INCIDENCE OF *CLOSTRIDIUM DIFFICILE* INFECTION IN SKILLED NURSING FACILITY RESIDENTS TREATED WITH ANTIBIOTICS COMPARED TO TREATMENT WITH ANTIBIOTICS AND PROBIOTICS

By

Robin S. Bilan
MSN, Clarion, Edinboro, and Slippery Rock Universities, 2010
BSN, Clarion University, 2008

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1/14/2019	Kara L PhD, CRNP
Date	Committee Chair
1/14/2019	Lucille A Morrison DNP, CRNP
Date	Committee Member
1/14/2019	
Date	Committee Member
1-18-19	
Date	Dean, College of Health Sciences and Human Services

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Committee Signature Page

Student Name _____

Committee Chairperson _____

Committee Member _____

Committee Member _____

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Robin S. Bilan, MSN, RN, NP-C

Abstract

Clostridium difficile is a microbe that may cause a severe intestinal infection in vulnerable individuals such as those who are ill and taking antibiotics, or the elderly living in skilled care facilities. Use of probiotic supplements have shown in some studies to decrease the incidence of *Clostridium difficile* infection (CDI). Does the use of probiotic supplements in residents of a skilled nursing facility in western Pennsylvania receiving antibiotic therapy reduce the incidence of CDI? This retrospective study reviewed electronic medical records of 164 residents in a skilled nursing facility, including residents receiving antibiotics, and those receiving antibiotics and probiotics. Limitations included the size of the study sample, the age and condition of the patient including possible previous CDI history, and the time frame of transposition of laboratory analysis results to the electronic medical record. Results revealed a statistically significant difference in the rate of antibiotic-related diarrhea between patients receiving antibiotics and those receiving antibiotic therapy with probiotic supplements. In this study, no patients receiving probiotics and antibiotics were positively diagnosed by laboratory analysis with CDI. This study indicates the need for further studies related to use of probiotic supplements in patients receiving antibiotic therapy.

Keywords: *Clostridium difficile* infection, probiotics, antibiotic associated diarrhea

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Chapter 1

Introduction

The discovery and development of antibiotics has profoundly impacted the treatment and survival of patients with infections (Gaynes, 2017). While nearing a century from when antibiotics were first discovered, current challenges face health care providers in prescribing therapies to the patients of today regarding antimicrobial treatment (Fromage, 2018). According to Fromage, antimicrobial resistance to currently prescribed antibiotics continues to increase with this trend predicted to continue at an alarming rate. The use of antibiotics may result in related infections caused by opportunistic microbes such as *Clostridium difficile*, inflicting significant symptoms and life-threatening illness for patients (Harvard Health Publishing, 2010). *Clostridium difficile* Infection (CDI) has been diagnosed in persons treated with antibiotics (Brown et al., 2016). The treatment for CDI includes antibiotic therapy (Liubakka & Vaughn, 2016).

Background of the Problem

The word, antibiotic, brings connotations of treating an infection (Harvard University, 2010). The literal meaning from the Greek translation is "life-killing" according to Vocabulary.com (n.d.). Anthony van Leeuwenhoek is credited with discovering bacteria in 1676, studying canal water with his creation, the microscope (Porter, 1976). Bacterial infection was identified as a major cause of mortality with little available for effective treatment prior to antibiotics (Runcie, 2015). The first antibiotic was identified in 1928 when Alexandar Fleming detected bacterial growth-altering properties of a mold which later became known as penicillin (Tan & Tatsumura, 2015). Ending the life of an identified or suspected bacterium with a medicinal substance may have been the original intent of Selman Waksman, the scientist first known to use the word "antibiotic" in 1943 (Clardy, Fischback, & Currie, 2009).

Infections caused by bacteria continue to be treated by clinicians prescribing antibiotics (Runcie, 20015). The treatment has now taken on a different meaning for many providers and patients. Terms such as "antimicrobial resistance" and "antibiotic related" has now become part of the conversation where antibiotics are discussed in the health care setting (Furber, Allison, & Hindley, 2017). Antibiotic resistance, a frightening term to the lay person and the health care industry alike, began as early as 1940 (Davies & Davies, 2010). This was when, according to Furber, et al. (2017), penicillinase, otherwise, known as a bacterial adaptation to the antibiotic properties of penicillin, was first documented by those closely studying the properties of bacteria and medicinal interactions. Davies and Davies (2010) reported many bacteria have since become resistant to multiple forms of antibiotic drugs, including those recommended as treatment for the offending pathogen. To further complicate the issue and confound health care providers, many of these multi-drug resistant bacteria are now classified as "nosocomial" – or hospital related infections (Davies & Davies, 2010, p. 475). This infers the infection occurred during or related to health care treatment including antibiotic use according to the authors.

Super bugs, a modern colloquialism for microbial organisms which have undergone multiple mutations resulting in resistance to numerous antibiotic preparations are the most virulent threat on the radar of both researchers and health care providers (Davies & Davies, 2010). One of these such infections is *Clostridium difficile* infection (CDI). *Clostridium difficile* is a toxin-producing bacterium found in the natural environment, often in soil, in fresh water, and in meats (Liubakka & Vaughn, 2016). *Clostridium difficile* was identified in 1935 as a group of anaerobic bacteria that live in the intestinal tract of some healthy individuals (Harvard Health Publishing, 2010). Anaerobes live and reproduce without oxygen. According to Liubakka and Vaughn (2016), *Clostridium difficile* may be found as natural flora, or colonization, causing no

illness in the intestinal tract of some human hosts, while others with CDI develop severe symptoms which may include perforation of the intestine and death. Liubakka and Vaughn (2016) noted in patients with symptomatic CDI, there is usually a history of current or recent exposure to antibiotics.

According to Bien, Palagani, and Bozko (2013), *Clostridium difficile* is normal intestinal flora in humans from infancy until approximately 2 years of age with no symptoms, and are normally kept in check by other normal flora of the human gastrointestinal system, only existing in 1-2 % of healthy adults. Bien, et al. (2013), reported this is subject to change to when dysbiosis, or disturbance in the balance of normal intestinal flora occurs, common with exposure to antibiotics. According to Bien et al. (2013), this may result in an abundance of *Clostridium difficile* bacteria in the intestinal tract, and cause CDI. Liubakka and Vaughn (2016) report antibiotics cause a decrease in the number and types of normal microbial flora in the intestine which results in an environment which permits florid growth of *Clostridium difficile* and subsequent CDI. *Clostridium difficile* are also spore forming bacteria. Harvard Health Publishing (2010) wrote spore forming bacteria are difficult to eradicate with antibiotics and are hard to eliminate on surfaces. This creates the possibility for horizontal transmission of spores from surfaces to patients via the oral-fecal route according to Liubakka and Vaughn (2016).

In 2015, the Centers for Disease Control and Prevention (CDC) described the clinical symptoms of CDI to be watery diarrhea, fever, loss of appetite, nausea, and abdominal pain and tenderness. The CDC (2015) also lists antibiotic exposure as the first risk factor for persons to develop CDI. Other risk factors, according to the CDC, include the persons 65 or older, and being either hospitalized or a resident of a skilled nursing facility. Liubakka and Vaughn (2016)

also noted exposure to *Clostridium difficile*, gastric acid suppression, gastrointestinal tract surgery, disease, or manipulation, and chemotherapy as risk factors for CDI. The CDC (2015) identified CDI as the most common culprit in healthcare related infections in United States' hospitals. Liubakka and Vaughn (2016) noted recurrence of the infection is common in those treated for CDI. These authors also reported exposure to *Clostridium difficile* spores in the health care environment as a significant risk factor contributing to CDI. One possible solution to preventing the development of CDI is the use of probiotic supplements. Liubakka and Vaughn (2016) reported the use of probiotics often considered for prevention of *Clostridium difficile* infection. According to Liubakka and Vaughn (2016), several probiotic compounds have been shown to decrease the incidence of antibiotic associated diarrhea.

The theoretical model of Change to Evidence-based Practice by Rosswurm and Larrabee (1999) is the guiding framework for this study. Clinicians using an evidence-based approach to use of antibiotics and treatments for CDI are in the forefront of lowering the rates of CDI and mitigating the associated sequelae according to the CDC (2015).

Statement of the Problem

Residents of skilled nursing facilities are at risk for CDI when treated with antibiotics. Administration of probiotic supplements has shown to decrease the incidence of antibiotic associated diarrhea in patients (Liubakka & Vaughn, 2016). There is no established protocol to prescribe probiotics for eligible patients receiving antibiotic therapy to reduce the incidence of CDI. The cost of probiotic therapy is not routinely covered by health insurance (Rodgers, Kirley, & Mounsey, 2013).

Research Question

Does the use of probiotic supplements in residents of skilled nursing facilities receiving antibiotic therapy reduce the incidence of *Clostridium difficile* infection?

Hypotheses

H_0: There will be no decrease in the incidence of *Clostridium difficile* infection in skilled nursing facility residents receiving antibiotic therapy with probiotic supplements when compared to residents receiving antibiotic therapy with no probiotic supplements.

H_a: There will be a decrease in the incidence of *Clostridium difficile* infection in skilled nursing facility residents receiving antibiotic therapy with probiotic supplements when compared to residents receiving antibiotic therapy with no probiotic supplements.

Definition of Terms

Antibiotic – antibacterial drug with the "ability to destroy or interfere with the development of a living organism" (Lilley, Collins, & Snyder, 2017, p. 599).

Clostridium difficile infection (CDI) – an abundance of Clostridium difficile bacteria in the intestinal tract of humans (Bien et al., 2013). Symptoms of CDI include frequent watery diarrhea, fever, loss of appetite, nausea, and abdominal pain and tenderness (CDC, 2015).

Skilled Nursing Facility – a health-care institution that meets federal criteria for Medicaid and Medicare Reimbursement for nursing care including especially the supervision of the care of every patient by a physician, the employment full-time of at least one registered nurse, the maintenance of records concerning the care and condition of every patient, the availability of nursing care 24 hours a day, the presence of facilities for storing and dispensing drugs, the implementation of a utilization review plan, and overall financial planning including an annual operating budget and a 3-year capital expenditures program (*Merriam-Webster's*, 2014).

Evidence-based Practice – assimilation of "individual clinical expertise with the best available external clinical evidence from systematic research" (Sackett, Rosenberg, Gray, Haynes, & Richardson, 1996, p. 71).

Probiotic – food ingredient, supplement, or drug containing living non-harmful bacteria that provide a health benefit or improve the physical condition of the person receiving the supplement (Hill et al., 2014).

Need for the Study

Individuals diagnosed with bacterial infections receive antibiotics to treat the infection (Lilley et al., 2017). Antibiotics may disturb the normal intestinal flora of the person with the infection, elevating the risk of CDI (Flatley, Wilde, & Nailor, 2015). The administration of probiotic supplements concomitantly with antibiotic therapy may alter this dysbiosis and slow, or prevent the development of antibiotic associated diarrhea, or CDI (Liubakka & Vaughn, 2016). Few studies have been conducted regarding the incidence of CDI with concomitant use of probiotics and antibiotic therapy. No studies were available for review which were conducted in a skilled nursing facility where residents are elderly and primarily receive oral antibiotics. This retrospective study purposed to ascertain if skilled nursing facility residents receiving concomitant antibiotics and probiotics have a lower incidence of CDI than those receiving antibiotics without any probiotic supplementation.

Significance of the Problem

According to the CDC (2015), CDI was responsible for nearly half million infections in patients in the United States in one single year. Ma, Brensinger, Wu, and Lewis (2017) noted CDI to be the most common health-care associated infection, with a price tag of approximately 5 billion dollars per year to the United States health care system. CDI also contributes significantly

to the morbidity and mortality rate of patients (Ma et al., 2017). The CDC notes persons developing CDI typically become very ill within a short time. Infection with *Clostridium difficile,* whether due to dysbiosis related to antibiotic exposure, advanced age, poor health, or contact with *Clostridium difficile* spores in a health care facility is a serious health threat reaching epidemic status in the United States (Liubakka & Vaughn, 2016).

According to Liubakka and Vaughn (2016) patients who develop CDI while receiving treatment consisting of prescribed antibiotic therapy have a high recurrence rate of infection, approximately 13-29%. Secondary recurrences are more problematic, with a rate of 40% of diagnosed patients experiencing additional recurrence (Liubakka and Vaughn, 2016). Following initial treatment with a course of the antibiotic metronidazole, recurrences are treated with a more expensive oral vancomycin course of therapy (Libuakka and Vaughn). According to Liubakka and Vaughn, (2016) Dificid, or fidaxomicin, is the third line for recurrent infection, with cost being a major concern. According to Cruz (2012), fidaxomicin costs at least $3,500 for a 10-day course, compared to $1,200 for a therapeutic course of oral vancomycin, and $21.00 for a commonly prescribed course of oral metronidazole. These costs continue to escalate as Reveles, Backo, Corvino, Zivkovic, and Broderick (2017) reported the cost of treating a hospitalized patient with fidaxomicin to be approximately $14, 442 per patient compared to $14,179 dollars for a course of therapy with oral vancomycin. A 10-day course of oral metronidazole carries a price tag of approximately $30 depending on insurance coverage according to Epocrates.com (2018).

One possible solution to prevention of CDI is the use of probiotic supplements concomitantly with antibiotic therapy. Liubakka and Vaughn (2016) reported probiotics are often considered for prevention of *Clostridium difficile* infection, treatment of *Clostridium difficile*

infection, and as adjuncts to therapy for *Clostridium difficile* infection. Liubakka and Vaughn (2016) reported that probiotic compounds have been reported to decrease the incidence of antibiotic associated diarrhea. Liubakka and Vaughn (2016) noted probiotics are not regulated by the Federal Food and Drug and Administration. Commercial health insurance plans also do not reimburse for the cost of probiotic therapy (Rodgers et al., 2013).

Probiotics, while holding promise, are limited in use due to lack of sufficient evidence and risk of adverse reactions in the patient with *Clostridium difficile* infection according to Liubakka and Vaughn (2016).

Assumptions

Assumptions of this study include:

1. Not all patients receiving antibiotic therapy develop CDI.
2. Not all patients diagnosed with CDI had prior or concomitant antibiotic therapy.
3. Not all patients receiving antibiotic therapy are prescribed probiotics.

Summary of the Problem

CDI is a significant problem for the patient and the clinician (Ma, et al., 2017). There are many contributing factors to the development of CDI, including exposure to antibiotics. One possible mitigating factor is probiotic supplementation with few studies supporting definitive recommendation (Liubakka & Vaughn, 2016). Conducting a retrospective study of a vulnerable population, while taking into consideration what has already been presented by researchers and clinicians, is a solid way to establish evidence-based practice (Rosswurm & Larrabee, 1999).

Chapter 2

Review of Related Literature

In review of the related literature, several areas were discussed by numerous experts regarding *Clostridium difficile* infection symptoms, diagnosis, and treatment. First, is an overview of CDI including predisposing factors, symptoms, and diagnostic methods. Second, includes treatments, first line, second line, and further recurrence, or drug resistant strains of CDI. Third, includes incidence methods of surveillance and prevention, including antibiotic stewardship and probiotic supplementation.

Predisposing Factors and Symptoms

Ma et al. (2017) wrote CDI is the most common health-care associated infection in the United States. CDI is primarily related to recent prior or current antibiotic use (CDC, 2015). Other predisposing factors according to Liubakka and Vaughn (2016) included the elderly population (age 65 or older), a person hospitalized in acute care, or a resident of a skilled nursing facility. Brown et al. (2016) identified horizontal transmission via the fecal-oral route of transmission common in residents requiring assistance with activities of daily living in the long-term care facility environment as a significant risk factor in this vulnerable population. Liubakka and Vaughn (2016) also noted such risk factors as transmission via care-givers' hands, visitor contact, and environmental factors including stethoscopes, toileting equipment, thermometers, and utensils.

Bien, Palagaini, and Bozko (2013) noted a dysbiosis, or disturbance in normal intestinal flora may occur for varying reasons, including previous or current antibiotic exposure could be a predisposing factor for CDI. The alteration of normal flora by antibiotic exposure allowing a proliferation of a virulent *Clostridium difficile* growth and associated toxin production (Flatley,

Wilde, & Nailor, 2015) may be devastating to an already compromised patient. Flatley et al. (2015) noted the antibiotics frequently associated with CDI include cephalosporins, fluoroquinolones, and clindamycin. Other medications, such as antacids and proton-pump inhibitors commonly prescribed for a variety of gastric issues, alter the digestive tract environment and decrease the acidity of the stomach, creating an environment for a potential proliferation of *Clostridium difficile* (Brown et al., 2016). Liubakka and Vaughn (2016) noted recent gastrointestinal tract surgery, enteral feeding tube placement and feeding, and the presence of irritable bowel disease are additional risk factors for CDI.

According to Liubakka and Vaughn (2016) symptoms may begin slowly, with patients experiencing mild abdominal upset, cramping, and non-bloody diarrhea. Liubakka and Vaughn (2016) reported the patient then may begin to experience fever and chills, nausea, anorexia, more frequent and liquid stools, an elevated white blood cell count, and a rise inflammatory factors including marked elevations in c-reactive protein. Possible sequelae include a systemic inflammatory response, colitis, toxic megacolon, colonic rupture, end organ failure including liver, renal, and respiratory failure requiring mechanical ventilation, and death (Liubakka & Vaughn, 2016).

Diagnosis

Diagnosis of CDI has become progressively more precise, but colonization vs. infection more difficult to discern according to Liubakka and Vaughn (2016). Liubakka and Vaughn (2016) noted patients with a previous CDI may shed spores and test positive for the infection weeks to months beyond the abatement of the illness. Ylisiurua, Koskela, Vainio, and Tuokko (2013) indicted that clinical signs and symptoms as well as detection of *Clostridium difficile* toxins are necessary for an accurate diagnosis of CDI. Flatley et al. (2015) wrote only patients

with liquid, or unformed stools should be tested utilizing enzyme linked assay (ELISA) testing for *Clostridium difficile* toxins A and B. According to Liubakka and Vaughn (2016) a stool culture, once the gold standard for CDI testing, has been replaced with polymerase chain reaction (PCR) assay testing. PCR assay testing is a more precise method according to Ylisiurua et al. (2013) and far less time intensive than all previously used testing methods to diagnose CDI.

Treatments

Treatment recommendations are standardized according to severity of disease (Liubakka & Vaughn, 2016) with the following recommendations:

Mild to moderate disease includes treatment with metronidazole 500 mg orally three times a day for 10 days. If metronidazole is not tolerated or there is no clinical improvement, then vancomycin 125 mg orally 4 times a day for 10 days is an adequate substitution. Fidaxomicin 200 mg orally twice a day for 10 days is nearly equally expensive to oral vancomycin but easier to manage with less dosing times required for the patient according to Reveles et al. (2017).

If the patient remains symptomatic, or becomes more clinically ill, a combination of oral vancomycin 500 mg orally 4 times daily with addition of intravenous metronidazole 500 mg every 8 hours and a vancomycin enema of 500 mg in 500 ml normal saline are recommended in addition to a surgical consult. Recurrent infections, becoming more common according to Liubakka and Vaughn (2016), are treated with Fidaxomicin and possibly rafiximin 400 mg twice daily.

Liubakka and Vaughn (2016) indicated fecal microbiota transplant (FMT) is being recommended for immunosuppressed patients, patients with a third symptomatic recurrence, and those not responding to standard treatments. Patients with recurrence of CDI are often found to

have multiple drug resistant strains of CDI, making treatment more complex and FMT a viable alternative to antibiotic treatment (Liubakka & Vaughn, 2016). Liubakka and Vaughn also pointed out that the process of FMT is regulated by the United States Food and Drug Administration and involves donor stool subjected to rigorous screening procedures. The transplant may be administered via upper endoscopy, pill ingestion, colonoscopy, enema, rectal tube, or sigmoidoscopy, utilizing fresh or frozen stool (Liubakka & Vaughn, 2016).

Incidence

In 2015, Lessa et al. reported CDI was responsible for nearly 500,000 infections with 29,000 associated deaths in the United States. Lessa et al. (2015) reported a 1.3% death rate in patients 30 days after initial diagnosis of a community associated CDI. Health care associated infections had a recurrence rate of nearly 21% and a death rate of 9.3 % within 30 days of diagnosis (Lessa et al., 2015). Ma et al. (2017) noted a 50% increase in hospitalizations for CDI between the years 2000 and 2010. Liubakka and Vaughn (2016) reported an increase in nearly 100 cases of CDI per 100,000 population in the health care setting.

Prevention

The CDC (2015) has made prevention of CDI a national priority. Multiple approaches to prevention are plausible: limitation and judicious use of antibiotic therapy; strict isolation to prevent horizontal transmission; and use of probiotics according to the CDC. The CDC (2015) has conducted multiple studies indicating a decrease in antibiotic use, by as little as 10%, may reduce the incidence of CDI by approximately 34%. The CDC (2015) has developed stewardship programs to improve antibiotic prescribing and is funding further research into eliminating hospital acquired infections; thereby decreasing the number of patients acquiring CDI.

The CDC (2015) identified the implementation of isolation procedures to prevent the horizontal spread to both patients and health care personnel are recommended: use of appropriate personal protective equipment for health care personal; appropriate room placement for patients; and sanitation being instituted. Liubakka and Vaughn (2016) wrote that probiotic supplements may play a role in prevention of antibiotic associated diarrhea, but with several issues limiting the use of these substances. Liubakka and Vaughn (2016) specifically listed probiotic compounds containing *Saccharomyces boulardii* and *Lactobacillus* as known to decrease the incidence of diarrhea in patients taking antibiotics. Use of these substances in CDI, as adjunctive therapy, has not shown to be of value and may be harmful to critically ill or immunosuppressed patients (Liubakka & Vaughn, 2016). Liubakka and Vaughn (2016) observed that probiotics are not regulated by the United States Food and Drug Administration and are not a covered treatment by most insurance companies. Professional medical societies have recommended not using probiotics in patients diagnosed with CDI due to the risk of invasive infections with *Lactobacillus* and possible systemic fungal infections in immunosuppressed patients (Liubakka & Vaughn, 2016).

Theoretical Framework

Rosswurm and Larrabee's (1999) Model for Change to Evidence Based Practice is applicable to the advanced practice nurse in the clinical setting. There are 6 integral steps to the model according to Rosswurm and Larrabee (1999):

Step 1: Assess the need for change in practice. Including stakeholders, collecting internal data about the current practice, and identifying a problem are part of the initial assessment and identifying a need for change.

Step 2: Link problem interventions and outcomes. Identifying interventions and activities and designating desired outcomes utilizing standardized classifications and terminology assist the advanced practice nurse in developing a plan.

Step 3: Synthesize the best evidence. Review of the literature and previously established protocols related to the practice of concern.

Step 4: Design – practice change. Following the protocol review, adapt or change said protocol if necessary to adhere to an evidence-based practice model of care for the patient.

Step 5: Implement and evaluate. The authors recommend doing a pilot study of the new protocol and evaluating the results.

Step 6: Integrate and maintain. Communicate recommended changes to stakeholders with education materials provided to staff to reinforce or change practice.

Summary of Review of the Related Literature

The problem of CDI is complicated and increasing in scope and severity in the United States health care system according to the CDC (2015). Prevention, early detection, effective isolation precautions and careful monitoring of patients suspected or diagnosed may help mitigate both the severity and spread of CDI in skilled nursing facilities. Concomitant use of probiotics with antibiotics may prevent the development of antibiotic associated diarrhea and possibly CDI (Liubakka & Vaughn, 2016). A retrospective study of patients on antibiotics with and without concomitant use of probiotics would provide valuable information related to this potentially deadly disease.

Chapter 3

Methodology

The purpose of this quantitative, retrospective study was to ascertain if residents in a skilled nursing facility who received antibiotics with concomitant probiotic supplements had a lower rate of CDI than residents who received antibiotics without probiotic supplementation.

Research Design

This was a retrospective study of a casual comparative convenience sample of 164 electronic medical records of skilled nursing facility residents selected to audit antibiotic use, probiotic use, and diagnosis of CDI. Approval was obtained by a skilled nursing facility in rural western Pennsylvania. The study was commenced after approval by the Institutional Review Board of Clarion University of Pennsylvania.

Setting

The setting was a skilled nursing facility in rural western Pennsylvania. The facility agreed to a retrospective study of electronic medical records.

Sample

The sample was a casual comparative sample of 164 random skilled nursing facility resident electronic medical records. Residents who had not received antibiotic therapy were excluded from the study. Residents receiving antibiotic therapy and antibiotic therapy with concomitant probiotic therapy were included in the study data.

Ethical Considerations

No research or protocol review was conducted until approval granted by the Institutional Review Board of Clarion University of Pennsylvania. No identifying information regarding resident name, birthdate, or otherwise identifiable information was included in the chart review data or study results. No identifiable information related to the skilled nursing facility was included in the study results.

Instrumentation

An Excel spreadsheet was utilized to denote:

- random number assigned to resident chart
- any previous or current prescription for antibiotic therapy
- any previous or current concomitant prescription for probiotic supplementation
- any previous or current testing or diagnosis of CDI within 6 weeks of antibiotic therapy

Data Collection

Following approval from the Institutional Review Board of Clarion University (IRB 23-18-9), data collection was completed by this nurse practitioner with a form created to collect and collate data during electronic medical record review.

Figure 1: Data Collection Form

Random Resident Number	Antibiotic /Name and Dose/Therapy Course	Probiotic Name/Dose	Symptoms of CDI	Testing for CDI (+) or (-)

Figure 1: Data collection form used to collect and collate data.

Summary of Methodology

The methodology utilized was a casual comparative sample of resident electronic medical records recording antibiotic and probiotic therapy, antibiotic related symptoms, and positive or negative testing for CDI. The protocol from the skilled nursing facility related to suspicion, isolation, and treatment of clients with symptoms or diagnosis with CDI was examined and recommendations for protocols identified to reflect evidence-based practice with education as approved by administration of the skilled nursing facility. A consultant reviewed and calculated collated data for statistical significance.

Chapter 4

Results and Discussion

Following approval by the Clarion University of Pennsylvania Institutional Review Board, a quantitative, a retrospective study was conducted with a review of resident electronic medical records at a skilled nursing facility in rural western Pennsylvania. Discussion of findings of the review related to the incidence of CDI in residents treated with antibiotics compared to residents treated with antibiotics and probiotics are presented.

Results

The electronic medical records of 164 residents were reviewed by this nurse practitioner. This nurse practitioner reviewed the electronic medical records of 164 residents. Ninety-nine residents received antibiotic therapy. Fifty-five residents received antibiotic therapy with concomitant probiotic supplements. As shown in Figure 2, few residents received no antibiotic therapy. Seven residents did not receive antibiotic therapy and were excluded from this retrospective study.

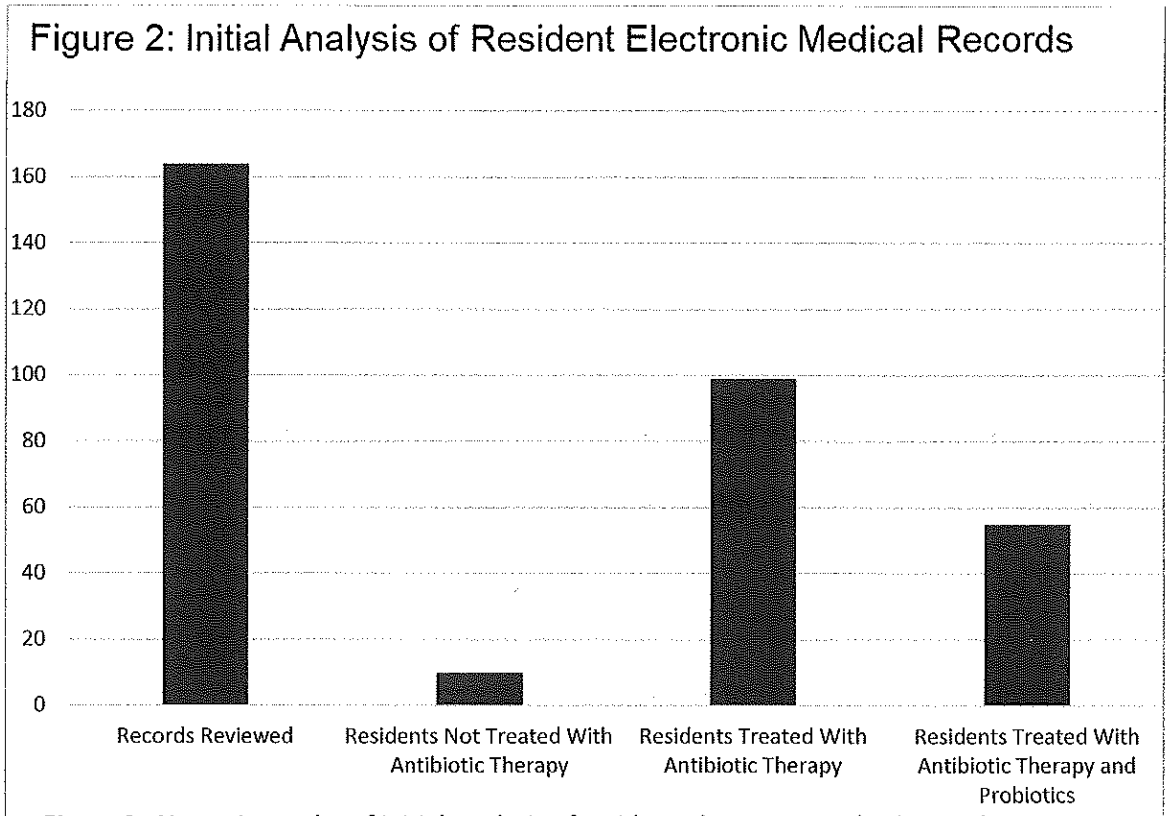

***Figure 2*: Numeric results of initial analysis of resident electronic medical record review.**

Further analysis, as shown in Figure 3, demonstrated twelve of the residents who received antibiotics developed symptoms of CDI including diarrhea. This compares to one of the resident group receiving antibiotic therapy and probiotics who developed symptoms of CDI including diarrhea.

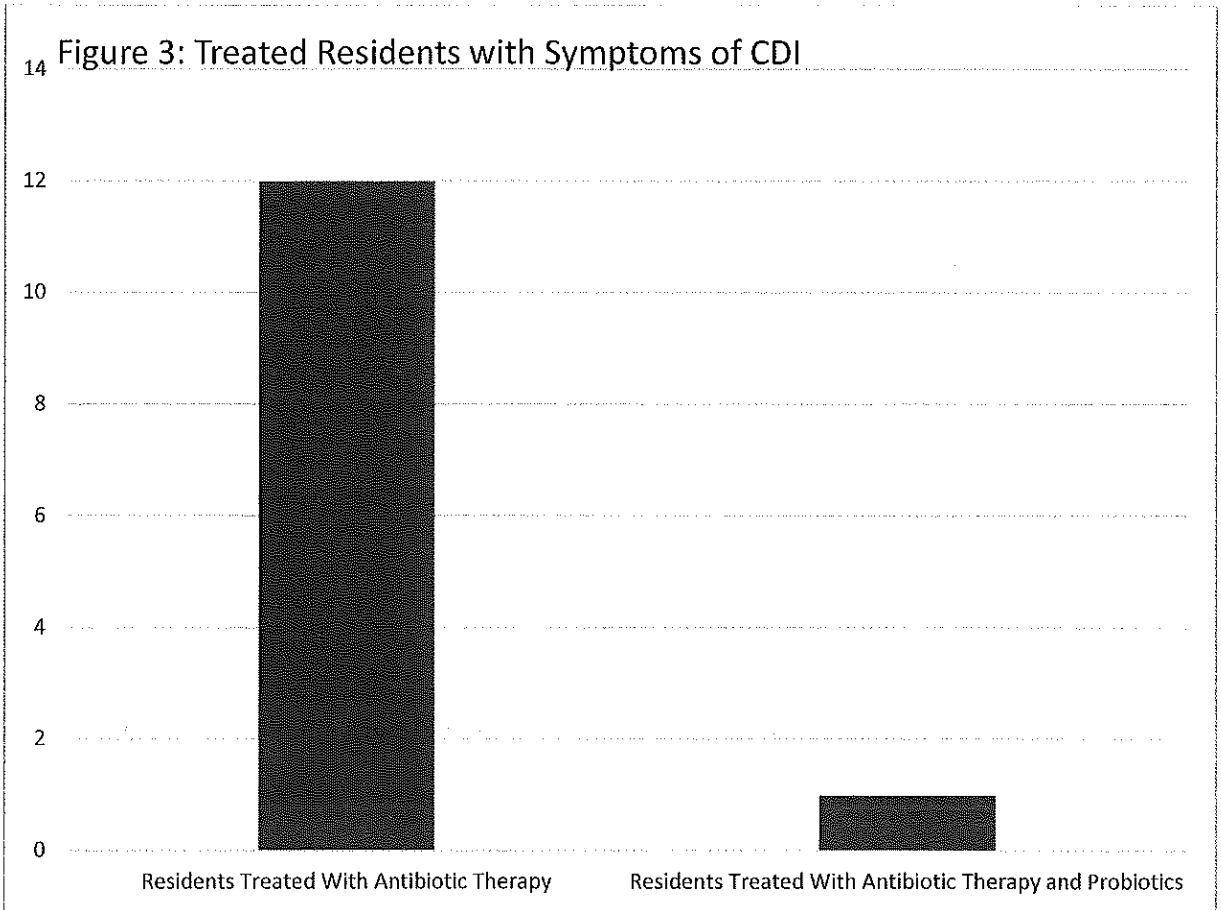

Figure 3: Number of residents who exhibited symptoms of CDI after medication therapy.

Figure 4 demonstrates the difference in number of residents in the two groups testing positive for *Clostridium difficile* infection. Testing for *Clostridium difficile* infection returned with clinical laboratory results reported positive CDI in three residents receiving antibiotic therapy and development of CDI symptoms including diarrhea. No positive laboratory CDI testing was demonstrated in the resident receiving antibiotics and probiotics who developed symptoms of CDI including diarrhea.

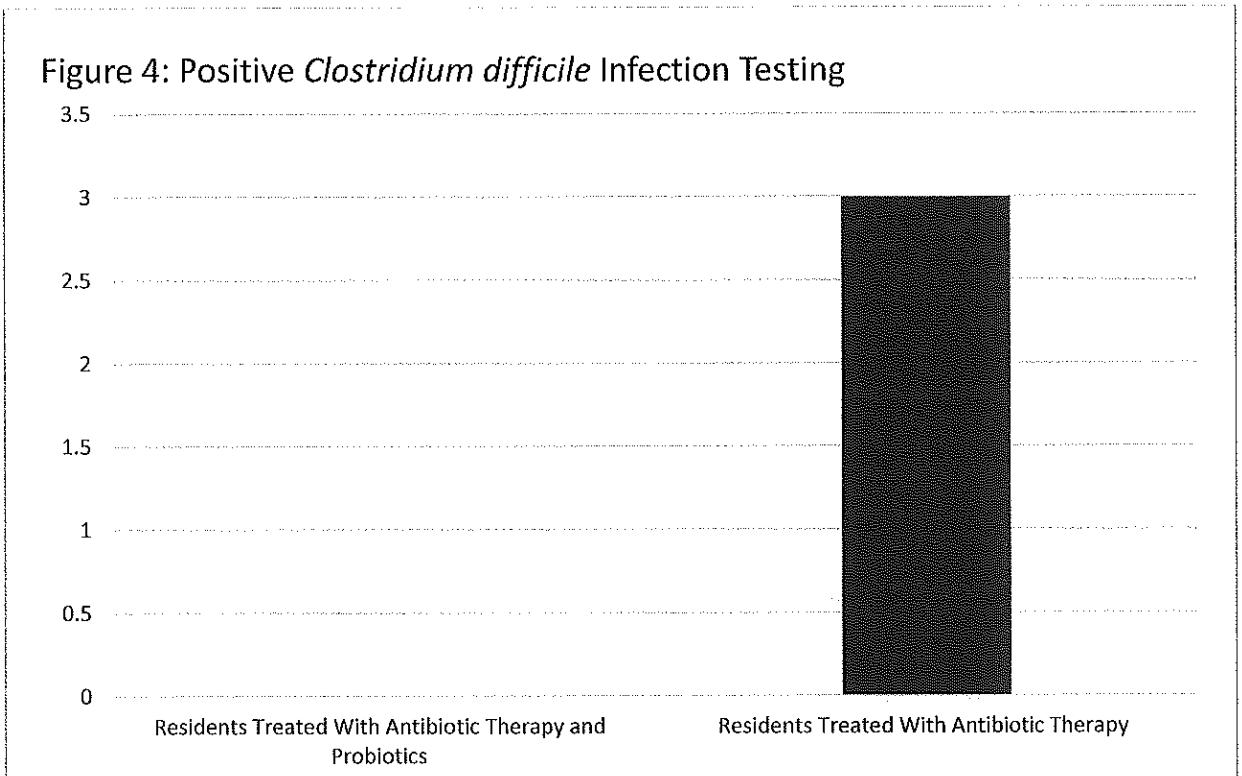

Figure 4: Number of residents with laboratory testing returning positive *Clostridium difficile* infection.

Discussion of Results

After completion of the quantitative, retrospective study it was found that 12.1% of the residents treated with antibiotic therapy developed symptoms consistent with CDI and were tested for this infection. Residents receiving antibiotic therapy and probiotic supplements who demonstrated symptoms consistent with CDI and were tested for the infection was 1.8 percent. Twenty-five percent of the residents receiving antibiotic therapy developing symptoms including diarrhea were diagnosed as positive for CDI. No residents receiving probiotics concomitantly with antibiotic therapy tested positive for CDI. Table 1 represents the numbers of residents in each group.

Table 1

Residents Receiving Antibiotic Therapy and Antibiotics with Probiotics with Development of Symptoms and CDI Testing

Antibiotic Therapy	CDI Symptoms	+ CDI	Probiotic Therapy	CDI Symptoms	+CDI
99	12	3	55	1	0

Note: + CDI = positive laboratory testing result for *Clostridium difficile* infection

A Fisher's exact test demonstrated a two-tailed p value equaling 0.0330, a statistically significant difference between outcomes of residents receiving antibiotic therapy and residents receiving antibiotic therapy with probiotic supplements.

Hypotheses Results

The following hypotheses were formulated in the planning of this retrospective study.

H_0: There will be no decrease in the incidence of *Clostridium difficile* infection in skilled nursing facility residents receiving antibiotic therapy with probiotic supplements when compared to residents receiving antibiotic therapy with no probiotic supplements. This hypothesis was not proved with the study results. The null hypothesis is rejected.

There is evidence to support the following research hypothesis:

H_a: There will be a decreased incidence of *Clostridium difficile* infection in skilled nursing facility residents receiving antibiotic therapy with probiotic supplements when compared to residents receiving antibiotic therapy with no probiotic supplements.

Limitations

A limitation of this quantitative, retrospective study is the sample size related to incidence of CDI and antibiotic use with or without concomitant probiotic supplementation. The sample size may not be representative to have adequate statistically significant results. Additional limitations include the resident, including physical condition, age, co-morbidities, and possibly previously diagnosed CDI. The facility electronic medical record with possible limited transposition of paper medical record information is another limitation of the study. An additional limitation is the type and course of antibiotic therapy and probiotic therapy differed from resident to resident.

Summary

A retrospective chart review of residents in a skilled nursing facility being treated with antibiotic therapy and antibiotic therapy and probiotics was conducted at a rural skilled nursing facility in Western Pennsylvania. The results demonstrated a statistically significant difference in the number of residents diagnosed with CDI symptoms or CDI receiving antibiotic therapy compared to the diagnosis of CDI symptoms or CDI in patients receiving antibiotic therapy with concomitant probiotics. The null hypothesis is rejected.

Chapter 5

Summary, Conclusions, and Recommendations

Summary of Findings

Infections are treated with antibiotics (Runcie, 2015). Antibiotics are effective in treating bacterial infections, but also may cause intestinal dysbiosis which may lead to an overgrowth of opportunistic bacteria such as *Clostridium difficile* according to Bien et al. (2013). *Clostridium difficile* infection is associated with moderate to severe illness in patients and may result in death (Liubakka & Vaughn, 2016). While no established protocol exists, research has shown a decrease in the incidence of antibiotic diarrhea with the concomitant administration of probiotics according to Liubakka and Vaughn (2016). This retrospective, quantitative study reviewed the electronic medical records of residents in a rural skilled nursing facility. The study included residents receiving antibiotic therapy and antibiotic therapy with concomitant probiotic therapy. Records were reviewed for the reporting of CDI symptoms such as diarrhea, and subsequent clinical laboratory testing for CDI.

Study results demonstrated a statistically significant difference in the number of residents receiving antibiotic therapy experiencing CDI symptoms and positive laboratory testing as compared to the number patients receiving antibiotic therapy and concomitant probiotics.

Implications for Advanced Practice Providers

While the evidence did not support the null hypothesis formulated for this retrospective study, the considerable limitations of the study must be considered when extrapolating the results into implications for advanced nursing practice. The small sample size, the age and condition of the residents, and the possible previously unknown CDI diagnosis in residents all must be considered having an impact on study results.

With those limitations tempering the study results, the theoretical framework of Rosswurm and Larabee's (1999) Model for Change to Evidence-based Practice provides significant guidance to improving resident care for a vulnerable population receiving antibiotic therapy in a skilled nursing facility. One case of CDI, while possibly devastating to a resident, may be transmitted horizontally through ineffective isolation or handwashing techniques (CDC, 2015). Review of both isolation procedures and patient care protocols for residents receiving antibiotic therapy at the skilled nursing facility demonstrated surveillance and action plans consistent with the CDC's recommendations to prevent the horizontal spread of CDI. This encompasses Step 1 of Rosswurm and Larrabee's (1999) Model for Change to Evidence-based Practice. This first step is an assessment of the need for change in practice.

Step 1 of Rosswurm and Larrabee's (1999) model may also incorporate the antibiotic stewardship guidelines developed by the CDC (2015) to improve antibiotic prescribing through

protocols and recommendations to clinicians. Review of antibiotic stewardship at the skilled nursing facility demonstrated stringent protocols and reporting of antibiotic use. Improving the outcome of patients prescribed antibiotic therapy includes synthesizing the best evidence in making prescriptive decisions, the third step of the Model for Change to Evidence-based Practice (Rosswurm & Larrabee, 1999). Liubakka and Vaughn (2016) observed the concomitant use of probiotics with antibiotics possibly preventing the development of antibiotic diarrhea and possible CDI, however, there are no definitive clinical guidelines at this point. Clinicians must continue to surveil research findings for adequate antibiotic stewardship and situations where probiotic supplements may be appropriate for patients being treated with antibiotic therapy.

Implications for clinicians to prescribe within the guidelines of antibiotic stewardship recommendations may prevent the development of antibiotic resistant organisms, including *Clostridium difficile* (CDC, 2015).

Recommendations for Further Research

Further research regarding antibiotic therapy and prevention of CDI are imperative to improve patient outcomes, cut costs, and hinder the development of antibiotic resistant microbes (Liubakka & Vaughn, 2016). Several ways this research may have been performed differently include categorizing the antibiotic therapy into specific pharmacotherapeutic classifications with subsequent results or tracking antibiotic therapy for a definitive purpose such as urinary tract infection treatment. Other changes to the research such as surveilling residents diagnosed with diarrhea including possible causes, test results, and treatments. Research identifying residents within a provider practice to receive antibiotics or antibiotics with consistent formulary and dosing schedules of probiotics is a definitive way to study results over a protracted length of

time. A presentation of this study results was presented to the administration of the skilled nursing facility.

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