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Diabetes, Obesity, Geographic Location of the Patient and Clostridium difficile Infection in the United States

Mary (Maribeth) Greenway
Walden University

Walden University

College of Health Professions

This is to certify that the doctoral dissertation by

Maribeth Greenway

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Review Committee
Dr. Srikanta Banerjee, Committee Chairperson, Public Health Faculty
Dr. Zin Htway, Committee Member, Public Health Faculty
Dr. Susan Nyanzi, University Reviewer, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
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Abstract

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by

Maribeth Greenway

MEd, University of Virginia, 2001

BA, University of Virginia, 1980

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Clostridium difficile infection (CDI) is a major nosocomial threat to be reckoned with in the current health care setting in the United States. Advancing age, underlying chronic disease associated with inflammation (including Diabetes Mellitus Type I ([DMI]), Diabetes Type II ([DMII]), and obesity), trauma, immunodeficiency and other factors that diminish the overall health of an individual, and increase an individual's susceptibility to CDI. The ecological framework was used to determine the relationship between geographic, chronic diseases and the occurrence of infectious diseases. To continue enhancing knowledge related to CDI susceptibility this quantitative study used the 2010 National Hospital Discharge Survey as the source of data to examine the relationship between specific health conditions, geographic location of the patient, and subsequent development of CDI in the acute care setting. Both established relationships and potential novel associations were explored utilizing International Classification of Disease-9 codes and evaluated for association with CDI. Binary logistic regression demonstrated that the independent variables of DM II (OR=1.17, 95% CI= 1.01-1.35, $p < 0.05$), advancing age, obesity, and a history of inflammatory bowel disease had a statistically significant influence over contracting CDI. Unanticipated results revealed an association between CDI and DMI, and a geographic association between patients admitted in the southern region of the United States and an increased susceptibility to CDI. The recognition of factors that make people more susceptible to *Clostridium difficile* infection will encourage a more personalized initial evaluation and a specific individualized course of treatment with improved outcomes regarding patient health and quality of life, resulting in significant positive social change in health care settings in the United States.

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Dedication

This dissertation is dedicated to Frank Greenway, my husband, who always encouraged me to pursue my dreams, including my doctorate degree. His endless support and infinite patience will always be appreciated.

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Chapter 1: Introduction to the Study

Introduction to the Study

Clostridium difficile infection is a significant nosocomial pathogen that frequently infects patients who have previously received antibiotic therapy. It is the most significant nosocomial pathogen to be reckoned with in the health care setting. *Clostridium difficile* infection is detrimental to the health care system in terms of cost, detrimental to human life in terms of morbidity and mortality, and detrimental to the overall health and quality of life of the patients infected with the organism. Awareness of factors that make an individual particularly susceptible to development of *Clostridium difficile* infection will allow for adoption of proactive preventive strategies that could help alleviate the morbidity and mortality currently associated with *Clostridium difficile* infection. Knowledge of CDI susceptibility factors coupled with patient-specific proactive strategies would reduce costs associated with treatment of the infection, as well as improving quality of life and overall population health of those affected, representing positive social change.

Inflammation may be a contributing factor as to whether a person is more susceptible to acquisition of *Clostridium difficile* infection. Chronic diseases such as Diabetes Mellitus Type II and obesity are associated with increased levels of inflammatory cytokines, which may contribute to susceptibility to infection. Initial stress response in these disorders initially have a positive physiologic value but over time (because the stress is not alleviated) the chronic inflammation can translate into a pathological outcome (Reilly, Saltiel, 2017). Rates of nosocomial *Clostridium difficile* infections appear to be higher in certain geographic regions of

the United States. This study examined the relationships between susceptibility to *Clostridium difficile* infection with respect to the comorbidities of Diabetes Mellitus Types I and II, and obesity. The influence of geographic location of the affected patient was also investigated.

Understanding patient populations and their potential susceptibility to acquisition of nosocomial *Clostridium difficile* infection might influence caregivers to more carefully devise a treatment plan for these patients. This study revealed factors that make patients more susceptible to infection, including comorbidities of the patient that make CDI infection more likely. Reduced initial infection can positively affect the patient population in many ways. These ways included reduced length of stay, reduced expense to both the patient and the health care system (Kurti, et al, 2015), improved quality of life for the patient, and reduced secondary *Clostridium difficile* infection in the visitor/family population. It has been verified that patients released from health care facilities with CDI contribute to community-acquired *Clostridium difficile* infection not only in family members but also in domestic pets (Loo, Brassard, Miller, 2016). Reduced initial patient infections would also translate into diminished *Clostridium difficile* infections transmitted to health care workers and other individuals in contact with the organism in the healthcare setting, especially the more susceptible individuals taking antibiotics (Aguirre-Garcia, et al, 2020). Patients with initial *Clostridium difficile* infection are also more likely to have relapses of infections that were not completely resolved. Recurrence of *Clostridium difficile* infection occurs in approximately 20% of patients with initial infection (Eyre et al, 2012) and is difficult to treat. The use of antibiotic therapy has been verified to be a significant predisposing factor in development of *Clostridium difficile* infection in the health care setting. It has been noted that fluoroquinolones, which include the broad-spectrum antibiotics ciprofloxacin and

levofloxacin, have the capability to eliminate normal gut flora. This makes the individual more susceptible to *Clostridium difficile* infection. For this reason, when treating a patient that is potentially more susceptible to *Clostridium difficile* infection, a physician should initially evaluate the situation with the patient carefully to ascertain whether or not antibiotic therapy is actually necessary. In the event that antibiotic therapy is necessary, the physician should evaluate the infection carefully, possibly taking the time to order a culture and sensitivity in order to determine the exact organism causing the infection. In this way, the physician could select an agent that targets the patient's specific infectious organism, rather than haphazardly utilizing a broad-spectrum antibiotic that wipes out the gut normal flora, subsequently leaving the patient more susceptible to *Clostridium difficile* infection. Recognizing factors that make people more susceptible to infection and relapse/reinfection will allow for individualized targeted therapy which will translate to improved outcomes and positive social change both for patients and health care systems alike.

Background

Clostridium Microbiology and Clinical Description

Clostridium spp. represents a group of gram-positive spore-forming rods that typically require an anaerobic atmosphere to grow. *Clostridium* can be found environmentally, especially in soil. *Clostridium* also makes up a small portion of the normal flora of the intestinal tract of mammals. Endospore formation is a hallmark of the *Clostridium* species. The spores are very hardy and resistant to traditional disinfection strategies. For this reason, *Clostridium* is a challenging pathogen to eradicate in the healthcare and long-term care setting. *Clostridium*

difficile-associated disease has been viewed primarily as a nosocomial infection for the past 2 decades in the hospital and long-term care settings. The organism was identified in 1978 as theprimary causative agent of diarrhea precipitated by antibiotic therapy and is associated with development of subsequent pseudomembranous colitis (DePestel & Aronoff, 2013). Antibiotics most frequently associated with *Clostridium difficile* infection include Fluoroquinolones (Cipro, Levaquin), Penicillins (amoxicillin, ampicillin) Clindamycin (Cleocin) and Cephalosporins (Suprax; Mayo Clinic, 2017). Pseudomembranous colitis, which can also be known as *Clostridium difficile* colitis (Mayo Clinic, 2017), presents with the symptoms of fever, diarrhea, cramps, nausea, and stools that contain blood and/or pus (Mayo Clinic, 2017). Other clinical presentations of *Clostridium difficile* infection include septicemia, perforated colon, shock, toxic megacolon, and even death (De Pestel & Aronoff, 2013). The organism produces two toxins, toxin A (enterotoxin) and toxin B (cytotoxin). These toxins affect the way fluids are absorbed in different parts of the intestines. (Lylerly, et al, 1982). Clinical disease associated with these organisms can often be associated with the production of exotoxins by these bacilli, which are the causative entities of the clinical presentation of the disease. In the clinical laboratory *Clostridium difficile* infection is most frequently diagnosed through the detection of exotoxins A and B, which are produced by the organism.

Clostridium difficile **Epidemiology**

A person is most susceptible to *Clostridium difficile* infection if they are undergoing treatment with antibiotics for another infection. Although *Clostridium difficile* is frequently normal flora of the human gut, broad-spectrum antibiotics can wipe out a large percentage of the normal flora, leaving the hardy *Clostridium difficile* bacilli to multiply rapidly, replacing the

previous gut microbiota. The elderly, those individuals greater than or equal to 65 years of age, are much more susceptible to *Clostridium difficile* infection than younger adults and children. Those individuals greater than or equal to 85 years of age are at the highest risk (De Pestel & Aronoff, 2013). The use of proton pump inhibitors by the patient has been implicated in increased susceptibility to development of *Clostridium difficile* infection subsequent to antibiotic therapy (McDonald, Milligan, Frenette, Lee, 2015). Individuals who are immunosuppressed are at greater risk to develop *Clostridium difficile* infection than the normal population. These individuals include cancer patients receiving radiation or chemotherapy, patients suffering from HIV infection, transplant patients, malnourished patients, patients with congenital immunodeficiencies, alcoholics, and patients with underlying chronic comorbidities (Costa, et al, 2014, De Pestel & Aronoff, 2013). Individuals who smoke are more likely to develop *Clostridium difficile* infections. People who have had previous gastrointestinal surgeries are also more susceptible. Individuals who must receive enteral feedings also have increased odds of developing *Clostridium infection* (De Pestel & Aronoff, 2013). Specific comorbidities have been associated with increased susceptibility to *Clostridium difficile* infection. Patients with ulcerative colitis and Crohn's disease are more likely to develop infection than the general population (Ananthakrishnan, et al, 2008). Obesity, as evaluated through the use of height and weight values, seems to be a risk factor for increased susceptibility to development of *Clostridium difficile* infection (Bishara, et al, 2013, Leung, et al, 2013). Diabetes has also been cited as a contributing factor in increased susceptibility to *Clostridium difficile* infection (Shakov, et al, 2011).

Clostridium difficile as a Significant Health and Economic Burden

In 2015, the Centers for Disease Control and Prevention (CDC) reported that approximately 500,000 individuals in the United States suffered from *Clostridium difficile* infection. Statistics cited by the CDC state that "1 out of every 11 patients aged 65 or older with a healthcare-associated *C. difficile* infection died within 30 days of diagnosis", which represents approximately 80% of deaths associated with *Clostridium difficile* infection (CDC, 2017b). Overall, 29,000 individuals of the 500,000 previously mentioned died within 30 days of being diagnosed with this enteric infection. In the United States 15,000 people per year who acquire *Clostridium difficile* infection in the health care setting eventually die of the disease. This situation represents a significant health burden, making antibiotic stewardship a responsibility of paramount importance to prevent initial *Clostridium difficile* infection. After infection has been documented, the disease is easily transmissible in the clinical and long-term care settings due to the resistance of the endospores to heat, desiccation, and chemical exposure. These spores are easily passed from person-to-person and can endure on environmental surfaces for extended periods of time without expiring, making *Clostridium difficile* an extremely communicable disease. In addition to the overt health concerns associated with *Clostridium difficile* infection, it is worthy to mention the toll the disease takes upon its victims. Patients may experience 10-15 watery stools per day, which come on with little warning (Mayo Clinic, 2017c). Additionally, patients can also experience abdominal tenderness, and general malaise. The affected individual's quality of life may be compromised immensely. Nosocomial *Clostridium difficile* infection also extends the hospital stay of the patient, leading to greatly increased expense to the patient and the health care system. In 2009, a patient who developed *Clostridium difficile*

infection during the course of their hospital stay increased their cost of stay by $24,400.00 (De Pestel & Aronoff, 2013), which is reflected in the increased cost due to the extended inpatient status of the individual. Nanwa, et al., on page1 of their 2016 article, report that the "attributable mean CDI costs ranged from $8,911 to $30,049 for hospitalized patients" when records from 1988-2014 were analyzed. Zhang et al. on page 7 of their 2016 article, estimated the "total annual CDI-attributable cost in the United States is estimated US$6.3 (Range: $1.9–$7.0) billion".

Because *Clostridium difficile* infection is problematic on so many levels (economic, healthcare burden, patient disease pathology, quality of life, significant cause of nosocomial infection) and remains a healthcare challenge that has defied resolution, it is worthy of further research. With this study I established relationships between susceptibility of infection and predisposing factors that enhance chance of infection. Geographic relationships between patient location and enhanced chance of developing infection were also explored. By studying covariates that may contribute to an individual's susceptibility to disease, interventions may be designed to lessen the development of *C. difficile* infection.

Problem Statement

Clostridium difficile infection is a recognized healthcare challenge with regard to nosocomial pathogens, especially in patients receiving antibiotic therapy for prior infection (Loo, et al., 2011). This pathogen is the primary organism associated with acquired diarrhea following treatment with antibiotics, and the disease can progress to pseudomembranous colitis, a serious health threat. *Clostridium difficile* represents a significant source of healthcare-acquired infection, and for this reason, *Clostridium difficile* infection is especially problematic in the

hospital and long-term care setting. Although community-acquired cases are recognized, the majority of *Clostridium difficile* infections are documented in healthcare settings, where the infection is associated with economic burden (Hunter, et al., 2016; Lessa, et al., 2015; McGlone, et al., 2012) as well as significant morbidity and mortality (Dubberke & Olsen, 2012). The infection also seriously compromises quality of life for some individuals (Garey, et al., 2016). The infection is particularly dangerous for the very young, the elderly, those with comorbidities, and individuals who are immunosuppressed (Loo, 2011).

Recent research has revealed that people with underlying comorbidities may be more likely to acquire *Clostridium difficile* infections than the normal population. These underlying comorbidities include Diabetes Mellitus Type I, Diabetes Mellitus Type II, and obesity. Not only are these individuals more likely to get the infection, but they also have higher morbidity and mortality associated with the infection (Bishara, et al., 2013), (Chakra, et al., 2014). They are also more likely to have recurrences of *Clostridium difficile* infection than the normal population. If it could be ascertained these three disease scenarios predispose individuals to both acquisition of *Clostridium difficile* infection and subsequent reinfection or refractory infection, perhaps prophylactic options could be used in these specific patient populations in the battle against nosocomial *Clostridium difficile* infection. There have been limited studies executed establishing a statistical relationship between these diseases and increased susceptibility and increased refractoriness to traditional treatment options with respect to *Clostridium difficile infection*. For this reason, the number of healthcare acquired *Clostridium difficile* infections continue to rise, resulting in great expense to the healthcare facilities. *Clostridium difficile*

infection frequently prolongs the length of patient hospital stays, increasing costs. It is estimated even a simple case of nosocomial *Clostridium difficile* infection increases patient cost of stay an additional 9000 U.S. dollars (McGlone, et al., 2012). *Clostridium difficile* infection also contributes to significant morbidity and mortality regarding affected populations.

Literature review revealed there is an information gap with respect to multifaceted prevention strategies to reduce initial *Clostridium difficile* infections. Discovering and verifying predisposing factors will certainly result in improved outcomes. It is difficult to ascertain why individuals in certain geographic areas seem more likely to develop infections, but this phenomenon has been recently noted globally and now *Clostridium difficile* infection has a significant presence in Asia, which previously had not been an endemic area. Studying the various regions of the United States with respect to *Clostridium difficile* infection revealed interesting results in that patients in the South seemed more susceptible to CDI. It seems normal gut flora differs from individual to individual, and another gap in the literature questions if the make-up of the gut flora predisposes an individual to infection. It appears the gut flora of obese individuals differs from that of lean individuals, so obesity may lend itself to more likelihood of *Clostridium difficile* infection. Researchers also question why some individuals seem to have resistance to *Clostridium difficile* colonization, although they may have factors that would seemingly make them more susceptible. The research also does not thoroughly address factors that lead to especially poor outcomes in certain patients.

Purpose of Study

The purpose of this study was to establish whether or not Diabetes Mellitus Type I, Diabetes Mellitus Type II, and obesity, or a combination of these disorders, predisposes the

affected individual to increased likelihood of development of a nosocomial *Clostridium difficile* infection in the acute healthcare hospital settings. The study also explores whether or not there is a geographic component related to susceptibility to *Clostridium difficile* infection specific to the United States. Assessment of the problem was accomplished through the review of secondary data found in the 2010 National Hospital Discharge Survey, with concentration on adult patients with toxin-documented *Clostridium difficile* infection in the acute hospital setting. Statistical analysis of this data will prove or disprove whether certain physical pathologies and/or geographic location of the patient can be associated with enhanced susceptibility to *Clostridium difficile* infection. This would help address gaps in the literature pertaining to a correlation between the aforementioned comorbidities and *Clostridium difficile* infection. This was a quantitative study utilizing linear regression. For linear regression/correlation to be utilized, the effects of three or more independent variables on a dependent variable must be analyzed. In this study, the dependent variable was whether or not the patient develops *Clostridium difficile* infection. Independent variables were the patient's age, whether patients have Diabetes Mellitus Type I, whether the patients have Diabetes Mellitus Type II, the geographic region of the country where the patient was hospitalized, whether they had previous abdominal surgeries, and whether they had suffered from previous inflammatory bowel disease.

Research Questions and Hypotheses

Research Question 1: Is there a relationship between obesity and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling

for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$1: There is not a statistically significant association between obesity and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a1: There is a statistically significant association between obesity and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 2: Is there a relationship between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$2: There is not a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a2: There is a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 3: Is there a relationship between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$3: There is not a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a3: There is a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 4: Is region significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$4: Region is not significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a4: Region is significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Theoretic Framework of the Study

A permutation of the ecological system was selected as the theoretical framework of this study. An ecological approach in public health "focuses on both population-level and individual-level determinants of health and interventions" (ACHA, 2018). On a population level,

Clostridium difficile is the most common nosocomial infection seen in the healthcare and long-term care setting. It is almost always associated with antibiotic treatment. On an individual level, there are factors that make one more susceptible to *Clostridium* difficile infection, such as Diabetes Mellitus Type I, Diabetes Mellitus Type II, and obesity. Microbial ecology investigates the bacteria and its relationship with the environment: how the microbe behaves is dependent upon the microbe itself, other microbes present in the same environment, their relationship with each other, and modifications observed when the environment changes. The traditional ecological system model examines an individual's behavior with respect to their environment by placing the individual as the center of several circles of influence that increase in size and complexity. This model is utilized widely in public health. Traditional use of this model in public health examines behaviors on an individual level and how these behaviors affect health. On a more global level, the model examines larger circles of influence that influence health, such as public policy. The first level of influence is interpersonal relationships; with respect to *Clostridium difficile*, this would be the interaction of *Clostridium* with other gut flora bacteria. The next level in the model would be community; this level is factors in the gastrointestinal system that influence the gut normal flora. The final influence would be large systems: the body in its entirety and its influence upon the gut microbiota. This study is interested in investigation of pathology existing in the body as a whole (large systems) and the influence it exerts upon susceptibility of an individual to *Clostridium difficile* infection. The roles of Diabetes Mellitus Type I, Diabetes Mellitus Type II, obesity, previous abdominal surgeries and inflammatory bowel disease was studied. In statistics, a covariate "is a variable that is possibly predictive of

the outcome under study" (Educalingo, 2018). These covariates potentially influence the probability of developing *Clostridium difficile* infection and the severity of the disease if contracted. Examination of the various circles of influence could assist in identifying the best intervention point for maximum efficacy (Sallis, et al., 2015). *Clostridium difficile* is an organism that frequently is present as normal flora in many individuals. In antibiotic therapy, other normal flora organisms are reduced in number as a side effect of treating the primary infection. This allows for enhanced growth of *Clostridium difficile*, as there are limited competing organisms to keep their numbers in check (Walter, et al., 2018). If *Clostridium difficile* is successful in proliferation, it is likely that the patient will develop infection. The covariates previously mentioned contribute to enhanced susceptibility and severity in nosocomial *Clostridium difficile* infection.

Nature of the Study

The Use of the National Hospital Discharge Summary as a Source of Secondary Data

Assessment of the problem was accomplished through the use of the National Hospital Discharge Summary from the year 2010. Reviews were performed on patients with toxin-documented *Clostridium difficile* infection in the acute care hospital setting in four major geographic regions in the United States, which include all 50 states and the District of Columbia. This review was performed in an effort to ascertain health factors in specific patient populations that contribute to susceptibility to initial Clostridium difficile infection and/or refractoriness to treatment. International Classification of Disease codes were utilized in order to ascertain the existence of comorbidities that may influence susceptibility to infection. Only patient information for adults 18 years of age or older was utilized in this study.

Additionally, in the acute care setting, the Standardized Infection Ratio can also be used to interpret the change of a nosocomial infection rate over time. The pre-existing conditions examined included Diabetes Mellitus Types I and II, and obesity. The International Classification of Disease codes were utilized to establish obesity. The nature of this study was quantitative. Variables that were examined were age, sex, whether the patient was overweight or obese, and whether the patient was an individual with Diabetes Mellitus Type I or II. Descriptive statistics were utilized to produce numeric descriptions of these variables. Age as a variable was measured as scale-interval level. Sex (gender) was measured through a nominal – dichotomous level, with "1" representing male, and "2" representing female. Whether the patient was overweight or obese was measured as nominal variable based upon the International Classification of Disease (ICD-9) code. Obesity was identified through the use of ICD-9 codes into the categories of "0" (not overweight) or "1" (overweight, obese, or morbidly obese); (assigned to the category HIBMI). Diabetes Mellitus Types I and II were measured individually on a nominal-dichotomous level, with "0" representing no diabetes, and "1" representing that the patient has Diabetes Mellitus Type I or Diabetes Mellitus Type II. Frequencies were ascertained and a statistics table was generated for the continuous variable of age. Ranges for the continuous variables were established through the use of minimum and maximum values in the statistics table. The categorical variables of sex, Diabetes Mellitus Type I, Diabetes Mellitus Type II, were then analyzed and frequency tables generated. Graphical descriptions of these variables were subsequently produced.

Previous bowel disease and abdominal surgeries were also investigated, as these factors increase likelihood of development of *Clostridium infection* (Leung et al., 2013). Multiple

regressions were utilized to ascertain whether or not a statistical relationship existed between each of the patient comorbidities and development of *Clostridium difficile* infection. Nominal variables were utilized to make this comparison. Bowel disease and abdominal surgery were represented on a nominal-dichotomous level, with "0" representing absence of the condition and "1" representing presence of the condition. These values were tested against presence or absence of *Clostridium difficile* infection, which was also represented on a nominal-dichotomous level, with "0" representing absence of the disease and "1" representing presence of the disease. I suspected that age was one of the confounding variables, because increasing age is a predisposing factor to development of *Clostridium difficile* infection. In addition, other potential confounding variables included pre-existing bowel disease and previous abdominal surgery.

Definition of Terms

This section serves to provide definitions of terms and concepts that were addressed in this study.

Adipose: of or relating to animal fat (Merriam-Webster Medical Dictionary, 2017).

Antibiotic: substance derived from a microorganism and able in dilute solution to inhibit or kill another microorganism (Merriam-Webster Medical Dictionary, 2017).

Body Mass Index: a measure of body fat that is the ratio of the weight of the body in kilograms to the square of its height in meters" (Merriam-Webster Medical Dictionary, 2017).

Colitis: inflammation of the colon (Merriam-Webster Medical Dictionary, 2017).

Comorbid: existing simultaneously with and usually independently of another medical condition (Merriam-Webster Medical Dictionary, 2017).

Diabetes: any of various abnormal conditions characterized by the secretion and excretion of excessive amounts of urine (Merriam-Webster Medical Dictionary, 2017).

Endospores: an asexual spore developed within the cell especially in bacteria (Merriam-Webster Medical Dictionary, 2017).

Epidemiology: a branch of medical science that deals with the incidence, distribution, and control of disease in a population (Merriam-Webster Medical Dictionary, 2017).

Exotoxin: a soluble poisonous substance produced during growth of a microorganism and released into the surrounding medium (Merriam-Webster Medical Dictionary, 2017).

Homeostasis: the maintenance of relatively stable internal physiological conditions (as body temperature or the pH of blood) in higher animals under fluctuating environmental conditions (Merriam-Webster Medical Dictionary, 2017).

Inflammation: a local response to cellular injury that is marked by capillary dilatation, leukocytic infiltration, redness, heat, and pain and that serves as a mechanism initiating the elimination of noxious agents and of damaged tissue (Merriam-Webster Medical Dictionary, 2017).

Immunocompetency: the capacity for a normal immune response (Merriam-Webster Medical Dictionary, 2017).

Immunodeficiency: inability to produce a normal complement of antibodies or immunologically sensitized T cells especially in response to specific antigens (Merriam-Webster Medical Dictionary, 2017).

Insulin: a protein hormone that is synthesized in the pancreas from proinsulin and

secreted by the beta cells of the islets of Langerhans that is essential for the metabolism of carbohydrates, lipids, and proteins, and that regulates blood sugar levels by facilitating the uptake of glucose into tissues (Merriam-Webster Medical Dictionary, 2017).

Insulin resistance: reduced sensitivity to insulin by the body's insulin-dependent processes (as glucose uptake, lipolysis, and inhibition of glucose production by the liver) that results in decreased activity of these processes or an increase in insulin production or both and that is typical of type 2 diabetes but often occurs in the absence of diabetes (Merriam-Webster Medical Dictionary, 2017).

Microbiota: the microscopic organisms of a particular environment (Merriam-Webster Medical Dictionary, 2017).

Microorganism: an organism of microscopic or ultramicroscopic size (Merriam-Webster Medical Dictionary, 2017)

Morbidity: the incidence of disease: the rate of illness (as in a specified population or group; Merriam-Webster Medical Dictionary, 2017).

Mortality: the proportion of deaths to population (Merriam-Webster Medical Dictionary, 2017).

Nosocomial: acquired or occurring in a hospital (Merriam-Webster Medical Dictionary, 2017).

Pathogen: a specific causative agent (such as a bacterium or virus) of disease (Merriam-Webster Medical Dictionary, 2017).

Pathogenicity: the quality or state of being pathogenic; degree of pathogenic capacity (Merriam-Webster Medical Dictionary, 2017).

Pathologic: altered or caused by disease (Merriam-Webster Medical Dictionary, 2017).

Population: a body of persons or individuals having a quality or characteristic in common (Merriam-Webster Medical Dictionary, 2017).

Pseudomembranous: characterized by the presence or formation of a false membrane (Merriam-Webster Medical Dictionary, 2017).

Susceptible: open, subject, or unresistant to some stimulus (Merriam-Webster Medical Dictionary, 2017).

Toxic: containing or being poisonous material, especially when capable of causing death or serious debilitation (Merriam-Webster Medical Dictionary, 2017).

Toxin: a colloidal proteinaceous poisonous substance that is a specific product of the metabolic activities of a living organism and is usually very unstable, notably toxic when introduced into the tissues, and typically capable of inducing antibody formation (Merriam-Webster Medical Dictionary, 2017).

Vulnerable: capable of being hurt; susceptible to injury or disease (Merriam-Webster Medical Dictionary, 2017).

Assumptions

It was assumed in this study that patients were accurately weighed and measured for height in such a way that a correct obesity assessment could be obtained. It was assumed that prescription of antibiotic therapy was correctly documented. It was assumed that laboratory documentation of *Clostridium difficile* infection was based upon confirmation of presence of *Clostridium difficile* toxin. It was also surmised that performance of the laboratory test was executed by a qualified laboratory professional in an appropriately certified laboratory governed

by standards outlined by the Clinical and Laboratory Standards Institute.

Additionally, it is assumed in this study those patients with the diagnosis of "diabetes", whether it be Diabetes Mellitus Type I or Type II, were appropriately diagnosed through the performance of supporting laboratory tests such as serum glucose, hemoglobin A1C, antidiuretic hormone and insulin levels by a qualified laboratorian in an appropriately certified laboratory.

Scope and Delimitations

Clostridium difficile infection has emerged as the most significant nosocomial infection in the United States in the hospital and long-term care settings. The disease is the number one cause of antibiotic-associated diarrhea in all age groups, but the disease is especially deadly in the elderly population over 65 years of age, where it is a significant cause of morbidity and mortality. The disease becomes even more dangerous if the patient suffers from obesity and/or Diabetes Mellitus Type I or Type II. The utilization of the 2010 National Hospital Discharge Summary will provide a substantial amount of data, which will address the aforementioned variables and their influence upon acquisition of *Clostridium difficile* infection after antibiotic use. Although the data is from 2010, it does not appear that a study of this type has been previously executed. This research would help address gaps in the literature pertaining to a correlation between the previously mentioned comorbidities and *Clostridium difficile* infection and also explored whether or not geographic location of the patient is an influencing factor. Because of the potential for skew in age distribution based of facilities sampled, age was tested as a confounding variable.

Limitations

The study used ICD-9 codes as a measure of obesity, which is generally appropriate. In cases where the patient may have retained fluid, however, the weight gain from the fluid could skew the BMI to the high side. Another consideration is that it is possible that not all patients with diarrhea were tested for *Clostridium difficile* infection, meaning some cases could be missed. In addition, the toxin test is the most frequently utilized screening test for *Clostridium difficile* infection. This test does not have high sensitivity, so it is possible that some cases of infection might have been missed (Bishara, et al., 2013). It is also possible that patients had other comorbidities not found upon chart review that contributed to susceptibility to *Clostridium difficile* infection. Retrospective chart reviews can also result in a smaller-than-desired sample size. Because chart review is essential for data collection, there is always the chance of data omission on the part of the individual documenting patient results, which can lead to gaps in data (Leung, et al., 2013). This study also had a slightly disproportionate number of older subjects because they represent approximately 65% of the population of our local acute care hospitals.

Significance

Clostridium difficile is a potentially deadly infection especially in vulnerable populations (Eckmann, et al., 2013). Post-antibiotic Clostridium difficile infection has been recognized for decades, but Clostridium difficile infection has morphed from a nuisance disease to a palpable public health threat (Wilkins & Lyerly, 2003), significantly compromising quality of life, in addition to being a significant expense to the medical community. *Clostridium difficile* is becoming increasingly more common both in the community and in the hospital setting and is a

contributing factor in the increasing length of hospital stays. *Clostridium difficile* infection is also becoming more common in the pediatric population, especially in infants and toddlers (Sammons, et al., 2013). It has been estimated that the aggregate cost of *Clostridium difficile* infection is 1.8 billion dollars annually (McGlone, et al., 2012). The incidence rate (or person-time rate) of an infection can be defined as the "number of new cases of disease during specified time interval" (CDC, 2012d). The CDC currently sponsors a surveillance program that tracks new *Clostridium difficile* cases across 35 counties in the states of "California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee" (CDC, 2017a). The most recent data provided by the CDC in 2017 was generated in 2015. In these specified geographic areas 17,354 cases of Clostridium difficile infection were reported out of a population of 11,682,427 people. There were 7,688 community-acquired cases, for an incidence rate of 65.81 per 1000 persons. There were 9,666 healthcare-acquired cases for an incidence rate of 82.74 per 1000 persons (CDC, 2017a). In 2014, in the state of Virginia 86 out of 106 hospitals reported healthcare-acquired *Clostridium difficile* infections in their facilities. The Standardized Infection Ratio (SIR) is a statistic used for comparison of infection rates from year to year to see if improvement is noted with respect to a number of nosocomial infections. Nosocomial infections tracked include central line-associated bloodstream infections, catheter-associated urinary tract infections, laboratory-identified hospital-onset bloodstream infections, surgical site infections, hysterectomy infections, colon surgery infections, and development of hospital-acquired *Clostridium difficile* infections (CDC, 2016e). In 2014, the state of Virginia had an SIR that was 7% above the national average for nosocomial *Clostridium difficile*

infection, which is quite concerning (CDC, 2016e). The national SIR was documented to be 0.92, while the Virginia SIR for *Clostridium difficile* infection was documented to be 0.99 (CDC, 2016e).

Clostridium difficile is a spore-forming organism (Kiser, et al., 2011), which makes it a formidable enemy, as it is very difficult to kill on surfaces (Guerrero, et al., 2012; Jabbar, et al., 2010; Landelle, et al., 2014). Refractive cases of infection and antibiotic-resistant strains of the organism make it even more dangerous as a pathogen. Awareness and subsequent adoption of novel preventive and treatment strategies, especially in vulnerable population, would help alleviate the significant morbidity and mortality currently associated with *Clostridium difficile* infection. This would reduce costs associated with treatment of the infection, improve quality of life and enhance overall population health. For these reasons, it would greatly behoove healthcare professionals to embrace strategies to recognize those individuals most susceptible to infection. Inflammation has been linked to increased susceptibility to infection, and is seen in obesity (Reilly & Saltiel, 2017). It is speculated that this inflammation may stem from alteration of the gut microbiota (Boulangé, et al., 2016). This inflammation leads to insulin resistance, which has been noted in both metabolic syndrome and Diabetes Mellitus, Type 2 (Reilly & Saltiel, 2017). Insulin resistance results in higher blood sugar levels, another contributing factor to *Clostridium difficile* infection (Butler, et al., 2005; Lin, et al., 2015).

This study investigates the relationship between Diabetes Mellitus Types I and II obesity and *Clostridium difficile* infection. As of the writing of this dissertation, *Clostridium difficile* infection is one of the most significant nosocomial infections to be reckoned with in the health care setting. *Clostridium difficile* infection can be a devastating illness in a number of ways.

Clostridium difficile infection adds a number of days to inpatient hospital stays, resulting in higher cost for both the patient and health care system. It results in compromised quality of life for the patient, as well as increased rates of morbidity and mortality for those infected, especially older individuals. Inflammation (associated with inflammatory cytokines) along with Diabetes Mellitus and obesity (also associated with inflammatory cytokines) seem to contribute to susceptibility to *Clostridium difficile* infection.

Implications for Social Change

Knowing factors that make an individual more likely to acquire *Clostridium difficile* infection will allow medical practitioners to be more proactive in both prophylactic and treatment strategies. Improved strategies will translate into reduced morbidity and mortality, as well as diminished hospital costs. This overall goal would result in better quality of life for those afflicted with the infection, as well as improved population health, resulting in positive social change. Whatever the cause or contributing factors, the overall goal would be to have improved outcome regarding *Clostridium difficile* infection. This can occur through improved healthcare practitioner education, improved patient education, and enhanced reporting practices by infection control preventionists. Shaping public policy to instill more stringent health policies regarding the reporting of *Clostridium difficile* infection would also improve outcomes. Moving forward in this way will allow the possibility of improved evidence-based prevention and treatment options (Debast, et al., 2014).

Summary

Clostridium difficile infection is currently the most significant communicable nosocomial infection in the hospital and long-term care setting. Post-antibiotic *Clostridium difficile* infection has been recognized for decades, but *Clostridium difficile* infection has morphed from a nuisance disease to a palpable public health threat, significantly compromising quality of life in addition to being a significant expense to the medical community. Refractive cases of infection and antibiotic-resistant strains of the organism makes it even more dangerous as a pathogen. Awareness of susceptible population, particularly those overweight patients, or individuals suffering from Diabetes Mellitus Type I or II could potentially alleviate the morbidity and mortality currently associated with *Clostridium difficile* infection. This could translate into diminished costs and improved quality of life and health for those afflicted. Awareness of epidemiologists and health care providers of a geographic component to susceptibility to the disease could also lead to more effective preventive strategies.

Chapter 2: Literature Review

Introduction

The literature review was conducted for various reasons. First, it was essential to gain a thorough understanding of how *Clostridium difficile*, as a biologic entity, was capable of causing significant communicable infection in the hospital and long-term care settings. This made it necessary to invest time in understanding the epidemiology of *Clostridium difficile* infection under normal circumstances. It was then necessary to investigate the factors that make individuals more susceptible to *Clostridium difficile* infection. Two particular conditions of interest were obesity, and Diabetes Mellitus, Types I and II. Other conditions of interest, which are pertinent to this study, included geographic location of the patient, inflammatory bowel disease, and previous abdominal surgeries. The literature was necessary to help illuminate gaps in the literature associated with *Clostridium difficile* infection. Although it was simple to find literature addressing obesity, diabetes, post-surgical status, and inflammatory conditions as contributing factors to susceptibility to infection in general, it was not as easy to link these predisposing factors specifically to the development to *Clostridium difficile* infection. It also appeared that information was lacking with respect to geographic location of the patient and susceptibility to *Clostridium difficile* infection.

Clostridium difficile infection has historically been a healthcare challenge, especially as a sequela to antibiotic therapy for another infection. It is the number one causative organism of antibiotic-associated diarrhea. *Clostridium difficile* is a spore-forming bacillus associated with significant morbidity and mortality, especially for the very young, the elderly, and the immunosuppressed. The organism is often present in very small numbers in healthy individuals.

The use of antibiotics often kills the normal bacteria present in the gut and allows the proliferation of the *Clostridium difficile* bacilli. The organism releases toxins that damage the colon and lead to the development of pseudomembranous colitis. Because *Clostridium difficile* is a spore-forming organism, it is more difficult to prevent and treat than many other pathogens seen in the health care setting. Patients suffering from *Clostridium difficile* infection frequently suffer from watery, bloody diarrhea, and the infection is easily spread by fecal contact on surfaces and on the hands of patients, visitors, or health care workers. The spores are resistant to drying, chemicals, and heat, and represent an excellent survival mechanism for the organism. The spores have the capability of survival for long periods on environmental surfaces and can even be carried from one point to another through the air. Novel prevention and treatment strategies directed against *Clostridium difficile* infection are being researched, and some potentially effective methods to combat *Clostridium difficile* infection have already been developed. It is questionable, however, how effective these strategies are, or whether they are actually being utilized at all.

It has recently been noted that there are a variety of factors that may predispose an individual to *Clostridium difficile* infection when undergoing antibiotic therapy. Certain medications and food items also can increase susceptibility to infection. The health status of the individual receiving antibiotic therapy may predispose them to increased susceptibility to infection. The literature review reveals that certain conditions make a person more likely to become ill with *Clostridium difficile*, especially when undergoing treatment for a primary infection. Susceptibility to *Clostridium difficile* infection has been noted when certain underlying comorbidities are present. Identification of these patients exhibiting reduced immunity to

Clostridium difficile infection could lead to modifications in the standard of care provided, resulting in reduced morbidity and mortality attributable to acquisition of *Clostridium difficile* infection. These patients are frequently hospitalized patients and patients residing in long-term care facilities, which gives health care practitioners easy access to provide preventive strategies.

Literature Search Strategies

The literature search was primarily executed using Google Scholar and the Walden University Library. Databases utilized included Medline, PubMed, ProQuest Central, EBSCO Host, and the CDC website and publications. The National Center for Health Statistics website was used to access the National Hospital Discharge Survey. Websites addressing specific ICD-9 codes were also utilized. The majority of researched articles were published between the years of 2010 and 2017, though a few older articles were utilized. Terms used in the article search strategy included *Clostridium difficile, Clostridium difficile risk factors, Clostridium difficile epidemiology, diabetes belt, inflammation, inflammation and infection, obesity, obesity and inflammation, obesity and infection, diabetes, diabetes and infection, diabetes and inflammation, inflammatory cytokines, abdominal surgery and Clostridium difficile infection, and inflammatory bowel disease and Clostridium difficile infection.* These searches yielded hundreds of articles of which approximately 50 articles were deemed most pertinent to this study.

Theoretical Foundation for the Study

The theoretical framework for this study was a permutation of the ecological systems theory. The traditional ecological systems theory is frequently utilized in behavioral studies and

places an individual in the center of a series of ovals that each represents an ever-widening circle of influence. These multiple influence levels can be examined in order to ascertain the best angle for a possible intervention (Sallis, et al., 2015). From an infection control standpoint, an ecological theory approach can be utilized. The balanced human microbiota (normal flora) represents the optimal goal of the ecological system (Costello, et al., 2012). Circles of influence were represented by ecologic influences that serve to either compromise or enhance the stability of the fragile microbiota such that the development of *Clostridium difficile* infection is either enhanced or hindered (Costello, et al., 2012; Smith, et al., 2005). "Understanding how the microbiota confers resistance against enteric pathogen and how antibiotics disrupt that resistance is the key to the prevention and cure of intestinal infections" (Stein, et al., 2013, p. 1). Factors that contribute to the successful invasion of *Clostridium difficile* were examined. *Clostridium difficile* in small numbers is frequently a normal inhabitant of the intestinal tract. Antibiotic therapy and change in the composition of normal flora allows the bacteria to flourish and overcome the normal microbiota (Walter, et al., 2018). Colonization of the intestine with *Clostridium difficile* bacteria and subsequent disease development represented the center of this framework. The circles of influence included host-related mechanisms that increase susceptibility to infection (inflammation, immunodeficiency, diabetes, obesity, presence of pre-existing colon disease, previous abdominal surgeries) (Ananthakrishnan, et al., 2008; Costa, et al., 2013; Dossett, 2009; Jung, et al., 2010; Kaplan, et al., 2008; Shakov, et al., 2011; Nguyen, et al., 2008; Sheridan, et al., 2012), characteristics of the *Clostridium difficile* organism itself (presence or absence of the organism, toxin production, serotype), and influences upon the

normal gut microbiota (obesity, use of antibiotics, probiotics). If the *Clostridium* can compete for resources with the normal gut microbiota in such a way that it can proliferate, chances are good that the patient with develop *Clostridium difficile* antibiotic-associated diarrhea With respect to the public health ecological foundation of the study, acquisition of *Clostridium difficile* infection is dependent upon both individual and population factors. At the individual level, a person taking antibiotics is more susceptible to *Clostridium difficile* infection than the general population. If they suffer from Diabetes Mellitus Type I or Diabetes Mellitus Type II, they are even more likely to contract the disease. Obesity also seems to play a contributing factor to acquisition of *Clostridium difficile* infection. Attention to gastrointestinal symptoms in the patient can lead to early diagnosis and treatment in the event of infection. From a community perspective, hygienic behaviors will prevent the spread of the disease through prevention of the spread of the spores. In the health care setting, the patient must be educated as to how to reduce the spread of the spores. The staff must also practice contact precautions so that reduction in the spread of the spores can be accomplished. Housekeeping personnel must also be similarly educated. In widening circles of influence, hospital policy regarding *Clostridium difficile* infection could be put into place. In addition, more stringent reporting policies to the state departments of health and the CDC might be considered.

Literature Review Related to Key Variables and Concepts

Factors that Predispose an Individual to Infection

An intact and fully functioning immune system is certainly the most efficient deterrent to development of infection in individuals of any age. Many factors can enhance immune system components to further improve resistance to infection, however. These factors include good

nutritional status, vaccination against common communicable pathogens, lack of stress, adequate amounts of sleep, and partaking in regular exercise routines (Stevens, 2017). A primary cause of immune system depression is simple aging. As an individual gets older, immunocompetence diminishes to a certain extent, leaving the individual more susceptible to development of infections (Giefing-Kröll, et al., 2015). Interestingly, gender and levels of sex hormones also contribute to immunocompetence, with higher testosterone levels of males exerting an immunosuppressive effect. For this reason, "men are more susceptible to many infections caused by viruses, bacteria, parasites, and fungi" (Giefing-Kröll, et al., 2015, p. 309). On the other hand, women seem more susceptible to contract sexually transmitted diseases. Congenital and acquired immunodeficiencies also contribute to increased susceptibility to infection. Immunodeficiencies may affect the innate immune system, the adaptive (humoral) immune system, or both arms of the immune system. AIDS (acquired immunodeficiency syndrome) is perhaps the best-known acquired immunodeficiency. AIDS affects the cellular immune system, infecting valuable helper T cells, which are necessary communication cells for the formation of antibodies (Stevens, 2017). An individual with AIDS is more susceptible to infection from all agents. Another condition associated with acquired immunodeficiency is the condition of severe burns. When skin is compromised, the barrier that prevents the entrance of microorganisms into the body is lost, resulting in infection. Congenital immunodeficiencies occur more commonly than one might expect. For example, congenital IgA deficiency, a defect of the adaptive (humoral) arm of the immune system, causes increased susceptibility to sinopulmonary infection, and is found in approximately 1 out of 125 individuals. The most serious immunodeficiencies affect both arms

of the immune system. Severe combined immunodeficiency involves lack of development of T cells and B cells, affecting both cellular and humoral immunity (Stevens, 2017). The disease presents in infancy with severe infection and significant morbidity and mortality.

Underlying chronic disease, traumas, and factors that diminish overall health also increase an individual's susceptibility to infection. The underlying mechanism of this process has yet to be thoroughly elucidated but is seems that chronic inflammation could be a contributing factor (Reilly & Saltiel, 2017). Chronic diseases implicated to be associated with increased susceptibility to infection include Diabetes Mellitus, Type 1, and Diabetes Mellitus Type 2 (Koh, et al., 2012). Another chronic illness speculated to be associated with increased infection susceptibility is inflammatory bowel disease, including Crohn's disease and ulcerative colitis. Surgeries, which compromise the protective components of skin and organ integrity, are associated with increased rates of infection (Choban, et al., 1995). Obesity has been implicated as a predisposing factor to greater than normal incidence of infection in an individual (Bishara, et al., 2013; Dossett, et al., 2009; Leung, et al., 2013). Hyperglycemia has also been speculated to be a culprit in increased incidence of infection (Butler, et al., 2005).

Epidemiology of *Clostridium difficile* Infection

Clostridium difficile, classically an exclusively nosocomial infection has now shown to be in the community. Recent epidemiological studies have shown that 26% of samples from both healthcare and non-healthcare sites tested positive for toxigenic *Clostridium difficile* strains. Shoe soles had the highest positivity rates, with 45% of samples testing positive for *C. difficile* ISDA, 2021) Community stewardship efforts are needed to reduce the risk of *C. difficile* in

communities and is a particularly devastating infection in susceptible individuals (Eckmann, Wasserman, Latif, Roberts, & Beriot-Mathiot, 2013). *Clostridium difficile* infection following antibiotic use has been recognized for many years, but *Clostridium difficile* infection has transitioned from a bothersome disease to a pathology that impacts public health, with significant morbidity and mortality (Wilkins & Lyerly, 2003). CDI is now recognized as an illness that seriously impacts quality of life, and a pathology that translates into a significant financial burden to the medical community, particularly the acute care facilities in which those stricken with the illness are already patients. *Clostridium difficile* is a contributing factor in the increasing length of hospital stays and the infection is not diminishing in prevalence in the community and acute care setting. *Clostridium difficile* infection is also becoming a palpable threat in those patients less than 18 years of age, especially in children of preschool age (Sammons, et al., 2013). In 2016 The Joint Commission Center for Transforming Healthcare reported the staggering financial costs that the care of patients with *Clostridium difficile* infection added annually to our healthcare systems. The figures from the National Institutes of Health incorporated data gathered between the years of 2005 through 2015. The average cost per case for hospital-acquired CDI was reported to be $34,157, while the average cost per case of community-acquired CDI was reported to be $21,448 per patient. The aggregate cost of *Clostridium difficile* infection in the United States was reported to be 6.3 billion dollars annually (The Joint Commission Center for Transforming Healthcare, 2016). The CDC currently sponsors a surveillance program that tracks the incidence rate of new *Clostridium difficile* cases across 35 counties across the United States. The incidence rate (or person-time rate) of an infection can be

defined as the "number of new cases of disease during specified time interval" (CDC, 2017).

The most recent data provided by the CDC in 2017, generated in 2015, demonstrated significant findings In the 35 counties studied, 17,354 cases of *Clostridium difficile* infection were reported out of a population of 11,682,427 people. There were 7,688 community-acquired cases, for an incidence rate of 65.81 per 1000 persons. There were 9,666 healthcare-acquired cases for an incidence rate of 82.74 per 1000 persons (CDC, 2017a). In 2015, in the state of Virginia 72 out of 81 hospitals reported healthcare-acquired *Clostridium difficile* infections in their facilities. The state of Virginia had an infection rate that was approximately equivalent to the national average (VDH, 2015), but our local health system had an infection rate that was approximately 7% above the national average for nosocomial *Clostridium difficile* infection (CDC, 2016e), which was quite concerning to me.

The ability of *Clostridium difficile* to form spores (Kiser, et al., 2011) makes it extremely challenging to kill the organism on surfaces (Guerrero, et al., 2012; Jabbar, et al., 2014). Refractive cases of infection and antibiotic-resistant strains of the organism make it even more dangerous as a pathogen.

Clostridium difficile infection is disproportionately found in increased numbers in the elderly population (DePestel, 2013), a population already utilizing increased health care resources. The appearance of a much more virulent strain, ribotype 027, makes it even a greater health threat (DePestel, 2013; Lessa, et al., 2012). The organism is a significant causative agent of nosocomial infection in the health care setting. "Recent data from 28 community hospitals in the southern United States suggest that *C. difficile* has replaced methicillin-

resistant *Staphylococcus aureus* as the most common cause of healthcare-associated infection" (Lessa, et al., 2012, p. S66). The incidence of *Clostridium difficile* infection is increasing, and geographically becoming more widespread. The infection is increasing in the community setting and affecting younger patients. As the epidemiology of *Clostridium difficile* infection changes, approaches to study and control of acquisition of infection must also be modified.

Inflammation in the Human Body

Inflammation is the body's protective response to infection, trauma, or malignancy. The inflammatory response is supposed to help remove infectious, cancerous, or foreign organisms or substances, resolve infection, and speed the healing process. Under stress situations, the body releases inflammatory cytokines, in particular interleukin-1, tumor necrosis factor, and interleukin-6. Interleukin-6 is often used as a marker to measure the magnitude of the inflammatory response. The cardinal signs of inflammation (fever, redness, swelling, pain, loss of function) are the body's physical response to the release of the inflammatory cytokines (Stevens, 2017). Sometimes an overstimulated immune system can actually damage the body more than help it.

Inflammation and Infection

The inflammatory response is the body's natural response to infection. The presence of a foreign entity is recognized in the innate response through the presence of cell-bound receptors that recognize the lipopolysaccharides in the cell membrane in the invading organism. Inflammatory cytokines help to recruit monocytes and macrophages to the site of infection. Phagocytosis commences when contact between the pathogen and the monocyte/neutrophil occurs, and the white cell binds the organism. The pathogen is drawn into the cell and digested.

Waste products are excreted to the outside of the cell. The release of interleukin-1 in the inflammatory process results in fever, which raises body temperature and inhibits bacterial growth. Interleukin-6 release is triggered by the presence of lipids located in the cell membrane of the invading microorganism. This cytokine promotes proliferation of antibody-secreting cells. Tumor necrosis factor serves to activate T cells that go on to communicate with B cells to produce antibody, "However, at higher levels, TNF can have deleterious systemic effects, leading to septic shock" (Stevens, 2017, p. 75). It is associated with pathologic inflammation, especially in autoimmune disorders.

Obesity and Inflammation

Obesity disrupts normal body homeostasis through "the production and release of pro-inflammatory cytokines that contribute to the triggering of the systemic acute-phase response which is characterized by elevation of acute-phase protein levels" (Rodríguez-Hernández, et al., 2013, p. 1). Inflammasomes found in adipose tissue have been shown to be associated with the inflammatory response in the obese individual. Obesity triggers inflammation in the adipose tissue, which results in an adaptive response designed to lessen stress in the body. In the body's effort to alleviate this stress, pathologic effects are often noted (Reilly & Saltiel, 2017). Homeostatic stress leads to acute inflammation and causes the body to "reset" normal blood levels of glucose and hormones. In the long run this attempt to reset homeostatic normal ranges in the body results in catecholamine resistance and insulin resistance. Insulin resistance is a condition where the body produces insulin but is not able to use it effectively (Roberts, et al., 2013). Insulin resistance is associated with development of Diabetes Mellitus Type II making this obesity-associated condition a significant health concern (Roberts, et al., 2013). Obesity is

also associated with increased production of numerous inflammatory cytokines, including C-reactive protein. "The proportion of people with elevated hs-CRP was significantly higher in those individuals with abdominal adiposity than control subjects, although they had a similar BMI" (Rodríguez-Hernández, et al., p. 3). It has recently been documented that the elevated C-reactive protein levels that can be found in obesity and may be associated with the development of an inflammatory response that executes detrimental effects upon the human body.

Diabetes and Inflammation

Diabetes Mellitus Type I is an autoimmune disorder characterized by progressive destruction of the beta cells of the islets of Langerhans of the pancreas (Stevens, 2017). Ten percent of individuals suffering from this disorder have the autoimmune form of the disease. In this situation, the body produces autoantibodies against insulin-producing cells of the pancreas. There is a genetic component to the disease, as well as an inflammatory component to development of the disease. "Progressive inflammation of the islets of Langerhans in the pancreas leads to fibrosis and destruction of most beta cells" (Stevens, 2017, p. 235). In some individuals, hypoinsulinemia is evident in the patient at a very young age, while in other it takes years for symptoms to appear. Hyperglycemia does not become evident until approximately 80% of insulin-producing cells in the pancreas are destroyed.

Diabetes/Hyperglycemia and Infection

Patients with diabetes/hyperglycemia are more susceptible to infection than individuals who are normoglycemic. "The main reason for which diabetes predisposes to infection appears to be abnormalities of the host response, particularly in neutrophil chemotaxis, adhesion and

intracellular killing, defects that have been attributed to the effect of hyperglycemia" (Koh, et al., 2012, p. 379). Mild hyperglycemia (up to 220 mgs/dl) is a normal body response to stress in individuals without diabetes (Butler, et al., 2005), but even these slightly elevated levels have now been shown to increase morbidity and mortality in affected individuals. Glucose metabolism is often compromised in injury and illness, and proinflammatory cytokines released in these conditions of body stress increase the release of glucose and may cause insulin resistance in some cases. Hyperglycemia, whether caused by Diabetes Mellitus Type I or II or simply through a patient being critically ill can lead to "changes in coagulability, impaired immune function, increased susceptibility to infection, and death is certain surgical patients" (Butler, et al., 2005, p. 965).

Potential Relationship between Geographic Regions in the United States and Diabetes

There are geographic variations in prevalence of diabetes and stroke throughout the United States. This may be an indication that there is also statistical significance associated with these regions with respect to *Clostridium difficile* infection. The CDC has identified geographic regions of 15 states that have high rates of diabetes when compared to the rest of the nation (CDC, n.d.). These states are primarily southern in location, and also represent geographic regions with high rates of obesity. The sum of these regions has been designated the "diabetes belt".

Obesity and Infection

Obesity is an independent health factor that has been associated with poor health outcomes independent of underlying disease. Many sources consider obesity a chronic disease in itself. (Choban, et al., 1995). Obesity has been associated with poor response to infection and

impaired protection from immunization (Sheridan, et al., 2012). Although the mechanism is not clear, obesity seems to impair cytotoxic T-cell response, and impair the formation of T-helper memory cells (Sheridan, et al., 2012). Obese patients "are at higher risk for post-operative infections such as pneumonia and surgical site infections, but the relationship between obesity and infections acquired in the intensive care unit (ICU) is unclear" (Dossett, et al., 2009, p. 137). It can be postulated that there may be an association between impaired immune response that has been documented in obesity and increased susceptibility to infection.

Diabetes and *Clostridium difficile* Infection

It has been established that there is an association between Diabetes Mellitus Types I and II and increased risk of infectious disease because of immune impairment. "The infectious diseases with increased risk in diabetes include *Clostridium difficile* infection" (Qu & Jiang, 2014, p. 285). Management of *Clostridium infection* in an immunocompetent individual is associated with proper macrophage function. The spore is phagocytosed, and the acidity of the phagolysosome contributes to the destruction of the spore, restricting the spread of infection. The individual with diabetes lacks the cytoplasmic acidity to effectively destroy the *Clostridium* spore, leaving it dormant and able to produce infection. Individuals with diabetes are also not effectively able to generate the cytotoxic oxygen radicals necessary for organism destruction. Not only are individuals with diabetes patients more susceptible to *Clostridium difficile* infection than the normal population, victims were younger than the general population (Hassan, et al., 2013). Exact reasons for this phenomenon are unclear.

Obesity and *Clostridium difficile* Infection

Obese patients are more susceptible to nosocomial infection than the general population

(Choban, et al., 1995). Obesity causes a change in the normal flora of the gut similar to that seen in patients with inflammatory bowel disease. This change in the gut microbiota makes an individual more susceptible to colonization with *Clostridium difficile* bacteria (Leung, et al., 2013). Overall, higher body mass index is associated with greater risk of nosocomial infection, including *Clostridium difficile* infection. "In a recent retrospective case control study, Bishara et al. demonstrated a higher BMI in all hospitalized patients with CDI compared with inpatient controls ($p < 0.001$)" ((Leung, et al., 2013, p. 1794).

Inflammatory Bowel Disease and *Clostridium difficile* Infection

Inflammatory bowel disease has been associated in a change in the microbiota of the gut and this change makes an individual more susceptible to infection with *Clostridium difficile*. "Studies have demonstrated that the increased incidence of CDI and colonization in IBD patients may be mediated by a derangement of gut flora" (Leung, et al., 2013, p. 1794). Regardless of the reason, patients with Crohn's disease or ulcerative colitis have greater morbidity and mortality from *Clostridium difficile* infection than the general population. "IBD may also be a risk factor for worse outcomes associated with *C difficile* infection compared with those without underlying IBD" (Ananthakrishnan, et al., 2008, p. 205).

The Use of the National Hospital Discharge Summary as a Source of Secondary Data

Assessment of the problem was accomplished through the use of the National Hospital Discharge Summary from the year 2010. Reviews were performed on patients with toxin-documented *Clostridium difficile* infection in the acute care hospital setting in four major geographic regions in the United States, which include all fifty states and the District of Columbia. This review was performed in an effort to ascertain health factors in specific patient

populations that contribute to susceptibility to initial *Clostridium difficile* infection and/or refractoriness to treatment. International Classification of Disease codes were utilized to ascertain the existence of comorbidities that may influence susceptibility to infection. Only patient information for adults eighteen years of age or older was utilized in this study. Additionally, in the acute care setting, the Standardized Infection Ratio could also be used to interpret the change of a nosocomial infection rate over time.

Summary

Critique of Methods

This study will quantitatively examine the relationships between obesity, Diabetes Mellitus Types I and II, and *Clostridium difficile* infection. Covariates that were controlled for include age, whether the patient suffered from Diabetes Mellitus Type I, whether the patient suffered from Diabetes Mellitus Type II, whether the patient was overweight, whether the patient had endured previous abdominal surgeries, and whether the patient had been diagnosed with inflammatory bowel disease. Obesity was determined using International Classification of Disease diagnosis codes. There are factors, however, which influence the validity of the determination of obesity. In cases in which the patient suffers from edema, weight gain from the fluid causes patient weight to be falsely increased. Another consideration is that it is possible that not all patients with diarrhea were tested for *Clostridium difficile* infection, meaning some cases could be missed. Physicians sometimes interpret initial diarrhea to be a side effect of the antibiotic utilized to treat initial patient infection, and do not take into consideration that the onset of diarrhea might be associated with *Clostridium difficile* infection. If diarrhea lasts more than 2 days or is accompanied by general malaise or fever, a *Clostridium difficile* screening test

should be performed. The toxin test for toxins A and B produced by the *Clostridium difficile* organism is the most frequently utilized screening test for *Clostridium difficile* infection. This test does not have high sensitivity, so it is probable that some *Clostridium difficile* infections might be missed (Bishara, et al., 2013). It is also possible that patients had predisposing factors not found upon chart review that contributed to susceptibility to *Clostridium difficile* infection. Predisposing factors would include decreased immunocompetence. Poor immune response would be found in patients suffering from malnutrition, patients suffering from congenital immunodeficiencies, patients infected with Human Immunodeficiency Virus, individuals receiving immunotherapy following organ transplantation, and people undergoing chemotherapy or radiation therapy for cancers. It is always the hope of the researcher that the sample size was large enough to lend rigor to the data obtained in the study, but this is not always the case, and smaller-than-anticipated sample size sometimes occurs. Utilization of data found in the National Hospital Discharge Summary hopefully generated a robust amount of data as there are over 155,000 patients evaluated for the year 2010. It should be noted that his study may have had a disproportionate number of older subjects because they represent approximately 65% of the acute care hospitalized population.

Knowledge Gap

Literature review revealed there is an increased rate of nosocomial infection in obese patients (Bishara, et al., 2013; Choban, et al., 1995, Dossett, et al., 2009) and individuals with diabetes (Butler, et al., 2005; Koh, et al., 2013). The relationship between Diabetes Mellitus Type I and *Clostridium difficile* susceptibility and Diabetes Mellitus type II and *Clostridium difficile* susceptibility has not been researched as thoroughly. Literature review revealed that

fecal evaluation demonstrates that many obese patients have a different proportion of various microbes in the gut when compared to non-obese patients. It is speculated that the altered microbiota makes an individual more susceptible to infection with various organisms including *Clostridium difficile* (Bishara, et al., 2013). A study in Israel that utilized a chart review of 6,300 hospitalized internal medicine patients concluded that increased BMI was associated with approximately double the rate of *Clostridium difficile* infection (Bishara, et al., 2013). The speculated cause of this increased infection rate was altered normal flora in the obese patients, but no actual fecal analysis was performed on these patients to verify this fact. The mean age of the patient population was 64 years, and this also makes a patient more prone to infection because immunocompetence declines with age.

Another study performed by Jason Leong and his colleagues in 2013 also attempted to prove an association between obesity and increased susceptibility to *Clostridium difficile* infection. This study cited the research performed by Bishara and his group targeting changes in gut normal flora as the causative factor for increased susceptibility to *Clostridium difficile*, but again, fecal analysis to support this theory was not performed. In the Leong study, the sample size was only 136 patients, which is rather small.

A study performed by Shakov and his colleagues in 2011 attempted to establish a relationship between diabetes and recurrence of *Clostridium difficile* infection. All patients in the study were diagnosed with *Clostridium difficile* infection. Initial infection was not studied; nonrelapse and relapse groups were the focus of the research. Two hundred fifty individuals with diabetes were included in the study. In the general population, relapses occur in approximately 20% of the population, but in individuals with diabetes included in this particular study, the

relapse rate was higher, though it was difficult to ascertain an exact value from the table provided. The mean age of the test subjects was approximately 73 years of age, which also makes a patient more prone to infection because diminishing immunocompetence is seen with declining age. An interesting fact presented in the article was the observation that the relapse group had a mean blood sugar of 147 mg/dl, while the nonrelapsing group had a mean blood sugar of 146 mg/dl. These two figures do not statistically differ, so it is difficult to conclude why some patients relapsed and some did not.

In 2014, Hassan and his colleagues reported that there seem to be an increase in *Clostridium difficile* infection in patients with Diabetes Mellitus Type II in the patient population that they associated with. They studied 159 hospitalized patients previously diagnosed with Diabetes Mellitus Type II who developed nosocomial hospital-acquired *Clostridium difficile* infection during the course of their stay. The researchers established that individuals with diabetes who acquired *Clostridium difficile* infection had a mean age of 53 years, which was younger than the individuals without diabetes that developed the infection. The researchers cited small sample size as a possible limiting factor in the validity of their study. The article did not address factors that might contribute to increased rate of infection in patients with Diabetes Mellitus Type II or why the patients were younger in age. The study also extrapolated the theory that results would be the same in patients with Diabetes Mellitus Type I although these patients were not included in the study.

Inflammatory cytokines are produced in both diabetes and obesity. These cytokines often cause reduced immunity against infection. Articles that addressed inflammation in these conditions did not extrapolate the data collected to explore the fact that inflammation in these

disorders could contribute to increased susceptibility to *Clostridium difficile* infection, representing a gap in current research. There were very few studies that could be found when the literature search was performed that addressed obesity, diabetes, inflammation, and *Clostridium difficile* infection. It is hoped that my research contributed data addressing these relationships that can be used to improve health outcomes for patients in these susceptible populations.

Geographic physical location of the affected patient with respect to nosocomial *Clostridium difficile* infection does not appear to have been thoroughly researched at this point in time. Four geographic areas of the United States were evaluated for prevalence of *Clostridium difficile* infection, and a regression study was performed to ascertain whether or not geographic location was an influence with regard to acquisition of *Clostridium difficile* infection. These geographic regions included all 50 states and Washington DC, and were subdivided into the Northeast, the Midwest, the South, and the West. Investigations as to whether there is a geographic relationship between CDI and site of patient hospital admission has been limited up to this point.

Clostridium difficile is a potentially deadly infection, especially in vulnerable populations. The scope of infection is increasing, as the number of community-acquired infections is on the rise and pediatric infections are becoming more common. In the United States, the number of obese individuals and individuals suffering from Diabetes Mellitus Type II is also increasing. Extended hospital stays due to *Clostridium difficile* infection are on the rise, and the economic burden of *Clostridium difficile* infection is staggering. It is estimated that the total cost of Clostridium difficile infection per year is 8.2 billion dollars. *Clostridium difficile* infection has progressed from a nuisance disease to a formidable pathogen that compromises

quality of life as well as health.

It was hoped that the use of information from the 2010 National Hospital Discharge Summary highlighted the relationships between susceptibility to nosocomial *Clostridium difficile* infections to make them more obvious. Previous studies implied that having Diabetes Mellitus Type I or II or being overweight seemed to contribute to susceptibility to infection on the whole. Investigation of other factors such as patient geographic location, presence of inflammatory bowel disease and a history of previous abdominal surgeries could potentially have predictive value with respect to development of *Clostridium difficile* infection. Statistically ascertaining the influence of these factors individually and cumulatively should clarify how strongly they contribute to development of infection, and lead to preventive strategies to lessen the health and financial burden caused by this infection.

Chapter 3: Research Method

Introduction

I sought to determine why nosocomial *Clostridium difficile* infection rates are higher in certain geographic regions of the United States when the comorbidities of obesity and Diabetes Mellitus Types I and II are taken into consideration. The purpose of this study is to establish whether or not these inflammatory conditions predispose affected adults to increased likelihood of development of a nosocomial *Clostridium difficile* infection in the acute hospital healthcare settings. Assessment of the problem was accomplished through the use of data gleaned from the 2010 National Hospital Discharge Survey with a focus on patients with toxin-documented *Clostridium difficile* infection in hospital settings gathered from four geographic regions of the United States. Obesity established through the examination of ICD-9 codes. Other conditions of interest which are pertinent to this study included inflammatory bowel disease and abdominal surgeries. These conditions will also be confirmed through the use of ICD-9 codes. Length of stay of the patient infected with *Clostridium difficile* will also be assessed, as *Clostridium difficile* infection frequently leads to increases in length of stay for the afflicted patient.

Research Design and Rationale

Assessment of the problem was accomplished through the review of secondary data found in the 2010 National Hospital Discharge Survey, with concentration on adult patients with toxin-documented *Clostridium difficile* infection in the acute hospital setting. A chart review was performed in an effort to ascertain health factors in specific patient populations that contribute to susceptibility to initial *Clostridium difficile* infection and/or refractoriness to treatment. As of 2021, collaborative studies linking inflammatory conditions with susceptibility

to *Clostridium difficile* infection have not been well-researched. An observational retrospective chart review also allows data to be collected with relative ease without having to obtain specific consent from the patient. In this study, the dependent variable was whether or not the patient acquired *Clostridium difficile* infection after antibiotic therapy in the healthcare facility. Covariates included whether the patient suffered from Diabetes Mellitus Type I, whether the patient suffered from Diabetes Mellitus Type II, whether the patient was overweight, obese, or morbidly obese, whether the patient had endured previous abdominal surgeries, and whether the patient had been diagnosed with inflammatory bowel disease.

Study Population

The study population for this research protocol was discharged patients in the non-institutional hospital setting from four distinct geographic regions of the United States that have acquired *Clostridium difficile* infection. For the purpose of this study, exclusively adult patients between the ages of 18 and 90 were utilized. Pediatric inpatients in community hospitals and patients from children's hospitals were excluded from this study. Patients from military and Veterans Administration hospitals were also excluded from this study. Patients from long term care facilities were also excluded from this study.

Sampling Strategy

Secondary data was used for this study. Information was obtained from the 2010 National Hospital Discharge Survey. This study gathered information from 203 short-stay

hospitals dispersed over four distinct geographical regions of the United States. The hospitals included were required to have at least six inpatient beds to be considered for the survey. Data collection from the hospitals was executed one of two ways. Data collected through the manual

method was reviewed and transcribed to abstract forms by medical records personnel. Another way manual data was collected was through the work of the United States Census Bureau which completed the manual forms and forwarded the forms to an outside source for coding and then made sure the information was received by the National Hospital Discharge Survey administrators. Data collected through the automated method was purchased by the National Center for Health Statistics and subsequently sampled by the National Hospital Discharge Survey personnel.

Sample Size

The goal of statistical power analysis was to optimize the size of the sample being studied to be most useful when attempting to study a particular effect. Statistical power strives to assure that an effect was detected in a sample as long as the effect exists in reality. As the sample size increases, the power of the study increases. Data review revealed a sample size of 151,511 individuals, which was an adequate number of subjects to lend rigor to statistics generated in the study. Initially, the data review was necessary to ascertain how many of those individuals suffered from *Clostridium difficile* infection. Then I created a second group of individuals of the same age and sex who do not suffer from *Clostridium difficile* infection to serve as the control group.

Mathematical calculation utilizing the z-test family can be used to establish sample size. The sample size was calculated utilizing G*Power 3.1.9.2 software. "z-test family" was selected followed by selection of the "logistic regression" option. The A priori analysis was selected to calculate the optimal sample size based upon an odds-ratio option of 1.3, and the Prob(Y=1/X=1)

H_0 value of 0.2. The alpha value was entered as 0.05 and the power was entered as 0.95. The X parm m was entered as [0] and X parm s was entered as [1]. The program calculated a minimum sample size of 988.

Table 1

Variable Descriptions

Variable	Type of Variable	Representation of Measure
Gender	Nominal-dichotomous	0 = male 1 = female
Age	Scale	Actual age of patient
Obesity	Nominal-dichotomous	0 = BMI < 25 1 = BMI >/= 25
Individuals with Diabetes Mellitus Type I	Nominal-dichotomous	0 = individuals without Diabetes Mellitus Type I 1 = individuals with Diabetes Mellitus Type I
Individuals with Diabetes Mellitus Type II	Nominal-dichotomous	0 = individuals without Diabetes Mellitus Type II 1 = individuals with Diabetes Mellitus Type II
Bowel Disease	Nominal-dichotomous	0 = individuals with bowel disease 1 = individuals without bowel disease
Abdominal Surgery	Nominal – dichotomous	0 = individuals with abdominal surgery 1 = individuals without abdominal surgery
Geographic Location	Nominal	1 = Northwest 2 = Midwest 3 = South 4 = West

Descriptive statistics were utilized to produce numeric descriptions of these variables. Age as a variable was measured as scale-interval level. Sex (gender) was measured through a nominal – dichotomous level, with "0" representing male, and "1" representing female. Obesity was identified through the use of ICD-9 codes into a nominal – dichotomous level categorized as HIBMI, with "0" representing a BMI of less than 25, and "1" representing a BMI of 25 or greater. Diabetes Mellitus Types I and II were studied as separate entities on a nominal-dichotomous level, with "0" representing no diabetes, and "1" representing that the patient had diabetes. Individuals with diabetes were also identified through the use of ICD-9 codes, with differentiation by patient as to whether the patient suffered from Diabetes Mellitus Type I or Diabetes Mellitus Type II. Frequencies were generated for the continuous variable of age. ICD-9 codes were used to find overweight individuals, with a code of 278.02 indicating that an individual was overweight, a code or 278.0 indicating non-specified obesity and a code of 276.01 indicating morbid obesity. Ranges for the continuous variables were established through the use of minimum and maximum values in the statistics table. The categorical variables of sex and Diabetes Mellitus Types I and II were then analyzed and frequency tables generated. Graphical descriptions of these variables were subsequently produced. Previous bowel disease and abdominal surgeries were also investigated, as these factors increase likelihood of development of *Clostridium* infection (Leung et al., 2013). ICD-9 codes were utilized to find these conditions in the data and to statistically evaluate the influence of these conditions. ICD-9 codes that were utilized include 54.0, representing abdominal incision, 560.89 representing inflammatory bowel disease. Chronic colitis was represented by the code 556.1.

The bulk of statistical analysis performed on the data in this study was logistic regression.

This was an optimal test to determine whether or not a relationship could be established between certain presumed predisposing factors in the patient and the likelihood of that patient developing a *Clostridium difficile* infection. The presence or absence of *Clostridium difficile* infection was the dichotomous dependent variable, while the independent variables studied included age, Diabetes Mellitus Type I, Diabetes Mellitus Type II, obesity, previous abdominal surgeries, history of inflammatory bowel disease and the geographic region of the acute care facility where the individual was a patient. These factors were considered covariates. Logistic regression was chosen for statistical analysis of the data because it is helpful in establishing whether an independent variable has a measurable relationship with the dependent variable. Logistic regression was selected to help to either establish or disprove whether there is a statistically significant relationship between the independent variable of presence or absence of select comorbidities and development of nosocomial *Clostridium difficile* infection. The Chi square test for independence could help to ascertain whether there could be a relationship between categorical variables in this study. Nominal variables could be utilized to make this comparison. Bowel disease and abdominal surgery could be represented on a nominal-dichotomous level, with "0" representing absence of the condition and "1" representing presence of the condition. These values could be tested against presence or absence of Clostridium difficile infection, which could also be represented on a nominal-dichotomous level, with "0" representing absence of the disease and "1" representing presence of the disease. It was suspected age was one of the confounding variables, because increasing age is a predisposing factor to development of *Clostridium difficile* infection. In addition, other potential confounding variables include length of facility stay, pre-existing bowel disease and previous abdominal surgery.

The geographic region that each patient lives in was also investigated. “1” indicates that the patient was hospitalized the Northeast, “2” indicates that the patient was hospitalized in the Midwest, “3” indicates that the patient was hospitalized in the South, and “4” indicates that the patient was hospitalized in the West.

Data Analysis Plan

The data was obtained from the 2010 National Hospital Discharge Survey. All patients examined for statistical correlation as the dependent variable in the study have a diagnosis of *Clostridium difficile* infection as demonstrated through a laboratory confirmed stool toxin or DNA test. Survey data used included patient age, sex, and race, whether they suffered from Diabetes Mellitus Type I or II, and whether they were overweight or not. Other areas of interest included whether the patient had been previously diagnosed with inflammatory bowel disease, and whether or not the patient had experienced previous abdominal surgeries or not. Logistic regression was utilized in order to determine whether or not the aforementioned variables influenced the outcome (development of nosocomial *Clostridium difficile infection*). Data was analyzed through the use of SPSS version 25.0. The logistic regression was used to address the research questions and hypotheses put forth in the study. These research questions and hypotheses were as follows:

Research Question 1: Is there a relationship between obesity and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$1: There is not a statistically significant association between obesity and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after

controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a1: There is a statistically significant association between obesity and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 2: Is there a relationship between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0 2$: There is not a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium* difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

$H_a 2$: There is a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 3: Is there a relationship between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0 3$: There is not a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a3: There is a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 4: Is region significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$4: Region is not significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a4: Region is significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Threats to Validity

Descriptive statistics were utilized to evaluate the percentage of data evaluated for specific geographic regions. The Northeast is represented by region 1 and includes the states of Maine, New Hampshire, Vermont, Massachusetts, Connecticut, Rhode Island, New York, New Jersey, and Pennsylvania. The Midwest is represented by region 2 and includes the states of Michigan, Ohio, Illinois, Indiana, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska and Kansas. The South is represented by region 3 and includes the states of Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi. Arkansas, Louisiana,

Oklahoma and Texas. The West is represented by region 4 and includes the states of Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Hawaii and Alaska.

Table 1

Geographic Distribution of Study Population

Geographic Region	Number of Test Subjects in Each Geographic Region	Percent of Test Subjects in Each Geographic Region
1 (Northeast)	28563	18.8%
2 (Midwest)	45631	30.1%
3 (South)	61729	40.7%
4 (West)	15628	10.3%
Total	151551	100.0%

Validity of the study may be affected by uneven distribution of data by geographic region, with the majority of the patient population hospitalized in region 3 (the South) and the least number of patients hospitalized in region 4 (the West).

Internal validity is a reflection on how well the experiment has been performed. When an experiment has been executed proficiently the chance of confounding is greatly reduced. When confounders are reduced the researcher can explore alternate possibilities for outcomes of a study with confidence. External validity reflects the reproducibility of a study. If predisposing factors lend themselves to similar outcomes in the various geographic settings, then external validity has been maintained.

Ethical Concerns

Ethical concerns were minimal in this study. In this study human participants were not directly encountered, because a secondary data source was used. Any individual who chooses to utilize this data set commits to maintaining the confidentiality of subjects. If the identity of any patient is accidentally discovered, the user of the data is forbidden to use this knowledge and the breach must be reported to the director of the National Center for Health Statistics. The likelihood of discovering the identity of a patient included in this study through the data provided is very slim. The data is contained in a document known as the National Hospital Discharge Survey, which is a matter of public record. Patient names are not included in the document; a file of this document is stored on the hard drive of my computer.

Limitations

The National Hospital Discharge Survey has been utilized since 1965 to collect a variety of medical and demographic data that can be statistically evaluated to gather hospital utilization data for short-term stay facilities. In 1988 geographic groupings were added to enhance the information generated, Unfortunately, in 2008 the number of hospitals surveyed was reduced by 50% resulting in increases of Relative Standard Error rates. For this reason, each facet of data studied should have at least thirty discharge summaries so that the Relative Standard Error was less than 30%. Errors could also occur if hospital response to the survey was missing or incomplete, or if information was inaccurately transcribed from the patient medical record to the transport form.

Summary

A secondary data set was utilized to establish if there is a relationship between nosocomial *Clostridium difficile* infection, Diabetes Mellitus Types I and II, and obesity. Simultaneously data from four different regions of the United States was examined to establish whether *Clostridium difficile* infection prevalence correlates with specific geographic regions of the United States. Of particular interest was the geographic regions incorporating the "diabetes belt" and geographic regions where obesity is recognized to be more common. As the data set is limited it was difficult for the evaluator to establish whether factors outside the data set which made a person more susceptible to *Clostridium difficile* infection were present. A possible threat to validity was an uneven distribution of patients in the various geographic regions and the fact that survey results from only 203 hospitals were included in the data. Conclusions based upon the results of the data may lack the property of generalization to other populations or sites. That being said, it is important to note that the data set included over 155,000 patients, which was a large enough sample size to yield statistically rigorous outcomes.

Chapter 4: Analysis and Presentation of Data

Introduction

The National Hospital Discharge Survey was used until 2010 at short-stay hospitals in the United States in order to gather pertinent information on the patients who had been admitted there. "Data from the NHDS are available annually and are used to examine important topics of interest in public health and for a variety of activities by governmental, scientific, academic, and commercial institutions" (CDC, 2015a). The dataset encompasses a population of 151,551 individuals who were discharged from nonfederal acute-care hospitals in 2010.

Exploratory Study Results

Patients diagnosed with *Clostridium difficile* (ICD-9 code 00845) are the primary focus of this study. Variables V17 through V31 (a total of 15 variables) address International Classification of Disease diagnosis codes for the entire data set. V17 represents the first disease coded for the patient, V18 the second disease coded, V19 the third disease coded, and so on. If the patient had numerous pathologies, up to 15 diagnoses were recorded, with V31 being the last potential disease variable recorded (see Table 3).

Table 2

Number of Patients Diagnosed with Clostridium difficile *Infection According to Diagnosis Number*

Variable	Number of affected patients
V17: C. diff diagnosis #1	374
V18: C. diff diagnosis #2	167
V19: C. diff diagnosis #3	158
V20: C. diff diagnosis #4	156
V21: C. diff diagnosis #5	111
V22: C. diff diagnosis #6	81
V23: C. diff diagnosis #7	52
V24: C. diff diagnosis #8	25
V25: C. diff diagnosis #9	10
V26: C. diff diagnosis #10	18
V27: C. diff diagnosis #11	12
V28: C. diff diagnosis #12	10
V29: C. diff diagnosis #13	7
V30: C. diff diagnosis #14	2
V31: C. diff diagnosis #15	3
Total	1186

Note: This table represents patients diagnosed with Clostridium difficile infection in order of diagnosis code. Each patient has the potential of being assigned up to 15 different diagnosis codes. V17 represents the first diagnosis code applied to the patient, and V31 the final diagnosis code being applied to the patient.

Utilizing the information in the NHDS, a total of 1186 patients in the study had a diagnosis of *Clostridium difficile* infection. This figure does not reflect the age restriction that the study population was 18 years of age or older. When age restrictions were applied, a total of 129,242 patients remained in the study population. Of that population, 1135 patients in the study population were documented to suffer from *Clostridium difficile* infection.

Table 3

Number of Patients Diagnosed with Clostridium difficile Infection

CD

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	*C.diff* (-)	128106	99.1	99.1	99.1
	C.diff (+)	1135	.9	.9	100.0
	Total	129241	100.0	100.0	
Missing	System	1	.0		
Total		129242	100.0		

Statistics

CD

N	Valid	1135
	Missing	0

CD

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	*C.diff* (+)	1135	100.0	100.0	100.0

Variable: Sex

After ascertaining the number of individuals diagnosed with the infection, I then assessed the sex of the study population. Although sex was not selected as a variable to be studied, the data indicates that the sampling frame is 40.3% male and 59.7% female.

Table 4

Sex of Patients in the Study Population

Statistics

Sex

N	Valid	129242
	Missing	0

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid:	Male	52042	40.3	40.3	40.3
	Female	77200	59.7	59.7	100.0
	Total	129242	100.0	100.0	

The dataset was then reexamined including only patients suffering from *Clostridium difficile* infection. Initial review of data regarding sex of the entire population revealed 40.3% males and 59.7% females. Restricting the data set to only those individuals suffering from *Clostridium difficile* infection demonstrated a population that was 43.4% male and 56.6% female.

Table 5

Sex of Patients in the Study Population Suffering from Clostridium difficile Infection

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	493	43.4	43.4	43.4
	Female	642	56.6	56.6	100.0
	Total	1135	100.0	100.0	

Note: the data indicates that the patient population suffering from Clostridium difficile infection is 43.4% male and 56.6% female.

The data indicates that in the patients suffering from *Clostridium difficile* in this population, 43.4% were male and 56.6% were female. 493/52041 = .947% of males were positive for *Clostridium difficile* infection, while 642/77200 = .832% of females in the population were positive for *Clostridium difficile* infection.

A logistic regression pertaining to sex of patients in the study population suffering from *Clostridium difficile* infection was performed. The predictor variable of sex was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, sex, in the logistic regression analysis, was found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.650, SE = .045, Wald = 10557.816, $p <$ .001. The unstandardized Beta weight for the predictor variable sex B = -131, SE = .045, Wald = 4.776, $p <$ .001. This analysis generated an odds ratio of 0.877.

Conclusion with Respect to Sex

Since males were baseline in this regression, the odds ratio of .877 indicates that females are almost 14% less likely to develop *Clostridium difficile* infection than males. The *p*-value of .029 reveals that sex is statistically significant in the development of Clostridium difficile infection in the National Hospital Discharge Summary population from 2010.

Variable: Mortality

The next variable examined was the discharge status of the study population. The primary focus was to establish whether the patient was alive or deceased upon discharge. It was also interesting to observe whether the patient subsequently was discharged to a secondary facility.

Table 6

Discharge Status of Patients in the Study Population

Discharge status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**Routine Discharge Home**	95621	74.0	74.0	74.0
	Left AMA	1516	1.2	1.2	75.2
	Short term care facility	3543	2.7	2.7	77.9
	Long term care facility	15620	12.1	12.1	90.0
	Alive no destination specified	6736	5.2	5.2	95.2
	Dead	2705	2.1	2.1	97.3
	Not reported	3501	2.7	2.7	100.0
	Total	129242	100.0	100.0	

Note: It is noted that 2705 patients were deceased upon discharge.

Sex of the study population who were dead upon discharge was then examined.

Table 7

Sex of Patients in the Study Population who were Dead upon Discharge

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	1337	49.4	49.4	49.4
	Female	1368	50.6	50.6	100.0
	Total	2705	100.0	100.0	

Analysis of the patient population who were dead upon discharge revealed that 49.4% of the study population were male and 50.6% of the study population was female.

Sex of the study population suffering from *Clostridium difficile* infection who were dead upon discharge was then examined.

Table 8

Sex of Patients in the Study Population Diagnosed with Clostridium difficile Infection who were Dead upon Discharge

Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	36	45.6	45.6	45.6
	Female	43	54.4	54.4	100.0
	Total	79	100.0	100.0	

Analysis of the patient population suffering from *Clostridium difficile* infection revealed that of the 79 deceased patients in this group, 45.6% of the population were male and 54.4% were female.

Variable: Race and Ethnicity

Race/ethnicity of the patient population in this study was then examined.

Table 9

Ethnicity of Patients in the Study Population

Ethnicity

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**White**	83915	64.9	64.9	64.9
	Black/ AA	17789	13.8	13.8	78.7
	Am. Indian/ Alaskan Native	320	.2	.2	78.9
	Asian	1573	1.2	1.2	80.2
	Native of Hawaii/ Pacific Islander	43	0	0	80.2
	Other	6288	4.9	4.9	85.1
	Multiple Races	89	.1	.1	85.1
	Not Stated	19225	14.9	14.9	100.0
	Total	129242	100.0	100.0	

With respect to ethnicity, the data indicates a patient population that is 64.9% White, 13.8% Black/African American, 0.2% American Indian/Alaskan Native, 1.2% Asian, 0% Native Hawaiian/Other Pacific Islander, 4.9% “Other”, 0.1% Multiple Race and 14.9% did not state their race.

The data set was then reexamined including only patients suffering from *Clostridium difficile* infection. These results are displayed in Table 11:

Table 10

Ethnicity of Patients in the Study Population Diagnosed with Clostridium difficile Infection

Ethnicity

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**White**	857	75.5	75.5	75.5
	Black/ AA	111	9.8	9.8	85.3
	Am. Indian/ Alaskan Native	1	.1	.1	85.4
	Asian	14	1.2	1.2	86.6
	Other	44	3.9	3.9	90.5
	Not Stated	108	9.5	9.5	100.0
	Total	1135	100.0	100.0	

The data generated from patients suffering from *Clostridium* infection indicates a patient population that is 75.5% White, 9.8% Black/African American, 0.1% American Indian/Alaskan Native, 1.2% Asian, 0.0% Native Hawaiian/Other Pacific Islander, 3.9% “Other”, 0.0% Multiple Race and 9.5% did not state their race.

Analysis of the population diagnosed with *Clostridium difficile* infection who were dead at discharge was then performed. These results are displayed in Table 12.

Table 11

Ethnicity of Patients in the Study Population Diagnosed with Clostridium difficile Infection who were Dead upon Discharge

Ethnicity

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	White	59	74.7	74.7	74.7
	Black/ AA	9	11.4	11.4	86.1
	Am. Indian/ Alaskan Native	1	1.3	1.3	87.3
	Other	3	3.8	3.8	91.1
	Not Stated	7	8.9	8.9	100.0
	Total	79	100.0	100.0	

Data assessment of those dead at discharge indicates a patient population that is 74.7% White, 11.4% Black/African American, 1.3% American Indian/Alaskan Native, 3.8% “Other”, and 8.9% did not state their race.

Variable: Marital Status

Marital status of the patient population in this study was then examined. These results are displayed in Table 13.

Table 12

Marital Status of Patients in the Study Population

Marital status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**Married**	25997	20.1	20.1	20.1
	Single	14003	10.8	10.8	30.9
	Widow	9015	7.0	7.0	37.9
	Divorced	4933	3.8	3.8	41.7
	Separated	723	.6	.6	42.3
	Not stated	74571	57.7	57.7	100.0
	Total	129242	100.0	100.0	

The dataset indicates that 20.1% of the population was married, 10.8% of the population was single, 7.0% of the population was widowed, 3.8% of the population was divorced, .6% of the population was separated, and 57.7% of the population did not state their marital status.

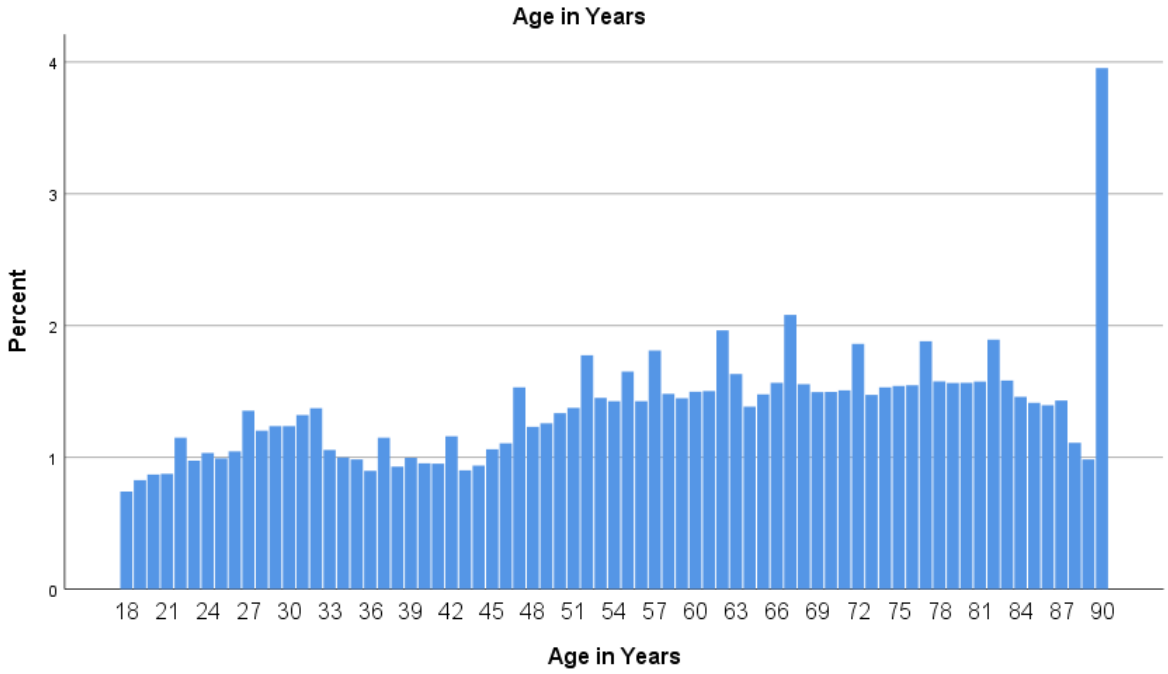
Variable: Age

Data analysis initially examined the ages of all individuals in the patient population. The data shows that 9.3% of patients discharged in the study were newborns. The dataset indicates that there were 22,204 individuals under the age of 18. Age restrictions were imposed upon the data set because the focus of this study is adults only. For this reason, data from the pediatric population were not included in the study. Of the 151,551 individuals addressed in the study, 85.3% of patients were 18 years of age or older. Utilizing this percentage, 129,209 patients fell into the adult age group. It is stated in the NHDS data set that all patients 90 years of age or

greater were counted as 90 years of age. 3.4% of patients fell in this age group. When the dataset is examined, patients of Medicare age (65 years of age and older) make up 35% of the patients.

Figure 1

Histogram: Study Population Age in Years



The mean age of the study population is 57.86 years of age while the median age of the study population is 60 years of age. The mode of the study population is 90 years of age, which in this study represents all individuals 90 years of age and greater. Ages 18 to 90 were evaluated on an individual basis for statistical significance.

A logistic regression analysis to investigate whether age contributed significantly to acquisition of *Clostridium difficile* infection was performed. The predictor variable of age was tested a priori to verify that there was no violation of the assumption of the linearity of the logit.

The predictor variable, age, in the logistic regression analysis, was found to contribute to the model. The unstandardized Beta weight for the Constant; B = -6.900, SE = .126, Wald = 2982.001, $p < .001$. The unstandardized Beta weight for the predictor variable age B = .034, SE = .002, Wald = 371.114, $p < .001$. The estimated odds ratio favored an increase likelihood of acquisition of *Clostridium difficile* infection of 1.034 with every year increase in age. (Exp B = 1.034), 95% Confidence Interval (1.031, 1.038) for development of *Clostridium difficile* infection for each one unit increase in age.

It can be concluded that the probability of *Clostridium difficile* infection is related to increasing age. The Sig. values produced for each age of the patients in the study demonstrate varying probabilities for each of the age values from 18 years of age until >/= 90 years if age. It is not surprising that younger ages carry very high Sig. values, as it is much less likely to have *Clostridium difficile* infection at younger ages. The data indicates a correlation between age and *Clostridium difficile* infection for patients 61 years of age and greater. It can be concluded that age is a statistically significant predictor of *Clostridium difficile* infection. An individual 61 years of age or older is more susceptible to acquisition of *Clostridium difficile* infection when compared to probability of infection in those individuals less than 61 years of age. The data reveals that there are three exceptions to this observation occurred at 40 years of age, 51 years of age, and 58 years of age.

In conclusion, with every year increase in age the odds of acquiring *Clostridium difficile* infection increase by 1.03.

Variable: Inflammatory Bowel Disease

Inflammatory Bowel Disease, coded IBD in the data analysis performed, is the variable indicative of whether the patient suffered from IBD or not. Inflammatory bowel disease collectively includes the diagnoses of Ulcerative Colitis and Crohn's Disease. These results are displayed in Table 14.

Table 13

Inflammatory Bowel Disease (IBD) of Patients in the Study Population

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Do not have IBD	128188	99.2	99.2	99.2
	Have IBD	1016	.8	.8	100.0
	Total	129204	100.0	100.0	
Missing	System	5	.0		
Total		129209	100.0		

N*ote: In this patient population, 1016/129204, or 0.8% of the patients, have inflammatory bowel disease. 128188/129204, or 99.2% of the patients did not suffer from inflammatory bowel disease.*

The case processing summary revealed that there were N = 129203 patients evaluated in the regression. n = 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the patient population of interest, 1016 individuals had been diagnosed with IBD. Of the patients with inflammatory bowel disease, 22 were simultaneously diagnosed with *Clostridium difficile* infection,

A logistic regression analysis was performed to investigate whether inflammatory bowel disease contributed significantly to acquisition of *Clostridium difficile* infection. The predictor variable of inflammatory bowel disease was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, inflammatory bowel disease,

in the logistic regression analysis, was found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.738, SE = .030, Wald = 24767.393, $p < .001$. The unstandardized Beta weight for the predictor variable inflammatory bowel disease B = .927, SE = .218, Wald = 18.150, p < .001. The estimated odds ratio favored an increase likelihood of acquisition of *Clostridium difficile* infection of 2.527 with every unit increase in inflammatory bowel disease. (Exp B = 2.527), 95% Confidence Interval (1.650, 3.872) for development of *Clostridium difficile* infection for every one unit increase in inflammatory bowel disease. The hypothesis that inflammatory bowel disease is not a significant predictor of *Clostridium difficile* infection is rejected because the *p*-value (Sig.), which is 0, is smaller than the critical *p*-value of .05.

There is a statistically significant correlation between IBD and development of *Clostridium difficile* infection.

Variable: Abdominal Surgery

Abdominal Surgery, designated in the data set as AS, is a variable demonstrating that the patient experienced abdominal surgery.

Table 14

Patients in the Study Population Who Have Experienced Abdominal Surgery (AS)

AS (abdominal surgery)

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Did not have abdominal surgery	126015	97.5	97.5	97.5
	Had abdominal surgery	3187	2.5	2.5	100.0
	Total	129202	100.0	100.0	
Missing	System	7	.0		
Total		129209	100.0		

In this patient population, 126015/129202 or 97.5% of the patient population has not had abdominal surgery. 3187/129202, or 2.5% of the patient population had experienced abdominal surgery.

Review of the regression revealed that there were N = 129209 patients evaluated in the regression. n = 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the entire patient population, 3187 individuals had experienced abdominal surgery. Of this population, 32 patients also experienced *Clostridium difficile* infection.

A logistic regression analysis was utilized to investigate whether previous abdominal surgery contributed significantly to acquisition of *Clostridium difficile* infection. The predictor variable of previous abdominal surgery was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, previous abdominal surgery,

in the logistic regression analysis was not found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.730, SE = .030, Wald = 24459.206, $p < .001$. The unstandardized Beta weight for the predictor variable previous abdominal surgery B = .139, SE = .180, Wald = .593, and $p = .442$. Results also revealed that Exp B = 1.149, and the 95% Confidence Interval was (.807, 1.636). The *p*-value of .442 did not indicate the association of development of *Clostridium difficile* infection when a patient had experienced previous abdominal surgery.

Hypothesis-Based Study Results

The purpose of this study is to establish whether or not Diabetes Mellitus Type I, Diabetes Mellitus Type II, obesity, or a combination of these disorders predisposes the affected individual to increased likelihood of development of a nosocomial *Clostridium difficile* infection in the acute healthcare hospital settings. The study also explores whether or not there is a geographic component related to susceptibility to *Clostridium difficile* infection. Research questions to be addressed are as follows:

Research Question 1: Obesity

RQ1: Is there a relationship between obesity and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$1: There is not a statistically significant association between obesity and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a1: There is a statistically significant association between obesity and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Obesity was examined as a potential predictor of *Clostridium difficile* infection. For this study obesity was evaluated based upon ICD-9 codes. The three subcategories initially evaluated were classified as overweight (OW), obese (OB) and morbidly obese (MOB). These three categories were subsequently combined into the larger category of HBMI. Patients documented to have a BMI greater than or equal to 25 based upon ICD-9 codes were placed in this category. These results are displayed in Table 16.

Table 15

Patients in the Study Population Determined to be Overweight (HIBMI) Based upon ICD-9 Codes

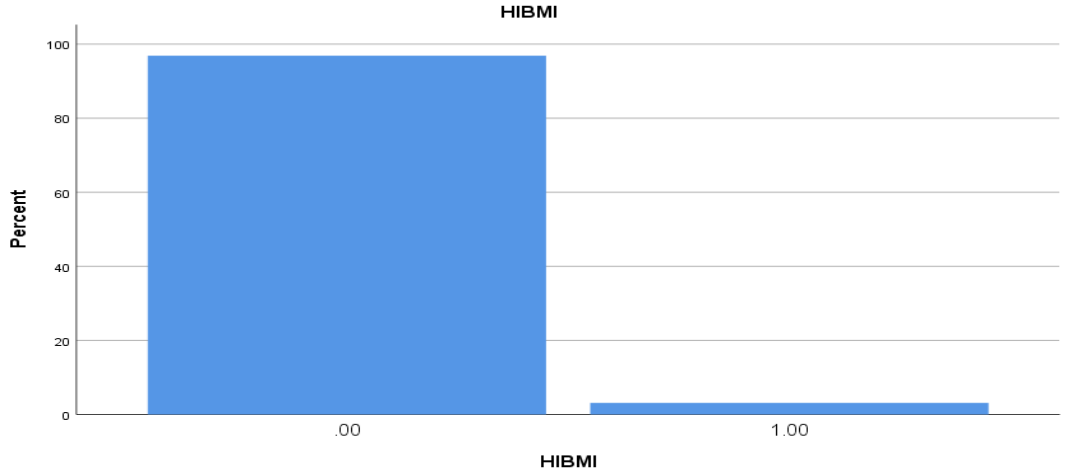
Overweight vs Not Overweight

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Not overweight	125153	96.9	96.9	96.9
	Overweight	4051	3.1	3.1	100.0
	Total	129204	100.0	100.0	
Missing	System	5	.0		
Total		129209	100.0		

This categorical variable table indicates that 4051/129204 individuals, or 3.1% of the population has been documented through ICD-9 coding to be overweight. !25153/129204, or 96.9% of the population is documented to not be overweight.

Figure 2

Bar Chart of Percentage of Overweight Patients (0 = not overweight, 1 = overweight)



Logistic Regression: Overweight (HIBMI)

The case processing summary revealed that there were 129204 patients evaluated in the regression. 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the patient population of interest, 4051 individuals were documented to be overweight.

A logistic regression analysis was executed to investigate whether being overweight contributed significantly to acquisition of *Clostridium difficile* infection was performed. The predictor variable of obesity was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, obesity, in the logistic regression analysis, was found to contribute to the model. The unstandardized Beta weight for the

Constant; B = -4.714, SE = .030, Wald = 24495.69, $p < .001$. The unstandardized Beta weight for the predictor variable obesity B = -.451, SE = .211, Wald = 4.559, p < .001. The odds ratio (OR) is given by dividing the number of positive cases of *Clostridium difficile* infection by the negative number of *Clostridium difficile* cases in the study. The estimated odds ratio favored an increase likelihood of acquisition of *Clostridium difficile* infection of .637 with every unit increase in obesity. The estimated odds ratio favored an increase of nearly 16% (Exp B = .637), 95% Confidence Interval (.421, .964) for development of *Clostridium difficile* infection for every one unit increase in the event that the patient was overweight. For the variable HIBMI, the Sig. (*p*-value is) .033, so the null hypothesis would be rejected.

A secondary logistic regression was then performed to determine the significance of being overweight when the other covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease were taken into consideration. These results are displayed in Table 17.

Table 17

Regression Evaluating HIBMI as a Contributing Factor to CDI with Respect to the Covariates of Age, Sex, Abdominal Surgeries and Inflammatory Bowel Disease:

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Age in Years	.034	002	368.429	1	.000	1.034	1.031	1.038
	Sex (1)	.055	.060	.829	1	.363	1.056	.939	1.189
	IBD(1)	-1.080	.219	24.312	1	.000	.340	.221	.522
	AS(1)	-.125	.181	.476	1	.490	.883	.619	1.258
	HIBMI(1)	.216	.212	1.040	1	.308	1.241	.819	1.881
	Constant	-5.952	.355	281.637	1	.000	.003		

a. Variable(s) entered on step 1: Age in Years, Sex, IBD, AS, HIBMI.

A second logistic regression analysis was executed to investigate whether being overweight contributed significantly to acquisition of *Clostridium difficile* infection. The covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease were included in the analysis. The predictor variable of obesity was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, obesity, in the logistic regression analysis, was not found to contribute to the model when interpreted in light of the covariates age, sex, preexisting abdominal surgeries and IBD. The unstandardized Beta weight for the Constant; B = -5.952, SE = .0355, Wald = 281.637, $p < .001$. The unstandardized Beta weight for the predictor variable obesity B = -.216, SE = .212, Wald = 1.040, $p = .308$. Results also revealed that Exp B = 1.241, and the 95% Confidence Interval was (.819, 1.881). When explored with the accompanying covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease, the variable HIBMI, with a Sig. (*p*-value) of .308, is not a statistical contributor to acquisition of *Clostridium difficile* infection, so the null hypothesis would be accepted.

Conclusion for RQ1

It can be concluded that being overweight is in fact associated with increased incidence of *Clostridium difficile* infection when obesity is examined as the only variable explored in the bivariate regression. However, when the variable of being overweight is analyzed in a regression with the covariates of age, sex, preexisting abdominal surgeries and IBD, it loses statistical significance.

Research Question 2: Diabetes Mellitus Type I

Is there a relationship between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$2: There is not a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a2: There is a statistically significant association between Diabetes Mellitus Type I and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

The next category to be examined is Diabetes Mellitus Type I and its relationship to *Clostridium difficile* infection. The diagnosis of Diabetes Mellitus Type 1 was then evaluated as a possible correlate to *Clostridium difficile* infection. Examination of the data revealed that there were 129200 patients evaluated in the regression. 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the patient population of interest, 911 individuals were documented to have a diagnosis of Diabetes Mellitus Type I. Of these individuals 12 were also diagnosed with *Clostridium difficile* infection. The percentage of individuals diagnosed with both conditions in the study population is 12/911 = 1.32%. These results are displayed in Table 18.

Table 16

Patients in the Study Population Determined to Have Diabetes Mellitus Type I (DM1) Based upon ICD-9 Codes

DMI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No DM1	128289	99.3	99.3	99.3
	DM1	911	.7	.7	100.0
	Total	129200	100.0	100.0	
Missing	System	9	.0		
Total		129209	100.0		

This categorical variable table indicates that 911/129200 individuals, or 0.7% of the population has been documented through ICD-9 coding to be diagnosed with Diabetes Mellitus Type I. 128289/129200, or 99.3% of the population is documented to not have been diagnosed with Diabetes Mellitus Type I.

Logistic Regression: Diabetes Mellitus Type I (DMI)

A logistic regression analysis to investigate whether Diabetes Mellitus Type I contributed significantly to acquisition of *Clostridium difficile* infection was performed to determine whether or not an association existed. The predictor variable of previous diagnosis with Diabetes Mellitus Type I was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, previous diagnosis with Diabetes Mellitus Type I, in the logistic regression analysis was not found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.316, SE = .291, Wald = 220.628, $p < .001$. With regard to the

unstandardized Beta weight for the predictor variable previous diagnosis with Diabetes Mellitus Type I, B =-.413, SE = .292, Wald = 2.000, and p = .157. Results also revealed that Exp B = .662, and the 95% Confidence Interval was (.373, 1.173). The p-value of .157 did not indicate the association of development of *Clostridium difficile* infection when a patient had a previous diagnosis of Diabetes Mellitus Type I. For the variable DMI in the table above, the Sig. (p-value) is .157, so the null hypothesis would be accepted.

A secondary logistic regression was then performed to determine the significance of a patient having Diabetes Mellitus Type I when the other covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease were taken into consideration. These results can be seen in Table 19.

Table 17

Regression Evaluating DMI as a Contributing Factor to CDI with Respect to the Covariates of Age, Sex, Abdominal Surgeries and Inflammatory Bowel Disease:

Variables in the Equation

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Age in Years	.034	.002	377.965	1	.000	1.035	1.031	1.039
	Sex(1)	.055	.060	.833	1	.361	1.057	.939	1.189
	IBD(1)	-1.089	.219	24.704	1	.000	.337	.219	.517
	AS(1)	-.126	.181	.483	1	.487	.882	.619	1.257
	DM1(1)	-.987	.295	11.231	1	.001	.373	.209	.664
	Constant	-4.787	.411	135.892	1	.000	.008		

a. Variable(s) entered on step 1: Age in Years, Sex, IBD, AS, DM1.

An additional logistic regression analysis was performed to investigate whether Diabetes Mellitus Type I contributed significantly to acquisition of *Clostridium difficile* infection. This second logistic regression analysis was executed to investigate whether having Diabetes Mellitus Type I contributed significantly to acquisition of *Clostridium difficile* infection when the covariates of age, sex, preexisting abdominal surgeries, and inflammatory bowel disease were included in the analysis. The predictor variable of previous diagnosis with Diabetes Mellitus Type I was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, previous diagnosis with Diabetes Mellitus Type I, in the logistic regression analysis was found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.787, SE = .411, Wald = 135.892, $p < .001$. With regard to the unstandardized Beta weight for the predictor variable previous diagnosis with Diabetes Mellitus Type I, B =-.987, SE = .295, Wald = 11.231, and $p = .001$. Results also revealed that Exp B = .373, and the 95% Confidence Interval was (.209, .664). The *p*-value of .001 did indicate the association of development of *Clostridium difficile* infection when a patient had the previous diagnosis of Diabetes Mellitus Type I. When explored with the accompanying covariates of age, sex, preexisting abdominal surgeries and IBD, the variable DM1, with a Sig. (*p*-value) of .001, is a statistically significant contributor to acquisition of *Clostridium difficile* infection, so the null hypothesis would not be accepted.

Conclusion for RQ2

It can be concluded that having Diabetes Mellitus Type I is in fact associated with increased incidence of *Clostridium difficile* infection when Diabetes Mellitus Type I is examined in a regression with the covariates of age, sex, preexisting abdominal surgeries and

Inflammatory bowel disease, However, the variable of Diabetes Mellitus Type I loses statistical significance when it is the only variable explored in the bivariate regression.

Research Question 3: Diabetes Mellitus Type II

RQ3: Is there a relationship between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$3: There is not a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a3: There is a statistically significant association between Diabetes Mellitus Type II and development of *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

The next category to be examined is Diabetes Mellitus Type II and its relationship to *Clostridium difficile* infection.

Table 18

Patients in the Study Population Determined to Have Diabetes Mellitus Type II (DM2)

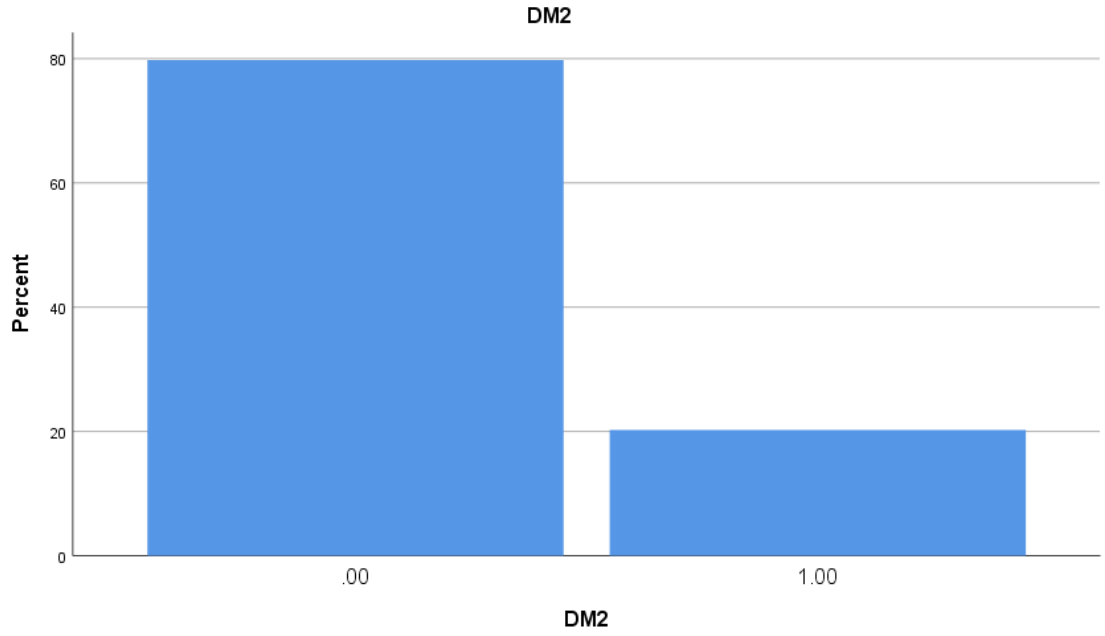
DM2 (Diabetes Mellitus Type II) based upon ICD-9 codes

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**Does not have DMII**	103067	79.8	79.8	79.8
	Has DMII	26133	20.2	20.2	100.0
	Total	129200	100.0	100.0	
Missing	System	9	.0		
Total		129209	100.0		

This categorical variable table indicates that 26133/129200 individuals, or 20.2% of the population has been documented through ICD-9 coding to be diagnosed with Diabetes Mellitus Type II. 103067/129200, or 79.8% of the population is documented to not have been diagnosed with Diabetes Mellitus Type II. This relationship can be seen in Figure 3.

Figure 3

Bar Chart of Percentages of Patients Diagnosed with Diabetes Mellitus Type II (0 = DMII neg; 1 = DMII pos)



Note: 20.2% of the study population has been verified through ICD-9 coding to have a diagnosis of Diabetes Mellitus Type II

Logistic Regression: Diabetes Mellitus Type II (DM2)

The case processing summary revealed that there were 129200 patients evaluated in the regression. 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the patient population of interest, 26133 individuals were documented to have a diagnosis of Diabetes Mellitus Type II.

A logistic regression analysis to investigate whether Diabetes Mellitus Type II contributed significantly to acquisition of *Clostridium difficile* infection. The predictor variable of previous diagnosis with Diabetes Mellitus Type II was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, previous diagnosis with Diabetes Mellitus Type II, in the logistic regression analysis was not found to contribute to the model. The unstandardized Beta weight for the Constant; B = -4.739, SE = .034, Wald = 19901.032, and $p < .001$. With regard to the unstandardized Beta weight for the predictor variable previous diagnosis with Diabetes Mellitus Type II, B =.062, SE = .073, Wald = .720, and $p = .396$. Results also revealed that Exp B = 1.064, and the 95% Confidence Interval was (.922, 1.227). The *p*-value of .396 did not indicate the association of development of *Clostridium difficile* infection when a patient had a previous diagnosis of Diabetes Mellitus Type II. The hypothesis that there is no association between a patient diagnosis of Diabetes Mellitus Type II and *Clostridium difficile* infection is accepted because the *p*-value (Sig.), which is .396, is larger than the critical *p*-value of .05.

A secondary logistic regression was then performed to determine the significance of a patient having Diabetes Mellitus Type II when the other covariates of age, sex, preexisting

abdominal surgeries and inflammatory bowel disease were taken into consideration. These findings can be seen in Table 21.

Table 19

Regression Evaluating DMII as a Contributing Factor to CDI With Respect to the Covariates of Age, Sex, Abdominal Surgeries and Inflammatory Bowel Disease:

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Age in Years	.034	.002	380.714	1	.000	1.035	1.031	1.038
	Sex(1)	.061	.060	1.040	1	.308	1.063	.945	1.197
	IBD(1)	-1.073	.219	23.990	1	.000	.342	.223	.525
	AS(1)	-.122	.181	.452	1	.501	.886	.621	1.262
	DM2(1)	-.156	.073	4.541	1	.033	.855	.741	.988
	Constant	-5.748	.295	378.613	1	.000	.003		

a. Variable(s) entered on step 1: Age in Years, Sex, IBD, AS, DM2.

An additional logistic regression analysis was performed to investigate whether Diabetes Mellitus Type II contributed significantly to acquisition of *Clostridium difficile* infection. This second logistic regression analysis was executed to investigate whether having Diabetes Mellitus Type II contributed significantly to acquisition of *Clostridium difficile* infection when the covariates of age, sex, preexisting abdominal surgeries and IBD were included in the analysis. The predictor variable of previous diagnosis with Diabetes Mellitus Type II was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, previous diagnosis with Diabetes Mellitus Type II,

in the logistic regression analysis was found to contribute to the model. The unstandardized Beta weight for the Constant; B = -5.748, SE = .295, Wald =378.613, $p < .001$. With regard to the unstandardized Beta weight for the predictor variable previous diagnosis with Diabetes Mellitus Type II, B =-.156, SE =.073 , Wald = 4.541, and $p = .033$. Results also revealed that Exp B = 855, and the 95% Confidence Interval was (.741, .988). The *p*-value of .033 did indicate the association of development of *Clostridium difficile* infection when a patient had the previous diagnosis of Diabetes Mellitus Type II. When explored with the accompanying covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease, the variable DMI1, with a Sig. (*p*-value) of .033, is a statistically significant contributor to acquisition of *Clostridium difficile* infection, so the null hypothesis would not be accepted.

Conclusion for RQ3

It can be concluded that having Diabetes Mellitus Type II is in fact associated with increased incidence of *Clostridium difficile* infection when Diabetes Mellitus Type II is examined in a regression with the covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease, However, the variable of Diabetes Mellitus Type II loses statistical significance when it is the only variable explored in the bivariate regression.

Research Question 4: Region

Is region significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$4: Region is not significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a4: Region is significantly associated with *Clostridium difficile* infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

The next category to be examined is geographic location of the patient and the relationship of the location of the patient to *Clostridium difficile* infection. Four geographic regions were explored. The Northeast region included the states of Maine, New Hampshire, Vermont, Massachusetts, Connecticut, Rhode Island, New York, New Jersey, and Pennsylvania. The Midwest region included the states of Michigan, Illinois, Ohio, Indiana, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, and Kansas. The South region included the states of Delaware, Maryland, the District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma, and Texas. The West region included the states of Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Hawaii, and Alaska. The distribution of the geographic location of the patients in this study can be seen in Table 22.

Table 20

Geographic Location of Patients in the Study Population; NE=Northeast NW=Midwest S=South W=West

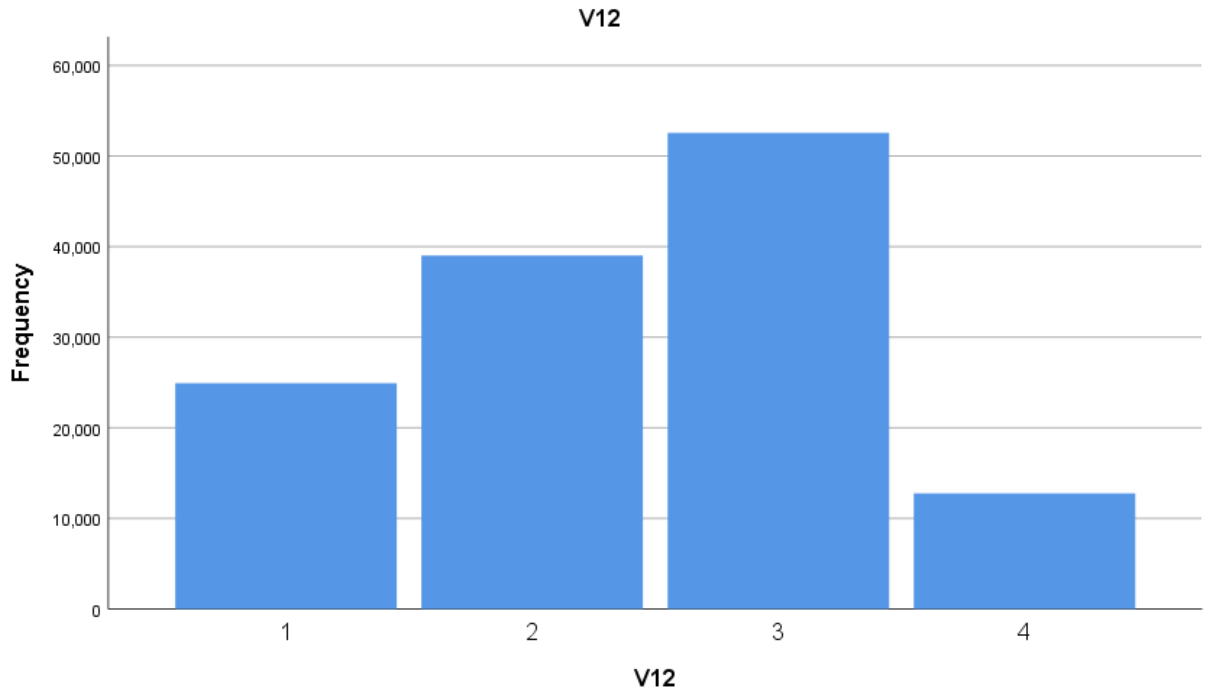
Geographic location of patient

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NE	24916	19.3	19.3	19.3
	MW	39008	30.2	30.2	49.5
	S	52527	40.7	40.7	90.1
	W	12757	9.9	9.9	100.0
	Total	129208	100.0	100.0	
Missing	System	1	.0		
Total		129209	100.0		

19.3% of the patients were from Region 1 (the Northeast), 30.2% of the patients were from region 2 (the Midwest), 40.7% of the patients were from Region 3 (the South) and 9.9% of the patients were from Region 4 (the West). Region 3 (the South) is most significantly represented by this data set. Geographic location of the patient is being investigated as to whether there is correlation with *Clostridium difficile* infection. This distribution can be seen in Figure 4.

Figure 4

Geographic Distribution of the Study Population.



Note: 24916 patients are from the Northeast (1), 39008 patients are from the Midwest (2), 52527 patients are from the South (3), and 12757 patients are from the West (4)

Logistic Regression: Geographic Location of Patient

Data analysis revealed that there were 129200 patients evaluated in the regression. 1135 of the patients had been diagnosed with *Clostridium difficile* infection. Of the patient population of interest, 24916 patients are from the Northeast, 39008 patients are from the Midwest, 52527 patients are from the South, and 12757 patients are from the West.

A logistic regression analysis was performed to investigate whether the geographic region of the patient contributed significantly to acquisition of *Clostridium difficile* infection. The predictor variable of geographic region of the patient was tested a priori to verify that there

was no violation of the assumption of the linearity of the logit. The predictor variable, geographic region of the patient, in the logistic regression analysis, was found to contribute to the model. Four geographic regions were examined. The overall *p*-value for the variable was .092, which is not statistically significant in itself, but when each region was assessed individually, patients from the South demonstrated a p-value of .013, which is statistically significant. The unstandardized Beta weight for the Constant; B = -4.659, SE = .066, Wald = 5030.506, and $p < .001$. The unstandardized Beta weight for the predictor variable of geographic region South is B = -.311, SE = .126, Wald = 6.141, and $p = .013$. The estimated odds ratio favored an increase likelihood of acquisition of *Clostridium difficile* infection of .733 with every unit increase in being from the South. The estimated odds ratio favored an increase of nearly 36% (Exp B = .733), 95% Confidence Interval (.573, .937) for development of *Clostridium difficile* infection for each one unit increase in the event that the patient was admitted to an acute care facility in the South. In this model, Geographic Location is statistically significant with respect to Region 3 (South) as manifested by a Sig. (probability) value of .016, which is below the cutoff value of .05.

A secondary logistic regression was then performed to determine the significance of the geographic region of the patient when the other covariates of age, sex, preexisting abdominal surgeries and IBD were taken into consideration. This can be seen in Table 23.

Table 21

Regression Evaluating Geographic Location of Patient as a Contributing Factor to CDI with Respect to the Covariates of Age, Sex, Abdominal Surgeries and Inflammatory Bowel Disease

Variables in the Equation

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Age in Years	.034	.002	370.841	1	.000	1.035	1.031	1.038
	Sex(1)	.057	.060	.907	1	.341	1.059	.941	1.192
	IBD(1)	-1.077	.219	24.174	1	.000	.341	.222	.523
	AS(1)	-.127	.181	.495	1	.482	.881	.618	1.255
	Geographic Reg			3.991	3	.262			
	V12(1)	.232	.126	3.410	1	.065	1.262	.986	1.614
	V12(2)	.200	.120	2.759	1	.097	1.221	.965	1.545
	V12(3)	.224	.117	3.681	1	.055	1.251	.995	1.573
	Constant	-5.947	.312	362.856	1	.000	.003		

a. Variable(s) entered on step 1: Age in Years, Sex, IBD, AS, V12(geographic region)

An additional logistic regression analysis was performed to investigate whether geographic region of the patient contributed significantly to acquisition of *Clostridium difficile* infection. This second logistic regression analysis was executed to investigate whether geographic region of the patient contributed significantly to acquisition of *Clostridium difficile* infection when the covariates of age, sex, preexisting abdominal surgeries and IBD were included in the analysis. The predictor variable of geographic region was tested a priori to verify that there was no violation of the assumption of the linearity of the logit. The predictor variable, geographic region, in the logistic regression analysis was found to contribute

less significantly to the model than when evaluated without the covariates. The unstandardized Beta weight for the Constant; B = -5.947, SE = 312, Wald =362.856, $p < .001$. With regard to the unstandardized Beta weight for the predictor variable geographic region, Region 3 held statistical significance in the initial univariate analysis. Evaluation of Region 3 with respect to the covariate analysis revealed B =.224, SE =117, Wald = 362.856, and $p = .055$. Results also revealed that Exp B =1.251, and the 95% Confidence Interval was (.995, 1.573). The *p*-value of .055 did not indicate as strong of an association of development of *Clostridium difficile* infection when a patient had geographic origin from the South. When explored with the accompanying covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease, the variable of patient geographic origin of the South, with a Sig. (*p*-value) of .055, is not a strongly statistically significant contributor to acquisition of *Clostridium difficile* infection, so the null hypothesis will not be rejected.

Conclusion for RQ4

It can be concluded that the geographic region that the patient was hospitalized in is in fact associated with increased incidence of *Clostridium difficile* infection when the geographic region of the South is examined in a regression when it is the only variable explored in the bivariate regression. In this situation geographic location is statistically significant with respect to Region 3 (South) as manifested by a Sig. (probability) value of .013, which is below the cutoff value of .05. When the geographic region of the South is explored with the covariates of age, sex, preexisting abdominal surgeries and inflammatory bowel disease, the variable of geographic region of patient hospitalization, the South, loses statistical significance.

A regression was then performed examining the combined effects of the independent variables age, sex, Diabetes Mellitus Type I, Diabetes Mellitus Type II, previous abdominal surgeries, presence of inflammatory bowel disease, and the conditions of being overweight.

Table 22

Regression Addressing the Combined Effects of the Independent Variables of Age, Sex, Diabetes Mellitus Type I, Diabetes Mellitus Type II, Previous Abdominal Surgeries, Presence of Inflammatory Bowel Disease, and the Conditions of Being Overweight as Contributing Factors to CDI

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	HIBMI(1)	-.186	.213	.763	1	.382	.831	.548	1.260
	DM1(1)	-.956	.295	10.508	1	.001	.384	.216	.685
	DM2(1)	.144	.073	3.864	1	.049	1.155	1.000	1.334
	IBD(1)	-1.080	.219	24.301	1	.000	.340	.221	.522
	AS(1)	-.129	.181	.509	1	.476	.879	.617	1.253
	Sex(1)	-.059	.060	.950	1	.330	.943	.838	1.061
	Age in Years	.034	.002	380.756	1	.000	1.035	1.032	1.039
	Constant	-4.883	.420	135.374	1	.000	.008		

a. Variable(s) entered on step 1: HIBMI, DM1, DM2, IBD, AS, Sex, Age in Years.

The Variables in Equation Table, including the Wald test, was utilized to determine statistical significance for each of the independent variables. This information can be reviewed by utilizing the "Sig." column, which represents probability. A Sig. value of .05 or less signifies

statistical significance. From these results it can be established that Age in Years (p = .000), IBD (p = .000), DM1(p = .001) and DM2 (p = .049) contributed significantly to the likelihood of *Clostridium difficile* infection, but AS (p = .476) did not contribute significantly to patient acquisition of *Clostridium difficile* infection. The information in this table also includes the Odds Ratio (OR) which can be used to predict the probability of an event occurring. Predictive value for each variable tells the significance of each individual independent variable when the significance of variables not being evaluated is held constant. This established the influence of a 1-unit change of the independent variable on the dependent variable. In the above table, the OR demonstrates that with every year increase in age the odds of acquiring *Clostridium difficile* infection increase by 1.035.

Another regression was then performed examining the combined effects of the independent variables age, sex, geographic location, Diabetes Mellitus Type I, Diabetes Mellitus Type II, previous abdominal surgeries, presence of inflammatory bowel disease, and the condition of being overweight. This regression can be seen in Table 25.

Table 23

Regression addressing the combined effects of the independent variables age, sex, geographic location, Diabetes Mellitus Type I, Diabetes Mellitus Type II, previous abdominal surgeries, presence of inflammatory bowel disease, and the condition of being overweight upon CDI

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR	95% C.I. for OR Lower	Upper
Step 1[a]	Age in Years	.034	.002	379.095	1	.000	1.035	1.031	1.039
	Sex	.060	.060	.994	1	.319	1.062	.944	1.195
	Geographic location NE			4.090	3	.252			
	Geographic location MW	.233	.126	3.424	1	.064	1.262	.986	1.615
	Geographic location S	.201	.120	2.793	1	.095	1.223	.966	1.547
	Geographic location W	.228	.117	3.820	1	.051	1.256	.999	1.580
	DM1(1)	-.955	.295	10.494	1	.001	.385	.216	.686
	DM2(1)	.148	.074	4.024	1	.045	1.159	1.003	1.339
	HIBMI(1)	.179	.213	.708	1	.400	1.196	.788	1.814
	AS(1)	-.135	.181	.556	1	.456	.874	.613	1.246
	IBD(1)	1.076	.219	24.107	1	.000	2.932	1.908	4.505
	Constant	-6.395	.424	227.996	1	.000	.002		

a. Variable(s) entered on step 1: Age in Years, sex, geographic location, DM1, DM2, HIBMI, AS, IBD.

The Variables in Equation Table, including the Wald test, was utilized to determine statistical significance for each of the independent variables. This information can be reviewed by utilizing the "Sig." column, which represents probability. A Sig. value of .05 or less signifies statistical significance. From these results it can be established that Age in Years (p = .000), IBD (p = .000), DM1(p = .001) and DM2 (p = .045) contributed significantly to the likelihood of *Clostridium difficile* infection. V12 (geographic location 3), which represents patients in the United States from the South may also demonstrate statistical significance (p = .051) but Abdominal Surgery (p = .456) did not contribute significantly to patient acquisition of *Clostridium difficile* infection.

Summary of Data Analysis

Data analysis of frequencies and binary logistic regression reveals some expected outcomes and some surprises. It was not surprising that the data revealed that increasing age leads to increasing likelihood of *Clostridium difficile* infection. It also was not surprising that it was revealed that a history of Inflammatory Bowel Disease (Ulcerative Colitis and Crohn's Disease) predisposed an individual to an increased likelihood of *Clostridium difficile* infection. It was not speculated that a history of Diabetes Mellitus Type I would enhance likelihood of *Clostridium difficile* infection, and evaluation of the data demonstrated that this lack of association was true for the univariate analysis, but the multivariate analysis revealed a correlation between acquisition of *Clostridium difficile* infection and a history of Diabetes Mellitus Type I. For Diabetes Mellitus Type I the multivariate analysis revealed significance, while the univariate analysis did not. This could be due to omitted variable bias. The performance of a regression of only one predictor may result in inconsistent or erroneous results

and must be interpreted carefully. Although it was expected that a history of abdominal surgery would increase the likelihood of *Clostridium difficile* infection, the data did not support this hypothesis. It was anticipated that there may be an association between Diabetes Mellitus Type II and increased susceptibility to *Clostridium difficile* infection, but the data from the univariate analysis did not support this hypothesis. However, the data generated from the multivariate analysis indicated an association. The lack of correlation in the univariate analysis between Diabetes Mellitus Type II in the study group and acquisition of *Clostridium difficile* infection was unexpected. Again, since the regression was performed on a singular predictor, omitted variable bias may be to blame. It was also anticipated that there might be an association between increased Body Mass Index and increased susceptibility to *Clostridium difficile* infection. Univariate regression analysis supported this theory, while multivariate analysis did not. The lack of correlation in the multivariate analysis between high Body Mass Index in the study group and acquisition of *Clostridium difficile* infection was also unexpected. Diabetes Mellitus Type II and obesity are frequently associated with increased susceptibility to infection. Another surprising result revealed by the data was the association between increased *Clostridium difficile* infection and the patient being discharged from a hospital designated geographically in the South, which includes the states of Delaware, Maryland, the District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma and Texas. The association established by the univariate analysis ($p = .013$) was stronger than the association established in the multivariate analysis ($p = .051$).

Chapter 5: Discussion, Conclusions, and Recommendations

The purpose of this study was to establish whether Diabetes Mellitus Type I, Diabetes Mellitus Type II and obesity, or a combination of these disorders predisposes the affected individual to increased likelihood of development of a nosocomial *Clostridium difficile* infection in the acute healthcare hospital settings. The study also explored whether there is a geographic component related to susceptibility to *Clostridium difficile* infection.

Variables 17–31 in the data set represented patient diagnoses based upon ICD-9 coding. Upon discharge, the patients were assigned one to 15 codes, dependent upon the diagnosis of their illness/debilitation. Discharge diagnoses of interest included the diagnosis of *Clostridium difficile* infection, Diabetes Mellitus Type I, Diabetes Mellitus Type II, the presence of Inflammatory Bowel Disease, a history of abdominal surgery, and whether the patient was overweight or not. All overweight, obese, and morbidly obese patients were grouped into the single category of HIBMI. Research questions addressed in the study were as follows:

Research Question 1: Is there a relationship between obesity and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$1: There is not a statistically significant association between obesity and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a1: There is a statistically significant association between obesity and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 2: Is there a relationship between Diabetes Mellitus Type I and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$2: There is not a statistically significant association between Diabetes Mellitus Type I and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a2: There is a statistically significant association between Diabetes Mellitus Type I and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 3: Is there a relationship between Diabetes Mellitus Type II and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$3: There is not a statistically significant association between Diabetes Mellitus Type II and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a3: There is a statistically significant association between Diabetes Mellitus Type II and development of Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Research Question 4: Is region significantly associated with Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery?

$H_0$4: Region is not significantly associated with Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

H_a4: Region is significantly associated with Clostridium difficile infection in patients hospitalized in the acute care setting, after controlling for age, sex, preexisting bowel disease, and previous abdominal surgery.

Discussion and Conclusions

The data of the entire population was evaluated regarding age, sex, and geographic location. Because the study only addressed adults, data evaluated were restricted to those patients greater than 17 years of age. Initial data analysis examined the ages of the patient population. Nine percent (9.3%) of patients discharged in the study were newborns. The data set indicates that 22,204 individuals under the age of 18 were included in the total population. Because the study focused upon adult patients, the data from the pediatric population were not included in the study. Of the 151,551 individuals addressed in the study, 85.3% of patients were 18 years of age or older. Utilizing this percentage, 129,273 patients fell into the adult age group. It is stated in the NHDS data set that all patients 90 years of age or greater were counted as 90 years of age; 3.4% of patients fell in this age group. Variable 3 is a nominal variable associated with age (1=Years 2=Months 3=Days). Data included revealed that 89.4% of the ages were

reported in years, 0.9% of the ages were reported in months, and 9.8% of the ages were reported in days.

Since the study focuses upon adult patients, the data from the pediatric population would not be included in the study. For the purpose of this study, data analyzed from Variable 3 were restricted to the value of "1" only (years). To further restrict the ages of the patients to only those individuals 18 years of age or older, Variable 4, also an age variable, was subsequently restricted to values > 17. Variable 4 is a scale variable associated with age in terms of years, months, or days (If units=years: 00-90; If units=months: 01-11; If units=days: 00-28). Ages 91 and over were recoded to 90. This revealed that the mean age of the patient population was 57.96 years of age. The mode was 60 years of age. The patient populating being studied was reduced from 151,551 individuals to 129,273 individuals greater than 17 years of age.

The total patient population having an ICD-9 classification of *Clostridium difficile* infection was 1,135 individuals. The mean age of this population was 70.13 years of age, which was older than the mean age of the general population in the study of 57.96 years old. Because there was no age differentiation for those individuals 90 years of age and older, it is likely that the mean age of this population may have been higher.

Regarding sex, data evaluated with application of age restriction indicated that the patient population was 40.3% male and 59.7% female. The data indicated that in the patients suffering from *Clostridium difficile* in this population, 43.5% were male and 56.5% were female. A greater percentage of female inpatients suffered from CDI than their male counterparts.

Regarding race, the age-restricted data indicated a patient population that was predominantly White. 64.9% of the patients were White, 13.8% were Black/African American, 0.2% were American Indian/Alaskan Native, 1.2% were Asian, 0.0% were Native Hawaiian/Other Pacific Islander, 4.9% reported their race as "Other", and 0.1% reported Multiple Race as their ethnicity. 14.9% did not state their race.

The age restricted data of patients suffering from *Clostridium* infection again indicated a patient population that was predominantly White. 75.5% of the patients were White, 9.8% were Black/African American, 0.1% were American Indian/Alaskan Native, 1.2% were Asian, 0.0% were Native Hawaiian/Other Pacific Islander, 3.9% reported their race as "Other", and 0.0% reported Multiple Race as their ethnicity. 9.5% did not state their race.

Discharge status of the entire patient population was assessed, which was quite important to the study at hand. Status of particular interest was whether the patient had died. Analysis of the entire patient population revealed that 2784 patients, or 1.8% of the patient population was deceased upon discharge.

Sex of the entire patient population that had died was assessed. Of the 2784 individuals who were dead upon discharge, 49.5% were male and 50.5% were female. The data was reexamined utilizing age restriction criteria, only examining data from patients 18 years of age or greater. Analysis of the age-restricted patient population revealed that 2705 patients, or 2.1% of the patient population were deceased upon discharge. Sex of the age-restricted group who were dead upon discharge was then examined. Analysis of the age-restricted patient population revealed that of the 2705 deceased patients, 49.4% of the population were male and 50.6% were

female. Sex evaluation of patients who were dead upon discharge and who suffered from *Clostridium difficile* infection was then performed. Analysis of the patient population suffering from *Clostridium difficile* infection revealed that of the 79 deceased patients in this group, 45.6% of the population were male and 54.4% were female.

Data were assessed in the *Clostridium difficile* patient group that addressed geographic origin of the patient population. Patient admissions were grouped into 4 broad geographic regions. These regions included the West, the Northeast, the Midwest and the South. Patients from the West comprised the smallest group analyzed. This group consisted of 91 individuals. 36 of the patients were male, and 55 of the patients were female. Regarding race, 71.4% were White, 9.9% were Black, 5.5% were Asian, 12.1% were Not Specified, and 1.1% were listed as "Other". Regarding age, 3.3% of patients were 18-29 years of age, 4.4% of patients were 30-39 years of age, 12% of patients were 40-49 years of age, 8.8% of patients were 50-59 years of age, 23% of patients were 60-69 years of age, 24.3% of patients were 70-79 years of age, 18.7% of patients were 80-89 years of age, and 5.5% of patients were 90 years of age or greater. 2.2% of patients suffered from Diabetes Mellitus Type I, 23.1% of patients suffered from Diabetes Mellitus Type II, 3.3% of patients suffered from obesity, and 2.2% of patients suffered from both Diabetes Mellitus Type II and obesity. 4.4% of the patients were dead at discharge. Of this demographic, 100% were White, 25% suffered from Diabetes Mellitus Type II, 50% were Male and 50% were female. The mean age of death for this demographic was 80.75 years of age.

Patients from the Northeast comprised the next group analyzed. This group consisted of

234 individuals. 96 of the patients were male, and 138 of the patients were female. Regarding race, 78.8% of patients were White, 8.1% of patients were Black, 2.5% of patients were Asian, 8.1% of patients were categorized as "Not Specified", 1.3% of patients were listed as "Other", and 0.4% of patients were listed as "Nothing". Regarding age, 1.7% of patients were 18-29 years of age, 4.3% of patients were 30-39 years of age, 8.5% of patients were 40-49 years of age, 7.8% of patients were 50-59 years of age, 10.3% of patients were 60-69 years of age, 21.4% of patients were 70-79 years of age, 32.9% of patients were 80-89 years of age, and 10.7% of patients were 90 years of age or greater. 0% of patients suffered from Diabetes Mellitus Type I, 16.7% of patients suffered from Diabetes Mellitus Type II, 3.4% of patients suffered from obesity, and 1.7% of patients suffered from both Diabetes Mellitus Type II and obesity. 3.8% of the patients were dead at discharge. Of those dead at discharge, 66.7% were White, and 33.3% were listed as "Other". 0.4% of these patients suffered from Diabetes Mellitus Type II. 22.2% of these patients were Male and 77.8% of these patients were female. The approximate mean age of death for this demographic was 84.22 years of age. This value is estimated because 4 of the patients who died were listed as greater than or equal to 90 years of age, so the approximate mean age of death listed was probably slightly lower than the actual value.

Patients from the Midwest comprised the next group analyzed. This group consisted of 335 individuals. 162 of the patients were male, and 173 of the patients were female. Regarding race, 77% of patients were White, 6% of patients were Black, 0.3% of patients were Asian, 15.2% of patients were "Not Specified", and 1.5% of patients were listed as "Other". Regarding age, 3.3% of patients were 18-29 years of age, 3% of patients were 30-39 years of age, 6.9% of patients were 40-49 years of age, 13.4% of patients were 50-59 years of age, 17.3% of patients

were 60-69 years of age, 23.6% of patients were 70-79 years of age, 26.4% of patients were 80-89 years of age, and 5.7% of patients were 90 years of age or greater. 2.1% of these patients suffered from Diabetes Mellitus Type I, 20.6% of these patients suffered from Diabetes Mellitus Type II, 4.2% suffered from obesity, and 2.1% suffered from both Diabetes Mellitus Type II and obesity. 6.3% of the patients were dead at discharge. Of those patients dead at discharge, 71.4% were White, 19% were listed as "Not Specified", and 9.6% were Black. 0.9% of those patients suffered from Diabetes Mellitus Type II, and 0.3% were documented to be overweight. 47.6% of those patients were Male and 52.4% were female. The approximate mean age of death for this demographic was 75.67 years of age. This value is estimated because 2 of the patients who died were listed as greater than or equal to 90 years of age, so the approximate mean age of death listed is probably slightly lower than the actual value.

Patients from the South comprised the largest group analyzed. This group consisted of 477 individuals. 203 of the patients were male, and 274 of the patients were female. Regarding race, 73.4% of patients were White, 14.9% of patients were Black, 0% of patients were Asian, 4.8% of patients were "Not Specified", and 6.9% of patients were listed as "Other". Regarding age, 2.3% of patients were 18-29 years of age, 2.7% of patients were 30-39 years of age, 7.1% of patients were 40-49 years of age, 11.5% of patients were 50-59 years of age, 17.8% of patients were 60-69 years of age, 22.9% of patients were 70-79 years of age, 23.4% of patients were 80-89 years of age, and 7.8% of patients were 90 years of age or greater. 1.3% of these patients suffered from Diabetes Mellitus Type I, 24.3% suffered from Diabetes Mellitus Type II, 7.1% suffered from obesity, and 3.6% of these patients suffered from both Diabetes Mellitus Type II and obesity. 8.8% of the patients were dead at discharge. Of those patients dead at discharge,

73.8% were White, 19% were Black, and 7.2% were listed as “Other”. 21.4% of patients dead at discharge suffered from Diabetes Mellitus Type II, and 2.4% of these patients were obese. 52.4% were Male and 47.6% were Female. The approximate mean age of death for this demographic was 72.3 years of age. This value is estimated because 3 of the patients who died were listed as greater than or equal to 90 years of age; for this reason, the approximate mean age of death listed is probably slightly lower than the actual value.

In summary regarding geographic region, 19.3% of the patients were from Region 1 (the Northeast), 30.2% of the patients were from region 2 (the Midwest), 40.7% of the patients were from Region 3 (the South) and 9.9% of the patients were from Region 4 (the West). Region 3 (the South) is still most significantly represented by this data set. Examination of the adult population revealed 20.6% of the patients were from Region 1 (the Northeast), 30.2% of the patients were from region 2 (the Midwest), 41.5% of the patients were from Region 3 (the South) and 7.7% of the patients were from Region 4 (the West). Region 3 (the South) remains most significantly represented by this data set.

The study revealed a variety of interesting findings, both inspected and unexpected. Literature review implicated age as a significant predictor of susceptibility to *Clostridium difficile* infection. It was not surprising that the data generated in the study supported the literature. Younger patients demonstrated less incidence of *Clostridium difficile* infection than older patients, though it was interesting to note that for each decade of life from 18 years of age until greater than 90 years of age the number of infections consistently rose. Exceptions were noted at 40 years of age, 51 years of age, and 58 years of age. A strong association between age

and *Clostridium difficile* infection was especially evident in those individuals 61 years of age and greater. Overall, the data revealed that with every year increase of age the odds of acquiring *Clostridium difficile* infection increased by 1.03.

Literature review also revealed that underlying chronic disease, traumas, and factors that diminish overall health also increased an individual's susceptibility to infection. Overall, it was speculated that chronic inflammation is a contributing factor to infection susceptibility. One type of chronic infirmity that seems to predispose an individual to *Clostridium difficile* infection is inflammatory bowel disease, such as ulcerative colitis and Crohn's disease. Patients with Crohn's disease or ulcerative colitis have greater morbidity and mortality from *Clostridium difficile* infection than the general population. In the study population, 0.8% (1016 individuals) were documented to suffer from inflammatory bowel disease. Of these 1016 individuals, 22 had concurrent *Clostridium difficile* infections. Statistical analysis revealed an odds ratio of .009 and a *p*-value of .000. It can be concluded that inflammatory bowel disease is a statistically significant predictor of *Clostridium difficile* infection. This conclusion coincided with documentation in the literature.

Abdominal surgery, particularly colorectal surgery, has been cited in the literature as a cause of increased susceptibility to *Clostridium difficile* infection in patient populations. 2.5% of the study population (3187 individuals) had experienced abdominal surgery. Of the 3187 individuals who had experienced abdominal surgery, 32 patients were simultaneously diagnosed with *Clostridium infection*. Binary logistic regression generated a *p*-value of 0.442, which is larger than the critical *p*-value of 0.05. Based upon the data generated in the study, abdominal surgery was not a statistically significant predictor of *Clostridium difficile* infection. This

information contradicted information found in the literature review.

Obesity was examined as a potential predictor of *Clostridium difficile* infection. The literature review cited obesity as a factor that increases susceptibility to *Clostridium difficile* infection for two main reasons. The first reason is that obesity triggers the production of inflammatory cytokines that contribute to *Clostridium difficile* infection. The second reason is that obesity causes a change in the types of organisms that comprise the gut normal flora, making it easier for *Clostridium difficile* to thrive in the gastrointestinal tract. For the purpose of this study, all individuals documented to have a BMI greater than 25 were evaluated. These individuals were placed in the created category of HIBMI. The study revealed that 3.1% (4051 individuals) in the study population were documented to be overweight. For the variable of HIBMI the analysis revealed a p-value of .033, supporting literature findings that obesity does indeed contribute to *Clostridium difficile* infection. 23 of the documented 1135 patients suffering from *Clostridium difficile* infection were overweight.

As mentioned previously, chronic disease has been implicated in increased susceptibility to infection overall. It is speculated that increased inflammation is the contributing factor. Two disease states, Diabetes Mellitus Type I and Diabetes Mellitus Type II, are of particular interest. Diabetes Mellitus Type I, an autoimmune disorder, had not been addressed quite as extensively in the literature as Diabetes Mellitus Type II regarding its relationship to increased susceptibility to infection. It was decided to investigate whether there was a relationship between Diabetes Mellitus Type I and increased susceptibility to *Clostridium difficile* infection. Evaluation of the patient population revealed that 0.7% (911 individuals) carried a diagnosis of Diabetes Mellitus Type I. The case process summary revealed that of the 911 patients in the study population

diagnosed with Diabetes Mellitus Type I, only 12 of the patients also carried the diagnosis of *Clostridium difficile* infection. Binary logistic regression generated a *p*-value of 0.154, which was higher than the critical *p*-value of 0.05. Although there was not significant literature review addressing the relationship between Diabetes Mellitus Type I and *Clostridium difficile* infection, the conclusion was reached that Diabetes Mellitus Type I was not a significant predictor of *Clostridium difficile* infection.

Diabetes Mellitus Type II has been cited frequently in the literature as a contributing factor to enhanced susceptibility of an individual to infection. In the study population, 26132 individuals, or 20.2% of the study population were diagnosed with Diabetes Mellitus Type II based upon ICD-9 diagnostic codes. The case process summary revealed that of the 26132 patients in the study population diagnosed with Diabetes Mellitus Type II, 241 of the patients also carried the simultaneous diagnosis of *Clostridium difficile* infection. This represents only 0.92% of the patient population. On the other hand, of the 1135 patients in the study, 241 carried the diagnosis of Diabetes Mellitus Type II. This represents 21.2% of individuals with the diagnosis of *Clostridium difficile* infection. Binary logistic regression generated a *p*-value of 0.396, which is higher than the critical *p*-value of 0.05. Based upon data generated in the binary logistic regression, the conclusion was reached that Diabetes Mellitus Type II is not a significant predictor of *Clostridium difficile* infection.

Data generated addressing geographic location of the study population turned out to be of significance. 19.3% of the patients were from the Northeast (24916 individuals), 30.2% were from the Midwest (39008 individuals), 40.7% of the individuals were from the South (52527 individuals) and 9.9% of the population (12757 individuals) were from the West. Geographic

location of the individual was investigated as a potential predictor of *Clostridium difficile* infection. Logistic regression with respect to the individuals from the Northeast category revealed a *p*-value of 0.416. This value is greater than the critical *p*-value of 0.05. Based upon data generated in the binary logistic regression, the conclusion was reached that a patient being from the Northeast is not a significant predictor of *Clostridium difficile* infection. Next logistic regression with respect to the individuals from the Midwest category was performed. Data generated revealed a *p*-value of 0.561. This value is greater than the critical *p*-value of 0.05. Based upon data generated in the binary logistic regression, the conclusion was reached that a patient being from the Midwest is not a significant predictor of *Clostridium difficile* infection. Next logistic regression with respect to the individuals from the South category was performed. In this case data generated revealed a *p*-value of 0.013. This value is significantly less than the critical *p*-value of 0.05. Based upon data generated in the binary logistic regression, the conclusion was reached that a patient being from the South is a significant predictor of *Clostridium difficile* infection. Finally, data from individuals from the West were examined. Logistic regression with respect to the individuals from the West category revealed a *p*-value of 0.092. This value is greater than the critical *p*-value of 0.05. Based upon data generated in the binary logistic regression, the conclusion was reached that a patient being from the West was not a significant predictor of *Clostridium difficile* infection. Data revealed that overall, geographic location is a significant predictor of Clostridium difficile infection with respect to the South. This was demonstrated by a *p*-value of 0.013.

A subsequent multiple logistic regression was then performed utilizing the multiple independent variables of age, sex, Diabetes Mellitus Type I, Diabetes Mellitus Type II,

previous abdominal surgeries, presence of inflammatory bowel disease, and the condition of being overweight. Multiple logistic regressions performed utilizing the sum of these independent variables generated slightly different results than when the independent variables were run individually in a binary logistic regression format. From the evaluation of the multiple regressions data generated revealed p-values of significance for several of the independent variables. Independent variables that generated *p*-values of less than 0.05 when statistical evaluation was performed included age in years, with a *p*-value of 0.000. The odds-ratio generated when the independent variable of age was examined revealed that the chance of acquiring *Clostridium difficile* infection increased 1.035 with every additional year of advancing age. Regression results revealed that inflammatory bowel disease, with a p-value of 0.000, and Diabetes Mellitus Type I, with a *p*-value of .001 were also significant predictors of acquisition of *Clostridium difficile* infection. Data generated with Diabetes Mellitus Type II also revealed a significant *p*-value of .049. On the other hand, a history of abdominal surgery generated a *p*-value of 0.476, so it can be concluded that a diagnosis of previous abdominal surgery would not contribute significantly to acquisition of *Clostridium difficile* infection.

An additional regression was then performed to evaluate the combined effects of age, sex, Diabetes Mellitus Type I, Diabetes Mellitus Type II, geographic location, previous abdominal surgeries, presence of inflammatory bowel disease, and the condition of being overweight. A *p*-value of .05 or less indicates statistical significance. These results revealed statistical significance for the independent variables of age in years, (*p*-value = .000), and inflammatory bowel disease *(p*-value = .000). Both Diabetes Mellitus Type I (p-value of .001) and Diabetes Mellitus Type II (*p*-value of .045) ended up being statistically significant, while

geographic location (South) demonstrated a *p*-value of .051 when this multiple regression was performed, demonstrating a seemingly diminished significance when compared with the simple binary regression executed with geographic location as the independent variable and *Clostridium difficile* infection the dependent variable.

Reviewing all data generated both consistencies and inconsistencies that are revealed when current data is compared with data previously described in the literature. The literature described many situations as contributing factors to increased susceptibility to infection overall. These predisposing pathologies included congenital/acquired immunodeficiencies, chemotherapy, radiation therapy and post-transplant immunosuppressive therapies. The presence of inflammatory conditions was also documented to contribute to increased probability of infection. Obesity was reported to be one of these conditions that predisposes an individual to increased likelihood of infection. Obesity is noted to be associated with increased presence of inflammatory cytokines and a change in gut normal flora that is thought to contribute to an enhanced environment for the development of infection. Diabetes Mellitus Type II, an acquired disorder associated with elevated blood sugar, increased inflammation, and insulin resistance with respect to cellular uptake of glucose was also documented to be associated with increased overall susceptibility to infection. Diabetes Mellitus Type I, an autoimmune disease where autoantibodies destroy the insulin-producing alpha cells of the islets of Langerhans in the pancreas was also cited in the literature as a predisposing factor for infection, but there did not seem to be as strong of an association between infection and Diabetes Mellitus Type I as there was between infection and the presence of Diabetes Mellitus Type II in an individual. The literature also cited advancing age as a factor in increased susceptibility to infection.

Sex was a factor that was not truly addressed in the literature review that provided the foundation for this study. It would have been useful if it had been an initial consideration as a potential area of interest regarding susceptibility to *Clostridium difficile* infection. Subsequent literature review from a 2016 article examining sex and *Clostridium difficile* infection over a 12-year period in an acute care facility in Spain revealed some interesting outcomes. "In both sexes, a gradient in age-specific rates was observed" (Esteban-Vasallo, et al, 2016), which was not surprising, and supported by data generated in this study. However, the Madrid study revealed that a "significantly increasing trend was detected in women of age 45-84 years" (Esteban-Vasallo, et al, 2016, p. 1037). Although a gender/sex age relationship was not explored in this study, it was noted that a greater percentage of male patients suffered from *Clostridium difficile* infection than female patients. The NHDS data revealed a patient population of age 18 and greater that was 43.4% male and 56.6% female. When further examined, the data generated from the patients of the National Hospital Discharge Summary demonstrated that males were more likely to suffer from *Clostridium difficile* infection than females. Results generated in this study reveal that the sex of the patient was a statistically significant predictor of *Clostridium difficile* infection. A female patient in this study was approximately14% less likely to acquire *Clostridium difficile* infection than a male patient in this study.

When examining pre-existing conditions that contributed to enhanced acquisition of *Clostridium difficile* infection, the literature cited the presence of the following pre-existing conditions as significant. If the patient suffered from inflammatory bowel diseases such as ulcerative colitis or Crohn's disease, their chance of developing *Clostridium difficile* infection

increased. 1016 individuals in the patient population were diagnosed with inflammatory bowel disease. Of these individuals, 22 demonstrated concurrent *Clostridium difficile* infection. Data generated through performance of regression studies supported the fact that there is an association between inflammatory bowel disease and the development of *Clostridium difficile* infection. Both in the simple binary regression and the multiple regression setting, a *p*-value of .000 was generated, demonstrating clear association between inflammatory bowel disease and increased likelihood of *Clostridium difficile* infection. Another underlying factor that was documented to enhance development of *Clostridium* infection mentioned in the literature was if the patients had a history of abdominal surgery/surgeries. In the patient population of interest, 3187 individuals had a history of previous abdominal surgery. Of these individuals, 32 had a diagnosis of *Clostridium difficile* infection. A *p*-value of .442 was generated when a binary regression was performed using AS (abdominal surgery) as the independent variable, and *Clostridium difficile* as the dependent variable. Data generated in this study did not indicate an association between previous abdominal surgery and acquisition of *Clostridium difficile* infection, which refutes information cited in the literature.

The literature cited advancing age as a predisposing factor to increased susceptibility to all infection, but also as a predisposing factor to acquisition of *Clostridium difficile* infection. As the body ages, cellular and humoral immune function gradually declines, so it is not surprising that susceptibility to all types of infection increases. The data generated in this study supported literature findings that stated that the older the patient is, the more likely they are to acquire a *Clostridium difficile* infection. This study revealed that in individuals 18 years of age and older,

with few exceptions, the odds of a person of acquiring *Clostridium difficile* infection increases by 1.03 with each year of advancing age.

Diabetes and *Clostridium* infection both represent significant challenge with respect to patient outcome in the acute care setting. There was much less literature addressing the influence on infection rates of patients with Diabetes Mellitus Type I versus those suffering from Diabetes Mellitus Type II. This is most likely because Diabetes Mellitus Type I only represents 5% of diabetes mellitus cases. Even so, it seemed a worthwhile endeavor to determine whether any conclusions could be drawn between patients diagnosed with Diabetes Mellitus Type I and acquisition of *Clostridium difficile* in the patient population of interest. In the patient population being studied, 911 individuals, or 0.7% of the population had been diagnosed with Diabetes Mellitus Type I. Of these individuals, 12 had also been diagnosed with *Clostridium difficile* infection. The p-value generated in the binary regression was .154, which would not be considered statistically significant. However, when a multiple regression was performed utilizing several independent variables, the *p*-value for Diabetes Mellitus Type I was .001, indicating associative significance with *Clostridium difficile* infection. Although there was little information in the literature associating Diabetes Mellitus Type I and *Clostridium difficile* infection, regressions performed in this study revealed a possible link between the two pathologies.

Based upon literature review, there is an overall increased susceptibility to infection in patients suffering with Diabetes Mellitus Type II, as well as an increased incidence of *Clostridium difficile* infection. It was anticipated that a binary regression comparing Diabetes Mellitus Type II patients with those suffering from *Clostridium* would show significant

association. The *p*-value generated in the bivariate regression comparing the dependent variable of *Clostridium difficile* infection with the independent variable of Diabetes Mellitus Type II was .396, which supported the null hypothesis that there was not an association. This was not an anticipated finding of the study. When Diabetes Mellitus Type II was examined in the context of a multivariate analysis, the *p*-value generated was .049, which would indicate statistical significance. This result would be the more anticipated expectation based upon pertinent literature.

Obesity has been implicated as a predisposing factor to greater than normal incidence of infection in an individual. Obesity has been associated with increased inflammatory cytokines, and insulin resistance, which both can be considered as predisposing factors to infection. Above normal BMI has also been associated with increased susceptibility of nosocomial infection, including *Clostridium difficile* infection. Initially three categories of BMI were established for the condition of being overweight based upon ICD-9 codes, but these categories were eventually condensed into one code for purpose of data analysis. The code utilized was HIBMI and consisted of all individuals in the patient population with Body Mass Index (BMI) measurements of 25 or greater, encompassing the categories of overweight, obese, and morbidly obese. Examination of the data revealed that 3.1% of the study population (4051/129204) were overweight. There were 1135 patients in the study who were diagnosed with *Clostridium difficile* infection. Twenty-three of these patients were concurrently diagnosed as being overweight. Bivariate logistic regression utilizing HIBMI as the independent variable and *Clostridium difficile* infection as the dependent variable. Generated a p-value of .033, which is smaller than the critical p-value of .05 necessary to accept the null hypothesis. For the bivariate

regression it was concluded that being overweight was, in fact, associated with increased incidence of *Clostridium difficile* infection. This conclusion was an anticipated result, supported by the literature. Interestingly, when multiple regressions were executed to establish the influence of the numerous independent variables upon the dependent variable of *Clostridium difficile* infection, HIBMI generated a p-value of .031, further reinforcing the conclusion that there is a relationship between being overweight and increased susceptibility to *Clostridium difficile* infection.

Geographic location of the patient was a facet of *Clostridium difficile* infection not truly addressed in the literature. Patient geographic location was, however, a variable in the 2010 National Hospital Discharge Survey. As geographic location had not been explored in the literature as a factor in *Clostridium difficile* infection, the variable was of particular interest. Of the study population, 24916 patients were from the Northeast, 39008 patients were from the Midwest, 52527 patients were from the South, and 12757 patients were from the West. Overall, for all geographic regions, logistic regression revealed a *p*-value of .091, which in and of itself was not statistically significant. However, when each geographic region was examined individually, some interesting results ensued. Data from the Northeast revealed a *p*-value of .416, data generated from the Midwest generated a *p*-value of .561, and data from the West generated a p-value of .092, none of which bear statistical significance. Data generated from the regression with the condition of being from the South as the independent variable and *Clostridium difficile* infection being the dependent variable did reveal statistical significance, a result that was not predicted or anticipated. The *p*-value for this regression was .013, which

supported the rejection of the null hypothesis, and supported the association between being a patient in an acute care facility in the South and increased incidence of *Clostridium difficile* infection, possibly a new discovery.

Limitations

There were several limitations regarding the data utilized in this study. Susceptibility to *Clostridium difficile* infection has a definite association with the treatment of patients with certain antibiotics. Antibiotics commonly associated with acquisition of *Clostridium difficile* infection include cephalosporins, fluoroquinolones, amoxicillin, clindamycin. erythromycin, clarithromycin, azithromycin, and penicillin. At the onset of this study, it was believed that it would be possible to ascertain which antibiotics that the patient had taken before or during their admissions, but this information was not available. Another limitation to the data in the study was the uncertainty as to whether the condition of the patient being overweight, obese, or morbidly obese was verifiably recorded in the list of diagnoses for each patient. Regarding the geographic location of the patient admissions, it was impossible to verify whether the patient resided in the geographic location of the acute care facility where they were patients, or if they were visitors to the area.

Recommendations

Review of the patient data revealed many areas of potential future research regarding patients with *Clostridium difficile* infection. One of the major potential associations noted when reviewing the data was that a greater than anticipated number of patients with *Clostridium difficile* infection also suffered from sepsis. It was difficult to ascertain whether the patients succumbed to sepsis because of their underlying *Clostridium difficile* infection, or whether the

presence of sepsis contributed to their acquisition of *Clostridium difficile* infection. It also seemed that a greater than anticipated number of the patients suffered from varying degrees of kidney disease ranging from mild compromised kidney function to severe disease. Many suffered from end stage renal failure. It was impossible to determine if the kidney disease contributed to the susceptibility of the patient to *Clostridium difficile* infection or whether the *Clostridium infection*, as a toxin-producing organism, led to the onset of kidney failure. It was also noted that many of the patients with *Clostridium difficile* infection also suffered from cancer, heart disease and autoimmune disorders. It is an established fact that immune function diminishes with age, and that incidence of *Clostridium difficile* infection increases with age. Prevalence of cardiovascular disease, including arteriosclerosis, atherosclerosis, peripheral vascular disease, myocardial infarction, and coronary artery disease also increase with advancing age. These were frequent diagnoses in the patients with *Clostridium difficile* as determined through ICD-9 diagnoses. It would be interesting to explore the associations between these additional comorbidities and their potential association with *Clostridium difficile* infection.

Clostridium difficile infection is the most significant nosocomial pathogen that is dealt with on a daily basis in the health care setting. This disease is a significant cause of morbidity and mortality for the patient, is an important source of financial burden in the acute and long-term care facilities, and greatly compromises quality of life for the patient. This study has the potential to be an instrument of social change in that awareness of novel factors that make an individual particularly susceptible to development of *Clostridium difficile* infection will allow for adoption of proactive preventive strategies that could improve outcomes for the particularly vulnerable patient populations. These strategies could reduce susceptibility in those patients

sensitive to *Clostridium* infection, and in those who acquire the infection, new strategies could help diminish the morbidity and mortality currently associated with this infection. This would reduce costs associated with treatment of the infection and would alleviate the stress on already challenged health care personnel. New knowledge would improve current strategies to battle the disease as well as improving quality of life and overall population health of those affected, representing positive social change. A healthier community translates into a healthier nation. Recognizing factors that make people more susceptible to infection and relapse/reinfection will allow for individualized targeted therapy which will translate into improved outcomes and positive social change both for patients and health care systems alike. Whatever the cause or contributing factors, the overall goal would be to have improved outcomes regarding *Clostridium difficile* infection. Strategies for improvement could include enhanced healthcare practitioner education, accompanied by better patient education, and enhanced reporting practices by infection control preventionists. Shaping public policy to instill more stringent health policies regarding the reporting of *Clostridium difficile* infection would also improve outcomes. Moving forward in this way will allow the possibility of improved evidence-based prevention and treatment options for *Clostridium difficile* infection. (Debast, et al., 2014).

One of the ten essential public health services (EPHS) is to communicate effectively to inform and educate (CDC, 2020). This can be accomplished by educating the population about the importance of antibiotic stewardship and taking antibiotics responsibly to decrease rates of *Clostridium difficile* infection. According to the EPHS Framework, communities should educate in order to contribute towards policy development.

References

Abou Chakra C. N., Pepin J., Sirard S., & Valiquette, L. (2014) Risk factors for recurrence, complications and mortality in Clostridium difficile infection: A systematic review. *PLoS One, 9*(6), e98400. https://doi.org/10.1371/journal.pone.0098400

Ades, P. A., Savage, P. D., Marney, A. M., Harvey, J., & Evans, K. A. (2015). Remission of recently diagnosed type 2 diabetes mellitus with weight loss and exercise. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *35*(3), 193–197. https://doi.org/10.1097/HCR.0000000000000106

American College Health Association. (2018). *Ecological model.* https://www.acha.org/HealthyCampus/HealthyCampus/Ecological_Model.aspx

Ananthakrishnan A. N., McGinley E. L., & Binion D. G. (2008). Excess hospitalisation burden associated with Clostridium difficile in patients with inflammatory bowel disease. *Gut, 57*(2), 205-10. https://doi.org/10.1136/gut.2007.128231

Arnlöv J., Ingelsson E., Sundström J., & Lind L. (2010). Impact of body mass index and the metabolic syndrome on the risk of cardiovascular disease and death in middle-aged men. *Circulation, 121*(2), 230-6. https://doi.org/10.1161/CIRCULATIONAHA.109.887521

Arrieta-Cruz, I. & Gutiérrez-Juárez, R. (2016). The role of insulin resistance and glucose metabolism dysregulation in the development of Alzheimer´s disease. *Rev Invest Clin, 68*(2), 53-8.

Bishara, J., Farah, R., Mograbi, J., Khalaila, W., Abu-Elheja, O., Mahamid, M., & Nseir, W. (2013). Obesity as a risk factor for Clostridium difficile infection. *Clin Infect Dis, 57*(4), 489-93. https://doi.org/10.1093/cid/cit280

Boulangé, C. L., Neves, A. L., Chilloux, J., Nicholson, J. K., & Dumas, M. E. (2016). Impact of the gut microbiota on inflammation, obesity, and metabolic disease. *Genome Med, 8*(1), 42. https://doi.org/10.1186/s13073-016-0303-2

Breault, J. L. (2013). Bioethics in practice - A quarterly column about medical ethics: ethics of chart review research. *Ochsner J, 13*(4), 481-2.

Burke, K. E. & Lamont, J. T. (2014). Clostridium difficile infection: A worldwide disease. *Gut Liver, 8*(1), 1-6. https://doi.org/10.5009/gnl.2014.8.1.1

Butler, S. O., Btaiche, I. F., & Alaniz C. (2005). Relationship between hyperglycemia and infection in critically ill patients. *Pharmacotherapy, 25*(7), 963-76. https://doi.org/10.1592/phco.2005.25.7.963

Centers for Disease Control and Prevention. (n.d.). *CDC Identified diabetes belt.* https://www.cdc.gov/diabetes/pdfs/data/diabetesbelt.pdf

Centers for Disease Control and Prevention. (2017). *Clostridiodes difficile (CDI) infection tracking.* https://www.cdc.gov/hai/eip/cdiff-tracking.html

Centers for Disease Control and Prevention. (2012d). *Morbidity frequency measures.* https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson3/section2.html

Centers for Disease Control and Prevention. (2015). *National and state healthcare-associated infections progress report.* https://www.cdc.gov/HAI/pdfs/progress-report/hai-progress-report-2015.pdf

Centers for Disease Control and Prevention. (2016e). *Virginia healthcare associated infection progress report.* https://www.cdc.gov/hai/pdfs/stateplans/factsheets/va.pdf

Centers for Disease Control and Prevention. (2017a). *Clostridium difficile Infection (CDI) tracking.* https://www.cdc.gov/hai/eip/clostridium-difficile.html

Centers for Disease Control and Prevention. (2017b). *Nearly half a million Americans suffered from Clostridium difficile infections in a single year.* https://www.cdc.gov/media/releases/2015/p0225-clostridium-difficile.html

Centers for Disease Control and Prevention (2017c). *Prevalence of obesity among adults and youth: United States, 2015–2016.* https://www.cdc.gov/nchs/products/databriefs/db288.htm

Centers for Disease Control and Prevention (2021). *Virginia HAI data and reports*. https://www.cdc.gov/hai/stateplans/state-hai-plans/va.html

Choban PS, Heckler R, Burge JC, Flancbaum L. (1995). Increased incidence of nosocomial infections in obese surgical patients. *Am Surg*. 61(11):1001-5.

Costa CL, Quesada-Gómez C, de Carvalho CB, González RH, Gifoni MA, Ribeiro RA, & de Castro Brito GA. (2014). Community-acquired diarrhea associated with Clostridium difficile in an HIV-positive cancer patient: first case report in Latin America. *Int J Infect Dis.* 26:138-9. https://doi.org/10.1016/j.ijid.2014.06.010

Costello EK, Stagaman K, Dethlefsen L, Bohannan BJ, & Relman DA. (2012). The application of ecological theory toward an understanding of the human microbiome. *Science*. 336(6086):1255-62. https:/doi.org/10.1126/science.1224203.

Debast SB, Bauer MP, & Kuijper EJ; European Society of Clinical Microbiology and Infectious Diseases. (2014). European Society of Clinical Microbiology and Infectious Diseases: update of the treatment guidance document for Clostridium difficile infection. *Clin Microbiol Infect*. Suppl 2:1-26. https://doi.org/10.1111/1469-0691.12418

Depestel DD, & Aronoff DM. (2013). Epidemiology of Clostridium difficile infection. *J Pharm Pract.* 26(5):464-75. https://doi.org/10.1177/0897190013499521.

Dossett LA, Dageforde LA, Swenson BR, Metzger R, Bonatti H, Sawyer RG, & May AK. (2009). Obesity and site-specific nosocomial infection risk in the intensive care unit. *Surg Infect (Larchmt).* 10(2):137-42. https://doi,org/10.1089/sur.2008.028

Dubberke ER, & Olsen MA. (2012). Burden of Clostridium difficile on the healthcare system. *Clin Infect Dis.* 55 Suppl 2(Suppl 2): S88-92. https://doi.org/10.1093/cid/cis335

Eckmann C, Wasserman M, Latif F, Roberts G, & Beriot-Mathiot A (2013). Increased hospital length of stay attributable to Clostridium difficile infection in patients with four co-morbidities: an analysis of hospital episode statistics in four European countries. *Eur J Health Econ*. 14(5):835-46. https://doi.org/10.1007/s10198-013-0498-8

Educalingo.com. (2018). Covariate. https://educalingo.com/en/dic-en/covariate

Esteban-Vasallo MD, Naval Pellicer S, Domínguez-Berjón MF, Cantero Caballero M, Asensio Á, Saravia G, & Astray-Mochales J. (2016). Age and gender differences in Clostridium difficile-related hospitalization trends in Madrid (Spain) over a 12-year period. *Eur J Clin Microbiol Infect Dis.* 35(6):1037-44. https://doi.org/10.1007/s10096-016-2635-7

Evans, Oman II, M., Starley, B., Galagan, J. C., Yabes, J. M., Evans, S., & Salama, J. J. (2016). Tea and recurrent Clostridium difficile infection. *Gastroenterology Research and Practice.* https://www.hindawi.com/journals/grp/2016/4514687/

Eyre, D. W., Walker, A. S., Wyllie, D., Dingle, K. E., Griffiths, D., Finney, J., O'Connor, L., Vaughan, A., Crook, D. W., Wilcox, M. H., Peto, T. E., & Infections in Oxfordshire Research Database (2012). Predictors of first recurrence of Clostridium difficile infection: implications for initial management. *Clinical infectious diseases* : an official publication of the Infectious Diseases Society of America, 55 Suppl 2(Suppl 2), S77–S87. https://doi.org/10.1093/cid/cis356

Forhan M, & Gill SV. (2013). Obesity, functional mobility and quality of life. *Best Pract Res Clin Endocrinol Metab*. 27(2):129-37. https://doi.org/0.1016/j.beem.2013.01.003

G Power Manual. (n.d.). http://www.gpower.hhu.de/fileadmin/redaktion/Fakultaeten/Mathematisch-Naturwissenschaftliche_Fakultaet/Psychologie/AAP/gpower/GPowerManual.pdf

Garey KW, Aitken SL, Gschwind L, Goddu S, Xie Y, Duff C, Barbut F, Shah DN, & DuPont HL. (2016). Development and validation of a Clostridium difficile health-related quality-of-life questionnaire. *J Clin Gastroenterol*. 50(8):631-7. https://doi.org/10.1097/MCG.0000000000000473

Gastro.org. (n.d.). Ulcerative Colitis ICD9 Codes. https://www.gastro.org/practice/clinical-service-line/525-325PNQ_13-2_PDF_Document_Updates_ICD-9_codes_-_UC_Final.pdf

Guerrero DM, Nerandzic MM, Jury LA, Jinno S, Chang S, & Donskey CJ. (2012). Acquisition of spores on gloved hands after contact with the skin of patients with Clostridium difficile infection and with environmental surfaces in their rooms. *Am J Infect Control.* 40(6):556-8. https://doi.org10.1016/j.ajic.2011.08.002

Guh AY, Mu Y, Baggs J, Winston LG, Bamberg W, Lyons C, Farley MM, Wilson LE, Holzbauer SM, Phipps EC, Beldavs ZG, Kainer MA, Karlsson M, Gerding DN, & Dumyati G. (2018). Trends in incidence of long-term-care facility onset Clostridium difficile infections in 10 US geographic locations during 2011-2015. *Am J Infect Control*. 46(7):840-842. https://doi,org/10.1016/j.ajic.2017.11.026

Hardt C, Berns T, Treder W, & Dumoulin FL. (2008). Univariate and multivariate analysis of risk factors for severe Clostridium difficile-associated diarrhoea: importance of co-morbidity and serum C-reactive protein. *World J Gastroenterol.* 21;14(27):4338-41. https://doi.org/10.3748/wjg.14.4338

Hassan SA, Rahman RA, Huda N, Wan Bebakar WM, & Lee YY. (2013). Hospital-acquired Clostridium difficile infection among patients with type 2 diabetes mellitus in acute medical wards. *J R Coll Physicians Edinb*. 43(2):103-7. https://doi.org/ 10.4997/JRCPE.2013.203

He, M., Miyajima, F., Roberts, P., Ellison, L., Pickard, D. J., Martin, M. J., Connor, T. R., Harris, S. R., Fairley, D., Bamford, K. B., D'Arc, S., Brazier, J., Brown, D., Coia, J. E., Douce, G., Gerding, D., Kim, H. J., Koh, T. H., Kato, H., Senoh, M., …& Lawley, T. D. (2013). Emergence and global spread of epidemic healthcare-associated Clostridium difficile. *Nature genetics,* 45(1), 109–113. https://doi.org/10.1038/ng.2478

Hess-Fischel, A. (2017). What is Insulin? https://www.endocrineweb.com/conditions/type-1-diabetes/what-insulin

Hunter JC, Mu Y, Dumyati GK, Farley MM, Winston LG, Johnston HL, Meek JI, Perlmutter R, Holzbauer SM, Beldavs ZG, Phipps EC, Dunn JR, Cohen JA, Avillan J, Stone ND, Gerding DN, McDonald LC, & Lessa FC. (2016). Burden of nursing home-onset Clostridium difficile infection in the United States: Estimates of incidence and patient outcomes. *Open Forum Infect Dis.* 18;3(1): ofv196. https://doi.org/10.1093/ofid/ofv196

ICD9Data.com. (n.d.). Overweight, Obesity and Hyperalimentation. http://www.icd9data.com/2013/Volume1/240-279/270-279/278/default.htm

ICD9Data.com. (n.d.). Procedure Code 54. Operations on the Abdominal Region. http://www.icd9data.com/2012/Volume3/42-54/54/default.htm

Indiana.edu. (n.d.). Internal validity. http://www.indiana.edu/~p1013447/dictionary/int_val.htm

Infectious Disease Society of America (2021). C. difficile is Everywhere – Even on the Bottom of Footwear. https://www.idsociety.org/news--publications-new/articles/2021/c.-difficile-is-everywhere--even-on-the-bottom-of-footwear/

Jabbar U, Leischner J, Kasper D, Gerber R, Sambol SP, Parada JP, Johnson S, & Gerding DN. (2010). Effectiveness of alcohol-based hand rubs for removal of Clostridium difficile spores from hands. *Infect Control Hosp Epidemiol*. 31(6):565-70. https://doi.org/10.1086/652772

The Joint Commission Center for Transforming Healthcare (2016). Reducing Clostridium difficile infections. https://www.centerfortransforminghealthcare.org/improvement-topics/reducing-c-diff-infections/

Kim YK, Shin JS, & Nahm MH. (2016). NOD-like receptors in infection, immunity, and diseases. *Yonsei Med J.* 57(1):5-14. https://doi.org/10.3349/ymj.2016.57.1.5

Kiser, K., Payne, W., & Taft, T. (2011). *Clinical Laboratory Microbiology: A Practical Approach*. Pearson Education Inc. Upper Saddle River, NJ.

Koh GC, Peacock SJ, van der Poll T, & Wiersinga WJ. (2012). The impact of diabetes on the pathogenesis of sepsis. *Eur J Clin Microbiol Infect Dis.* 31(4):379-88. https://doi.org/10.1007/s10096-011-1337-4

Labtestsonline. (2017). Clostridium difficile and Clostridium difficile toxin testing. https://labtestsonline.org/understanding/analytes/cdiff/tab/test/

Landelle C, Verachten M, Legrand P, Girou E, Barbut F, & Brun-Buisson C. (2014). Contamination of healthcare workers' hands with Clostridium difficile spores after caring for patients with C. difficile infection. *Infect Control Hosp Epidemiol*. 35(1):10-5. https://doi.org/10.1086/674396

Leontis, L. (2017). Type 2 diabetes: Key facts. https://www.endocrineweb.com/conditions/type-2-diabetes/type-2-diabetes-overview

Lessa, F. C., Gould, C. V., & McDonald, L. C. (2012). Current status of Clostridium difficile infection epidemiology. *Clinical infectious diseases*: an official publication of the Infectious Diseases Society of America, 55 Suppl 2(Suppl 2), S65–S70. https://doi.org/10.1093/cid/cis319

Lessa FC, Winston LG, & McDonald LC; (2015). Emerging Infections Program C. difficile Surveillance Team. (2015). Burden of Clostridium difficile infection in the United States. *N Engl J Med.* 11;372(24):2369-70. https://doi.org/10.1056/NEJMc1505190

Leung J, Burke B, Ford D, Garvin G, Korn C, Sulis C, & Bhadelia N. (2013). Possible association between obesity and Clostridium difficile infection. *Emerg Infect Dis*. 19(11):1791-8. https://doi.org/10.3201/eid1911.130618

Lin HJ, Hung YP, Liu HC, Lee JC, Lee CI, Wu YH, Tsai PJ, & Ko WC. (2013). Risk factors for Clostridium difficile-associated diarrhea among hospitalized adults with fecal toxigenic C. difficile colonization. *J Microbiol Immunol Infect*. 48(2):183-9. https://doi.org/10.1016/j.jmii.2013.08.003

Lockwood, W. (2017). Clostridium Difficile: A Growing Problem. http://www.rn.org/courses/coursematerial-72.pdf

Loo VG, Bourgault AM, Poirier L, Lamothe F, Michaud S, Turgeon N, Toye B, Beaudoin A, Frost EH, Gilca R, Brassard P, Dendukuri N, Béliveau C, Oughton M, Brukner I, & Dascal A. (2011). Host and pathogen factors for Clostridium difficile infection and colonization. *N Engl J Med*. 365 (18):1693-703. https://doi,org/10.1056/NEJMoa1012413. PMID: 22047560

Mayo Clinic. (2017c). C. difficile infection. https://www.mayoclinic.org/diseases-conditions/c-difficile/symptoms-causes/syc-20351691

Mayo Clinic. (2017a). Metabolic Syndrome. https://www.mayoclinic.org/diseases-conditions/metabolic-syndrome/symptoms-causes/syc-20351916

Mayo Clinic. (2017b). Pseudomembranous Colitis. http://www.mayoclinic.org/diseases-conditions/pseudomembranous-colitis/symptoms-causes/syc-20351434

McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, Dubberke ER, Garey KW, Gould CV, Kelly C, Loo V, Shaklee Sammons J, Sandora TJ, & Wilcox MH. (2018). Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis.*19;66(7): e1-e48. https://doi.org/10.1093/cid/cix1085

McGlone SM, Bailey RR, Zimmer SM, Popovich MJ, Tian Y, Ufberg P, Muder RR, & Lee BY. (2012). The economic burden of Clostridium difficile. *Clin Microbiol Infect*. 18(3):282-9. https://doi.org/10.1111/j.1469-0691.2011.03571.x

MDCALC (2018). Charlson Comorbidity Index (CCI). https://www.mdcalc.com/charlson-comorbidity-index-cci

Merriam-Webster Medical Dictionary. (2017). Medical Terms and Abbreviations. https://www.merriam-webster.com/medical

Nanwa N, Kendzerska T, Krahn M, Kwong JC, Daneman N, Witteman W, Mittmann N, Cadarette SM, Rosella L, & Sander B. (2015). The economic impact of Clostridium difficile infection: a systematic review. *Am J Gastroenterol*. 110 (4):511-9. https://doi.org/ 10.1038/ajg.2015.48

National Center for Health Statistics. (2012). National Hospital Discharge Survey (2010). http://www.cdc.gov/nchs/nhds.htm

Neogen. (2017). Clostridium difficile agar; product information. foodsafety.neogen.com/pdf/Acumedia_PI/7385_PI.pdf

Nguyen GC, Kaplan GG, Harris ML, & Brant SR. (2007). A national survey of the prevalence and impact of Clostridium difficile infection among hospitalized inflammatory bowel disease patients. *Am J Gastroenterol*. 103(6):1443-50. https://doi,org/10.1111/j.1572-0241.2007.01780.x

Noorani HZ, Soni N, Pitrak D, Belinson S, & Aronson N. (2012). Future research needs for prevention and treatment of Clostridium difficile infection: Identification of future research needs from comparative effectiveness review No. 31 [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 May. Report No.: 12-EHC100. https://pubmed.ncbi.nlm.nih.gov/23326897/

Olanipekun TO, Salemi JL, Mejia de Grubb MC, Gonzalez SJ, & Zoorob RJ. (2016). Clostridium difficile infection in patients hospitalized with type 2 diabetes mellitus and its impact on morbidity, mortality, and the costs of inpatient care. *Diabetes Res Clin Pract*. 116: 68-79. https://doi.org/10.1016/j.diabres.2016.04.021

Pattani, R., Palda, V. A., Hwang, S. W., & Shah, P. S. (2013). Probiotics for the prevention of antibiotic-associated diarrhea and Clostridium difficile infection among hospitalized patients: systematic review and meta-analysis. *Open medicine*: a peer-reviewed, independent, open-access journal, 7(2), e56–e67. https://pubmed.ncbi.nlm.nih.gov/24348885/

Pavlov, V. A., & Tracey, K. J. (2012). The vagus nerve and the inflammatory reflex--linking immunity and metabolism. *Nature reviews. Endocrinology*, 8(12), 743–754. https://doi.org/10.1038/nrendo.2012.189

Peggy Lillis Foundation. (2018). Fighting C. diff. through education and advocacy. https://peggyfoundation.org/about-plf/missionvision/?gclid=EAIaIQobChMItPuljpXN3gIVhp-zCh2h3ghnEAAYASAAEgKLBfD_BwE

Pincus T, Chua JR, & Gibson KA. (2016). Evidence from a multidimensional health assessment questionnaire (MDHAQ) of the value of a biopsychosocial model to complement a traditional biomedical model in care of patients with rheumatoid arthritis. *J Rheum Dis.* 2023:212-233. https://doi.org/10.4078/jrd.2016.23.4.212

Qu HQ, & Jiang ZD. (2014). Clostridium difficile infection in diabetes. *Diabetes Res Clin Pract.* 105 (3):285-94. https://doi.org/10.1016/j.diabres.2014.06.002

Reilly SM, & Saltiel AR. (2017). Adapting to obesity with adipose tissue inflammation. *Nat Rev Endocrinol.* 13(11):633-643. https://doi.org/10.1038/nrendo.2017.90

Rettner, R. (2016). Diabetes by State: Full List of State Rankings. https://www.livescience.com/57072-diabetes-american-state-rankings.html

Rettner, R. (2015). Most and Least Obese States: Full Rankings. https://www.livescience.com/50973-obesity-rates-full-rankings.html

Reveles KR, Lee GC, Boyd NK, & Frei CR. (2014). The rise in Clostridium difficile infection incidence among hospitalized adults in the United States: 2001-2010. *Am J Infect Control.* 42(10):1028-32. https://doi.org/10.1016/j.ajic.2014.06.011

Rodríguez-Hernández H, Simental-Mendía LE, Rodríguez-Ramírez G, & Reyes-Romero MA. (2013). Obesity and inflammation: epidemiology, risk factors, and markers of inflammation. *Int J Endocrinol*. 2013;2013:678159. https://doi.org/10.1155/2013/678159

Sallis, J. F., Owen, N., & Fisher, E. (2015). Ecological models of health behavior. Health behavior: theory, research, and practice. 5th ed. San Francisco: Jossey-Bass, 43-64. http://riskybusiness.web.unc.edu/files/2015/01/Health-Behavior-and-Health-Education.pdf#page=503

Sammons JS, Toltzis P, & Zaoutis TE. (2013). Clostridium difficile infection in children. *JAMA Pediatr.* 167 (6):567–573. https://doi.org/10.1001/jamapediatrics.2013.441

Shakov R, Salazar RS, Kagunye SK, Baddoura WJ, & DeBari VA. (2011). Diabetes mellitus as a risk factor for recurrence of Clostridium difficile infection in the acute care hospital setting. *Am J Infect Control*. 39(3):194-8. https://doi.org/10.1016/j.ajic.2010.08.017

Sheridan PA, Paich HA, Handy J, Karlsson EA, Hudgens MG, Sammon AB, Holland LA, Weir S, Noah TL, & Beck MA. (2012). Obesity is associated with impaired immune response to influenza vaccination in humans. *Int J Obes (Lond).* 36(8):1072-7. https://doi.org/10.1038/ijo.2011.208

Smith, K. F., Dobson, A. P., McKenzie, F. E., Real, L. A., Smith, D. L., & Wilson, M. L. (2005). Ecological theory to enhance infectious disease control and public health policy. Frontiers in ecology and the environment, 3(1), 29–37. https://doi.org/10.1890/1540-9295(2005)003[0029:ETTEID]2.0.CO;2

Smith-Marsh, D. (2017). Type 1 Diabetes overview. https://www.endocrineweb.com/conditions/type-1-diabetes/type-1-diabetes-overview

Stein RR, Bucci V, Toussaint NC, Buffie CG, Rätsch G, Pamer EG, Sander C, & Xavier JB. Ecological modeling from time-series inference: insight into dynamics and stability of intestinal microbiota. PLoS *Comput Biol*. 9(12): e1003388. https://doi.org/10.1371/journal.pcbi.1003388

Stevens, C. (2017). Clinical Immunology and Serology: A Laboratory Perspective. F.A. Davis Company. Philadelphia, PA

TechLab. (2017). C.DIFF QUIK CHEK COMPLETE 30525C. http://www.techlab.com/diagnostics/c-difficile/c-diff-quik-chek-complete-30525c-30550c-t30525c-t30550c/

TechLab. (2017). C. DIFFICILE TOX A/B II T5015. http://www.techlab.com/diagnostics/c-difficile/c-difficile-tox-ab-ii-t5015/

TechLab. (2017)). TOX A/B QUIK CHEK T5033. http://www.techlab.com/diagnostics/c-difficile/tox-ab-quik-chek-t5033/

The State of Obesity. (2017). Virginia State Obesity Data. https://stateofobesity.org/states/va

Tickler IA, Goering RV, Whitmore JD, Lynn AN, Persing DH, & Tenover FC; Healthcare Associated Infection Consortium. (2014). Strain types and antimicrobial resistance patterns of Clostridium difficile isolates from the United States, 2011 to 2013. *Antimicrob Agents Chemother*. 58(7):4214-8. https://doi.org/10.1128/AAC.02775-13

UCLA Institute for Digital Research and Education. (n.d.). Logistic Regression/SPSS Annotated Output. https://stats.idre.ucla.edu/spss/output/logistic-regression/

Vassar, M., & Holzmann, M. (2013). The retrospective chart review: important methodological considerations. *Journal of educational evaluation for health professions*, 10, 12. https://doi.org/10.3352/jeehp.2013.10.12

Virginia Department of Health. (2016). Diabetes Burden Report for the State of Virginia. www.vdh.virginia.gov/content/uploads/sites/75/2016/.../Diabetes-Burden-Report.pdf

Virginia Department of Health (2016). Diseases and Organisms; Clostridium difficile. http://www.vdh.virginia.gov/surveillance-and-investigation/hai/organisms/

Virginia Department of Health (2015). Virginia Healthcare-Associated Infections Report. https://www.vdh.virginia.gov/content/uploads/sites/13/2016/10/2015ConsumerReport.pdf

Vrieze A, Van Nood E, Holleman F, Salojärvi J, Kootte RS, Bartelsman JF, Dallinga-Thie GM, Ackermans MT, Serlie MJ, Oozeer R, Derrien M, Druesne A, Van Hylckama Vlieg JE, Bloks VW, Groen AK, Heilig HG, Zoetendal EG, Stroes ES, de Vos WM, Hoekstra JB, & Nieuwdorp M. 92012). Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. *Gastroenterology.*143(4):913-6.e7. https://doi.org/10.1053/j.gastro.2012.06.031

Wade DT, & Halligan PW. (2004). Do biomedical models of illness make for good healthcare systems? *BMJ.* 11;329(7479):1398-401. https://doi.org/10.1136/bmj.329.7479.1398

Walter J, Maldonado-Gómez MX, & Martínez I. (2017). To engraft or not to engraft: an ecological framework for gut microbiome modulation with live microbes. *Curr Opin Biotechnol.* 49:129-139. https://doi.org/10.1016/j.copbio.2017.08.008

Washington Post. (2014). Infections by C. diff bacteria are on the rise and can cause serious problems. https://www.washingtonpost.com/national/health-science/infections-by-cdiff-bacteria-are-on-the-rise-and-can-cause-serious-problems/2017/10/13/371c824e-93eb-11e7-aace-04b862b2b3f3_story.html?noredirect=on&utm_term=.9ec404efb6fc

Wendt JM, Cohen JA, Mu Y, Dumyati GK, Dunn JR, Holzbauer SM, Winston LG, Johnston HL, Meek JI, Farley MM, Wilson LE, Phipps EC, Beldavs ZG, Gerding DN, McDonald LC, Gould CV, & Lessa FC. (2014). Clostridium difficile infection among children across diverse US geographic locations. *Pediatrics.* 133(4):651-8. https://doi.org/10.1542/peds.2013-3049

Zhang S, Palazuelos-Munoz S, Balsells EM, Nair H, Chit A, & Kyaw MH. (2016). Cost of hospital management of Clostridium difficile infection in United States-a meta-analysis and modelling study. *BMC Infect Dis.* 25;16(1):447. https://doi.org/ 10.1186/s12879-016-1786-6.

Appendix A: Age Run as a Continuous Variable

Table A1

Binary logistic regression: Study population age in years vs Clostridium difficile infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129208	100.0
	Missing Cases	1	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128073	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR
Step 0	Constant	-4.726	.030	25127.286	1	.000	.009

(140)

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	Age in Years	401.335	1	.000
	Overall Statistics		401.335	1	.000

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	436.948	1	.000
	Block	436.948	1	.000
	Model	436.948	1	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	12571.027[a]	.003	.035

a. Estimation terminated at iteration number 8 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	26.827	8	.001

Contingency Table for Hosmer and Lemeshow Test

		CD = .00		CD = 1.00		
		Observed	Expected	Observed	Expected	Total
Step 1	1	12712	12700.133	16	27.867	12728
	2	13286	13272.799	26	39.201	13312
	3	13046	13056.281	64	53.719	13110
	4	12783	12796.824	84	70.176	12867
	5	13788	13776.676	84	95.324	13872
	6	12202	12208.066	111	104.934	12313
	7	12754	12782.379	163	134.621	12917
	8	12177	12184.129	165	157.871	12342
	9	12253	12257.118	198	193.882	12451
	10	13072	13038.596	224	257.404	13296

Classification Table[a]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 1	CD	.00	128073	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. The cut value is .500

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	Age in Years	.034	.002	371.114	1	.000	1.034	1.031	1.038
	Constant	-6.900	.126	2982.001	1	.000	.001		

a. Variable(s) entered on step 1: Age in Years.

Appendix B: Inflammatory Bowel Disease (IBD) Run as a Nominal Variable

Table B1

Binary Logistic Regression of Study Population Diagnosed with IBD vs Clostridium difficile Infection

Contingency Table for Hosmer and Lemeshow Test

		CD = .00		CD = 1.00		
		Observed	Expected	Observed	Expected	Total
Step 1	1	128068	128068.000	1135	1135.000	129203

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR
Step 0	Constant	-4.726	.030	25126.862	1	.000	.009

Variables not in the Equation

			Score	Df	Sig.
Step 0	Variables	IBD(1)	19.477	1	.000
	Overall Statistics		19.477	1	.000

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	IBD (1)	.927	.218	18.150	1	.000	2.527	1.650	3.872
	Constant	-4.738	.030	24767.393	1	.000	.009		

a. Variable(s) entered on step 1: IBD.

Appendix C: High Body Mass Index (HIBMI) Run as a Nominal Variable

Table C1

Case processing summary

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128068	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Categorical Variables Codings

			Parameter coding
		Frequency	(1)
HIBMI	.00	125152	.000
	1.00	4051	1.000

Table C2

Binary Logistic Regression of Study Population Diagnosed with HBMI vs Clostridium difficile Infection

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128068	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Categorical Variables Codings

			Parameter coding
		Frequency	(1)
HIBMI	.00	125152	.000
	1.00	4051	1.000

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129203	100.0
	Missing Cases	6	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-4.726	.030	25126.862	1	.000	.009

Variables not in the Equation

			Score	Df	Sig.
Step 0	Variables	HIBMI(1)	4.637	1	.031
	Overall Statistics		4.637	1	.031

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	5.280	1	.022
	Block	5.280	1	.022
	Model	5.280	1	.022

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	13002.608[a]	.000	.000

a. Estimation terminated at iteration number 8 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	.000	0	.

Contingency Table for Hosmer and Lemeshow Test

		CD = .00		CD = 1.00		
		Observed	Expected	Observed	Expected	Total
Step 1	1	4028	4028.000	23	23.000	4051
	2	124040	124040.000	1112	1112.000	125152

Variables in the Equation

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	HIBMI(1)	-.451	.211	4.559	1	.033	.637	.421	.964
	Constant	-4.714	.030	24495.691	1	.000	.009		

a. Variable(s) entered on step 1: HIBMI.

Appendix D: Diabetes Mellitus Type I (DMI) Run as a Nominal Variable

Table D1

Binary Logistic Regression of Study Population Diagnosed with DMI vs Clostridium difficile Infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129199	100.0
	Missing Cases	10	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Categorical Variables Codings

		Frequency	Parameter coding (1)
DMI	.00	128288	1.000
	DMI	911	.000

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128064	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR
Step 0	Constant	-4.726	.030	25126.523	1	.000	.009

Variables not in the Equation

			Score	Df	Sig.
Step 0	Variables	DM1(1)	2.028	1	.154
	Overall Statistics		2.028	1	.154

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	DMI(1)	-.413	.292	2.000	1	.157	.662	.373	1.173
	Constant	-4.316	.291	220.628	1	.000	.013		

a. Variable(s) entered on step 1: DMI.

Appendix E: Diabetes Mellitus Type II (DMII) Run as a Nominal Variable

Table E1

Binary Logistic Regression of Study Population Diagnosed with DMII vs Clostridium difficile Infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129199	100.0
	Missing Cases	10	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Categorical Variables Codings

			Parameter coding
		Frequency	(1)
DM2	.00	103067	.000
	1.00	26132	1.000

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128064	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR
Step 0	Constant	-4.726	.030	25126.523	1	.000	.009

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	DM2(1)	.720	1	.396
	Overall Statistics		.720	1	.396

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	DM2(1)	.062	.073	.720	1	.396	1.064	.922	1.227
	Constant	-4.739	.034	19901.032	1	.000	.009		

a. Variable(s) entered on step 1: DM2.

Appendix F: Geographic Region (V12) Run as a Nominal Variable

Table F1:

Binary logistic regression: Geographic location of patient (V12) vs Clostridium difficile infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129207	100.0
	Missing Cases	2	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128072	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR
Step 0	Constant	-4.726	.030	25127.201	1	.000	.009

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	V12	6.470	3	.091
		V12(1)	.002	1	.966
		V12(2)	.338	1	.561
		V12(3)	5.783	1	.016
	Overall Statistics		6.470	3	.091

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	V12			6.433	3	.092			
	V12(1)	-.069	.085	.663	1	.416	.933	.789	1.103
	V12(2)	-.047	.080	.338	1	.561	.954	.815	1.117
	V12(3)	-.311	.126	6.141	1	013	.733	.573	.937
	Constant	-4.659	.066	5030.506	1	.000	.009		

a. Variable(s) entered on step 1: V12 (geo loc).

Appendix G: Binary Logistic Regression: Age, Sex, DMI, DMII, AS, IBD and HIBMI

Clostridium difficile Infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129189	100.0
	Missing Cases	20	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Categorical Variables Codings

		Frequency	Parameter coding (1)
V5	1	52026	.000
(sex)	2	77163	1.000
DM1	.00	128278	1.000
	DM1	911	.000
DM2	.00	103058	1.000
	1.00	26131	.000
IBD	.00	128173	1.000
	1.00	1016	.000
AS	.00	126002	1.000
	1.00	3187	.000
HIBMI	.00	125138	.000
	1.00	4051	1.000

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128054	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-4.726	.030	25125.676	1	.000	.009

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	HIBMI(1)	4.639	1	.031
		DM1(1)	2.028	1	.154
		DM2(1)	.719	1	.396
		IBD(1)	19.472	1	.000
		AS(1)	.591	1	.442
		sex(1)	4.768	1	.029
		Age in Years	401.326	1	.000
	Overall Statistics		442.667	7	.000

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	469.854	7	.000
	Block	469.854	7	.000
	Model	469.854	7	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	12537.786[a]	.004	.038

a. Estimation terminated at iteration number 8 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	16.296	8	.038

Contingency Table for Hosmer and Lemeshow Test

		CD = .00		CD = 1.00		
		Observed	Expected	Observed	Expected	Total
Step 1	1	12533	12522.540	16	26.460	12549
	2	12890	12882.333	29	36.667	12919
	3	12958	12964.476	58	51.524	13016
	4	12750	12757.166	75	67.834	12825
	5	12625	12621.156	80	83.844	12705
	6	12972	12970.214	105	106.786	13077
	7	12624	12648.032	153	128.968	12777
	8	12923	12929.347	170	163.653	13093
	9	12795	12804.953	212	202.047	13007
	10	12984	12953.783	237	267.217	13221

Classification Table[a]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 1	CD	.00	128054	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. The cut value is .500

Correlation Matrix

		Constant	HIBMI(1)	DM!(1)	DM2(1)	IBD(1)	AS(1)	Sex(1)	Age in Years
Step 1	Constant	1.000	-.042	-.686	-.198	-.496	-.400	-.073	-.213
	HIBMI(1)	-.042	1.000	-.006	.062	-.003	.018	-.021	.079
	DM1(1)	-.686	-.006	1.000	.046	.017	.011	-.011	-.094
	DM2(1)	-.198	.062	.046	1.000	.017	.000	-.041	.073
	IBD(1)	-.496	-.003	.017	.017	1.000	-.046	.003	-.039
	AS(1)	-.400	.018	.011	.000	-.046	1.000	.010	-.016
	Sex(1)	-.073	-.021	-.011	-.041	.003	.010	1.000	-.003
	Age in Years	-.213	.079	-.094	.073	-.039	-.016	-.003	1.000

Variables in the Equation

								95% C.I.for OR	
		B	S.E.	Wald	df	Sig.	OR	Lower	Upper
Step 1[a]	HIBMI(1)	-.186	.213	.763	1	.382	.831	.548	1.260
	DM1(1)	-.956	.295	10.508	1	.001	.384	.216	.685
	DM2(1)	.144	.073	3.864	1	.049	1.155	1.000	1.334
	IBD(1)	-1.080	.219	24.301	1	.000	.340	.221	.522
	AS(1)	-.129	.181	.509	1	.476	.879	.617	1.253
	Sex(1)	-.059	.060	.950	1	.330	.943	.838	1.061
	Age in Years	.034	.002	380.756	1	.000	1.035	1.032	1.039
	Constant	-4.883	.420	135.374	1	.000	.008		

a. Variable(s) entered on step 1: HIBMI, DM1, DM2, IBD, AS, Sex, Age in Years.

Appendix H: Binary Logistic Regression: Age, sex, geographic location of patient, DMI, DMII, AS, IBD, and HBMI vs *Clostridium difficile* infection

Case Processing Summary

Unweighted Cases[a]		N	Percent
Selected Cases	Included in Analysis	129188	100.0
	Missing Cases	21	.0
	Total	129209	100.0
Unselected Cases		0	.0
Total		129209	100.0

a. If weight is in effect, see classification table for the total number of cases.

Dependent Variable Encoding

Original Value	Internal Value
.00	0
1.00	1

Categorical Variables Codings

			Parameter coding		
		Frequency	(1)	(2)	(3)
V12 (geo loc)	1	24916	1.000	.000	.000
	2	39001	.000	1.000	.000
	3	52515	.000	.000	1.000
	4	12756	.000	000	.000
IBD	.00	128172	.000		
	1.00	1016	1.000		
DM!	.00	128277	1.000		
	DM1	911	.000		
DM2	.00	103057	1.000		
	1.00	26131	.000		
HIBMI	.00	125137	1.000		
	1.00	4051	.000		
AS	.00	126001	1.000		
	1.00	3187	.000		
sex	1	52025	1.000		
	2	77163	.000		

Block 0: Beginning Block

Classification Table[a,b]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 0	CD	.00	128053	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. Constant is included in the model.

b. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-4.726	.030	25125.591	1	.000	.009

Variables not in the Equation

			Score	df	Sig.
Step 0	Variables	Age in Years	401.335	1	.000
		Sex(1)	4.770	1	.029
		V12(Geo loc)	6.469	3	.091
		V12(1)	1.301	1	.254
		V12(2)	.002	1	.966
		V12(3)	.341	1	.559
		DM!(1)	2.027	1	.154
		DM2(1)	.719	1	.397
		HIBMI(1)	4.639	1	.031
		AS(1)	.591	1	.442
		IBD(1)	19.471	1	.000
	Overall Statistics		446.408	10	.000

Block 1: Method = Enter

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	474.195	10	.000
	Block	474.195	10	.000
	Model	474.195	10	.000

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	12533.427[a]	.004	.038

a. Estimation terminated at iteration number 8 because parameter estimates changed by less than .001.

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	16.208	8	.039

Contingency Table for Hosmer and Lemeshow Test

		CD = .00		CD = 1.00		
		Observed	Expected	Observed	Expected	Total
Step 1	1	13119	13105.433	14	27.567	13133
	2	12786	12780.203	31	36.797	12817
	3	12851	12858.510	59	51.490	12910
	4	12739	12742.884	72	68.116	12811
	5	12823	12828.265	91	85.735	12914
	6	12923	12918.908	103	107.092	13026
	7	12732	12754.938	154	131.062	12886
	8	12860	12865.765	170	164.235	13030
	9	12799	12802.204	207	203.796	13006
	10	12421	12395.891	234	259.109	12655

Classification Table[a]

			Predicted		
			CD		Percentage
	Observed		.00	1.00	Correct
Step 1	CD	.00	128053	0	100.0
		1.00	1135	0	.0
	Overall Percentage				99.1

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	OR	95% C.I.for OR Lower	Upper
Step 1[a]	Age in Years	.034	.002	379.095	1	.000	1.035	1.031	1.039
	V5 (sex)	.060	.060	.994	1	.319	1.062	.944	1.195
	V12(geo loc)			4.090	3	.252			
	V12(1)	.233	.126	3.424	1	.064	1.262	.986	1.615
	V12(2)	.201	.120	2.793	1	.095	1.223	.966	1.547
	V12(3)	.228	.117	3.820	1	.051	1.256	.999	1.580
	DM1(1)	-.955	.295	10.494	1	.001	.385	.216	.686
	DM2(1)	.148	.074	4.024	1	.045	1.159	1.003	1.339
	HIBMI(1)	.179	.213	.708	1	.400	1.196	.788	1.814
	AS(1)	-.135	.181	.556	1	.456	.874	.613	1.246
	IBD(1)	1.076	.219	24.107	1	.000	2.932	1.908	4.505
	Constant	-6.395	.424	227.996	1	.000	.002		

a. Variable(s) entered on step 1: Age in Years, sex, V12 (geo loc), DM1, DM2, HIBMI, AS, IBD.