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The Use of Probiotics to Prevent Antibiotic Associated Diarrhea: Current Primary Care Practice and Introduction of an Evidence Based Practice Protocol

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The Use of Probiotics to Prevent Antibiotic Associated Diarrhea:

Current Primary Care Practice and Introduction of an Evidence Based Practice Protocol

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Doctoral research Project submitted to the School of Nursing at

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Abstract

Antibiotic associated diarrhea (AAD) is defined as the self limiting diarrhea that occurs during or following a course of antibiotics (Bartlett, 2002; Dendukuri, Costa, McGregor, & Brophy, 2005; Pimental & Choure, 2009; Sullivan & Nord, 2005; Vrabie & Aberra, 2009). Despite strong support for the use of probiotics in the outpatient setting for preventing AAD, there is lack of probiotic utilization by primary care providers in the outpatient setting. Current literature indicates that one of the barriers to probiotic use is medical doctors' (MDs) and nurse practitioners' (NPs) attitude and lack of knowledge regarding the use of probiotics in preventing antibiotic associated diarrhea. The purpose of this study was to evaluate the current attitude and knowledge of providers (MD, NP and physician assistant [PA]) in a primary care practice in central and eastern Connecticut. Current attitude towards the use of probiotics to prevent AAD was positive ($p=0.083$). The level of providers knowledge increased by 17.53% ($p=0.002$). NPs showed a greater increase in knowledge in the post test than MDs ($F(21)=59.345$, $p=0.005$). The second purpose of the study was to introduce an evidence-based protocol, during an educational intervention, for use in the adult outpatient setting. The third purpose of the study was to evaluate providers' use of probiotics as documented in the Electronic Medical Record after the introduction of an educational intervention. There was a 50% increase in the number of providers recommending probiotics when prescribing an antibiotic. The result of this study showed providers have a positive attitude toward the use of probiotics to prevent AAD. There was also an increase in the provider knowledge of probiotic use after an educational intervention and the introduction of an evidence-based protocol. There was also an increase in the number of providers who recorded their recommendation of a probiotic when prescribing an antibiotic. Educational programs can be successful in introducing any evidence-based protocol. Further

research is needed to evaluate if this increase in the use of probiotics is sustained. Further research is also needed to evaluate the extent providers implement the evidence-based protocol within their practice.

Problem

Statement of the Problem

Many episodic visits to primary care providers are due to complaints related to an infective process; cellulitis, sinusitis, community acquired pneumonia, etc. These are appropriate and reasonable conditions for antibiotic treatment. All antibiotics have the potential side effect of diarrhea which puts the patient at risk for antibiotic associated diarrhea (AAD), this risk is increased if the patient has co-morbidities or advanced age. Preventing AAD improves patient health outcomes. The current treatment for AAD is to stop the prescribed antibiotic; evidence supports AAD prevention by adding a probiotic to the treatment regime. Probiotics have not been used widely or consistently in the adult outpatient setting. One of the barriers to probiotic use is lack of provider knowledge of probiotics to prevent AAD. The purpose of this study is to discover what providers attitude and knowledge about probiotics and if an educational intervention increases probiotic use in the outpatient adult setting.

AAD affects one in five adults prescribed antibiotics (Avadhani & Miley, 2011; Weichseilbaum, 2009). When a probiotic is taken concurrently with an antibiotic, AAD is reduced to one in ten adults (Avadhani & Miley, 2011; Weichseilbaum, 2009). Several meta-analyses support the use of probiotics to prevent AAD in the adult population (Avadhani & Miley, 2011; Cremonini, et al, 2002; D'Souza, Rajkumar, Cooke, & Bulpitt 2002; Kale-Pradhan, Jassal & Wilhelm 2010; McFarland 2010; Sazawal, et al 2006; Szajewska & Mrukowicz 2005). Only a few studies specifically describe the use of probiotics in the adult outpatient population (Armuzzi, et al., 2001). The evidence supports the use of probiotics to prevent AAD in the adult outpatient population. It is not clear if probiotics are currently used by primary care providers.

Information discussing provider attitude and knowledge in the use of probiotics to prevent AAD is minimal. Hermosilla (2009) reports that after an educational session there was an increase in probiotic prescribing in a medical intensive care unit. Camras (2008) proposed an educational project to be done at an adult primary care practice however results were not reported in her paper. Nichols, Grobe and Roche (2005) report on a web based survey they used to determine what advice general practitioners give to patients regarding probiotics. Nichols, et al. concludes that greater than 50% of the general practitioners advise probiotics in certain clinical scenarios.

The main purpose of this study is to evaluate the knowledge and attitude toward the use of probiotics to prevent AAD. The study evaluated approximately 70 providers (MD, NP, and PA) in a primary care and urgent care practice located in central and eastern Connecticut. The secondary purpose is to introduce an evidence-based protocol for the use of probiotics to prevent AAD accomplished by an in person educational intervention. The final purpose of this study is to identify if knowledge increases and practice changes following the educational intervention.

Goals of the Project

- To get at least 50% participation from the 70 providers to complete the study.
- To design an evidence-based protocol for the use of probiotics to prevent AAD in the outpatient adult setting.
- To present an educational intervention introducing the evidence-based protocol to the provider staff.
- To document and analyze current antibiotic and probiotic prescribing habits of Primary Care Providers.

- To present results to the medical staff at the conclusion of this project.

Evidence of the Problem

Antibiotics continue to be prescribed in large numbers. According to the American College of Physicians (2011), 133 million courses of antibiotics are prescribed each year. These are for wide ranging infections, e.g.: sinusitis, community acquired pneumonia, cellulitis, urinary tract infections, etc. There is variation of specific antibiotic prescribed, depending on presumed infective bacteria, co-morbidities, and bacteria sensitivities. The use of any antibiotic for any infection can cause AAD. This indicates that increasing the number of antibiotics increases the incidence of AAD.

The incidence of AAD is reported as between 5 -30% of adults prescribed antibiotics (Avadhani & Miley, 2011; Bartlett, 2002; Hickson, et al, 2007; Jenkins, et al 2005; McFarland, 1998; Pimental & Choure, 2009; Sullivan & Nord, 2005; Teitelbaum & Walker, 2002; Weichselbaum, 2009). These numbers represent the total incidence of AAD both inpatient and outpatient. McFarland (2008) states that outpatient incident rates of diarrhea for every 100 visits for diarrhea 34 are for AAD. Using these reported incidences, approximately 29 million adults in the United States experienced AAD during a course of outpatient antibiotic treatment in the year 2001. Despite these numbers the true incidence of AAD in the outpatient adult population is higher; in a study by Gessert & Rubin (2011), they conclude that AAD is underreported.

In the outpatient setting, antibiotic associated gastrointestinal side effects are often the reason a patient stops the antibiotic, but this information is not regularly reported to the provider by the patient (Armuzzi, et al, 2001). Anastasio, et al, (1992) report a discontinuance rate for erythromycin due to diarrhea as between 4%-25%. Damrongmane and Ukarapol (2007) report

two thirds of the pediatric patients with AAD the antibiotic was stopped without medical advice. The inpatient setting is a controlled environment; the administration of medications is controlled by facility practice guidelines, while there is no control in the outpatient setting. In conclusion, the prevention of the side effect of AAD is averted then the full antibiotic course is likely to be finished. By inference there would be a decrease in *Clostridium difficile* cases, as *C. difficile* is considered a subset of AAD for the purposes of this study.

A review of the existing literature supports the prophylactic use of probiotics to prevent AAD in the adult inpatient setting. In the outpatient setting there is the challenge of different infective processes and different antibiotic treatments. The reviewed studies were not diagnosis specific nor were they antibiotic specific and most did not control for these variables. This is helpful in the outpatient setting when the choice of antibiotic is generally broader for the range of infective processes treated. The support of concurrent probiotic use in a wide variety of diagnostic and treatment combinations becomes very helpful in the outpatient adult setting (Armuzzi, et al, 2001; Avadhani & Miley, 2011; Cremonini, et al., 2002; Kale-Pradhan, Jassal & Wilhelm, 2010; McFarland, 2010; Sazawal, et al, 2006; Szajewska & Mrukowicz, 2005).

Armuzzi, et al., (2001), Avadhani and Miley, (2011), Cremonini, et al., (2002), Kale-Pradhan, Jassal and Wilhelm, (2010), McFarland, (2010), Sazawal, et al., (2006) and Szajewska and Mrukowics, (2005), all focused on reducing AAD in the inpatient setting, this speaks to a need for further investigation of the use of probiotics in the outpatient setting. The conclusions of these meta-analyses are applicable in the outpatient setting for use of probiotics for the prevention of AAD. These supplements are readily available over the counter and their use in the outpatient setting is relatively unknown.

Armuzzi, et al., (2001), is an outpatient adult study that addresses probiotic use for the prevention of AAD. This study looked at 60 healthy adults who were asymptomatic, *Helicobacter pylori* positive in an outpatient setting. Study participants were randomized to either probiotic or placebo while receiving standard treatment with a macrolide antibiotic; an antiparasitic and proton pump inhibitor. They used *Lactobacillus GG* 6×10^9 CFU for 14 days, in the treatment arm of the study. The probiotic was given the week of *H. pylori* eradication therapy and the week after. They report a significant reduction of AAD, (RR=0.1; CI 95% 0.1-0.9). They conclude that *L. GG* is effective in reducing the incidence of AAD in the adult outpatient setting.

It is unclear why there are so few studies of probiotics for the prevention of AAD in the adult outpatient setting. The researcher proposes that probiotics are over the counter supplements sold direct to consumer and monetary allocation for these types of studies may not benefit the companies. Studies that look at provider attitude and knowledge would direct educational programs to increase awareness of the benefits of probiotics. For probiotics to be considered evidence based practice these studies need to be done to provide support for their use.

Community Needs Assessment

In a demonstration project started in 2007, the medical team of a rural eastern Connecticut skilled nursing facility (SNF) noted an increase in the incidence of diarrhea. This prompted a review to determine the root cause of this increase. Increases in antibiotic usage, due to an outbreak of upper respiratory infection, lead to these cases of AAD. It was felt that there must be a way to treat or prevent diarrhea associated with antibiotics. The protocol shows a reduction in AAD to zero over a five year time frame. This protocol consists of the

administration of a probiotic every time a course of antibiotics is prescribed. The protocol continues to be in place at this SNF.

If the introduction of a probiotic can reduce AAD in the SNF population can the same reduction be realized in the outpatient adult setting? It is well documented that probiotics are effective in reducing the incidence of AAD in the pediatric outpatient setting but there is little documentation supporting the use of probiotics for adults. This gap in the literature provides an opportunity for research.

Several personal discussions were undertaken with specialists within the researchers' provider community. In a discussion on November 9, 2011 the local infectious disease specialist, Eugene M. Ciccone, MD, agrees that there is a need for the use of probiotics in adults and further study is need in the outpatient adult setting. Ajit J. Kokkat, MD, a local gastroenterologist, also supports the use of probiotics in the adult population and agrees that there is a need for further study in the population. Dr. Kokkat reviewed and endorsed the proposed protocol. The information was also reviewed by Lynn M. Rapsilber, MSN, APN-BC, APRN, specializes in gastroenterology; is an advocate of the use of probiotics to prevent AAD. Ms. Rapsilber also reviewed and endorsed the protocol. This project was formally approved by Kent Stahl, MD, Chief Executive Officer and Medical Director of Hartford Medical Group. A formal stakeholder letter can be found in Appendix 4. As the medical director, Dr Stahl is supportive of the need for research within the adult population. This study has also been discussed and approved by the office medical director, Michael A. Kilgannon, MD.

Stakeholders

Key stakeholders include the decision makers Hartford Medical Group (HMG). These decision makers include the Chief Executive Officer/Chief Medical Officer, Kent Stahl, MD and the Chief Operating Officer, John Fundock, PA. They supported the provided time during the medical staff meeting for the educational intervention.

Review of Literature

Antibiotic associated diarrhea is accepted to refer to the diarrhea that occurs during or following a course of antibiotics (Bartlett, 2002; Dendukuri, et al, 2005; Pimental & Choure, 2009; , Sullivan & Nord, 2005; Vrabie & Abera, 2009). The incidence of AAD is reported as between 5 -30% (Bartlett, 2002; Hickson, et al, 2007; Pimental & Choure, 2009; Sullivan & Nord, 2005; Teitelbaum & Walker, 2002). Bartlett (2002) breaks down these percentages by offending antibiotic: ampicillin, 10-25%; amoxicillin-clavulanate, 10-25%; cefixime, 15-20%; and all others cephalosporins, fluoroquinolones, azithromycin, clarithromycin, erythromycin, and tetracycline, 2-5%. Jenkins, et al (2005) report 30% of patient can experience AAD. For the purposes of this study *C. difficile* is considered a subset of AAD.

Diarrhea can pose a serious problem for any patient beyond the nuisance factor. Diarrhea leading to dehydration and electrolyte imbalance complicates the treatment of a simple infection. Add this to any potential co-morbid conditions a patient may have and a life threatening situation can ensue. The prevention of all types of diarrhea associated with antibiotic use would decrease negative outcomes, avoid adverse events, save healthcare dollars and decrease the likelihood of the patient stopping the antibiotic therapy prematurely due to diarrhea. The use of narcotics and antidiarrheal medications combined with the derangement of the intestinal flora has been postulated to potentially cause the complication of toxic mega-colon. In the outpatient setting

preventing diarrhea means a course of antibiotics is completed as directed, as well as both direct and indirect healthcare costs are reduced. The current approach to AAD is to discontinue the offending antibiotic (Bartlett, 2002).

It is generally accepted that the cause of AAD is exposure to antibiotics, oral or parenteral (Bartlett, 2002; Rohde, Bartolini & Jones, 2009; Vogel, 1995; Vrabie & Aberra, 2009). Other risk factors include: use of fluoroquinolones, neonates born prematurely, severe illness, prolonged antibiotics use, nasogastric intubation, age greater than 65 years, male gender, use of proton pump inhibitor, medical patient, increased length of hospital stay, gastrointestinal surgery or gastrointestinal manipulation, immunodeficiency, narcotic use and antidiarrheal medications (Bartlett, 2002; Rohde, Bartolini & Jones, 2009; Vogel, 1995; Vrabie & Aberra, 2009).

There are currently no clinical guidelines for the use of probiotics in the outpatient setting. A search of the National Guideline Clearinghouse, the Cochrane Library, Pub Med, and CIAHL, from 1980 to present, yielded evidence and suggestion of probiotic use but no guidelines that outline safety, dosing, adverse events and recommended protocols. A search using the term antibiotic associated diarrhea in the National Guideline Clearinghouse returned 61 possible guidelines but none were specific for AAD. The closest guideline; “World Gastroenterology Organisation (WGO) practice guideline: acute diarrhea,” however, this guideline does not address diarrhea specifically associated with antibiotics. It does address the use of probiotics: “Controlled clinical intervention studies and meta-analyses support the use of the specific probiotic strains and products in the treatment and prevention of rotavirus diarrhea in infants. However, all effects are strain-specific and need to be verified for each strain in human studies. Extrapolation from the results of even closely related strains is not possible, and

significantly different effects have been reported” (WGO, 2008, page 9). A search of the Cochrane Library found 29 citations with the search antibiotic associated diarrhea. Two of these were considered applicable to this paper. One entitled “Probiotics for the prevention of pediatric antibiotic-associated diarrhea” is a full review with recommendations (Johnston, Supina, Ospina, & Vohra, 2007). This report is specific for the pediatric population and has limited applicability to the adult population. The other report, “Probiotics for the prevention of *Clostridium difficile* antibiotic-associated diarrhea in adults and children,” is only in the development stage with no standards put forth at this time (Pillai & Nelson, 2008).

Antibiotic Associated Diarrhea

Probiotics have a role in the prevention of AAD. A probiotic is defined by the World Health Organization as “Live microorganisms which when administered in adequate amounts confer a health benefit on the host,” (Weizman, Asli & Alsheikh, 2005; World Health Organization, 2001, page 5). The Cochrane Collaboration has approved a review that states probiotic treatment was demonstrated to be beneficial versus placebo in the prevention of pediatric AAD (Johnson, et al, 2008). The literature discussing prevention of AAD in the adult population using probiotics has many small studies that make comparisons between the studies challenging (Armuzzi, et al, 2001; Davidson, Hibberd, Calderwood, & Baron, 2009; Dendukuri, et al, 2005; Sullivan & Nord, 2005). Acknowledging current studies are disparate there is evidence for the use of probiotic monotherapy to prevent AAD in adults in the inpatient setting (D’Sousza, Rajkumar, Cooke & Bulpitt, 2002; Santosa, Farnworth & Jones, 2006; Sullivan & Nord, 2005). In a randomized control study (RCT) by Hickson, et al, (2007) researchers gave inpatients a probiotic drink that contained three different probiotics which showed a significant reduction in the incidence of AAD ($p=0.007$). Wallace (2009) notes that a dose dependent effect

improved outcomes of AAD when the dose was 5.5 to 20 billion colony forming unit (CFU) per day. Of the 10 studies evaluated by Wallace, five studies looked at monotherapy using *Lactobacillus sporogenes*, *Lactobacillus GG* or *Saccharomyces boulardii* and all decreased the incidence of AAD. None of the studies were able to agree on which probiotic to use, dose of probiotic and length of use (D'Sousza, et al, 2002; Dendukuri, et al, 2005; Miller & Fraser, 2009). Accumulated evidence states that probiotics reduce the risk of AAD particularly the probiotics *S. boulardii* and *L. GG* (Wallace, 2009; Weichseilbaum, 2009). Avadhani and Miley's (2011) meta-analysis concludes that probiotics provide a relative risk reduction of 44% for AAD.

The following is a review of the seven meta-analyses found during literature search. These meta-analyses focus on the adult inpatient population although some did include the pediatric inpatient and outpatient population. There is one RCT on AAD in the outpatient adult population, this study is also described.

Avadhani and Miley's (2011) meta-analysis includes eight RCT evaluating probiotic efficacies in the prevention of AAD. They include two studies that report negative results with respect to the use of probiotics in preventing AAD. The perspective of this meta-analysis is prevention of AAD and *C. difficile*-associated diarrhea (CDAD) in hospitalized adults. This review paper focused on their results for AAD. All eight of the articles include results for AAD. A random effects model in the MASTARI software and the Mantel-Haenszel relative risk ratio was used to analyze the eight studies. The Forest Plot showed an overall favoring of probiotics in the prevention of AAD. They report an overall $Z=4.75$ with a $p \leq 0.001$. The relative risk ratio was 0.56 (95% CI, 0.44-0.71). They do report heterogeneity as being low to moderate (29.12) owing to the fact that two studies had negative results. No funnel plot was reported.

They conclude concurrent use of probiotics was effective in preventing AAD in the adult hospitalized patient.

Cremonini, et al, (2002) review seven RCT for their meta-analysis and report an age range of two weeks to elderly age groups. This analysis also includes a study with negative results; it is the same study that is reported as negative in the previous meta-analysis. This review does not stratify the studies evaluated for setting; this information was extracted from the discussion and the studies themselves when available. These authors investigated probiotic monotherapy to prevent AAD. There were two different probiotics represented in this analysis: *Lactobacillus GG* and *S. boulardii*. The Forest Plot showed an overall favoring of probiotics in the prevention of AAD. This data was analyzed using STATA Software version 6.0 from Texas University. An overall Z score was not reported. The test for homogeneity gave $X^2 = 6.001$; $df = 6$; $p = 0.42$. Mantel-Haenszel was used to calculate the combined relative risk reported as 0.3966 (95% CI, 0.275-0.571). This study reported a funnel plot with no asymmetry observed. These authors conclude probiotics reduce the risk of AAD.

D'Souza, Rajkumar, Cooke, & Bulpitt (2002) present a meta-analysis that evaluated the efficacy of probiotics in the prevention and treatment of AAD. This analysis included pediatrics and adults, two of the studies report pediatric results. This meta-analysis utilized the QUOROM statement. The outcome measure is the percentage of patients in either arm of the study without diarrhea. They also performed three separate analyses split by probiotics type: *S. boulardii* and *lactobacilli* or *enterococci*. A pooled analysis of all nine studies is also included in the discussion. The Mantel-Haenszel method is applied to determine the benefit of treatment versus placebo. No publication bias is shown in the funnel plot. The relative risk for all nine studies is reported as 0.37 (95% CI; 0.26 – 0.53). Homogeneity for all nine trials is $p = 0.246$. The Forest

plot favors probiotics preventing AAD. This meta-analysis concluded there is evidence that probiotics provide protection against AAD. These authors state that probiotics prevent AAD but it does not treat AAD.

Kale-Pradhan, Jassal & Wilhelm (2010) performed a meta-analysis of *Lactobacillus* in both pediatric and adult patients. They looked at *Lactobacillus* as monotherapy for the prevention of AAD. They analyzed ten RCT but this paper focused on the results for the adults, which are reported separately. The risk reduction for the adults is reported as 0.24 (95% CI, 0.08 – 0.75) using Mantel-Haenszel calculation. Heterogeneity was well controlled $\text{Tau}^2 = 1.41$; $\text{Chi}^2 = 30.19$; $\text{df} = 5$ ($p < 0.0001$), $I^2 = 83\%$. The overall Z score was reported as 2.46 ($p = 0.01$). A Forest plot showed *Lactobacillus* does prevent AAD in adults. They reported a potential publication bias as the funnel plot graph is asymmetric owing to one of the adult studies had a very small n . They also report the dose of *Lactobacillus* ranges from 2×10^9 – 4×10^{10} colony forming units (CFU). It is of interest to note that the pediatric arm of this meta-analysis did not reach statistical significance. This study concludes that *Lactobacillus* monotherapy prevented AAD in the adult population.

McFarland (2010) presents a systematic review and meta-analysis of *S. boulardii* in adult patients. McFarland looked at multiple disease states but this paper concentrated on the meta-analysis for AAD contained in her review. The author reported on ten RCT in adults using *S. boulardii* as monotherapy. The Forest plot favors *S. boulardii* as preventing AAD. This analysis showed a pooled relative risk of 0.47 (95% CI, 0.35 - 0.63, $p < 0.001$). The author reported that heterogeneity was well controlled $X^2 = 10.8$, $p = 0.29$. The author also reported no publication bias was found either in Begg's test ($p = 0.93$) or the funnel plot. The investigator also reported that the number needed to treat with *S. boulardii* to prevent on case of AAD was 10.2. An

overall Z score was not reported. This study reported that the use of *S. boulardii* monotherapy is effective in preventing AAD. This was pooled data of both inpatient and outpatient so no specific conclusion can be drawn regarding adult outpatient data.

Sazawal, et al (2006) performed a meta-analysis that evaluated the use of probiotics in all types of acute diarrhea; AAD was a subset that was reported separately. The inclusion criteria for this analysis looked at RCT that were masked and placebo controlled. For inclusion the study design is an experimental arm and a control arm that “differed only by the provision of a probiotic and in which the risk of acute diarrhea in each arm was presented,” (Sazawal, et al, 2006, p. 374). Articles published in both English and French were considered for inclusion by the authors. They reported on 16 articles that yielded 19 separate AAD studies, one of the articles had two arms and another had three arms to the study. Ten of the articles focused on adults and six on children. The risk reduction was reported as 52% (95% CI, 0.35 – 0.65) with a $p = 0.001$, for all ages. Heterogeneity test was reported as $I^2 = 53\%$ (95% CI, 40-68). The Forest Plot is not reported for AAD. Overall, probiotics were shown to have a protective effect. When community is the setting probiotics were still shown favorably but not as strong as the overall effect 0.94 (95% CI, 0.87 – 1.02). The pooled n of the community is 1927; adults and children cannot be teased out since one of the community studies did not report the age groups separately. This study also reports a number needed to treat as being for every four adults receiving probiotics one will have acute diarrhea prevented. This study correctly comments that very few trials have been carried out in the community regarding probiotics and the prevention of diarrhea. Those that have been done looked at travelers’ diarrhea or infectious diarrhea, none in this analysis focused on AAD. These authors found that effect size of probiotic prevention of AAD type was the highest compared to all other types of acute diarrhea.

Szajewska & Mrukowicz (2005) analyzed five RCT that evaluated *S. boulardii* for the prevention of AAD. They used STATSDIRECT software and QUOROM standards to analyze the data. The total *n* is 1076. They reported a risk ratio of 0.43 (95% CI, 0.23-0.78). This analysis included both children and adults. Unfortunately, the age groups are not reported separately. The Forest Plot does favor the use of probiotics to prevent AAD. By excluding one of the trials they were able to achieve homogeneity ($X^2 = 2.9$; $p = 0.4$) and maintain significance, 0.33 (95% CI, 0.22-0.5). They report no publication bias or small sample bias. This analysis reported on five studies and was the smallest of the meta-analyses. They report the number needed to treat to prevent AAD is ten. This analysis supports the conclusion that *S. boulardii* reduces the risk of AAD.

Armuzzi, et al. (2001) report on a RCT in which they gave outpatient adults probiotics during a specific antibiotic treatment. The investigators randomized sixty healthy asymptomatic *Helicobacter pylori* positive adults to probiotic and placebo. They used a preparation of *Lactobacillus GG* (6×10^9 CFU) for 14 days; during the week of treatment and the week after treatment. The treatment was seven days of rabeprazole 20 mg twice a day, clarithromycin 500 mg twice a day and tinidazole 500 mg twice a day. The probiotic was given twice a day one and half hours after the administration of the antibiotic. Of all of the side effects of antibiotic use included in the study only diarrhea is significant between the two groups ($p=0.026$). They reported a difference in diarrhea rates: placebo being 26.6% versus probiotic 3.3% during the treatment week. During week two the placebo group had 10% diarrhea and the probiotic group 3.3% diarrhea. The diarrhea was self reported as mild for all participants, which in the context of the study is defined as 'observed by could be disregarded'. It should also be noted that the study

participants were all medical personal (physicians, nurses, biologists, or administrators). This study shows that probiotics are effective in reducing AAD in the outpatient adult population.

In summary, the seven meta-analyses and one RCT all report a reduction of diarrhea when probiotics are used to prevent AAD. They all agree that several different probiotics are safe to use in a wide variety of diagnoses, antibiotics, patient populations and settings. What is lacking are studies done in the adult outpatient population. The limitations of these analyses are there is overlap of the studies contained across the meta-analysis, there is no agreement on which probiotic is the most efficacious, and there is no agreement on dose.

Prescriber Attitude, Knowledge and Habits

There is no research regarding what is current practice in the primary care setting of probiotic prescribing, in the United States. This may be related to provider lack of education of efficacy and safety of probiotics. This may also be related to provider attitude to alternative medication use. The next section illustrates prescriber attitude and knowledge of probiotic use.

Hermosilla (2009) looked at attitude and knowledge of prescribers towards probiotics in an intensive care setting. The author found that an educational offering increased both physician (MD) and nurse knowledge and attitudes. However, in the large intensive care setting staff was not stable and the effect did not appear to be sustained. The prescriber group consisted of MDs only. The author reports a two fold increase in probiotic prescriptions after the educational offering. Pre-education session showed 2% ($n=2$) of the patients receiving antibiotics were prescribed a probiotic. After the educational session 5% ($n=4$) were prescribed a probiotic. While this is an increase in the prescribing of probiotics it is a small increase, Hermosilla (2009) reports a p value of 0.003.

Nichols, Grob, and Roche (2005) sent a web-based questionnaire to outpatient primary care providers in Surrey, England. They reported a 16.6% response rate (n=99). Of the responders, they found 54% of providers have advised patients on the value of taking probiotics. Seventy-three percent reported they believed probiotics reduce the incidence of diarrhea. This study was not specific to AAD.

In summary, these findings show a lack of comprehensive information describing provider attitude, knowledge and prescribing habits toward probiotics, the studies emphasize the importance of educating providers on the pathophysiology, efficacy and safety of probiotics in the prevention of AAD.

Theoretical Framework

The Stetler Model of Research Utilization to Facilitate Evidence-Based practice was used to frame this study (Gawlinski & Rutledge, 2008; Snyder, Facchiano, & Brewer, 2011; Stetler, 2001). This model supports implementation of practice changes at both the individual and the organizational levels (Gawlinski & Rutledge, 2008; Stetler, 2001). Stetler (2001, p. 274) states in her first assumption that the “formal organization may or may not be involved in an individual’s utilization of research.” This model is also well suited to the provider who has the ability to evaluate knowledge within their own field of expertise and to evaluate if that evidence supports a practice change (Snyder, Facchiano, & Brewer, 2011). At this time the primary care practice, where the implementation occurred, has no formal process for the integration of evidence-based practice (EBP). However, they do have an organizational roadmap for defining initiatives using five pillars: service excellence, quality, people, growth, and financial strength. The integration of EBP supports the quality pillar of the balanced scorecard. The quality pillar is

defined as “insuring that an infrastructure is in place to drive clinical and service excellence.”

The implementation of EBP would not only support clinical excellence within this pillar it would provide a process for the implementation of future EBP projects.

Stetler’s (2001) model has five phases: preparation, validation, comparative evaluation/decision making, translation/application, and evaluation. The following describes the use of Stetler’s model in this project. The preparation phase was started as part of a demonstration project at a local SNF, using frail elderly patients. This project leads to inquiring if the same outcomes could be applied in the outpatient adult setting. The literature review done for the proposed study focused on meta-analyses, accepted as Level I evidence. As indicated earlier there are no published evidence-based practice guidelines available. Based on an analysis of the studies reviewed a practice protocol can be recommended. A randomized controlled trial was part of the literature review as it best matched the population and setting of the proposed study. The researcher chose to use meta-analysis as the basis of the literature review as the key stakeholder is a MD who values Level 1 evidence. The use of Level 1 evidence provides a strong support for the proposed educational intervention.

Phase II, Validation, was done as a critique of the meta-analyses and one RCT; these showed that the findings were supportive of the use of probiotics in preventing AAD. A conclusion of the literature review found several areas that needed to be specified in the present study such as provider attitude and knowledge toward the use of probiotics to prevent AAD. In an unpublished study of a quality improvement project done in a long term care facility, the implementation of concurrent use of antibiotics and probiotics has reduced the incidence of AAD in this population to zero. This project was developed in response to an increase of diarrhea in the facility population. A literature review was done and a protocol was presented to the medical

staff for approval. After approval by the medical staff it was implemented. After approximately 18 months the protocol was reviewed, a cost analysis was performed and the protocol was streamlined. This protocol continues to be successfully used at the facility. The above issues impact on the practice utilization as described in Snyder, Facchiano, & Brewer (2011).

Comparative evaluation and decision making, Phase III, requires the synthesized information found in Phase II be applicable to the practice setting for a change in practice. The meta-analyses reviewed support the use of prophylactic probiotic use. There are barriers to the applicability of this information in the current practice setting. These barriers include provider attitude and knowledge. The proposed study has a good fit in the outpatient setting. The research study is feasible to complete in the proposed setting, substantiates the current evidence and impact to current practice.

Phase IV, translation and application, provided an insight into what the current state of practice and what barriers must be overcome for full application. The proposed study offered insight into the number of probiotics currently being recommended and this is correlated with the same provider groups' knowledge and attitude towards the use of probiotics.

Evaluation, Phase V of Stetlers' model was done when the data is collected and analyzed from the study. Refinements were made in the proposed probiotics protocol. Further research is suggested from the data analysis of the three different purposes of the study.

Project Plan

Project Design

This project design used two different methods. The first design was a description of the current use of probiotics in a large corporate primary care and urgent care practice group. The second project design was a pre and post test of probiotic knowledge and attitude of provider. These surveys were given before and after an educational intervention presenting a literature review supporting the use of probiotics to prevent AAD.

The descriptive project looked at the number of antibiotics and probiotics prescribed by this group at two points in time. The choosing of the time frame is arbitrary. This group of providers uses the Allscripts[®] electronic medical record which includes the recording of prescribed medications. A random week one month prior to the educational intervention was selected; a data report asked how many antibiotics have been prescribed during a seven day time frame. There was no restriction on the drug class of antibiotic or infective process. It was presumed that all prescribed antibiotics are appropriate to the infective process. This descriptive number was then paired with the descriptive number of how many probiotics were prescribed during this same seven day time frame. This data was analyzed by provider, MD, NP, and PA. This data provided information on the prescribing habits of primary care providers without intrusion by the researcher. This information is valuable in that are few reports of primary care prescribing habits with descriptive statistics. The disadvantage of this study design is the inability to provide generalization to any other group.

A pre and post test design utilizing a convenience sample of primary care providers who prescribe antibiotics was used. The inclusion criterion was all providers; MDs, NPs and PAs working at the same large practice group as described above. An email was sent to all providers in the group introducing them to the project. Basic demographic information including names were obtained. Only the researcher has access to the names of participants. The provider names

were converted to a numeric label during data entry. The participant label was used to compare the pre and post test results for an individual.

The pre-intervention survey was provided before the educational intervention was presented. The intervention is a power point presentation discussing evidence recommending the use of probiotics in the prevention of AAD (see Appendix 1 for the protocol and Appendix 7 for the educational intervention). A post intervention survey was provided just after the educational intervention presentation. It is understood that this design might have an effect on the prescribing habits of those who participate by virtue of presenting the information. It is unknown if the effect is long lasting.

The information was requested from the IT department. A random week in February 2012 was chosen. This represented approximately one month prior to the start of the educational intervention. The second data run was requested a week after the last educational intervention. The original plan was to wait a month after all interventions were completed but time constraints did not allow for the time to wait. The data came in an excel spreadsheet. The data was coded and loaded into IBM SPSS Statistics 20 software.

The second part of the study was an educational intervention with a pre and post test questionnaire. This was originally to be done at a staff meeting where all of the providers would be in attendance. Unfortunately, due to scheduling and time constraints this was not possible. Instead the educational intervention was provided at the individual provider offices in small groups. The presentation was kept consistent and providers were able to ask questions. The providers were assigned a number and all information was entered into the IBM SPSS Statistics 20 software system on the day it was obtained.

Sample

The study subjects were the 70 providers at a large multi-site primary care group. These providers consist of MDs, NPs and PAs. The MDs are both family practice and internal medicine specialties. The NPs are both adult and family specialties. The PAs also practice in primary care and urgent care specialties. With a sample size of $n=70$, small effect size (0.3) determined by Cohen's convention, and $\alpha=0.05$, the study has a minimum power of 0.6967 when using Lenth's website for calculation for a paired t -test (Lenth, 2006-9). Using the same sample size, alpha, and small effect size determined by Cohen's convention when using a table cited in Munro, (2005).

The original sample was 70 providers, MD, NP, and PA. These providers are a part of a large multi-site primary care group. The group is located in central and eastern Connecticut. The data received from the IT department revealed 71 providers had prescribed antibiotics in the selected week prior to the educational intervention. When the data was received from the IT department after all of the educational interventions were complete there were 73 providers who had prescribed antibiotics. Of the providers who prescribed antibiotics 27 completed the project. This represents only 37.5% of the available providers. This was significantly below the project goal of 50%. The greatest percentage of participants were the MDs at 15 participants, then the NPs at 8 participants and finally the PAs at 4 participants, please see Table 1.

Project Site

These providers are part of a large multi-site corporate practice consisting of both primary care and urgent care. The researcher is a provider at one of the primary care sites. These offices are located in central and eastern Connecticut. The researcher is affiliated with one

of the offices located in eastern Connecticut. This provider group is affiliated with a tertiary acute care center as part of an Accountable Care Organization (ACO). They serve a diverse population of patients, within urban, suburban and rural areas. They accept all major commercial insurance plans and Medicare but they do not accept new patients with Medicaid. This practice group is being used as a convenience to the researcher; as she has access to the providers and the data. There is a corporate culture of innovation and the CEO is supportive of this clinical research project. The formal letter of support from Dr. Kent Stahl is found in Appendix 4. Currently it is unknown as to how many antibiotics are prescribed and how many probiotics are being recommended in this provider group.

Educational Intervention

This project presented an evidence based protocol abstracted from the current literature review. This protocol, found in Appendix 1, was developed by the researcher. The protocol was sent to the local Gastroenterologist, an APRN with a specialty in Gastroenterology and Infectious Disease specialist for review. These providers gave feedback to the protocol and it was incorporated into the final protocol. The protocol was introduced to the providers during the educational intervention. The educational intervention consisted of:

- a review of translational research
- a review of AAD,
- gut pathophysiology,
- antibiotic disturbance of gut flora,
- overview of current literature
- presentation of the proposed protocol found in Appendix 1.

The education intervention consisted of a PowerPoint presentation describing several meta-analyses and randomized control trials supporting the use of probiotics for the prevention of AAD. The PowerPoint presentation can be found in Appendix 7. A protocol for the use of the probiotics in the outpatient adult setting was presented and discussed during the intervention. The providers attending were given a copy of the protocol, see Appendix 1. The providers were also given a handout for patients explaining probiotic use, see Appendix 5. There was positive feedback related to both the information presented and the handouts. Providers were encouraged to implement the protocol. The interventions went very well, the MDs were respectful. The researcher was not made to feel that the information was not valuable because of my professional title.

Instruments

Prior to the intervention a questionnaire was used to evaluate the office provider's attitude and knowledge of probiotics use. The questionnaire that was used was developed and tested by Nichols, Grob and Roche (2005), there is no identifying name for the questionnaire. They developed the questionnaire, which consists of 20 items, to look at multiple reasons for using probiotics. For the purposes of this study only the first four questions were used as a pre and post test for this project. The original questions developed and used by Nichols, Grob, and Roche (2009) is reproduced below. The first 4 questions and the last 7 questions are yes or no answers. The middle 6 questions responses are never, occasionally or frequently.

Nichols, Grob and Roche Provider Probiotic Questionnaire (2009):

Please answer yes or no for the following questions:

1. Which of the following apply to your advice to patient regarding probiotics:
 - A. I know of no reason to advise patients to take probiotics
 - B. Probiotic usage may be valid but I have not advised patients on this

- C. I have advised patients on the value of probiotics
2. Probiotics decrease the incidence of diarrhea
 3. Probiotics decrease the risk of thrush

Some of us are ‘trigger happy’ when it comes to prescribing antibiotics, but there is also the danger of failing to prescribe an antibiotic when an antibiotic is genuinely needed. Assuming you decide that an antibiotic is necessary, in which of these conditions have you advised a patient to take a probiotic with and/or after the course of antibiotics? Please answer never, occasionally, or frequently for the following questions:

4. Probiotics give a boost to host immunity
5. Children with acute suppurative otitis media
6. Healthy young patients with acute bronchitis
7. Elderly patients with pneumonia
8. Recurrent acute cystitis
9. Severe painful dental abscess
10. Diverticulitis with pyrexia

Other conditions have been found to respond to probiotics to a greater or lesser degree and probiotics have been suggested as part of a preventive strategy for some conditions. Have you advised patients to take probiotics for any of the following? Please answer yes or no for the following questions:

11. Severe eczema
12. Recurrent vaginal thrush
13. Crohn’s disease
14. Ulcerative colitis
15. To reduce the risk of bladder and bowel cancer
16. To reduce the risk of coronary artery disease
17. An infant recovering from viral gastroenteritis

Questions five through seventeen do not pertain to the proposed research project and therefore was not used for this project. The proposed questionnaire is attached in Appendix 2.

Permission was received from Dr. John Nichols and his co-author Dr. Paul Grob to use the questionnaire they developed (Nichols, Grob and Roche, 2009). Permission was granted in the form of an email dated August 10, 2011, see Appendix 6. The original questionnaire was designed to look at many other disease processes that probiotics may be helpful. As stated above only the first four questions pertained to this project. Question three was changed due to

terminology confusion between the United States and England. They used the term “thrush” meaning a vaginal yeast infection. The term “thrush” was changed for the purposes of this project. This project used the statement: “vaginitis due to yeast.” Thrush has a different connotation for United States providers.

Procedure

Institutional Review Board (IRB) approval was obtained from University of Massachusetts after a lengthy process. My protocol was approved March 1, 2012. This set my project timeline back by eight weeks as data collection had been slated to start the beginning of January. Formal approval from Dr. Kent Stahl was obtained on February 13, 2012, see Appendix 4. The project was introduced at the March Medical Directors meeting by Dr. Kent Stahl. An email was sent to the providers introducing the research project. The initial email included an overview of the research project and what participation requires. The email addresses of the providers were obtained from the shared email group of which the researcher is a part. An email was sent to all 71 providers to introduce the project. This email consisted of an outline of the project as well as the IRB information. A separate email was sent to all of the medical directors requesting to be included in a staff meeting for the purposes of presenting my educational intervention.

The educational intervention was accomplished by visiting individual office provider groups and presenting at their monthly provider staff meeting. Six offices were visited between the March 14, 2012 and April 15, 2012. This was an average of 4.5 providers at each presentation. One office had only one provider available and the others had four or five providers available. I was also able to capture three more providers after a meeting for the NPs

and PAs. A summary of the demographics of the providers who participated is found in Tables 1-4.

Data Collection

The first of data collection for this project was a data set from Electronic Medical Record (EMR) regarding the current probiotic prescribing habits of providers before and after the intervention of the educational program. The data requested was limited to adults, 18 years and older. An arbitrary week was selected prior to the educational intervention, February 5-11, 2012. A second arbitrary week was selected after the educational intervention, April 22-28, 2012. This was accomplished by filling out an “Analytics Report Request,” a reproduction of this form is found in Appendix 3. The form was submitted to the IT team. The data set parameters that were requested from the Information Technology (IT) team: the total number of antibiotics prescribed and total number of probiotics prescribed during that week for all patients older than 28 years, any provider, any antibiotic, any probiotic, any diagnosis. Since the data is to determine provider prescribing habits no patient identifier or patient demographics were requested. The same process was used for both weeks that the data set was requested.

The EMR used by the providers in the study was Allscripts®. This EMR can record both medications requiring prescriptions as well as over the counter medications. This information is stored in the medications section of the EMR and is to be reconciled at every visit.

Reconciliation is the means by which the provider determines that the current list of medications is accurate. One of the drawbacks of this study is that there is no way of knowing why the probiotic is not documented in the EMR; not prescribed or not documented. Whether the patient actually follows through with taking the probiotic is outside the scope of this study.

Prior to the educational intervention the providers filled out a one page survey that included both the demographics and the short questionnaire. The questionnaire consisted of demographic data and four questions. The four questions are listed in Appendix 2. The demographics included:

- Name (which is only used for matching the tests)
- Provider type: MD, NP, or PA
- Gender: Male or Female
- Age: 20-29, 30-39, 40-49, 50-59, 60-69, 70 or older
- Educational level: certificate, masters, MD or PhD

The surveys from each provider were entered into an IBM SPSS Statistics 20 software database for analysis.

Data Analysis

The analysis of the information collected from the Allscripts[®] EMR regarding current prescribing habits was done with descriptive statistics. This provides a snapshot of current clinical practice of the providers in this primary care group. This data are numbers for the entire provider group and are broken down by individual provider. This same data set was requested approximately two weeks after the last educational intervention. A comparison of the prescribing of both antibiotics and probiotics using descriptive statistics was done.

The data gathered from the questionnaire was analyzed by both descriptive statistics and a paired *t*-test. A paired *t*-test was utilized because the survey was identified by the provider name. The raw data with the name was only be seen by the researcher. The paired *t*-test was analyzed using IBM SPSS Statistics 20 software. The descriptive statistics were used to

compare the different provider groups, MD and NP, to see if there are differences in attitude and knowledge after the educational intervention and presentation of the clinical practice protocol.

The PA information was only used in the summary data and was not compared to the other providers since there a small number of PA participants ($n=4$).

Barrier to Project Implementation

This study is only looking at provider attitudes, knowledge and prescribing habits. One drawback of this study is the outcome of diarrhea in the patients was not determined. The questionnaire is only 4 questions long and this should not be a burden. The educational intervention was delivered in person. It is anticipated that due to the suggestion of a practice change by an NP to a largely MD group may create some resistance of implementation of this practice protocol.

The MDs did not voice any resistance to a practice change suggested by an NP. This was a barrier that was anticipated but was not encountered during the study. The response was positive from all the MDs. I felt more resistance from the NPs and PAs and had difficulty getting them to stay and listen to the educational program. It is unknown as to why the NPs and PAs were resistant; this could be a false perception by the researcher. The most challenging barrier was the reduced time line to provide the educational intervention to the providers. The scheduling was difficult due to provider meetings being only once a month. While the medical directors in each office were contacted directly, often it was the practice manager who scheduled the meeting. The practice manager was not necessarily aware of the project and often it took several emails to schedule the intervention.

Budgeting and Cost

The cost of this project was very minimal. Cost of the project is the time of the researcher. The request for the EMR data carried no cost. The questionnaire was created and printed on the researcher's personal computer. The expense of obtaining IBM SPSS Statistics 20 software was less than expected, \$44.94. However, the cost of gas to drive to each office was much greater than anticipated. The total mileage was 263 miles at 55.5 cents a mile comes to a total of \$145.97. The original budge was approximately \$300.00 this project came under budget by \$109.09. These expenses were absorbed by the researcher.

IRB Approval and Ethical Considerations

IRB approval from the University of Massachusetts, Amherst, was required as an expedited application as no patient identifying information is being collected. The use of the EMR information is purely numerical, how many antibiotics prescribed and how many probiotics are prescribed at the same time. The knowledge survey asked for a name and minimal demographic information on the providers. Names and demographic information were kept confidential. The results of the pre and post intervention survey have only been viewed by the researcher and researcher's primary advisor. The benefit to the providers was the participation in and educational offering on probiotics and the distribution of an evidence based practice protocol.

The University of Massachusetts IRB granted approval on March 1, 2012. Approval for the provider group was granted by Dr. Kent Stahl on February 13, 2012.

Time Line

Task	Deadline

Capstone project approval	December 20, 2011
UMass IRB approval	December 30, 2011
Hartford Medical Group (HMG) IRB approval	December 30, 2011
Contact each medical office at HMG to set up the educational session	January 5, 2012
Contact with HMG IT Department to request EMR data for the previous 7 days	January 10, 2012
Finalize the providers data set and analyze	January 10, 2012
Analyze the questionnaire	January 20, 2012
Educational sessions with each office to start	January 20, 2012
Educational sessions with each office to conclude	February 15, 2012
Analyze provider questionnaire	February 20, 2012
Contact with HMG IT Department to request EMR data for the previous 7 days	February 20, 2012
Analyze and compare EMR data	February 29, 2012

Results

Data Analysis

EMR Findings

The analysis of the information collected from the Allscripts® EMR regarding current prescribing habits provides a snapshot of current clinical practice of the providers in this primary care group. The information provided showed that 71 providers were listed as prescribers in this data set. In the first week of the data collection 764 antibiotics were prescribed in the one week period between the dates of February 5, 2012 to February 11, 2012. There were 4477 patient visit for these same 71 providers during this same time frame. This would be a prescribing rate for this group of 171 antibiotics per 1000 patient visits. Of the 71 providers prescribing antibiotics only two providers recorded recommending probiotics to five different patients. Both of these providers were NPs. This translates to five patients who have a probiotics recorded in the EMR at the same time as an antibiotic. For the period of April 22, 2012 to April 28, 2012 there were 73 providers prescribing and 504 antibiotics prescribed. Three providers prescribed probiotics to three different patients. These three providers were two MDs and one NP, the NP was a different NP from the two NP prescribers in the first data set. This is a 50% increase in the number of providers prescribing probiotics but a decrease in the number of patients. This may be explained by the decrease in the number of antibiotics prescribed during the second time frame.

Comparison of Prescribing Habits of MDs and NPs

A comparison of the prescribing habits of MD, NP and PA was also analyzed. For the week of February 5, 2012 to February 11, 2012, the prescribing habits are not different across the provider types ($F=2.217, p=0.110$). For the week of April 22, 2012 to April 28, 2012, the

prescribing habits across the provider types are had no significant difference ($F=1.268$, $p=0.261$). This is consistent with national prescribing habits between provider types (Gonzales, Barrett, Crane & Steiner, 1998, Ladd, 2005, & Roumie, et. al, 2005)

Provider Attitude toward Probiotics

The data reveals that 21 of the 27 (77.8 %) providers have advised probiotics prior to attending the educational presentation. After the presentation 24 (88.9%) providers stated that probiotics would be advised. Only two of the providers felt that probiotics may be valid but that they would not advise the use of these supplements. None of the providers chose the option, “I know of no reason to advise patients to take probiotics.”

Provider Knowledge of Probiotics

Knowledge questions two, three and four were combined to create a knowledge score. The percent of providers aware of probiotic use pretest was 58.02% the posttest percentage increased to 75.54%, see Table 8. This is a 17.52% increase in probiotic knowledge after the educational intervention. There was a significant difference ($p=0.001$) in the scores for pre-knowledge ($M = 4.92$, $SD = 1.521$) and post knowledge ($M = 3.81$, $SD = 1.021$). The correlation between the two measures was 0.274 ($p=0.176$).

Difference between MD and NP in Attitude and Knowledge

The paired t-test showed no significant difference in attitude towards the use of probiotics between the MDs (pretest: $n=15$, mean=2.87, $SD=0.352$ and posttest: $n=15$, mean=2.87, $SD=0.352$) and NPs (pretest: $n=8$, mean 2.88, $SD=3.54$ and posttest: $n=8$, mean=3.00, $SD=0.000$) For question one the pretest showed equal variances ($F=0.012$, $p=0.957$) and the posttest for

question one also showed equal variances, ($F=6.278$, $p=0.164$). The knowledge score showed a significant difference between MDs pretest ($n=15$, mean 5.2667, $SD=1.16292$) and NPs pretest ($n=8$, mean=3.7500, $SD=1.03510$). Again, there was a significant difference between MD posttest ($n=15$, mean=4.2000, $SD=1.08233$) and NP posttest ($n=8$, mean=3.0000, $SD=0.0000$). The paired t-test for the pretest knowledge score also showed a significant difference between MDs and NPs ($F(21)=0.034$, $p=0.006$). The paired t-test for the posttest knowledge score showed a significant difference between the MDs and NPs scores ($F(21)=59.345$, $p=0.005$).

Discussion

The purpose of this study was to evaluate the attitude and knowledge regarding the use of probiotics to prevent AAD in the outpatient adult setting. The results show that MDs and NPs have a positive attitude towards the use of probiotics. They have advised their patients on the value of these supplements. The results also show that MDs and NPs increased their knowledge of probiotics due to the educational intervention. However, it was found that NPs had a greater increase in their knowledge scores as compared to MDs.

The goal of introducing an evidence based protocol was accomplished. The protocol was presented to the providers and they were encouraged to use it. There was positive feedback during the educational sessions for the protocol. The providers indicated that the handout that described the protocol was helpful especially since it contained specific recommendations on dosing and length of treatment. Dr. Kent Stahl supported the use of this protocol within our primary care and urgent care practice.

The third purpose of this study was to evaluate the providers' use of probiotics as documented in the EMR. The initial data revealed that while providers have a positive attitude

towards probiotics and recommend probiotics they are not recording this in the EMR. After the education intervention the probiotics that were recorded in the EMR increased by 50%. There were two different prescribing providers both NPs who prescribed probiotics prior to the educational intervention. After the educational intervention there were three different providers that prescribed probiotics, two MDs and one NP. The extra step of recording the probiotic in the EMR is problematic. It is actually five extra mouse clicks to record another medication in the EMR, many providers feel overwhelmed with the amount of information they are required to record already. This has been a common complaint voiced at provider meetings within this group. In future studies with this group, if the providers could be incentivized to record the probiotics this might improve recording outcomes. If the providers could be shown a short cut within the EMR system that decreased the amount of mouse clicks to record this recommendation this might also improve the recording of probiotic recommendations.

When the knowledge scores were evaluated NPs showed a greater beginning knowledge of probiotic use as compared to MD. The NPs also increased their knowledge to a greater degree than MDs in the posttest.

The data also supported the assertion that there is no difference in the prescribing habits of MDs and NPs. This can be looked at two different ways. As a negative it could be interpreted as NPs should prescribe fewer antibiotics because they should be encouraging more self care interventions and utilize an antibiotic as the last resort. As a positive it supports the notion that NP practice is no different than MD practice. This group's antibiotic prescribing habits of 171 per 1000 is well below the national average of 302-304 per 1000 reported by Roumie, et al., (2005).

The goals of this project were not all met. The project fell short on the goal of 50% participation from the 70 providers' eligible, only 38% were recruited. This was due to the late approval from the IRB. The evidence-based protocol for the use of probiotics to prevent AAD was created and presented in the adult outpatient setting. The protocol appears to have been well received by the providers who attended the educational interventions. The interventions went smoothly and care was taken to present the information in the same way at each office. The goal of documenting and analyzing current antibiotic and probiotic prescribing habits was met. However, since probiotics are over the counter supplements this is really measuring the providers documentation of the probiotic in the EMR. There is no way to know if the patient actually followed this recommendation.

A limitation of this study were that the small number of providers that participated in the educational intervention. This study looked at the prescribing providers of a primary care and urgent care group; these results cannot be generalized to other provider populations. This study will be continued until the participants' number over 50. There are already three more offices scheduled to have the educational program in May and June.

In conclusion this study showed that primary care providers have a positive attitude towards the use of probiotics. It also showed that providers increased their knowledge of probiotic use as a result of an educational intervention. The actual prescribing rate of probiotics as recorded in the EMR was slightly higher after the educational intervention; however due to the small number of participants it may not be attributable to the educational intervention. It is proposed that actual recommendation of probiotics is higher but it is just not recorded in the EMR.

Future Directions

Further research is needed on the use of probiotics. The implementation of the proposed protocol could be one future study. Further research is needed on both the dosing of probiotics as well as the timing of probiotics. There is little research confirming the dosing of probiotics at five billion colony forming units. There is also little research specifically focused on when the probiotic should be given in relation to the antibiotic. The patients in the outpatient adult setting have not been well represented in current research. A qualitative study that addresses the patient experience with the use of probiotics would advance the body of literature for adults.

The abstract for this paper was submitted to American Association of Nurse Practitioners Foundation for a grant to continue research in this area. The grant is for best practices in the use of nutritional supplements. The deadline for submission is April 30, 2012 and the award presentation will be the 27th Annual American Association of Nurse Practitioners National Conference in Orlando, Florida.

Plans for Dissemination

The pathophysiology and the demonstration quality initiative that inspired this project have already been presented twice. The quality initiative has been presented in poster form at three different nursing conferences: the national DNP conference in San Diego California September 2010, Connecticut Advanced Practice Registered Nurse Society's annual conference May 2011, and CT Nursing Research Alliance Conference on 10/14/11. The poster received third place at the CT Nursing Research Alliance Conference and honorable mention at the Connecticut Advanced Practice Registered Nurse Society's conference. The pathophysiology and the quality initiative were presented at this year's Connecticut Advanced Practice Registered

Nurse Society's annual conference as a session choice. The results of this project are to be presented at Windham Community Memorial Hospital at Grand Rounds, to be scheduled in June.

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Author Note

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And to my friends and family who never tired of hearing of my work, and for listening to me say many times “what was I thinking?”

“...and so the Light and Dark were joined for awhile; just long enough for each of them to remember that their purpose was not to hate each other but to love each other simply because they were not each other.”
-unknown

Table 1**Percent of Providers by Title**

Professional Title	Frequency	Percent
MD	15	55.6%
NP	8	29.6%
PA	4	14.8%
Total	27	100%

Table 2**Percent of Providers by Gender**

Gender	Frequency	Percent
Male	10	37.0%
Female	17	63.0%
Total	27	100%

Table 3**Percent of Providers by Age**

Age Range	Frequency	Percent
20-29	0	0%
30-39	7	25.9%
40-49	8	29.6%
50-59	7	25.9%
60-69	3	11.1%
70+	0	0%
Missing	2	7.4%
Total	27	100%

Table 4**Percent of Providers by Educational Preparation**

Educational Level	Frequency	Percent
Certificate	1	3.7%
Masters	10	37.0%
MD	15	55.6%
DNP	0	00.0%
Missing	1	3.7%
Total	27	100%

Table 5**Question 1 Responses**

Questions 1	Pre-Test	Post-Test
Which of the following statement apply to your advice to patient regarding probiotics:		
a. I know of no reason to advise patients to take probiotics	0	0
b. Probiotic usage may be valid but I have not advised my patients on these supplements	5	2
c. I have advised patients on the value of taking probiotics	21	24
Missing	1	1
Total	27	27

Table 6**Question 2 Responses**

Questions 2	Pre-Test	Post-Test
Probiotics decrease the incidence of diarrhea		
Yes	25	26
No	0	0
Don't know	1	0
Missing	1	1
Total	27	27

Table 7**Question 3 Responses**

Questions 3	Pre-Test	Post-Test
Probiotics decrease the risk of vaginitis due to yeast		
Yes	15	20
No	4	4
Don't know	7	2
Missing	1	1
Total	27	27

Table 8**Question 4 Responses**

Questions 4	Pre-Test	Post-Test
Probiotics give a boost to immunity		
Yes	7	16
No	8	7
Don't know	11	3
Missing	1	1
Total	27	27

Table 9**Combined Knowledge Score**

Questions 2, 3, & 4	Pre-Test	Pre-Test Percent	Post-Test	Post-Test Percent
2. Probiotics decrease the incidence of diarrhea				
3. Probiotics decrease the risk of vaginitis due to yeast				
4. Probiotics give a boost to immunity				
Yes	47	58.02%	62	75.54%
No	12	14.81%	11	13.58%
Don't know	19	23.46%	5	6.17%
Missing	3	3.7%	3	3.7%
Total	81	100%	81	100%

Percent columns may not equal 100 due to rounding.

Appendix 1: Evidence-Based Protocol Describing the Use of Probiotics in the Adult Outpatient Population.

When an antibiotic is prescribed for any condition the following guidelines can be taken into consideration when also prescribing a probiotic.

Strain: *Lactobacillus*, *S. boulardii*, *Bifidobacterium* are the most studied probiotics. (Avadhani & Miley, 2011, Cremonini, et al, 2002, Edwards-Marshall, 2011, Hickson, et al, 2007, Hunter, 2004, Rohde, Bartolini, & Jones, 2009, Santosa, Farnworth, & Jones, 2006, Vrabie & Aberra, 2009, & Weichselbaum, 2009, Williams, 2010) .Culturelle, Align, Florastor or generic equivalent will be recommended since these OTC products contain one of the above mentioned probiotics.

Dose: 1 million to 100 billion CFUs QD to BID. (Avadhani & Miley, 2011, Cremonini, et al, 2002, Fox & Dang, 2004, Hickson, et al, 2007, Rohde, Bartolini, & Jones, 2009 & Santosa, Farnworth, & Jones, 2006)

Dose Timing: At least 2 hours from the dose of antibiotic. (Williams, 2010)

Therapy Duration: At least during the antibiotic treatment course and up to 6 weeks after completion. The average is 7-14 days. (Edwards-Marshall, 2011, Cremonini, et al, 2002 & Vrabie & Aberra, 2009)

Contraindications: *S. boulardii* should not be given with antifungals. (Williams, 2010)

Safety: Probiotics are generally considered safe. (Hickson, et al, 2007, Rulis, 2002 & Venugopalan, Shriner, Wong-Beringer, 2010)

Risk Factors for Sepsis: Immune compromised individuals (including debilitated state or malignancy) and Premature Infants are at risk for sepsis. Minor risk factors include: central venous catheter, impaired intestinal epithelial barrier, administering probiotic by jejunostomy, broad spectrum antibiotic to which the probiotic is resistant, probiotics with high mucosal adhesions, use of *Lactobacillus* and cardiac valvular disease. The presence of one major risk factor and two or more minor risk factors should caution the use of a probiotic (Boyle, Robins-Browne & Tang, 2006)

Appendix 2: Survey Questions:

1. Which of the following statements apply to your advice to patients regarding probiotics:
 - a) I know of no reason to advise patient to take probiotics.
 - b) Probiotic usage may be valid but I have not advised patients on these supplements
 - c) I have advised patient on the value of taking probiotics

2. Probiotics decrease the incidence of diarrhea:
Yes No Don't Know

3. Probiotics decrease the risk of vaginitis due to yeast:
Yes No Don't Know

4. Probiotics give a boost to host immunity
Yes No Don't Know

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Nichols, J. A. A., Grob, P. R., & Roche, N. (2005). A web questionnaire to determine the advice general practitioners give on probiotics. *Journal of Nutritional & Environmental Medicine*, 15(4) 212-222. doi:10.1080/13590840600692980.

Appendix 3**PEMR Analytics Report Request**

Name: _____ **Phone:** _____

Purpose of this report:

Criteria:(please check all that apply and enter specific information in space provided)

Organization Name:

Provider Names

Site Names

Diagnosis

Order Names

Result Names

Medication Names

Appointment Types

Task Types

Date/Date Range

Other

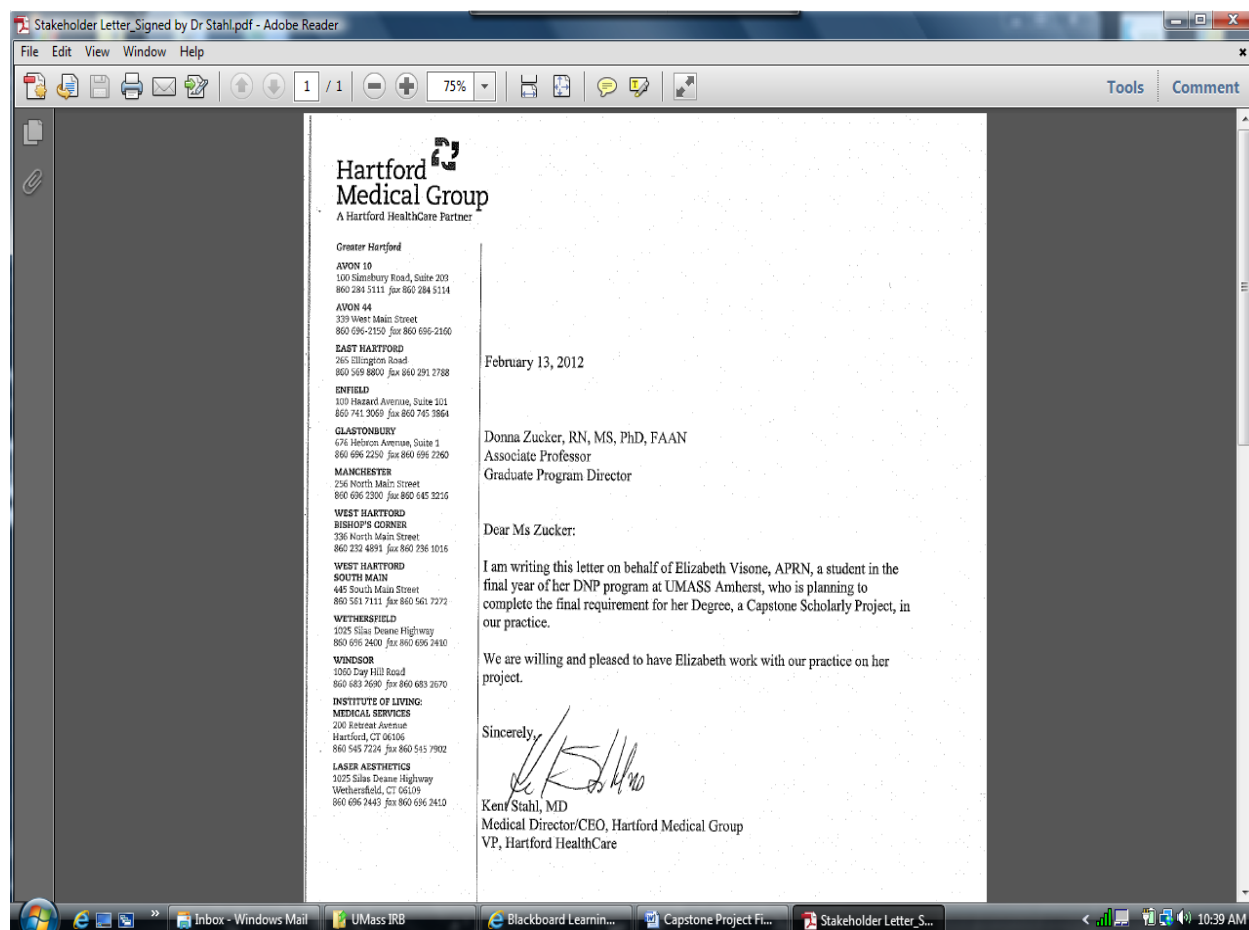
Include: Deceased Deactivated

Report Needed by:

Priority

Desired Output: (Ex: Pt full name, MRN, DOB, Phone, A1c, Provider, Date of last arrived appt)

Appendix 4: Stakeholder Letter



Appendix 5: Probiotic Handout for Patients**What are probiotics?**

Probiotics are bacteria found naturally in your large intestine. By taking probiotics you maintain or restore the balance of bacteria normally found in your body.

Why is my provider recommending I take a probiotic?

One of the side effects of antibiotics is diarrhea. This is because antibiotics kill the infection you are being treated for as well as the normal bacteria found in your intestine. When the normal bacteria are also wiped out diarrhea can occur. The probiotics help to maintain the normal bacteria so you don't get diarrhea.

Where can I get probiotics?

Most of the pharmacies and grocery stores carry both name brand probiotics and store brand probiotics, either one is fine. You may also look for probiotics at natural foods stores.

How much do they cost?

The cost is \$10 to \$40 dollars depending on the brand and size of the bottle.

How much should I take?

Your provider should tell you to either follow the package instructions or give you instructions on how many pills to take. 5 billion CFU are recommended but you should ask your provider how much you should take. Your provider should discuss how long you should continue the probiotic, usually at least as long as you are on the antibiotic.

When should I take them?

They should not be taken at the same time as the antibiotic but separated by 2 hours from your antibiotic dose.

What are the side effects of probiotics?

Probiotics are accepted as safe by the FDA. However, some people may experience gas cramps and gas bloating from probiotics. If this happens tell your provider. This will often happen if you take more than the recommended dose.

Appendix 6: Email from Dr. John Nichols and Dr. Paul Grob

----- Original Message -----

From: [John Nichols](#)

To: [Liz Visone](#)

Sent: Wednesday, August 10, 2011 4:40 AM

Subject: Fw: Fw: Web Questionnaire on Probiotics

Dear Liz,

My co-author has confirmed that you can use our q'aire in any way you wsh (see below).

Good luck.

John

----- Original Message -----

From: [PAUL GROB](#)

To: [John Nichols](#)

Sent: Wednesday, August 10, 2011 8:24 AM

Subject: Re: Fw: Web Questionnaire on Probiotics

hi fine

paul

--- On Fri, 5/8/11, John Nichols <drjaan@ntlworld.com> wrote:

From: John Nichols <drjaan@ntlworld.com>

Subject: Fw: Web Questionnaire on Probiotics

To: "Paul Grob" <paul.grob1@btinternet.com>

Date: Friday, 5 August, 2011, 22:06

Dear Paul,

This American nurse practitioner would like to use part of our questionnaire. I have no problem with this. Is it OK by you? I will try to find out more about her project.

Best wishes.

John

----- Original Message -----

From: [Liz Visone](#)

To: drjaan@ntlworld.com

Sent: Thursday, July 28, 2011 2:04 AM

Subject: Web Questionnaire on Probiotics

Dear Dr. Nichols,

I am a doctoral student in the United States working my dissertation/capstone project for graduation. I would like to use parts of your questionnaire in my project. I found the first four questions in your article appropriate for my project as a pre and post test. I will be suggesting a practice guideline for use in an outpatient primary care practice.

I would like to obtain permission to use your questions in my study, how would I go about doing this. Thank you for your help.

Elizabeth Visone, RN, MSN, APRN-BC

Nurse Practitioner

Doctoral Student

Appendix 7: Educational Intervention

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**The Use of Probiotics to Prevent Antibiotic
Associated Diarrhea:
Current Primary Care Practice and
Introduction of an Evidence Based Practice
Protocol**



**Elizabeth MB Visone, MS, RN, APRN-BC
DNP Candidate**

School of Nursing

Learning Objectives

- Understanding translational research
- Understanding normal gut ecology
- Understanding the effect antibiotics have on normal gut ecology
- Review of evidence of prophylactic probiotics to prevent antibiotic associated diarrhea
- Proposed evidence based protocol for the use of probiotics to prevent antibiotic associated diarrhea

Translational Research

- This is research that moves the “bench experiment” to the bedside
- Taking current research and quickly moving it to the bedside
- Understanding that while rigor is important, there are many more variables at the bedside and many cannot be controlled
- How does laboratory knowledge translate with real patients under real life conditions

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Normal Gut Ecology

- The gut contain 300-500 different bacterial species
- 30-40 species comprise the majority of bacteria
- Most of the gut bacteria is found in the colon

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Normal Gut Ecology

- pH in the stomach and small intestine prohibit bacterial colonization
- Unless you count *Helicobacter pylori*
- The entire community of bacteria in the gut has yet to be described

UMassAmherst

Normal Gut Ecology

- Humans are born with a sterile gut
- Gut bacteria is populated during the birth process and neonatal period
- The initial ecology of the gut as an infant dictates the ecology as an adult

Normal Gut Ecology

- The healthiest gut ecology is conferred by a vaginal birth and a breast fed infant
- Humans have a unique and stable gut ecology
- Human gut bacterial flora is like a finger print, no two people have the same community members in the same concentration

Normal Gut Ecology

anaerobic bacteria outnumber aerobic bacteria by a factor of
1:10

Anaerobes

- *Bacteroides*
- *Bifidobacterium*
- *Eubacterium*
- *Clostridium*
- *Peptococcus*
- *Peptostreptococcus*
- *Ruminococcus*

Aerobes

- *Escherichia*
- *Enterobacter*
- *Enterococcus*
- *Klebsiella*
- *Lactobacillus*
- *Proteus*

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Normal Gut Ecology

Functions of Gut Microflora:

- Metabolic
- Trophic
- Protective

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Normal Gut Ecology

Metabolic

- Fermentation
- Mucous Production
- Salvage of Energy

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Normal Gut Ecology

Trophic

- Epithelial Cell Growth & Development
- Host Immunity

Protective

- The intestine has the highest concentration of immunocompetent cells in the body
- Interface between the body and the external environment
- Ecological communities of bacteria in the gut are a defense against invasion of exogenous microbes and thus prevent infection

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The Effect of Antibiotics on Gut Ecology

Antibiotics:

- Select for resistant organisms
- Inhibit susceptible organisms

The Effect of Antibiotics on Gut Ecology

Alterations in Gut Mucosa:

- Changes in fermentation of carbohydrates and creation of mucous will change nutrient absorption ability of the host and inhibit immunological functions
- Abdominal pain most likely caused by diarrhea, bloating, and flatulence
- Selection of resistant organisms for continued growth produces an imbalance in the microflora

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The Effect of Antibiotics on Gut Ecology

Broad spectrum antibiotics are most often implicated

However

Any Antibiotic can cause AAD

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The Effect of Probiotics on Gut Ecology

A probiotic is defined by the World Health Organization as “Live microorganisms which when administered in adequate amounts confer a health benefit on the host.”

(World Health Organization, 2001)



The Effect of Probiotics on Gut Ecology

- Support the native bacteria of the gut
- Preservation of the native bacterial community
- Encourage mucous production
- Encourages the immunity functions of the native bacteria

UMassAmherst**DEFINITION OF AAD**

Antibiotic associated diarrhea (AAD) is the self limited diarrhea that occurs during or following a course of antibiotics

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Incidence of AAD

- 5-30% of adults prescribed an antibiotic
- 301.4 out of 1000 adults were prescribed an antibiotic in the year 2002
- **Resulting in 29 million adults in the US with AAD in the year 2002**

- Current treatment for AAD is to stop the offending antibiotic

- Antibiotic treatment is necessary

- Prevention of AAD is a better choice

The logo for UMass Amherst, featuring the text "UMassAmherst" in a serif font, with "UMass" in red and "Amherst" in white.

Evidence for the use of Probiotics to Prevent AAD

No evidence based clinical guidelines available for the prevention in AAD in adults

Evidence based clinical guidelines are available for the pediatric population

7 meta-analyses and 1 RCT evaluated the efficacy of probiotics to prevent AAD

META-ANALYSIS: Avadhani & Miley (2011)

- **Consists of 8 RCT evaluating probiotic efficacy in the prevention of AAD**
- **Includes 2 RCT that report negative results**
- **Focus was prevention of AAD & *C. difficile* in hospitalized adults**
- **Report a Relative Risk Ratio of 56%**
- **Conclude concurrent use of probiotics and antibiotics as effective in preventing AAD in the hospitalized adult patient**

META-ANALYSIS: Cremonini, et al (2002)

- **Consists of 7 RCT evaluating probiotic efficacy in the prevention of AAD**
- **Includes 1 RCT that report negative results**
- **Focus was prevention of AAD in an age range of 2 weeks to elderly**
- **Investigated probiotic monotherapy using *Lactobacillus GG* or *S. Boulardii***
- **Conclude probiotics reduce the risk of AAD**

UMassAmherst**META-ANALYSIS: D'Souza, Rajkumar,
Cooke, & Bullpitt (2002)**

- Consists of 9 RCT evaluating probiotic efficacy in the prevention & treatment of AAD
- *S. boulardii*, *lactobacilli* or *enterococci* were evaluated
- Focus was prevention of AAD in both adult and pediatric populations
- Relative Risk of 37%
- Conclude probiotics prevent AAD but do not treat AAD

UMassAmherst**META-ANALYSIS: Kale-Pradhan, Jassal & Wilhelm (2010)**

- Consists of 10 RCT evaluating probiotic monotherapy efficacy in the prevention of AAD
- *Lactobacillus* was evaluated
- Focus was prevention of AAD in both adult & pediatric populations, results were reported separately
- Relative Risk of 24%
- Conclude probiotics prevent AAD in the adult population

META-ANALYSIS: McFarland (2010)

- **Systemic review & meta-analysis of *S. boulardii* in adults**
- **10 RCT using *S. boulardii* as monotherapy**
- **Focus was prevention of AAD in both adult & pediatric populations, results were reported separately**
- **Relative Risk of 47%**
- **Conclude *S. boulardii* prevents AAD in the adult population both in the inpatient & outpatient setting**

META-ANALYSIS: Sazawal, et al (2006)

- **Meta-analysis evaluated 16 RCT focusing on the use of probiotics in all types of acute diarrhea**
- **All RCT in the analysis were masked & placebo controlled**
- **Focus was prevention of acute diarrhea in both adult & pediatric populations**
- **Relative Risk reduction of 52%**
- **Conclusion: of all types of acute diarrhea, probiotics have the greatest effect on preventing AAD**

UMassAmherst**META-ANALYSIS: Szajewska & Mrukowicz
(2005)**

- **Meta-analysis evaluated 5 RCT focusing on the use of *S. boulardii* for the prevention of AAD**
- **Includes both adult & pediatric populations**
- **Relative Risk reduction of 43%**
- **Conclusion: *S. boulardii* reduces the risk of AAD**

RCT: Armuzzi, et al (2001)

- **RCT with outpatient adults given probiotics during a specific antibiotic treatment**
- **Randomized 60 healthy asymptomatic *H. pylori* positive adults to probiotic or placebo**
- ***H. pylori* treatment: rabeprazole, clarithromycin, & tinidazole all BID**
- **Lactobacillus GG (6×10^9 CFU) or placebo BID for 14d; 1-1/2 hours after the antibiotic administration**
- **All the side effects of antibiotic use were included in the study, only diarrhea was significant ($p=0.026$)**

RCT: Armuzzi, et al (2001), continued

- **Diarrhea rates reported: placebo 26.6% versus probiotic 3.3%**
- **Side effects were self reported and all diarrhea was reported as mild for all participants**
- **Of note all the study participants were a convenience sample of medical personnel (MD, RN, biologists or administrators)**

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Study	Results
Avadhani & Miley (2011)	concurrent use of probiotics and antibiotics as effective in preventing AAD in the hospitalized adult patient
Cremonini, et al (2002)	Conclude probiotics reduce the risk of AAD
D'Souza, Rajkumar, Cooke, & Bullpitt (2002)	Conclude probiotics prevent AAD but do not treat AAD
Kale-Pradhan, Jassal & Wilhelm (2010)	Conclude probiotics prevent AAD in the adult population
McFarland (2010)	Conclude <i>S. boulardii</i> prevents AAD in the adult population both in the inpatient & outpatient setting
Sazawal, et al (2006)	Conclusion: of all types of acute diarrhea, probiotics have the greatest effect on preventing AAD
Szajewska & Mrukowicz (2005)	Conclusion: <i>S. boulardii</i> reduces the risk of AAD
Armuzzi, et al (2001)	All the side effects of antibiotic use were included in the study, only diarrhea was significant ($p=0.026$)
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Conclusions

- All 7 meta-analyses and 1 RCT agree that AAD is prevented when probiotics are included in the treatment plan
- There is a wide variety of probiotics, diagnoses, antibiotics, patient populations and settings reported
- There is an overlap of studies across the meta-analyses

Conclusions

While there is no agreement on the best probiotic or the optimal dose there are some guidelines that can be gleaned from the literature

Introduction of the Evidence-Based Protocol

**Evidence-Based Protocol
describing The Use of Probiotics
in the Adult Outpatient
Population**

When an antibiotic is prescribed for any condition the following guidelines can be taken into consideration when prescribing a probiotic for AAD prevention.

Introduction of the Evidence-Based Protocol**Strain**

Lactobacillus, *Bifidobacterium*, *S. boulardii* are the most studied probiotics.

(Avadhani & Miley, 2011; Cremonini, et al, 2002; Edwards-Marshall, 2011; Hickson, et al, 2007; Hunter, 2004; Rohde, Bartolini, & Jones, 2009; Santosa, Farnworth, & Jones, 2006; Vrabie & Abera, 2009; Weichselbaum, 2009; Williams, 2010)

Culturelle, Align, Florastor or generic equivalent can be recommended since these OTC products contain one of the above mentioned probiotics.

Introduction of the Evidence-Based Protocol

Dose

1 million to 100 billion CFUs QD to BID.

(Avadhani & Miley, 2011; Cremonini, et al, 2002; Fox & Dang, 2004; Hickson, et al, 2007; Rohde, Bartolini, & Jones, 2009; Santosá, Farnworth, & Jones, 2006; Wallace, 2009)

Introduction of the Evidence-Based Protocol

Dose Timing

At least 2 hours from the dose of antibiotic. This can be either before the antibiotic or after the antibiotic dose.

(Williams, 2010)

Introduction of the Evidence-Based Protocol

Therapy Duration

At least during the antibiotic treatment course and up to 6 weeks after completion. The average is 7-14 days.

(Edwards-Marshall, 2011; Cremonini, et al, 2002; Vrabie & Aberra, 2009)

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Contraindications

S. boulardii should not be given with antifungals.

(Williams, 2010)

UMassAmherst**Introduction of the Evidence-Based Protocol**

Safety

Probiotics are generally considered safe.

(Hickson, et al, 2007; Rulis, 2002; Venugopalan, Shriner, & Wong-Beringer, 2010)

Introduction of the Evidence-Based Protocol**Risk Factors for Sepsis**

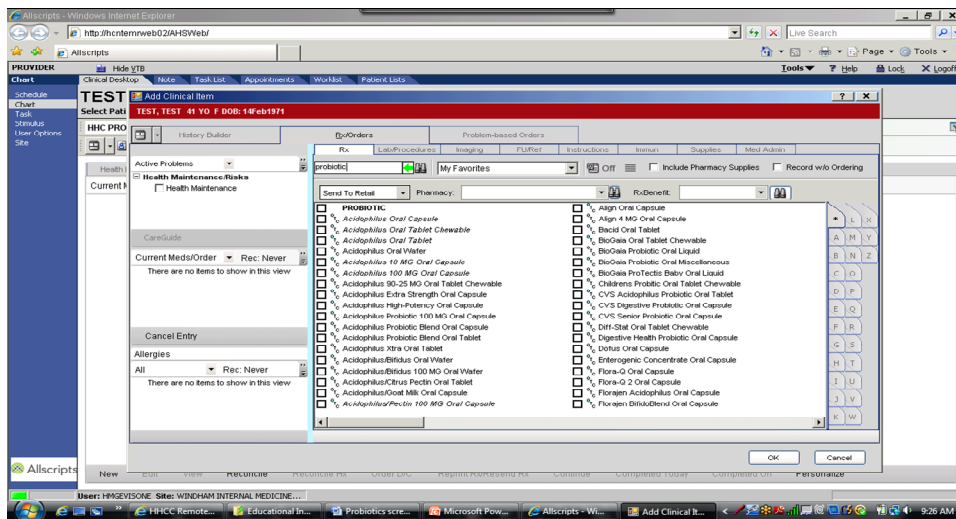
- Major risk factors include: immune compromised individuals (including debilitated state or malignancy) and premature infants are at risk for sepsis
- Minor risk factors include: central venous catheter, impaired intestinal epithelial barrier, administering probiotic by jejunostomy, broad spectrum antibiotic to which the probiotic is resistant, probiotics with high mucosal adhesions, use of *Lactobacillus* and cardiac valvular disease
- The presence of one major risk factor and two or more minor risk factors should caution the use of a probiotic

How to document Probiotics in Allscripts®

- When you are picking the antibiotic in Allscripts® medication section, you can also document the recommendation of a probiotic. You can document just Probiotic or you can document a specific OTC probiotic.
- If you search the term “probiotic” in the medication section the following screen shot is returned. You can select your favorites or just use the generic Probiotic.

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Screen Shot of Probiotic Search



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