THE ROLE OF PROBIOTICS IN THE PREVENTION OF ANTIBIOTIC-ASSOCIATED DIARRHEA

By
DEBRA M. CLEMENT

A project submitted in partial fulfillment of
The requirements for the degree of:

MASTER OF NURSING

WASHINGTON STATE UNIVERSITY
College of Nursing
August 2010

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Lorrie Dawson, PhD, ARNP, Chair

Melody Rasmor, MS, ARNP, FNP

Renee Hoeksel, PhD
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Abstract

By DEBRA M. CLEMENT
Washington State University
August 2010

Chair: Lorrie Dawson, PhD, ARNP

Antibiotic-Associated Diarrhea (AAD) is a serious complication of antimicrobial therapy. There is emerging interest in the health benefits of probiotics for a plethora of illnesses. Studies have demonstrated the efficacy of probiotics for respiratory infections, dental caries, irritable bowel syndrome and inflammatory bowel disease.\textsuperscript{1,2} Probiotics may also have a role in the prevention of AAD. From 1994 to 2003 U.S. citizens nearly tripled the amount spent on probiotic purchases.\textsuperscript{1} Probiotics are considered a natural and safe remedy by many. It is the nurse practitioner’s responsibility to advise and educate patients with the latest evidence-based information regarding the role of probiotic therapy in the prevention of AAD.

Keywords: probiotics, diarrhea, antibiotic-associated diarrhea
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Diarrhea can be a serious side effect of antibiotic therapy. Despite an increased focus on prudent prescribing of antimicrobial drugs the occurrence of antibiotic-associated diarrhea (AAD) remains a healthcare concern. AAD occurs in the outpatient setting in up to 30% of children and adults who receive antibiotics.\(^3,4,5\) AAD typically develops rapidly after the introduction of antibiotic therapy however onset can be delayed for six to eight weeks upon discontinuation.\(^4,6\)

AAD can lead to complications such as debilitating discomfort, incompleteness of prescribed antibiotic course, increased cost of care and toxic mega colon. Toxic mega colon is often caused by \textit{C. difficile} infection.\(^7\) \textit{C. difficile} infection is a serious and potentially life-threatening outcome of AAD. Historically, \textit{C. difficile} has been thought of as a nosocomial infection. The emergence of a hyper virulent form of \textit{C. difficile} has been recently identified that poses a threat to healthy individuals outside the acute care setting.\(^8\) The cost to prevent one case of AAD is estimated at $100 compared to an estimated $3669 cost to treat.\(^9\) Prevention of AAD could result in improved patient tolerance to antibiotics, completion of the antibiotic course, decreased mortality rates and less money spent overall on the treatment and management of the individual with AAD. Judicious antimicrobial prescribing and prevention is the key as no treatment exists for non \textit{C. difficile} AAD other than supportive care and removal of the problematic antibiotic.\(^6\)

There is emerging interest in whether probiotics can play a role in the prevention of AAD. A survey of advice given in the office setting by general practitioners to patients regarding probiotics concluded we have reached the "tipping point" on whether the provider offers information about probiotics.\(^10\) Probiotics are here to stay and it is the nurse practitioner's responsibility to be aware of the potential benefits, use and risks associated with probiotics in the prevention of AAD.
Theoretical Framework

Prevention is universally recognized as the key to good health. Encouragement of health promoting behavior is elemental to the success of preventative programs and outcomes that serve to keep individuals working and living in their communities and out of the acute care setting. Pender’s Health Promotion Model\(^{11}\) (HPM) is an example of a middle range theory that can serve as the basis for the nurse practitioner to assist individuals in meeting their preventative gastrointestinal health needs. In the setting of AAD prevention, a focus on health promotion facilitates and supports the practitioner to responsibly prescribe antimicrobials and prevent any untoward outcomes of antibiotic therapy.

The HPM provides the framework for addressing health beliefs and structuring care based on health promotion and wellness. There are several areas along the HPM spectrum where obstacles could exist and the nurse practitioner should be cognizant of these potential barriers. For example, an individual’s prior health related behaviors, their financial situation and interpersonal influences may all prevent an individual from experiencing a healthy outcome in preventing AAD.\(^{11}\)

The theoretical underpinnings of Pender’s HPM can be very helpful in directing the approach to patient care in the gastroenterology setting. The greatest impact of the HPM is at the behavioral outcome end of the model where the patient and provider have made a commitment to a plan of action and a resulting health promoting behavior occurs. Through understanding the pathogenesis of AAD and the current body of evidence in probiotic use, the nurse practitioner will be well-prepared to assist individuals in gastrointestinal disease prevention and health promotion.
Literature Review

Databases used to identify relevant literature included the Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE/PubMed and the United States National Library of Medicine (NLM). Key words used in the search were probiotics, diarrhea and antibiotic associated diarrhea. The search was limited to full text peer-reviewed research reports in English between the dates of 2005-2010. The types of articles in the MEDLINE/PubMed search were limited to clinical trials and randomized controlled trials.

Thirty-seven articles from the CINAHL database and 52 from the MEDLINE database were located. The NLM search resulted in 9 related articles. Titles and abstracts were then perused to establish whether the reference was relevant to provide evidence regarding the use of probiotics in the setting of antibiotic use and the prevention of AAD. The articles were then classified according to evidence of efficacy.

A total of 27 articles and studies met the inclusion criteria. Included in this number are five meta-analyses, the largest consisting of a review of 25 adult and pediatric studies and a Cochrane review of ten pediatric trials. On-line resources include the Centers for Disease Control and Prevention (CDC), World Health Organization (WHO) and the National Center for Complementary and Alternative Medicine (NCCAM).

Pathogenesis of AAD

Understanding the pathogenesis of AAD is important in preventing gastrointestinal illness and supporting digestive health promotion. AAD made its appearance in the 1950s with increased prescribing of broad spectrum antibiotics. Attention has focused on efforts to promote responsible antimicrobial prescribing since, yet AAD persists as a healthcare concern as the use of newer broad spectrum-antibiotics continues. AAD is commonly defined as three or more loose,
watery stools per day in the setting of antibiotic administration without other known causes.  

Secondary causes for diarrhea include non-antibiotic pharmacology agents such as drugs that affect gastrointestinal motility. Acute infections, parasites, chronic gastrointestinal maladies such as ulcerative colitis, Crohn's, irritable bowel syndrome and food allergies like those seen with celiac sprue disease or lactose intolerance are also possible sources of non AAD.  

AAD can occur within a day of antibiotic therapy or up to 8 weeks after its completion and affects up to 30% of individuals in the outpatient clinical setting. AAD is age-indiscriminate and rates are relatively similar between pediatric and adult populations. The effects can sometimes cause little trouble other than the inconvenience of watery diarrhea and mild cramping. AAD becomes more serious when colitis develops and abdominal pain, fever and electrolyte disturbances ensue. The most severe outcome of AAD is the development of a potentially life-threatening inflammation of the colon called pseudomembranous colitis (PMC). Complications of PMC include hypokalemia (37%), renal failure (27%), and hypoproteinemia (50%). The pathogenic organism known as C. difficile is almost always present in PMC. The toxins released by C. difficile may lead to toxic mega colon, sepsis and even death.

The specific organism responsible for AAD is unknown; however there is evidence C. difficile is the culprit in about one-third of cases. The CDC estimated minimum annual incidence of community-acquired C. difficile infection rates are 7.6 cases per 100,000 and 1 case per 5,000 in the setting of outpatient antimicrobial use. C. difficile diarrhea occurs when antibiotic exposure disrupts indigenous colonic flora allowing the C. difficile spores to transform to a vegetative state where toxin production wreaks havoc on the colonic mucosa. Other possible etiologies of AAD reported in the literature include Clostridium perfringes, Klebsiella oxytoca,
Staphylococcus aureus and Candida albicans however these findings remain inconclusive.⁴

The pathogenesis of AAD is thought to be primarily due to the local effects of the antibiotic on the normal flora of the gut. Colon flora is established after infancy and remains well balanced throughout life except when disrupted by antibiotic therapy. Over 400 microorganisms have been identified and are known to inhabit the gut.¹² This massive ecosystem provides natural protection from disease.

Antibiotics cause a disruption in the complex, well-balanced symbiotic relationship of intestinal microbiota. Suppression of the indigenous colon flora has three major effects: overgrowth of pathogens, altered gut flora metabolism and change in the physiology of the enteric nervous system.⁴ In the incidence of pathogen overgrowth, colonization resistance becomes compromised. Colonization resistance is a vital component of gut health. Resident intestinal microbiota exhibit colonization resistance by competing for nutrients with opportunistic pathogens, producing proteases that degrade toxins, and guarding and protecting pathogen receptor sites.⁴

Altered gut flora metabolism results in osmotic diarrhea and the impact is two-fold. Ingested carbohydrates are usually fermented by resident intestinal microbiota. However a reduction in the ecosystem leads to an excess of large osmotically active saccharides as well as a lack of fermented short chain fatty acids that are responsible for sodium and water resorption.⁴ This alteration in carbohydrate metabolism and reduction in the amount of short-chain fatty acids available for absorption leads to osmotic diarrhea.

In addition to pathogen overgrowth and altered metabolism, there is also evidence there is a disruption in the enteric nervous system when normal microbiota have been disturbed by antibiotics.⁴ However, there is limited research in this area and results remain inconclusive.
Antimicrobial use in the setting of pathogen exposure is undeniably the major risk factor for AAD.\textsuperscript{4,14} Antibiotics that make an individual especially prone to AAD include clindamycin, cephalosporins and penicillins.\textsuperscript{4} Broad spectrum antibiotics are the usual culprits.\textsuperscript{5} Lower risk antibiotics include fluoroquinolones and macrolides.\textsuperscript{4}

Antibiotics are troublesome for more than one reason. Clindamycin, the aminopenicillins and cephalosporins have mechanisms of action against anaerobic organisms.\textsuperscript{3} Anaerobes are prolific in the intestine and are responsible for metabolism of carbohydrates. Osmotic diarrhea will occur if sugars are left unmetabolized in the gut. Antibiotics also affect local gut flora while leaving other organisms unaffected which can lead to an overgrowth of pathogens such as \textit{C. difficile}. Finally, some antibiotics like erythromycin, can affect gut motility by promoting stimulation of receptors that increase bowel motility, causing diarrhea.\textsuperscript{3} Other risk factors for AAD include age, immunity status, co-morbidities, pathogen exposure and recent invasive procedures such as surgery.\textsuperscript{4}

\textbf{Probiotics}

The HPM framework embodies the concept of health promoting behaviors. Gaining knowledge regarding probiotic use in the prevention of AAD prepares the nurse practitioner to assist individuals in making evidence-based health promoting decisions. The nurse practitioner should understand how probiotics work in the prevention of AAD, identify commonly used strains, determine the most effective dose and be aware of the risks associated with their use.

In 1989 Fuller\textsuperscript{15} defined a probiotic as a “live microbial feed supplement which beneficially affects the host animal by improving its [intestinal] microbial balance”.\textsuperscript{15} The scientific exploration of probiotic use is still in its early stages according to the NCCAM.\textsuperscript{16} However, the concept of probiotics has been around for centuries. Since ancient times humans
have been eating fermented foods and drinking cultured milk products.\textsuperscript{15,16}

It is thought that probiotics offer resistance to disease in four ways: through the production of antimicrobial factors, by providing a physical barrier via competition for adhesion receptor sites, through competition for nutrients and by stimulation of innate immunity.\textsuperscript{15} In addition, there is evidence probiotics offer intestinal wall mucosa protection through specific peptides that regulate cell survival and growth.\textsuperscript{17}

One of the most detailed studies to date in regards to innate immunity involves mice as the study subjects and uses a probiotic containing eight different strains.\textsuperscript{18} In this study, researchers demonstrate that the probiotic stimulates epithelial innate immune responses resulting in the suppression of an intestinal inflammatory response. This study uses both in vivo and in vitro methods. It had been previously hypothesized that probiotics may have an anti-inflammatory effect on the gut. In this study, researchers find rather than suppression of inflammatory cytokines, the probiotics actually stimulate an immune response.\textsuperscript{18} In fact the preventive effect is that the intestine’s innate immunity rather than one’s acquired immunity is stimulated, hence a potentially harmful inflammatory cascade does not ensue.\textsuperscript{18}

\textit{Lactobacilli, bifidobacteria, streptococci} and \textit{enterococci} have all been identified as non-pathogenic microorganisms in the probiotic groups that are derived from humans.\textsuperscript{3} Of the groups, \textit{Lactobacillus} and \textit{Bifidobacterium} comprise most probiotics.\textsuperscript{16} Groups are further classified into species and strains. Some probiotics, like \textit{Saccharomyces boulardii} are yeasts and not of human origin.\textsuperscript{3,16}

\textit{Lactobacilli} in general enhance immunity by stimulating interleukin 12, 18 and \textit{y}-interferon in monocytes.\textsuperscript{5} \textit{Lactobacillus casei} and \textit{acidophilus} affect the immune response by promoting plasma cell IgA response.\textsuperscript{5} \textit{Lactobacillus rhamnosus} strain GG (LGG) is a lactic-acid
fermenting bacteria that is unique in that it has antimicrobial properties and it can survive the inhospitable acidity and bile of the gastrointestinal tract.\(^5\)

One study concludes that LGG–derived peptides have antibacterial properties against both gram-negative and gram-positive bacteria.\(^19\) In this study identification of peptides and antibacterial activity assays are performed to analyze the effect of LGG on \textit{E. coli} growth. Through anion exchange chromatography researchers found three small peptide molecules that exhibit antibacterial and heat resistant activity. Of the three peptides, the isolate identified as NPSRQERR has the most antibacterial properties and has the greatest thermostability.\(^19\)

Other organisms shown to be of most benefit are not of human origin, rather they are yeasts. Like \textit{Lactobacillus}, \textit{S. boulardii} is able to remain viable in the gut despite inhospitable conditions.\(^5\) This yeast can specifically have an effect upon \textit{C. difficile} as it produces an enzyme that disables toxins A and B of the \textit{C. difficile} vegetation.\(^5\) \textit{Saccharomyces} yeasts are thought to have a direct effect on absorption by increasing chloride absorption in the intestine thus decreasing the volume of diarrhea. In addition, there is evidence they have an effect upon the nitric oxide pathway that regulates water and electrolyte transport in the intestine.\(^3\)

\textbf{Efficacy}

There are five meta-analyses to date evaluating the efficacy of probiotics for AAD prevention. The analyses include studies of pediatric, mixed pediatric and adult inpatient and outpatient populations. In addition, the studies include varying strains and combinations of probiotics for trial use.

A meta-analysis\(^20\) of nine studies comprised of both adults and children (\(n=1300\)) reports a reduction in AAD by two thirds amongst the study groups taking probiotics (OR 0.37, CI 95%). A limitation of this meta-analysis\(^20\) is a lack of heterogeneity testing and publication bias. Of
note, a similar study\textsuperscript{21} includes five studies also reviewed by this meta-analysis\textsuperscript{20} and does test for heterogeneity and publication bias, neither of which are found. Overall, seven studies are included (n=881), reporting an odds ratio of 0.3966 with the administration of probiotics and the prevention of AAD.\textsuperscript{21} Trials with 15% or more losses to follow-up are excluded from this analysis.\textsuperscript{21}

Two of the meta-analyses have a pediatric focus.\textsuperscript{22,23} A study evaluating six pediatric trials (n=766) reports probiotics reduce the incidence of AAD an average of 60% with a number needed to treat (NNT) about nine.\textsuperscript{22} A review of six randomized placebo-controlled trials\textsuperscript{23} (n=707), five of which are included in the other pediatric focused analysis\textsuperscript{22}, also concludes there is a benefit of probiotic over placebo in the prevention of AAD (RR 0.43, CI 95%). This study reports treatment of 6 patients is required to prevent 1 case of AAD in the per-protocol analysis but the findings do not withstand intention-to-treat analysis (ITT).\textsuperscript{23} This can be attributed to two studies within the review that report extreme losses to follow-up (37% and 29%).\textsuperscript{23}

The largest meta-analysis\textsuperscript{24} of randomized controlled trials (RCT) to date evaluates 25 studies (n=2810) of which 13 (52%) report a reduction in AAD (RR=0.43, 95% CI 0.31, 0.58, \(p<0.001\)) in the probiotic group versus placebo. These findings are similar to those of the other, smaller meta-analyses.

A Cochrane Database of Systematic Reviews published in 2007 performed an analysis review of the literature of probiotics for the prevention of pediatric AAD.\textsuperscript{25} The Cochrane review evaluates evidence from ten randomized clinical studies (n=1986) including two trials not previously analyzed in any meta-analysis. The review reports probiotics do prevent AAD with ten being the number needed to treat to prevent one case.\textsuperscript{25} However, similar to Johnston et al.'s 23 meta-analysis in which there is evidence suggesting the promising benefit of probiotic in AAD
prevention, the studies reviewed by Cochrane do not stand up to ITT analysis. So the Cochrane review's final conclusion is that while the data is promising, it is inconclusive. Of note, the loss to follow up is quite significant in four of the trials included in the review ranging from 21% to 37%, thus influencing the ITT results dramatically.

With the exception of the studies that failed ITT analysis, all of the meta-analyses report a statistically significant decreased risk of AAD with co administration of a probiotic in the setting of antimicrobial use. Odds ratios range from 0.37 to 0.3966, relative risks average 0.43 and confidence intervals are consistently 95% amongst the studies.

**Strains and Dosing**

Probiotics are supplied in tablets, capsules, liquids and in foods such as yogurts, milk, miso, tempeh, some juices and soy based products. A beneficial product should contain at least more than one probiotic for which there is current evidence regarding its efficacy in the prevention of AAD. Organisms with good evidence include *Saccharomyces boulardii*, *Lactobacillus rhamnosus* GG, *Lactobacillus acidophilus*, *Lactobacillus bulgaricus* and *Bifidobacterium*. More studies are needed to establish strain and dosing guidelines as the strength and strain combinations usually vary between products. However, of the studies that report beneficial results most use 2 to 40 billion colony-forming units (CFUs) per day. A review of literature over the past twenty years concludes there is good strength of evidence for prevention of AAD in adults with administration of *S. boulardii* at a dose of 1 g daily and *Lactobacillus* GG at a dose of 1-2 billion CFUs daily in children. The Cochrane review is the first to analyze probiotic dose and specific strain, reporting doses in the range of at least 5 billion CFUs/day are the most beneficial. In addition, the analysis concludes the most effective strains are *Lactobacillus GG*,...
*Lactobacillus sporogenes* (now *B. coagulans*) and *S. boulardii*.

The largest meta-analysis\(^{24}\) to date reports *Lactobacillus GG* and *S. boulardii* have the most significant benefit for prevention of AAD at doses greater than 10 billion CFUs/day with a treatment course of at least three weeks. Similar findings are reported in a subgroup analysis where *Lactobacillus* GG, *L. sporogenes* and *S. boulardii* at strengths of 5 to 40 billion CFUs daily are found to be promising.\(^{23}\) This study does however caution that further research be conducted before specifically recommending routine probiotic use in pediatric populations.

*Lactobacillus* GG is used in several RTCs for the prevention of AAD.\(^5\) There are studies in both adult and pediatric populations that show promising results utilizing *Lactobacillus* GG. Of seven recent studies using *Lactobacillus* in their preparation, five report there is a reduction in AAD and the findings between studies is very similar in that 12%-17% of the probiotic groups develop AAD versus 34%-37% of the placebo groups.\(^{8,9,28,29,30,31}\) A meta-analysis also supports the use of this organism, reporting an odds ratio of 0.34 for the *Lactobacillus* treated study groups (95% CI 0.19-0.61; \(P<0.01\)).\(^{20}\)

Often the probiotic preparation included in the studies represents a combination of potentially beneficial organisms in addition to *Lactobacillus*. One such study (n=63) concludes only 5.9% of participants experience AAD compared to placebo when receiving a milk product containing a combination of *Lactobacillus* GG, La-5 and *Bifidobacteria lactis*.\(^{31}\) Another study combines *L. casei*, *L. bulgaricus* and *S. thermophilus* (n= 136), administering the probiotic combination to hospitalized patients receiving antibiotic therapy.\(^9\) Of the probiotic group 12% experience diarrhea versus 34% of the placebo group. In addition, *C. difficile* infection occurs in 17% of the placebo group whereas none of the probiotic group experience a *C. difficile* infection.

There are studies that suggest evidence for the benefit of probiotic therapy and the
prevention of AAD using microorganisms other than *Lactobacillus*. These studies are strong in design in that they are randomized, controlled double-blinded studies.⁶²⁸ A study using a combination of the probiotics *Bifidobacterium lactis* and *Streptococcus thermophilus* in infants and children concludes the incidence of AAD is decreased by 47.7% with application of the probiotic intervention.⁶ In addition, several single organism studies report the benefit of the yeast *S. boulardii* in the prevention of AAD, three of which are recent.²³,²⁸,³²,³³ One study (n=151) finds AAD occurrence in 1.4% of the group treated with the single organism *S. boulardii* preparation versus 9% of the placebo participants.³⁴ Another (n=269) reports 3.4% of the *S. boulardii* treated participants experience ADD compared to 17.3% in the non treated group.³³ In addition, ADD up to two weeks post antibiotic therapy is 8% compared to 28% for the placebo group. A study (n=466) specifically evaluating the use of *S. boulardii* in relation to antibiotic type reports a decrease in AAD of 5.7% versus 25.6% for placebo in the presence of ampicillin-sulbactam.³² Finally, a meta-analysis²⁰ looking at specific probiotic strains reports an odds ratio for *S. boulardii* of 0.39 (95% CI 0.25-0.62; *P*<0.001).

**Safety, Risks and Complications**

Probiotics are manufactured as food and dietary supplements, not as drugs, thus they are considered complementary and alternative medicine.¹⁶ The colon is complex and there is insufficient scientific identification of this vast microscopic ecosystem consisting of an estimated 10 to 100 trillion microorganisms.¹⁹ NCCAM cautions that varying preparations of different strains can lead to inconsistent results and that more scientific evidence is necessary regarding probiotics and their safety.¹⁶ Improved methods for identifying organisms and understanding the relationship with the healthy and unhealthy host must be explored.

Yet there have been scientific studies citing the safety of probiotics and the consensus is
they are quite safe for use in the general population. Bloating and flatulence are the most common side effects.\textsuperscript{27} Studies caution against the use of probiotics in premature infants, individuals who are immunocompromised, patients undergoing chemotherapy, have an already compromised intestinal mucosa or a central venous catheter.\textsuperscript{3,24,26,27} The safety of probiotics in populations such as the immunocompromised has not been established and the risk of probiotic sepsis should be a consideration.\textsuperscript{26,27} Theoretically probiotics could cause systemic infections, alter metabolism in a harmful way, over stimulate the immune system or result in gene transfer.\textsuperscript{16}

The WHO summarizes reports from 1988-2000 in which there are documented associations between consumption of a probiotic and a systemic infection.\textsuperscript{35} There are two documented cases of \textit{L. rhamnosus} infection possibly linked to probiotic consumption. In addition, there are thirteen reported cases of fungemia due to \textit{Saccharomyces} in patients who had contamination via a vascular catheter and seven cases of \textit{Bacillus subtilis} bacteremia, septicemia and cholangitis.\textsuperscript{35} The WHO emphasizes all the cases were in patients with underlying medical disease.

McFarland's meta-analysis\textsuperscript{24} reports 26 out of 31 trials evaluate for adverse events and in 24 of them no adverse events are found to be associated with the probiotic intervention. Side effects are thirst, constipation, and mild bloating or gas when compared with the placebo groups. No cases of septicemia are reported in any of the trials. Johnston, Supina, & Vohra\textsuperscript{23} as well as the Cochrane review\textsuperscript{25} also report no serious adverse events associated with probiotic use.

**Implications for Nurse Practitioners**

Although responsible antimicrobial prescribing is the best AAD prevention strategy, nurse practitioners must be aware of additional preventative measures to assure best outcomes. Prevention strategies are integral to health promotion and should be addressed at every patient...
visit. The nurse practitioner is in a unique position to assess and identify a patient’s preventative needs and health promotion outcomes utilizing Pender’s HPM\textsuperscript{11}. The areas within the HPM model where the nurse practitioner should focus are in regards to how a patient perceives the benefits of preventing AAD and recognizing perceived barriers to taking action. In the setting of AAD prevention the health promoting plan of action should consist of provider and patient agreement on measures to prevent adverse outcomes related to antimicrobial use, including the role of probiotics.

Given the public’s increasing interest in natural remedies and healthcare concern regarding the emergence of drug resistant organisms, there is little doubt probiotics are here to stay, more studies will be done, and patients will ask about them. Probiotics are a potentially cost-effective, safe tool to have in the nurse practitioner's health promotion arsenal. Nurse practitioners should be prepared to discuss the potential benefits, use and risks associated with probiotics in the prevention of AAD. Results from this review can serve as a basis for informed decision-making for the nurse practitioner in the area of probiotics and AAD prevention.

**Implications for Research**

There is emerging evidence suggesting the benefits of probiotics in the prevention of AAD. A review of the literature appears to support this benefit. However definitions, designs and interventions are inconsistent amongst many of the existing studies. More homogenous comparative studies of rigorous design and dose-ranging trials are needed.

Research has already been conducted on probiotic use for a variety of ailments, including AAD. Future studies will continue to evaluate the efficacy of probiotics in AAD prevention in addition to the use of probiotics in the prevention and treatment of colon cancer, bladder cancer, diabetes and rheumatoid arthritis.\textsuperscript{2}
Conclusion

AAD is a serious side effect of antibiotic therapy that can cause pain, discomfort, increased healthcare costs and even death.\textsuperscript{8,24} The effects of AAD may also prevent compliance and completion of antibiotic therapy for treatment of existing infections. Utilizing a health promotion (HPM) approach to care, the nurse practitioner is in a unique position to help individuals make evidence-based health care decisions. A review of the evidence finds probiotics do have a role in the prevention of AAD. Understanding the current evidence and integrating it into clinical practice will significantly impact AAD prevention and patient health promotion outcomes.
References


