcomes, as compared to individuals who were not infected or colonized with CRAB but were as ill or had similar underlying illness as patients with XRAB. A case-control study was performed using case reports from the Georgia Emerging Infections Program linked to hospital encounter information from the Georgia Hospital Discharge Database. Seventy-seven cases were propensity score matched using 118,000 potential controls by ICD-9/ICD-10 codes. Propensity score matching was conducted to ensure cases were being compared with individuals as likely as being infected with CRAB. Wilcoxon signed-rank tests were utilized to evaluate the differences in length of stay and time to re-admission between cases and matched controls. Length of stay, the time between a patient's first discharge and their next subsequent readmission, or frequency of incident hospitalization death were not significantly different between matched cases and controls. These findings may represent negligible outcomes attributable to CRAB when cases are appropriately matched with individuals with similar comorbidities, or a lack of power due to small sample size. Further exploration of attributable outcomes related to CRAB with larger sample sizes should be conducted to better understand the true morbidity and mortality associated with these infections.

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**DISCLAIMER**

The primary dataset used in this project was collected by the Georgia Emerging Infections Program (GAEIP). The GAEIP was not involved in the analyses presented in this thesis.

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# CHAPTER I: BACKGROUND

The use of antibiotics, or medicines for fighting infections caused by bacteria, has transformed the way in which we, as a society, approach modern medicine. (1) Various antibiotics are utilized to treat a multitude of diseases in both humans and animals. While antibiotics have undoubtedly been a medical advancement, overprescribing, with a lack of continued antibiotic development, has fueled bacterial resistance to this form of treatment. As a result, antibiotic resistance has been recognized as one of the current day's most concerning public health issues.

## *Surveillance of Carbapenem-resistant Acinetobacter baumannii Infections*

Carbapenem-resistant *Acinetobacter baumannii* is a type of Gram-negative bacteria that is of great concern due to its resistance to several groups of antibiotics, including last-line classes, such as the carbapenems. For this reason, surveillance is a vital aspect regarding understanding the true burden of disease and the overall influence of antimicrobial resistant infections on health outcomes. Surveillance efforts supported by CDC's Emerging Infections Program were designed to estimate the extent of certain gram-negative bacteria in the United States, as well as how these trends change over time. These surveillance data can also be used to investigate outcomes attributable to theses infection.

## *Mechanisms for Antibiotic Resistance*

Antibiotic resistance is described as the ability of "germs to develop the ability to defeat the antibiotics designed to kill them." (2) This is a naturally occurring phenomenon, as natural selection drives random mutation in bacteria. These random mutations may then be deemed

advantageous, when bacteria with the given trait replicate, fueling the development of antibiotic resistance. This process, however, is expedited and exacerbated by increased exposure of germs to antibiotics, as well as bacteria's resistance mechanisms. (3)

Commonly several different mechanisms work together to contribute to the resistance. (4) One of the primary ways in which bacteria does this is by producing carbapenem-hydrolyzing enzymes, known as carbapenemases. (5) There are three main mechanisms of resistance for Carbapenem-resistant *Acinetobacter baumannii* (CRAB): 1) enzymes inactivating antibiotics, 2) reduced entry into the target site of bacteria, and 3) alteration of the target or cellular functions due to mutations. (6)

The first mechanism that is seen in CRAB is through carbapenemases. Carbapenemases, in general, are considered to have very versatile hydrolytic capabilities. These enzymes possess the ability to hydrolyze various antibiotic classes, including cephalosporins and carbapenems, rendering many β-lactam antibiotics ineffective. One of the most predominant forms of carbapenemases found in individuals infected with CRAB are Carbapenem-hydrolyzing class D β-lactamases (CHDLs), which can also be referred to as OXA-type enzymes or oxacillinases. (5) Typically, an OXA-type carbapenemase presents only weak carbapenemase activity. However, a secondary resistance mechanism such as porin deficiencies or the overexpression of efflux pumps can increase this activity level. (7)

Another mechanism that allows CRAB to evade antibiotics is through the reduction of antibiotic entry into the target site of the bacteria. This can be inhibited in two main locations: the porin channels and the outer membrane protein, which both deliver antibiotics into the target proteins. Porins typically work with beta-lactamases to overcome the small size and number of porin channels in CRAB strains. This makes it increasingly challenging for antibiotics to

permeate the cell wall and thus, essentially renders them ineffective. (5) Another aspect of antibiotic evasion is feasible when efflux pumps remove antibiotics from target locales within the bacteria. Furthermore, point mutations can occur in enzyme encoding genes or porin channels. This can result in a decreased affinity for binding or alteration in the up-regulating cellular functions responsible for efflux pump production. (6)

The third central mechanism for carbapenem resistance is altering the target or cellular functions due to mutations. Particularly, Imipenem and Meropenem-resistant CRAB is associated with the loss of CarO, a heat-modifiable 29kDA outer membrane protein. (8) This mechanism also accounts for selective pressures that are in place due to the broad nature of antibiotics, as well as the dynamic transmission patterns between patients that can further the presence of carbapenem resistance. (6)

### *Risk Factors Associated with Carbapenem-resistant Acinetobacter baumannii Infections*

There are several comorbidities or conditions that make an individual more likely to experience a CRAB infection. Most of these individuals are immunocompromised or within intensive care or burn units. (9) Individuals in inpatient settings utilizing devices such as ventilators or invasive devices have increased risk of infection with CRAB. (10) CRAB infections can present as ventilator-associated pneumonia, bloodstream infection, urinary tract infection, meningitis, and wound infection. (10) CRAB infections rarely occur outside of a healthcare setting. (11) This bacterium can survive for extensive periods of time on inanimate objects such as bedrails, sink counters, computer keyboards, pillows, curtains, and other dry surfaces. (12) Moreover, this bacterium can survive under harsh environmental pressures, making it more likely to survive inadequate or sub-optimal cleaning of patient rooms and patient-

care equipment. This prolonged survival in patient's rooms may explain why patient risk for infection with CRAB is increased with longer hospital stays in a healthcare setting. (2) Ultimately, it is believed that individuals who experience a CRAB diagnosis will have more severe health outcomes, some of which might include a longer hospitalization, or more frequent readmissions to inpatient settings. However, several published studies estimating the impact of CRAB on patient's outcomes have utilized suboptimal comparison groups that are not comprised of patients with similar severity of illness to produce an unbiased estimate of attributable outcomes.

# CHAPTER II

## ABSTRACT

An Investigation of the Attributable Outcomes of Carbapenem-Resistant *Acinetobacter baumannii* (CRAB) Among Hospitalized Patients with Urinary Tract Infections or Bloodstream Infections
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Antibiotic resistance bacteria are an increasing area of concern due to poor outcomes attributable to these infections, resulting in morbidity and mortality. Carbapenem-resistance *Acinetobacter baumannii* (CRAB) has been deemed an "urgent" threat by CDC due to increasing resistance to this class of antibiotics. CRAB presents an extraordinary challenge for healthcare facilities, as infected or colonized patients can spread the bacteria when appropriate infection prevention and control procedures are inadequately executed. Patients with CRAB infections are usually very ill to begin with and estimates of attributable outcomes of CRAB infections may be imprecise due to biased selection of uninfected controls. This study explored if individuals with CRAB experience more severe outcomes, as compared to individuals who were not infected or colonized with CRAB. A case-control study was performed using case reports from the Georgia Emerging Infections Program linked to hospital encounter information from the Georgia Hospital Discharge Database. Seventy-seven cases were propensity score matched to 118,000 potential controls using ICD-9/ICD-10 codes. Propensity score matching was conducted to ensure cases were being compared with individuals as likely as being infected with CRAB. Wilcoxon signed-rank tests were utilized to evaluate the differences in length of stay and time to re-admission between cases and matched controls. Length of stay, the time between a patient's first discharge and their next subsequent readmission, or rate of incident hospitalization death were not significantly different between matched cases and controls. Further exploration of attributable outcomes related to CRAB with larger sample sizes should be conducted to better understand the true morbidity and mortality associated with these infections.

## INTRODUCTION

Antibiotic resistance is an emerging public health threat that requires attention. In 2019, it was estimated that 4.95 million deaths were associated with bacterial antimicrobial resistance. (13) Identifying viable treatments for these bacteria has become increasingly challenging, or even non-existent. Overprescribing of antibiotics are allowing bacteria to evade medications that have been seen as reliable treatment options for a plethora of infections and illnesses. (14) In conjunction with overprescribing, there is a lack of new drugs that are being developed to treat infections, with the last entirely new class of antibiotics being discovered over 30 years ago. (15) The current conditions surrounding antimicrobial usage and resistance are a reason for great concern.

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is a multi-drug resistant bacteria that is capable of evading carbapenem antibiotics. Carbapenem antibiotics are the antibiotic of last resort and are valuable in that they can be utilized broadly, but that they also have the greatest potency when it comes to treating both gram-positive and gram-negative bacteria. (16) Utilization of carbapenems is typically reserved for when other antibiotic classes are insufficient, however, increasing resistance to cephalosporin antibiotics has made the prescribing of carbapenems more common. (17) This ability for the bacteria to avoid antibiotics creates great concern for individuals who become infected. The Center for Disease Control and Prevention (CDC) estimated that roughly 8,500 individuals were hospitalized with CRAB in 2019, with about 8% of infected patients experiencing mortality. (2) Patients suffering from other comorbidities or complicated hospital stays are more likely to become infected with *Acinetobacter* spp. regardless of susceptibility profile; factors associated with these infections include lengthy hospital stays, those who have open wounds, or patients in need of invasive

devices. Because these infections occur in the sickest patient population, estimating the attributable outcome of CRAB has challenges, and requires comparisons to a patient population with similar severity of illness as the CRAB infected patients.

## METHODS

### *Study Design*

This study utilized a retrospective approach to test the hypothesis that hospitalized patients diagnosed with CRAB faced more severe attributable health outcomes then comparable patients not infected with CRAB. More specifically, an investigation was completed to determine if individuals with CRAB experienced a longer length of stay or a shorter time until readmission than individuals who were not diagnosed with CRAB.

### *Primary Data Source*

A matched case-control study was conducted utilizing two Georgia databases: the Georgia Discharge Data System (GDDS), as well as the Georgia Emerging Infections Program (EIP) Multi-site Gram-negative Surveillance Initiative (MuGSI) CRAB database. All patients hospitalized in the 8 county Health District 3 (HD3) within 30 days of a specimen culture were eligible for inclusion. Each unique hospital encounter was accompanied by data including patient identifiers, facility labels, and characteristics of the visit, including admission and discharge dates, diagnosis codes, and length of stay. GDSS is a database of all encounters from acute care hospitals. Summary data for each patient discharge from an acute care facility in Georgia is collected.

The MuGSI team at the Georgia EIP ascertained CRAB cases by conducting active, population-based surveillance for the eight counties surrounding the Atlanta area which is more formally known as Health District Three (HD3). An incident case is defined as an individual's first CRAB-positive culture that is resistant to one or more of the carbapenem antibiotics (Doripenem, Imipenem, or Meropenem), with minimum inhibitory concentration (MIC) values for resistance being determined by the Clinical & Laboratory Standards Institute.

### *1. Identification of Eligible Cases and Controls*

The Georgia Emerging Infections Program (EIP) conducts active, population-based surveillance for CRAB for the eight counties surrounding the Atlanta area, also known as Health District Three (HD3). CRAB cases were identified through routine queries of laboratory tests by EIP staff. Cases of CRAB were defined as a patient whose home address resides in HD3 with an *Acinetobacter baumannii* isolate recovered from a normally sterile site or urine. The isolate met EIP's case definition if Imipenem (MIC >=8), Meropenem (MIC >=8), or Doripenem (MIC >1) were resistant. Cases were linked to the GDSS, where complete discharge data was identified. For our study, we evaluated CRAB cases with positive specimen collected between April 2015 and July 2017. All individuals who had specimen collected as an outpatient without any hospitalization within three days of a positive specimen collection were excluded as eligible cases. Potential controls were selected from the GDDS by subsetting all encounters from the same facilities and months that case-patients were discharged.

### *2. Assessing Comorbidity Scores of Cases and Controls*

An integral part of the analysis plan was understanding from what type and to what extent the outcomes of both cases and controls entering the hospitals within HD3 was being influenced by comorbidities or underlying illnesses. The Charlson Comorbidity Index is a notable proxy variable for ascertaining this type of information about the study population. To be able to discern a score from the original dataset, ICD-9 and ICD-10 discharge information had to be addressed separately, as our case dataset spanned time periods that used both ICD-9 and ICD-10 codes. This was done by utilizing a National Association of Health Data Organization granted SAS MACRO. Once ICD-9 and ICD-10 discharge codes were separated for both the cases and the controls, the Comorbidity Package in R was utilized to read this assigned comorbidity scores. To confirm that Comorbidity scores were being assigned correctly, SAS MACROs created by the University of Manitoba were utilized. This reaffirmed the Charlson Comorbidity Score for each case, as well as the frequency of scores amongst the case-cohort.

### *3. Assigning of Admission Diagnosis Category*

Their first discharge ICD-9 or ICD-10 code from incident admission of all cases and eligible controls was manually translated into syndromes, using Codify by American Academy of Professional Coders' information as a reference. (18) Case-patients were classified into one of the following broader categories of discharge diagnosis: Epilepsy (N=2), Esophagitis (N=1), Diabetes (N=2), Plasma Protein Disorder (N=1), Sepsis (N=28), Diseases of the Circulatory System (N=3) Diseases of the Respiratory System (N=6), Diverticulosis of the Colon (N=2), Non-Urinary Tract Infection Diseases of the Genitourinary System (N=3), Urinary Tract Infection (N=5), or Medical Complications of Procedures (N=2).

### *4. Matching of Cases and Controls*

Cases and controls were matched to identify controls in the hospital that were as likely to suffer a CRAB infection as the cases. To do so, cases and controls underwent propensity score matching. First, eligible controls were created by performing frequency matching od all hospital encounters in the GDDS by facility and month of cases. Initially, 77 cases were eligible for matching, however, after cases with incomplete GDDS data were removed, 54 cases remained. Despite 23 cases being removed due to incomplete data, it is believed, based on various demographic factors, that the cases with complete data are rather representative of the cohort. Next, propensity score matching allowed for identification of patient-encounters at similar risk for CRAB infections as cases. Propensity score matching was based on Admission Diagnosis Category, Age Group, and whether they were diagnosed with renal disease during their incident admission. The 'MatchIt' package in R was utilized to identify controls apt for matching upon as likely to have CRAB. Out of the 54 cases that were eligible for matching, only 51 had suitable controls that were matched based on the selected criteria. This was based on the propensity score of a control being within 0.01 standard deviations of the propensity score of the case. Propensity score matching is a technique that ensures individuals in the matched control group were similar to their counterparts, the cases, who were ultimately diagnosed with CRAB.

### *5. Wilcoxon Signed-Rank Tests to Assess for Statistically Meaningful Differences*

In this study, Wilcoxon Signed-Rank Tests were utilized to determine whether certain variables related to a patient's attributable outcomes were statistically different between the cases and controls. Cases and controls had to be adequately matched prior to conducting these

analyses. All statistical tests considered *p* values of <0.05 were considered statistically significant. Data were analyzed using SAS 9.4 (Cary, NC, USA).

## RESULTS

Overall, seventy-seven cases were identified to study. Most of the cases identified as Black/African American (70.1%), and not Hispanic or Latino (96.1%). (Table 1) Most of these individuals within the matched study population were between the ages of 19 and 49 (36.4%). Specimens were collected almost entirely from urine (67.5% and blood (29.9%), with a small portion of them being collected from bone (2.6%). (Table 1) This likely indicates that individuals diagnosed with CRAB had an invasive device such as a catheter or central line inserted during their hospitalization, highlighting the risk for inappropriate or improper usage of these devices.

As expected, the case-cohort had a higher percentage of various comorbidities than what was identified in the control-cohort (Table 2) including myocardial infarction (5.6% vs. 2.7%), congestive heart failure (16.7% vs. 7.0%), peripheral vascular disease (1.9% vs. 1.6%), cerebrovascular disease (7.4% vs. 4.3%), dementia (3.7% vs 0.4%), chronic pulmonary disease (9.3% vs. 5.0%), diabetes with (1.9% vs. 1.2%) and without complications (13.0% vs. 3.8%), hemiplegia or paraplegia (14.8% vs. 0.4%), renal disease, (16.7% vs. 3.4%) and HIV/AIDS (5.6% vs. 0.8%). (Table 2)

Of the cases that were able to be matched to the Georgia Hospital Discharge Dataset, fifty-one were able to have a control identified that's propensity score was within 0.01 standard deviations of the case. Several different variable combinations and propensity score thresholds were attempted. Many of these included Charlson Comorbidity Score and Race as matching variables, however, this drastically decreased the number of matches available within upwards of

1.0 standard deviations of the case's propensity score. Ultimately, cases and controls were matched upon Admission Diagnosis Category, Age Group, and whether the patient was diagnosed with renal disease during their incident admission. Based upon the criteria, three cases matched to the GDDS were unable to be matched to a suitable control, and thus removed from further analysis. These three cases had Admission Diagnosis Categories that made it challenging to identify controls capable of being matched to. These categories included Medical Complications of Procedure and Plasma Protein Disorder.

Propensity score-matched cases and controls appear to be rather similar. In the control cohort, there were more females than males, which is different from the case-cohort where there are more males than females. The distribution of race is similarly representated between the propensity score-matched cases and controls. The main difference between these groups is that the case patients had higher Charlson Comorbidity Scores, as compared to the controls, in that 27.4% of cases has a score of 2 or greater, as compared to 2.0% of controls.

Overall, it was found that the duration of hospitalization for the incident admission was longer for cases (Median: 11.0 days, $CI_{95}$: 12.82, 23.69) compared to controls (Median: 7.0 days, $CI_{95}$: 8.17, 15.86) ($p = 0.10$). (Table 4) Similar statistical tests were conducted for the time between a patient's incident discharge date and their subsequent readmission into an inpatient setting. It took cases longer to be readmitted into an inpatient setting after their incident admission (Mean: 28.0 days, $CI_{95}$: 24.25, 61.63) than controls (8.0 days, $CI_{95}$: 8.56, 31.44) ($p = 0.19$). (Table 4) Lastly, cases died at a higher frequency during their incident hospitalization, as compared to controls. ($p = 0.25$). (Table 4)

# DISCUSSION

## *1. Analysis Interpretations and Discussion*

Three attributable outcomes were evaluated in this study: length of stay, time to first subsequent readmission, and incident hospitalization death. Of the three attributable outcomes, there was evidence of minor or no significant different between the cases and controls. This was rather surprising, and contrary to the hypothesis that patients with CRAB were likely to have longer lengths of stay, shorter times to subsequent readmission and be more likely to die during incident hospitalization. This could be a result of matching based on similar admission diagnoses, and not that based on the idea that CRAB patients suffer worse outcomes. Additionally, length of stay was only calculated amongst individuals who survived their incident hospitalization, and thus, were eligible for readmission.

Existing literature has found that patients with multi-drug resistant *Acinetobacter baumannii* infections have were more likely to die upon incident admission, as well as to have subsequent positive culture. These findings were statistically significant at an alpha of 0.01. In this study, however, the population was nearly 8,000 individuals, most of whom were males. (19) With this in mind, the small sample size should in this thesis's study population should be considered when examining the generalizable of this study. The findings do suggest that there were small differences observed between the cases and controls that might be of statistical importance should there have been a larger sample size analyzed that allowed for different matching criteria to be selected.

## *2. Data Quality and Sample Size*

In this study, data from the Georgia Emerging Infections Program, as well as the Georgia Hospital Discharge Dataset were utilized as a basis for exploring the attributable outcomes of CRAB. In general, CRAB is a rather rare diagnosis, that typically impacts individuals who are immunocompromised or in healthcare settings for extended periods of time. The Georgia EIP only conducts surveillance in the eight surrounding Metro-Atlanta area. Additionally, it was decided that, due to concerns regarding outpatient data collection and the ability to conduct follow-up reporting, the case cohort would only be made up of individuals who were treated for CRAB in inpatient settings. As a result of all these factors, the number of cases in the study's cohort was rather small. Further, 23 of the cases that were eligible for inclusion lacked complete data and thus were excluded from the analysis portion of this study.

### *3. Implications of Data Quality and Sample Size on Analytics*

There are several aspects of the study that could be influenced by the data quality and sample size, which can impact the validity of the overall findings. It can be challenging to study rare diseases, as these typically have small sample sizes. Furthermore, these cases likely represent individuals who are, in general, considerably sicker than the general population. This presented a great challenge when attempting to match based on Charlson Comorbidity Score, as only 31 cases had suitable controls when trying to match upon this variable. GDDS only records ten discharge codes for every patient's hospitalization. As a result, the overall comorbidity scores that were ascertained from these discharge codes are likely an underrepresentation of the true comorbidities of the individuals in this study. Upon manual review of the data collected on cases via full medical record reviews, it is estimated that less than 48% of the total comorbidities for these cases were captured by the discharge database diagnosis codes. EIP conducts analyses on

their cases, including Charlson Comorbidity Score ascertainment, which reaffirmed that Charlson Comorbidity Scores assigned through the GDDS were an underestimate of the true burden of morbidity in the study population.

## CHAPTER III: PUBLIC HEALTH IMPLICATIONS

Understanding the implications of *Acinetobacter baumannii* infections is of great importance when attempting to uncover the true burden of morbidity and mortality caused by multi-drug resistant organisms. Through this case-control study, attributable outcomes due to infection with CRAB were explored. CRAB is an infection that occurs among very sick hospitalized patients, and as a result, is difficult to accurately quantify CRAB infections and the attributable outcomes associated with these infections. Despite the small sample size, this study suggests that the outcomes attributable to CRAB may be overestimated by other researchers using less well-matched controls. It is evident that CRAB is a public health problem, however, the attributable morbidity and mortality of these infections requires careful study to accurately quantify. Further efforts should be made in discerning clinical infection from colonization to gain a better understanding of where to prioritize resources for prevention efforts.

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# TABLES

**Table 1. Demographics and clinical characteristics of CRAB cases with Complete Data obtained from 2015-2017 EIP surveillance data**

| | Patients with Positive CRAB Culture Matched to GDDS (N=54) | | Patients with Positive CRAB Culture Unmatched to GDDS (N=23) | |
|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** |
| **Patient Demographics** | | | | |
| *Sex* | | | | |
| Female | 15 | 27.8 | 9 | 39.1 |
| Male | 39 | 72.2 | 14 | 60.9 |
| *Age Categories (y)* | | | | |
| 0-18 | 0 | 0.0 | 0 | 0.0 |
| 19-49 | 17 | 31.5 | 11 | 47.8 |
| 50-64 | 12 | 22.2 | 4 | 17.4 |
| 65-79 | 20 | 37.0 | 2 | 37.0 |
| 80+ | 5 | 9.3 | 6 | 26.1 |
| *Race* | | | | |
| White | 13 | 24.1 | 5 | 21.7 |
| Black/African American | 38 | 70.4 | 16 | 69.6 |
| American Indian | 0 | 0.0 | 0 | 0.0 |
| Asian | 2 | 3.7 | 1 | 4.3 |
| Hawaiian/Pacific Islander | 0 | 0.0 | 0 | 0.0 |
| Unknown | 1 | 1.9 | 1 | 4.3 |
| *Ethnicity* | | | | |
| Hispanic or Latino | 0 | 0.0 | 0 | 0.0 |
| Not Hispanic or Latino | 53 | 98.1 | 21 | 91.3 |
| Unknown | 1 | 1.9 | 2 | 8.7 |
| **Infection Characteristics** | | | | |
| *Culture Source* | | | | |
| Non-sterile site | | | | |
| Urine | 37 | 68.5 | 15 | 65.2 |
| Any sterile site | | | | |
| Blood | 16 | 29.6 | 7 | 30.4 |
| Bone | 1 | 1.9 | 1 | 4.3 |
| **Specimen Collection Characteristics** | | | | |
| *Lab of Specimen Collection* | | | | |
| Southern Regional Hospital | 0 | 0.0 | 1 | 4.3 |
| Wellstar Cobb | 7 | 13.0 | 0 | 0.0 |

| | | | | |
|---|---|---|---|---|
| Emory Decatur Hospital | 4 | 7.4 | 0 | 0.0 |
| Emory University Hospital | 12 | 22.2 | 2 | 8.7 |
| Eastside Medical Center | 6 | 22.2 | 0 | 0.0 |
| Atlanta Medical Center | 5 | 11.1 | 8 | 34.8 |
| Grady Memorial Hospital | 1 | 9.3 | 1 | 4.3 |
| Wellstar Kennestone | 1 | 1.9 | 1 | 4.3 |
| Northside Atlanta Hospital | 0 | 0.0 | 1 | 4.3 |
| Wellstar North Fulton | 2 | 1.9 | 0 | 0.0 |
| Piedmont Atlanta Hospital | 10 | 18.5 | 4 | 17.4 |
| St. Joseph's Hospital | 3 | 5.6 | 0 | 0.0 |
| Piedmont Rockdale Hospital | 0 | 0 | 4 | 17.4 |
| Clinical Laboratory Services | 3 | 5.6 | 1 | 4.3 |
| *Location of Culture Collection* | | | | |
| Emergency Room | 19 | 35.2 | 8 | 34.8 |
| Intensive Care Unit | 13 | 24.1 | 1 | 4.3 |
| Long Term Acute Care Hospital | 2 | 3.7 | 8 | 34.8 |
| Long Term Care Facility | 3 | 5.6 | 1 | 4.3 |
| Observation Unit/Clinical Decision Unit | 1 | 1.9 | 0 | 0.0 |
| Outpatient Clinic/Doctor's Office | 1 | 1.9 | 1 | 4.3 |
| Surgery/Operating Room | 2 | 3.7 | 1 | 4.3 |
| Other Inpatient | 13 | 24.1 | 2 | 8.7 |
| Other Outpatient | 0 | 0.0 | 1 | 4.3 |
| **Epidemiological Classification** | | | | |
| Healthcare-Associated Community-Onset [a] | 19 | 35.2 | 16 | 70.0 |
| Long-Term Care Facility Onset [b] | 23 | 42.6 | 3 | 13.0 |
| Hospital Onset [c] | 12 | 22.2 | 4 | 17.4 |

[a] specimen collected $\leq$ 3 calendar days after acute care hospital admission or in an outpatient setting **and at least one of the following risk factors:** Acute care hospitalization within the past year, Surgery within the past year, Current chronic dialysis, Residence in Long-Term Care Facility (LTCF) within the past year (excluding current LTCF residence; see long term care facility onset), Admission to a Long Term Acute Care Hospital (LTACH) within the past year, Central venous catheter, urinary catheter, or other indwelling device in place in 2 calendar days prior to specimen collection, International travel within the year prior to specimen collection

[b] specimen collected in a LTCF, or patient was residing in a LTCF $\leq$ 3 calendar days prior to collection

[c] specimen collected >3 calendar days after acute care hospital admission

**Table 2. Demographics and clinical characteristics of CRAB cases Matched to Georgia Hospital Discharge Dataset and Controls**

| | Patients with Positive CRAB Culture Matched to GDDS (N=54) | | Controls (N=118,000) | |
|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** |
| **Patient Demographics** | | | | |
| *Sex* | | | | |
| Female | 15 | 27.8 | 65996 | 55.9 |
| Male | 39 | 72.2 | 45804 | 38.8 |
| *Age Categories (y)* | | | | |
| 0-18 | 0 | 0.0 | 1299 | 1.1 |
| 19-49 | 17 | 31.5 | 42768 | 36.2 |
| 50-64 | 12 | 22.2 | 29657 | 25.1 |
| 65-79 | 20 | 37.0 | 26738 | 22.7 |
| 80+ | 5 | 9.3 | 11338 | 9.6 |
| *Race* | | | | |
| White | 13 | 24.1 | 51030 | 43.2 |
| Black/African American | 38 | 70.4 | 53929 | 45.7 |
| American Indian/Alaskan | 0 | 0.0 | 366 | 0.3 |
| Asian | 2 | 3.7 | 1779 | 1.5 |
| Hawaiian/Pacific Islander or Other | 0 | 0.0 | 79 | 0.0 |
| Multiracial | 0 | 0.0 | 4617 | 3.9 |
| Unknown | 1 | 1.9 | 0 | 0.0 |
| Ethnicity | | | | |
| Hispanic or Latino | 0 | 0.0 | | |
| Not Hispanic or Latino | 53 | 98.1 | | |
| Unknown | 1 | 1.9 | | |
| **Infection Characteristics** | | | | |
| *Culture Source* | | | | |
| Non-sterile site | | | | |
| Urine | 37 | 68.5 | | |
| Any sterile site | | | | |
| Blood | 16 | 29.6 | | |
| Bone | 1 | 1.9 | | |
| **Specimen Collection Characteristics** | | | | |
| *Lab of Specimen Collection* | | | | |
| Southern Regional Hospital | 0 | 0.0 | | |
| Wellstar Cobb | 7 | 13.0 | | |

| | | | | |
|---|---|---|---|---|
| Emory Decatur Hospital | 4 | 7.4 | | |
| Emory University Hospital | 12 | 22.2 | | |
| Eastside Medical Center | 6 | 22.2 | | |
| Atlanta Medical Center | 5 | 11.1 | | |
| Grady Memorial Hospital | 1 | 9.3 | | |
| Wellstar Kennestone | 1 | 1.9 | | |
| Northside Atlanta Hospital | 0 | 0.0 | | |
| Wellstar North Fulton | 2 | 1.9 | | |
| Piedmont Atlanta Hospital | 10 | 18.5 | | |
| St. Joseph's Hospital | 3 | 5.6 | | |
| Piedmont Rockdale Hospital | 0 | 0 | | |
| Clinical Laboratory Services | 3 | 5.6 | | |
| **Location of Culture Collection** | | | | |
| Emergency Room | 19 | 35.2 | | |
| Intensive Care Unit | 13 | 24.1 | | |
| Long Term Acute Care Hospital | 2 | 3.7 | | |
| Long Term Care Facility | 3 | 5.6 | | |
| Observation Unit/Clinical Decision Unit | 1 | 1.9 | | |
| Outpatient Clinic/Doctor's Office | 1 | 1.9 | | |
| Surgery/Operating Room | 2 | 3.7 | | |
| Other Inpatient | 13 | 24.1 | | |
| Other Outpatient | 0 | 0.0 | | |
| **Epidemiological Classification** | | | | |
| Healthcare-Associated Community-Onset [a] | 19 | 35.2 | | |
| Long-Term Care Facility Onset [b] | 23 | 42.6 | | |
| Hospital Onset [c] | 12 | 22.2 | | |
| **Underlying Clinical Conditions** | | | | |
| None | 19 | 35.2 | 76559 | 65.0 |
| Myocardial Infarction | 3 | 5.6 | 3013 | 2.7 |
| Congestive Heart Failure | 9 | 16.7 | 7803 | 7.0 |
| Peripheral Vascular Disease | 1 | 1.9 | 1763 | 1.6 |
| Cerebrovascular Disease | 4 | 7.4 | 4797 | 4.3 |
| Dementia | 2 | 3.7 | 404 | 0.4 |
| Chronic Pulmonary Disease | 5 | 9.3 | 5546 | 5.0 |
| Rheumatoid Disease | 0 | 0.0 | 725 | 0.7 |
| Peptic Ulcer Disease | 0 | 0.0 | 566 | 0.5 |
| Mild Liver Disease | 0 | 0.0 | 1535 | 1.4 |
| Diabetes Without Complication | 7 | 13.0 | 4227 | 3.8 |
| Diabetes With Complications | 1 | 1.9 | 1364 | 1.2 |
| Hemiplegia or Paraplegia | 8 | 14.8 | 460 | 0.4 |
| Renal Disease | 9 | 16 | 3759 | 3.4 |

| | | | | |
|---|---|---|---|---|
| Cancer (any malignancy) | 1 | 1.9 | 5310 | 3.8 |
| Moderate or Severe Liver Disease | 0 | 0.0 | 727 | 0.7 |
| Metastatic Solid Tumor | 0 | 0.0 | 1519 | 1.4 |
| HIV/AIDS | 3 | 5.6 | 850 | 0.8 |

[a] specimen collected ≤ 3 calendar days after acute care hospital admission or in an outpatient setting **and at least one of the following risk factors:** Acute care hospitalization within the past year, Surgery within the past year, Current chronic dialysis, Residence in Long-Term Care Facility (LTCF) within the past year (excluding current LTCF residence; see long term care facility onset), Admission to a Long Term Acute Care Hospital (LTACH) within the past year, Central venous catheter, urinary catheter, or other indwelling device in place in 2 calendar days prior to specimen collection, International travel within the year prior to specimen collection

[b] specimen collected in a LTCF, or patient was residing in a LTCF ≤ 3 calendar days prior to collection

[c] specimen collected >3 calendar days after acute care hospital admission

**Table 3. Demographic and clinical characteristics of Propensity Score Matched CRAB Cases and Controls**

| | Case Patients with Positive CRAB Culture Matched via Propensity Score (N=51) | | Control Patients Matched to Positive CRAB Culture via Propensity Score (N=51) | |
|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** |
| **Patient Demographics** | | | | |
| *Sex* | | | | |
| Female | 15 | 29.4 | 27 | 53.0 |
| Male | 36 | 70.6 | 24 | 47.1 |
| *Age Categories (y)* | | | | |
| 0-18 | 0 | 0.0 | 0 | 0.0 |
| 19-49 | 16 | 31.3 | 16 | 31.3 |
| 50-64 | 11 | 21.6 | 11 | 21.6 |
| 65-79 | 19 | 37.3 | 19 | 37.3 |
| 80+ | 5 | 9.8 | 5 | 9.8 |
| *Race* | | | | |
| White | 13 | 25.5 | 23 | 45.1 |
| Black/African American | 35 | 68.9 | 27 | 53.0 |
| American Indian/Alaskan | 0 | 0.0 | 1 | 2.0 |
| Asian | 2 | 3.9 | 0 | 0.0 |
| Unknown | 1 | 2.0 | 0 | 0.0 |
| **Charlson Comorbidity Score** | | | | |
| 0 | 18 | 35.3 | 39 | 76.5 |
| 1 | 19 | 37.3 | 11 | 21.6 |
| 2 | 11 | 21.6 | 1 | 2.0 |
| 3 | 2 | 3.9 | 0 | 0.0 |
| 4 | 1 | 2.0 | 0 | 0.0 |

**Table 4. Attributable Outcomes for Propensity-Score Matched Cases and Controls**

| | Patients with Positive CRAB Culture Matched via Propensity Score (N=51) | | Controls Matched via Propensity Score (N=51) | | P-Value |
|---|---|---|---|---|---|
| | No. / Median | SD / % | No. / Median | SD / % | |
| **Attributable Outcomes** | | | | | |
| Length of Stay (Days) [a] | 11.0 | 2.7 | 7.0 | 1.9 | 0.10 |
| Time to Readmission (Days) [b] | 28.0 | 9.07 | 8.0 | 5.5 | 0.19 |
| Readmission [a] | | | | | |
| ≤ 30 Days | 18 | 35.3 | 18 | 35.3 | |
| ≤ 90 Days | 25 | 49.0 | 22 | 43.1 | |
| Death During Incident Hospitalization [a] | 5 | 9.8 | 2 | 3.9 | 0.25 |

[a] Excludes Individuals Who Died

[b] Includes Individuals Who Died