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Clinical use of probiotics: A survey of physicians' beliefs and practice patterns

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Clinical Use of Probiotics: A Survey of Physicians' Beliefs and Practice Patterns

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ABSTRACT

Background: Probiotics have the potential to be used as a preventive agent or adjuvant therapy for various medical conditions, and recent research is beginning to illuminate some of the associated benefits. Some clinicians currently prescribe probiotics in practice. Understanding physicians' beliefs and practice patterns regarding the use of probiotics will help identify current practices, barriers preventing their acceptance, and the sources of information that impact clinical practice.

Objective: To identify and describe physicians' beliefs and practice patterns regarding the use of probiotics.

Methods: A cross-sectional online questionnaire was administered to 130 physicians employed by or affiliated with Danville Regional Medical Center, a 350-bed, acute care facility located in Danville, VA. Data were analyzed using descriptive frequencies, Pearson's chi-square, and the Student's t-test.

Results: Of the 27 valid responses (20.8%), 55.6% of physicians reported using probiotics in clinical practice (n = 15). Those who used probiotics were significantly more likely to agree that probiotics have clinically beneficial effects ($p < 0.017$) and pose minimal risk ($p < 0.003$) than those who don't use probiotics (n = 12, 44.4%). Physicians using probiotics were also less likely to agree that more clinical evidence is needed to support the benefits of probiotics for their specialty ($p < 0.012$), and more likely to indicate "peer practice patterns" ($p < 0.032$) as prompting their use, whereas those not using probiotics were more likely to choose "original research

articles" ($p < 0.006$) as a source of information that would potentially change their practice with regard to probiotics.

Conclusions: Physicians' beliefs regarding the use of probiotics differ between those who recommend their use in clinical practice and those who do not. Physicians not using probiotics feel that more evidence-based research is needed to support their use in clinical practice.

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Introduction

The most universally accepted definition of a probiotic is “a live, microbial food supplement that beneficially affects the host animal by improving its intestinal microbial balance” (1). For a probiotic to be considered effective, it should have a beneficial effect on its host, be nontoxic and nonpathogenic, consist of a large number of viable cells and remain such through storage and use, and be able to survive and be metabolically active in the gut (1). Most probiotics for human use are lactic acid producers, such as lactobacilli and bifidobacteria. Research investigating probiotics for their health benefits has seen a rising trend in recent years. In 2009, there were 5,466 publications on probiotics cited on the U.S. National Library of Medicine journal literature search system (www.pubmed.gov), (1,571, or more than 28%, were reviews) (2), yet in contrast, there were only 85 publications from 1973 to 1998 (3). Probiotics have been positively associated with a variety of gastrointestinal benefits including relieving the symptoms of lactose malabsorption (4), preventing and treating viral or infectious diarrhea and reducing the symptoms of inflammatory bowel disease (5, 6). Treatment with probiotics has also been shown to improve immune activity in critically ill patients by aiding the maintenance of the intestinal mucosal barrier and enhancing immune responses (7). Some of the mechanisms suggested for the beneficial effects of probiotics include lowering intestinal pH, adherence to intestinal mucosa, production of acids that are bactericidal, decreasing permeability of gut mucosa, production of short chain fatty acids which have a

protective effect on the gut, stimulation/regulation of gut associated lymphoid tissue, mucus production and regulation of motility (5).

Clinical evidence demonstrating that probiotics may have a place in patient care as a prophylactic or adjuvant therapy is increasing, as is consumer demand for natural products. Probiotics have the potential to offer a natural alternative to attenuate the side effects of pharmacotherapy, treat symptoms of chronic disease, prevent acute illness, and act as an intervention against antibiotic-resistant pathogens (3).

Background Information

A search of the U.S. National Library of Medicine journal literature search system (www.pubmed.gov) yielded only two surveys addressing physicians' practices regarding probiotics. The earlier study, published in 2001, was conducted by a high school student to determine whether physicians recommended probiotics to their patients to prevent antibiotic-associated diarrhea (AAD). The survey results showed that 32% of respondents recommended probiotics when prescribing antibiotics. Furthermore, 31% of the physicians stated that they were not familiar with probiotics and only 18% were aware of any research on probiotics (8). The second study, published in 2010, sought to describe gastroenterologists' perceptions and use of probiotics in practice. All respondents (n = 56) in this survey believed that probiotics were safe for most patients, and 98% felt that probiotics have a role in the treatment of gastrointestinal illnesses or symptoms. This study reported that the two most common conditions for which gastroenterologists recommended probiotics were irritable bowel syndrome (IBS) and *Clostridium difficile*-associated diarrhea

(CDAD) (9). Currently, there is an inadequate amount of information regarding what affects physicians' practice patterns and beliefs regarding probiotic use, as well as the number of physicians who use them in practice.

Statement of Problem

While the evidence supporting the use of probiotics in clinical practice is mounting, it has yet to become a widely accepted practice among physicians in North America. At the present time, there is limited data regarding physicians' beliefs and practice patterns with respect to probiotics.

Purpose of the Study

The objective of this research is to ascertain physicians' beliefs and practice patterns regarding the clinical use of probiotics, and the sources of information that prompt their use.

Chapter 2: Review of Literature

Probiotics and Diarrhea

Much of the evidence points to benefits of using probiotics to treat diarrhea of various etiologies. Diarrhea has been defined as the condition in which there is a decreased consistency or increased frequency of bowel movements, with an increased fecal weight due to the greater liquidity of the stool (5). The preventive or therapeutic effects of probiotics for diarrhea have been investigated in conditions such as *Clostridium difficile* infection *(C. difficile),* antibiotic-associated diarrhea (AAD), acute diarrhea (both viral and bacterial), inflammatory bowel diseases, irritable bowel syndrome, tube feeding associated diarrhea, and diarrhea resulting from chemotherapy or radiation (5). Diarrhea is problematic because its occurrence increases the workload of caregivers and decreases patient comfort level and sense of dignity. Diarrhea in itself can lead to metabolic problems and malnutrition, which increases risks for the patient as well as healthcare costs.

Antibiotic-Associated Diarrhea and *Clostridium difficile* Infection

Antibiotic use and *C. difficile* infection often lead to diarrhea, as a consequence of altered gastrointestinal microbiota (3, 5,10). The research on the effectiveness of probiotics to prevent AAD and *C. difficile*-associated diarrhea (CDAD) is encouraging. In a randomized, placebo-controlled trial of 202 children, Vanderhoof and colleagues found that *Lactobacillus rhamnosus* GG (LGG) significantly reduced stool frequency ($p < 0.02$) and increased stool consistency ($p < 0.001$) in the treatment group (n = 93) compared to the placebo group (n = 95) during a 10-day course of oral antibiotic therapy (10). A meta-analysis of nine double blind,

randomized, controlled trials investigating the efficacy of probiotics in the prevention and treatment of AAD reported that certain strains showed a clear benefit in the prevention of AAD ($p < 0.001$), but these studies didn't support probiotics as an effective treatment of AAD (11). A Cochrane review (a systematic review conducted by the Cochrane Collaboration and based on the best available evidence to aid practitioners in determining the effectiveness of an intervention in a specific clinical application) (12) found that probiotics show promise for the prevention of AAD (nine of the ten trials show statistically significant results) in pediatric patients based on existing literature, but further studies are warranted to determine the effect of age and antibiotic treatment duration to properly assess efficacy (13). In a multi-center, randomized, double blind placebo controlled trial, *Saccharomyces boulardii*, a strain of yeast believed to be beneficial to the gastrointestinal tract, was shown to prevent diarrhea in tube-fed, critically ill patients ($p < 0.0023$), especially those with risk factors for diarrhea such as antibiotic use, hypoalbuminemia, non-sterile administration of enteral feeding, and CDAD (14). In a meta-analysis of trials of certain probiotics on AAD and CDAD, McFarland found that *S. boulardii,* LGG, and probiotic mixtures significantly reduced the incidence of AAD ($p < 0.001$), but only *S. boulardii* was effective in treating CDAD ($p < 0.005$) (15).

Acute Diarrhea

Acute diarrhea is also a condition where probiotics may provide a benefit and show promise for use as treatment. In a trial of 113 infants and toddlers with acute diarrhea, Henker and colleagues found that the administration of *Escherichia coli* strain Nissle 1917 reduced the median duration of diarrhea by 2.3 days ($p < 0.0007$)

(16). A similar study was conducted using two strains of *Lactobacillus* to treat hospitalized children with acute diarrhea. The findings showed that each of the two strains resulted in significant reductions in the duration of rotavirus excretion ($p < 0.02$) and length of hospital stay ($p < 0.03$); however, the reduction in duration of diarrhea of 20% was not significant ($p < 0.07$) (17). Van Niel and colleagues investigated nine randomized, controlled trials of *Lactobacillus* on acute infectious diarrhea in children. The meta-analysis showed that treatment with Lactobacillus reduced duration of diarrhea by 0.7 days (95% confidence interval (CI): 0.3-1.2 days) and frequency by 1.6 stools by day two of treatment (95% CI: 0.7-2.6 fewer stools) compared to the placebo group (18). In a review of 23 studies of children and adults, investigators concluded that probiotics reduced the risk of diarrhea and were beneficial in treating infectious diarrhea, reducing the mean duration of diarrhea by 30.48 hours (95% CI: 18.51-42.46 hours) (19). A meta-analysis of 34 trials on probiotics in the prevention of acute diarrhea showed that various strains reduced the incidence of acute diarrhea by 57% in children and 26% in adults (20). When examining acute diarrhea by type, the evidence showed a reduction in the risk of AAD by 52%, of traveler's diarrhea by 8%, and that of various other causes by 26%. There were no significant differences in effectiveness among the strains used in these studies. McFarland performed a meta-analysis of twelve probiotic treatments from seven randomized, controlled trials on traveler's diarrhea and concluded that certain strains had significantly reduced the risk of traveler's diarrhea ($p < 0.001$) and could provide a safe and effective method for prophylaxis (21). Other studies on the effect of probiotics on traveler's diarrhea have shown mixed results, likely due to

differences in the strains used, the traveled countries, local microflora, time of initiation of therapy, dosage, and compliance (5, 21).

Irritable Bowel Syndrome

Probiotics have also been proposed to treat the symptoms of irritable bowel syndrome (IBS). In a randomized, placebo controlled trial of 40 IBS patients, Sinn and colleagues found that probiotics resulted in a reduced score for abdominal pain/discomfort by more than 20% ($p < 0.003$) in comparison to placebo (22). A meta-analysis by Hoveyda and colleagues reviewed 14 randomized, placebo-controlled trials of probiotics on IBS. The studies varied in strains, dose, duration and strength of probiotics used. They found that overall symptoms were moderately improved, yet two of the studies failed to yield statistically significant improvements (23).

Inflammatory Bowel Disease

Probiotics have also been suggested to aid in inflammatory bowel diseases (IBD), although firm evidence is lacking. The most consistent results found that probiotics were effective in reducing the risk of recurrence in patients with non-active pouchitis compared to placebo (24-26). While some published studies suggest probiotics use may be beneficial for patients with Crohn's disease and ulcerative colitis, reviews of the existing data yields mixed findings (27-31).

***Helicobacter pylori* Infections**

Some research has examined the effectiveness of probiotics as a co-therapy for eradicating *Helicobacter pylori* infections (and reducing related diarrhea and dyspepsia from treatment) (32-35). The consistent finding among these studies was

that probiotics were beneficial in decreasing gastritis and bacterial load, but showed no effect on eradication.

Chemotherapy and Radiation Induced Diarrhea

In addition, probiotics have been shown to be beneficial in ameliorating diarrhea related to chemotherapy and radiation therapy. Osterlund and colleagues conducted a randomized, controlled trial of LGG on 150 patients diagnosed with colorectal cancer receiving either one of two chemotherapy regimens. Findings of this study showed that abdominal discomfort and diarrhea was reduced in the group receiving LGG ($p < 0.027$) compared with the placebo group, and there was no related toxicity (36). Delia and colleagues conducted a double blind, placebo-controlled trial on 490 patients who underwent adjuvant postoperative radiation therapy. Before the initiation of radiation, patients were either given VSL#3 (a probiotic mixture containing four strains of lactobacilli, three strains of bifidobacteria and one strain of streptococcus, manufactured by VSL Pharmaceuticals, Fort Lauderdale, MD) or placed in the placebo group at the initiation of radiation. More patients in the placebo group got diarrhea ($p < 0.001$), experienced more severe grades of diarrhea ($p < 0.001$), experienced more daily bowel movements ($p < 0.05$) and had a significantly shorter duration ($p < 0.001$) before loperamide (an anti-diarrheal drug) was required for treatment (37).

Necrotizing Enterocolitis

A recent Cochrane review found that administrating probiotics to preterm infants >1000 g at birth significantly reduced the risk of severe necrotizing

enterocolitis (NEC) (relative risk (RR) 0.32) and mortality (RR 0.43). The authors concluded that this supports a change in practice (38).

Adverse Effects Associated With Probiotics

Most scientific evidence indicates that probiotics are safe and reports of adverse effects are extremely rare. However, sepsis has been reported to occur in immunocompromised patients using probiotic supplements. In several cases of sepsis in which pathogen identification was performed, the infective and probiotic strains were indistinguishable. Since the probiotic strains can be found in the gastrointestinal tract of healthy people, the cause of infection was inconclusive (39). While probiotic supplementation is considered safe for healthy people, caution should be used in the immunocompromised because bacterial translocation and opportunistic infection can occur, increasing the risk of sepsis (40).

Limitations of Studies on Probiotics

While several probiotic preparations hold promise for clinical use, most researchers agree that larger, controlled trials are needed. To date, most of the trials have been small and contained methodological limitations. Research is challenging because specific strains, optimal dose, time of initiation, duration of therapy and patient adherence are complex variables in matching probiotic treatment to a specific indication within a patient population. Existing evidence is difficult for researchers to pool because of the heterogeneity among studies. Additionally, authors' recommendations can differ, based on the studies selected for inclusion and methods used to analyze the data.

However, Al Faleh and colleagues state that the evidence on probiotic

supplementation in preterm infants to prevent NEC supports a change in practice (37). The clinical recommendations from UpToDate® (41), an evidence-based, peer-reviewed resource for clinicians, states that the evidence related to probiotics and NEC is “exciting”; however, these studies varied considerably in strains/products used, doses, and dosing regimens, and caution should be used with the application of these findings. Practice guidelines from the World Gastroenterology Organization (42) state that evidence strongly supports the use of certain probiotic strains in preterm infants to reduce the incidence of NEC. This demonstrates that sources of information for clinical recommendations and how they are interpreted may vary.

Regulation of probiotics by the U.S. Food and Drug Administration (FDA) as a dietary supplement as opposed to the stringent testing required by drugs may also be a barrier in the widespread acceptance of probiotics in clinical practice due to lack of standardization of products and insurer reimbursement.

The use of probiotics in treatment and as preventative agents may result in reduced costs in healthcare and increased patient well-being, and their use poses little risk to otherwise healthy people. The benefits of probiotics should not be overlooked even though they urgently warrant further research to be accepted as a mainstay in clinical practice.

Chapter 3: Research Methods

Study Population

All currently practicing physicians employed by or affiliated with Danville Regional Medical Center (DRMC), located in Danville, Virginia, were invited to participate in the study. A list of e-mail addresses for all physicians was provided by the DRMC Human Resources Department. Overall, 146 subjects were contacted. Of those, 3 physicians were no longer practicing in Danville, and 13 survey invitations were found to be undeliverable, resulting in a study population of 130 physicians.

Methods

A cross-sectional survey study on physicians' beliefs and current practice regarding the clinical use of probiotics was conducted using the physician population of Danville, VA, during October and November of 2010. This study was approved by the E.M.U. College of Health & Human Services Human Subjects Review Committee on October 18, 2010 (Appendix A: CHHS HSRC Approval Letter) and also submitted to the DRMC Institutional Review Board, which determined that the study did not require their approval (Appendix D: DRMC IRB Response to Proposal). The survey questionnaire was developed and administered by the principal investigator using SurveyMonkey™ software. Once the questionnaire and participant list were created, the program notified participants via email to participate in the survey. Upon entering the survey, participants were presented with the informed consent (Appendix C: Informed Consent Form), which notified them of the purpose of the study, the confidentiality of individual responses, the voluntary nature of

participation, and the intended use of the research for scholarly purposes. Participants were required to give consent prior to entering the survey questionnaire. Once the participant completed the questionnaire, the responses were saved within the password-protected survey software and were only accessible by the principal investigator. The survey was open for a period of one month, from October 25 to November 25, 2010. Reminder messages were sent to non-responding physicians four times throughout the duration of data collection.

Survey Instrument

The investigator-designed survey consisted of 14 items divided into five categories: demographic information, practice characteristics, beliefs regarding probiotics, use of probiotics, and information regarding probiotic recommendation (Appendix D: Survey Instrument). The instrument consisted of multiple choice questions and 5-point Likert scales of agreement, with response categories ranging from “strongly disagree” to “strongly agree.” Three open-ended questions were also used to ascertain respondents’ age, medical specialty, and age characteristics of their patient population. The final two questions of the survey differed according to whether the physician responded that he or she did or did not use probiotics in clinical practice.

Data Analysis

Data collected by SurveyMonkey™ software was exported into the Microsoft Office Excel software program. Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS release 17.0.0, SPSS Inc, Chicago, IL). Descriptive statistics were obtained to summarize the demographics of the

respondents and their responses to the questions. Physicians were divided into two groups: those who recommended/used probiotics in practice and those who did not. Predicting factors for probiotics usage were analyzed using the Student's t-test and the Chi-square test. A $p < 0.05$ was considered statistically significant.

Chapter 4: Results and Analysis

Demographics

Responses totaled 27 from 130 eligible physicians (after accounting for undeliverable email and physicians no longer practicing in this area), yielding a 20.8% response rate. There were four physicians who opted out of the survey (3.1%). The respondents ranged in age from 35 to 58 years, with a mean age of 49 years; however, there were two missing responses to this question. The general demographic information is listed in Table 1. There were a higher number of male respondents (74.1%) than female (25.9%). The range of years of experience was as follows: <5 (7.4%), 6-10 (14.8%), 11-15 (18.5%), 16-20 (11.1%), 21-25 (29.6%), 26-30 (11.1%), and >30 (7.4%). The majority of physicians (92.6%) completed their specialty training in the United States. Respondents' specialties were grouped according to whether they were surgical (40.7%) or medical (59.3%). Of the individual specialties, obstetrics/gynecology (14.8%) and internal medicine (18.5%) were most highly represented.

Table 1. Demographics of respondents (n=27).

Demographic	Total (n)	% of Total
Gender		
Male	20	74.1%
Female	7	25.9%
Experience (years)		
<5	2	7.4%
6-10	4	14.8%
11-15	5	18.5%
16-20	3	11.1%
21-25	8	29.6%
26-30	3	11.1%
>30	2	7.4%
Training Outside the U.S.		
Yes	2	7.4%
No	25	92.6%
Surgical Specialty	**11**	**40.7%**
Anesthesiology/Pain Medicine	2	7.4%
General Surgery	1	3.7%
Obstetrics/Gynecology	4	14.8%
Ophthalmology	2	7.4%
Otolaryngology	1	3.7%
Thoracic Surgery	1	3.7%
Medical Specialty	**16**	**59.3%**
Emergency Medicine	1	3.7%
Family Medicine	2	7.4%
Gastroenterology	2	7.4%
Hematology/Oncology	1	3.7%
Internal Medicine	5	18.5%
Pediatrics	2	7.4%
Pulmonary Medicine	1	3.7%
Radiology	2	7.4%

Practice Characteristics

Information on practice characteristics was also obtained to determine whether there was any association with probiotic use (Table 2). The mean percentages of patient population age are as follows: pediatric (13.8%), adult (42.9%) and geriatric (43.3%). There were 19 physicians (70.3%) who worked in a private practice, six physicians (22.2%) who practiced in the hospital, and two physicians (7.4%) whose practice involved both settings. None of the respondents practiced in a long-term care facility or health clinic.

With respect to technological resources used in practice, 24 physicians (88.9%) reported using electronic medical records (EMR), while only three physicians (11.1%) did not. Respondents were also asked about the other types of technological resources that they used in their practice. Fifteen physicians (55.6%) reported using an online library database such as Cochrane, PubMed, or Medline; 13 (48.1%) used electronic professional journals; 12 (44.4%) used software applications for personal digital assistants (PDA) or smartphones; and 18 (66.7%) used other internet resources. There were no significant findings with practice characteristics as predictors for probiotic usage.

Table 2. Practice characteristics of physicians (n=27).

Practice Characteristic		
	Mean % of Responses	
Patient Population		
Pediatric (17 or younger)	13.8%	
Adult (18 to 64)	42.9%	
Geriatric (65 and older)	43.3%	
	Total (n)	**% of Total**
Practice Setting		
Private Practice	19	70.3%
Community Hospital	6	22.2%
Both	2	7.4%
EMR Usage		
Yes	24	88.9%
No	3	11.1%
Technological Resource Usage		
Online Library Database	15	55.6%
Electronic Professional Journals	13	48.1%
PDA or Smartphone Applications	12	44.4%
Other Internet Resources	18	66.7%

Physicians' Use and Beliefs on Probiotics

The percentage of physicians who reported currently recommending/using probiotics in clinical practice was 55.6%, while 44.4% did not use probiotics in practice. When responding whether they knew what constitutes a probiotic, 63% responded that they did, 14.8% did not, and 22.2% reported that they would like to learn more about it. Eighty-seven percent (n=13) of the physicians using probiotics in clinical practice reported knowing what constitutes a probiotic, while only 33% (n=4) of physicians not using probiotics had this knowledge, yielding a statistically significant difference ($p < 0.005$) between the groups (Table 3).

Table 3. Physician responses (n=27) to whether they know what constitutes a probiotic.

	Physicians Using Probiotics in Practice (n)	Physicians Not Using Probiotics (n)	*p* - value	
Yes	13	4	0.005	
No	0	4	0.039	
I would like to learn more about it	2	4	0.250	(NS)

NS = not significant

The frequencies of all responses regarding physicians' beliefs about probiotics are listed in Table 4. There is one missing response for this question. Overall, 57.7% of the 26 respondents agreed that probiotics have clinically beneficial effects, and 69.2% agreed that there are minimal risks associated with probiotic use. Half of all respondents agreed that physiologic effects of probiotics varied by strain, while the other half were undecided. Respondents were mostly undecided (53.8%) whether matching the most beneficial strain to a specific indication was a barrier in recommending probiotics to patients. Most physicians (61.5%) agreed that a lack of information regarding available probiotic supplements is a barrier to recommending them to patients and that they would benefit from education/training related to the use of probiotics in clinical practice. Few respondents (19.2%) disagreed that more clinical evidence is needed to support the benefits of probiotics for their specialty, while 46.1% agreed with this statement and 34.6% were undecided.

Table 4. Physicians' level of agreement (n=26) with statements about probiotics related to the beneficial effects, risks, physiologic effects of strains, available supplements, training and existing evidence.

		Total (n)	% of Total
Probiotics have clinically beneficial effects	Strongly Disagree	0	0.0%
	Disagree	1	3.8%
	Undecided	10	38.5%
	Agree	11	42.3%
	Strongly Agree	4	15.4%
There are minimal risks associated with the clinical use of probiotics	Strongly Disagree	0	0.0%
	Disagree	1	3.8%
	Undecided	7	26.9%
	Agree	16	61.5%
	Strongly Agree	2	7.7%
Physiologic effects of probiotics vary by strain	Strongly Disagree	0	0.0%
	Disagree	0	0.0%
	Undecided	13	50.0%
	Agree	13	50.0%
	Strongly Agree	0	0.0%
Matching the most beneficial probiotic strain to a specific indication is a barrier to recommending them to patients	Strongly Disagree	0	0.0%
	Disagree	7	26.9%
	Undecided	14	53.8%
	Agree	5	19.2%
	Strongly Agree	0	0.0%
Lack of information regarding available probiotic supplements is a barrier to recommending them to patients	Strongly Disagree	1	3.8%
	Disagree	2	7.7%
	Undecided	7	26.9%
	Agree	13	50.0%
	Strongly Agree	3	11.5%
I would benefit from education/training related to the use of probiotics in clinical practice	Strongly Disagree	1	3.8%
	Disagree	2	7.7%
	Undecided	7	26.9%
	Agree	14	53.8%
	Strongly Agree	2	7.7%
More clinical evidence is needed to support the benefits of probiotics for my specialty	Strongly Disagree	1	3.8%
	Disagree	4	15.4%
	Undecided	9	34.6%
	Agree	9	34.6%
	Strongly Agree	3	11.5%

The mean scores of responses by the two groups of physicians regarding their beliefs about probiotics are presented in Table 5. Scores were determined by assigning points to Likert Scale items as follows: Strongly Disagree =1, Disagree = 2, Undecided = 3, Agree = 4, and Strongly Agree = 5. Physicians who use probiotics in clinical practice were significantly more likely to agree that probiotics have clinically beneficial effects ($p < 0.017$) and that there are minimal risks associated with the clinical use of probiotics ($p < 0.003$). This group of physicians was also less likely to agree that more clinical evidence is needed to support the benefits of probiotics for their specialty ($p < 0.012$).

Table 5. Physicians' level of agreement with statements about probiotics related to the beneficial effects, risks, physiologic effects of strains, available supplements, training and existing evidence, presented as a mean score of the responses.

	Physicians Using Probiotics*	**Physicians Not Using Probiotics***	***p*-value**	
Probiotics have clinically beneficial effects	4.00	3.27	0.017	
There are minimal risks associated with the clinical use of probiotics	4.07	3.27	0.003	
Physiologic effects of probiotics vary by strain	3.53	3.45	0.705	(NS)
Matching the most beneficial probiotic strain to a specific indication is a barrier to recommending them to patients	2.87	3.00	0.635	(NS)
Lack of information regarding available probiotic supplements is a barrier to recommending them to patients	3.60	3.55	0.888	(NS)
I would benefit from education/training related to the use of probiotics in clinical practice	3.80	3.18	0.128	(NS)
More clinical evidence is needed to support the benefits of probiotics for my specialty	2.93	3.91	0.012	

*Each response was scored on a 1 – 5 scale: 1 = Strongly Disagree, 5 = Strongly Agree. Data presented represents the mean of physician responses to each of the statements.

NS = not significant

Information Sources Influencing Probiotics Use

Of the physicians who reported recommending or using probiotics in clinical practice, 87% reported seeing a clinical benefit from their use, while 13% did not. None of the physicians responded that there was a placebo effect only. This group of physicians was also asked to indicate which sources of information prompted them to recommend or use probiotics in clinical practice.

The sources with the highest number of responses were peer practice patterns (66.7%) and continuing medical education (53.3%). The group of physicians who did not use probiotics in clinical practice were asked to indicate the reasons (all that apply) for not recommending/using them. Three respondents skipped this question. The majority of the responses (58%) were “not convinced of the clinical benefit,” followed by “there are no clinical applications for probiotics in my specialty” (33%). Fear of liability (8%) and lack of prescriptive authority by the U.S. Food and Drug Administration (8%) were also selected. Negative experiences with prior use, or cost, were not factors in choosing not to recommend probiotics.

Physicians not using probiotics were also asked about the sources of information that would potentially change their practice patterns with regard to probiotics (Table 6). There were two missing responses for this question. The sources with the highest number of responses in this group were continuing medical education (66.7%) and original research articles (58.3%). When comparing sources of information that influence practice patterns between the two groups, those who use probiotics in practice were significantly more likely to select “peer practice

patterns" ($p < 0.032$) and significantly less likely to choose "original research articles" ($p < 0.006$).

Table 6. Sources of information that have prompted (those using probiotics in practice) or would potentially prompt (those not using probiotics in practice) physicians to use probiotics in their practice.

	Physicians Using Probiotics in Practice		Physicians Not Using Probiotics		*p*-value	
	Total (n)	% of Total	Total (n)	% of Total		
Continuing Medical Education	8	53.3%	8	66.7%	0.502	(NS)
Original Research Articles	1	6.7%	7	58.3%	0.006	
Review Articles	6	40.0%	5	41.7%	0.933	(NS)
Clinical Care Guidelines	4	26.7%	5	41.7%	0.431	(NS)
Peer Practice Patterns	10	66.7%	3	25.0%	0.032	
Internet Sources (UpToDate® Cochrane Database, Medline, etc.)	7	46.7%	3	25.0%	0.257	(NS)

NS = not significant

Chapter 5: Discussion

Physicians' Use of Probiotics

Most of the research on probiotics to date has been conducted to determine their efficacy as a therapeutic or preventive agent for various clinical applications. This paper describes the beliefs and practice of probiotic use among physicians, and it is one of only three studies to explore this topic. The results of this study indicate that more than half (55.6%) of the responding physicians use or recommend probiotics to patients, which is higher than the 32% reported by family physicians in the study by Edmunds in 2001 (8), but far lower than the 89% of gastroenterologists in the recent study by Williams and colleagues (9). This high rate of probiotic use would seem to be explained by the fact that most of the known clinical applications of probiotics are related to gastrointestinal benefits. In this study, of the physicians who reported recommending probiotics in practice, a majority (73.3%) practice medical specialties (as opposed to surgical specialties), which was expected since they are more likely to be involved in managing gastrointestinal symptoms. The results of this survey have also revealed that the physicians currently using probiotics were significantly more likely to know what constitutes a probiotic and believe that they are beneficial and pose minimal risk.

Physicians' Knowledge and Beliefs Regarding Probiotics

Are physicians knowledgeable about probiotics? Data from this survey reveals that 14.8% of physicians did not know what constitutes a probiotic, and 22.2% responded that they would like to learn more about it. In comparison, Edmunds reported that only 18% of the family physicians were aware of any

research on probiotics (8). The study by Edmunds (2001) was the first to explore the use of probiotics by physicians; however, its findings have lost relevance since a majority of published studies documenting the benefits of probiotics have emerged in the past decade.

This study also revealed that 61.5% of physicians felt they would benefit from education/training regarding the clinical applications of probiotics. Interestingly, a higher number of physicians currently recommending probiotics (73.3%) than those not using probiotics (45.5%) agreed that additional training would be beneficial. Fifty percent of physicians were undecided about whether the physiologic effects of probiotics vary by strain, and 53.8% were undecided as to whether matching the most beneficial strain to a specific indication was a barrier in recommending them to patients. This would suggest that while the body of evidence supporting the use of probiotics is growing, the information might not be reaching all physicians. In addition, the marketing efforts of probiotic supplement manufacturers may not be adequately directed towards physicians, as the majority (61.5%) of respondents in this study agreed that a lack of information regarding available probiotic supplements is a barrier in recommending them to patients.

Information Sources Regarding the Clinical Use of Probiotics

In this study, 63.7% of physicians not currently recommending probiotics, as well as 33.3% of physicians who do recommend them, felt that more clinical evidence is needed to support the benefits of probiotics. Further, 58% of physicians not recommending probiotics were reluctant to recommend because they were not convinced of the clinical benefit. While 98% of gastroenterologists in the study by

Williams and colleagues believed that probiotics are beneficial in the treatment of gastrointestinal illnesses, several reported that there is still a lack of convincing evidence to support their use (9). In this study, 58.3% of physicians not recommending probiotics reported that original research articles would prompt them to change their practice patterns. These data support the fact that there are limitations in existing studies and that additional large, randomized, controlled trials are needed for an increased number of physicians to adopt the use of probiotics in clinical practice.

This study found that physicians currently using probiotics in clinical practice were significantly more likely to indicate that peer practice patterns have prompted this practice and significantly less likely to indicate original research articles than those not recommending probiotics. Of these physicians, 87% reported seeing a clinical benefit from their use. These results may suggest that experience with positive outcomes from the use of probiotics is a larger influence on practice patterns than research. Furthermore, none of the physicians who don't use probiotics indicated that experience with adverse outcomes from the use of probiotics was the reason for not recommending them in practice.

Physicians' Demographics, Practice Characteristics, and Barriers With Regard to Probiotic Use

Due to the small number of respondents, a relationship between the use of probiotics and demographics could not be identified. Data regarding practice characteristics also failed to yield any significant findings. The use of technological resources in practice was comparable for both groups and did not indicate that

increased access to information such as online library databases or electronic professional journals was a predictor for probiotics use. The patient population of physicians' practices also failed to show that physicians treating geriatric patients or pediatric patients would be more likely to recommend probiotics. Finally, while the lack of prescriptive authority of probiotics (because they are not regulated by the FDA) was proposed as a deterrent to using them, our data indicated that this was not a major concern of physicians, nor was a fear of liability or costs associated with probiotic use.

Chapter 6: Conclusions and Future Recommendations

Conclusions

In summary, this study describes physicians' beliefs and practice patterns regarding the use of probiotics. The study, though small in scale and not without limitations, provides some insight into how physician beliefs differ based on current practice and the role that information plays in physician practice patterns with regard to probiotics. The key findings of this research are that there are a few significant differences regarding beliefs and sources of information related to the use of probiotics between the physicians who use them in clinical practice and those who do not. Those who use probiotics are more likely to believe that they have beneficial effects with minimal risks. The physicians who don't are less likely to know what constitutes a probiotic and more likely to believe that more clinical evidence is needed to support their use. Peer practice patterns were a more significant source of information that prompted the use of probiotics for physicians who recommend them, while those that don't use them were more likely to state that original research articles could change their practice regarding probiotics.

Implications of Study

There is limited research describing physicians' beliefs and the sources of information that could change their current practice patterns regarding probiotics. This study found that most physicians not using probiotics in practice are not doing so because they are not convinced of the clinical benefit. The majority of these physicians were undecided about whether probiotics are beneficial, pose minimal risk, or have effects that vary by strain. Further, this study has identified that lack of

information about available probiotic supplements was a barrier in recommending probiotics in practice for a majority of all respondents. While most physicians not using probiotics were more likely to state that original research articles would potentially change their practice, peer practice patterns were more likely to prompt physicians' current use of probiotics. These findings could suggest that evidence regarding the beneficial effects of probiotics and information regarding its clinical applications is not reaching some physicians. This study could be used as the basis for a larger study to determine the best way to reach physicians with the current research regarding the use of probiotics, educate them on clinical applications, and make them aware of available probiotic supplements.

Limitations of Study

While this research is helpful in describing physicians' beliefs regarding probiotics, findings must be viewed with caution due to the limitations of this study. The survey response rate was low (20.8%), yielding a very small sample size. Further, there were a few missing responses in the survey data, possibly affecting the findings for those questions. Another limitation is that the study population included all physicians practicing in a geographic area, which allowed for the inclusion of physicians whose specialties do not have clinical applications for probiotics. In this study, most of the physicians who reported not using probiotics practiced specialties in which there are no applications for probiotics, such as radiology, ophthalmology, and anesthesiology. Finally, the percentage of physicians currently using probiotics in practice who responded to the survey (55.6%) may be

high, as physicians who currently use probiotics in practice or have some knowledge of them may have been more likely to respond to the survey.

Recommendations for Future Research

Research exploring physicians' beliefs and practice patterns regarding probiotics is warranted. Future research should have a larger study population, such as a university hospital or multiple hospitals with differing geographic locations. The study population should only include those specialties that have potential clinical applications for probiotics. While a web-based survey can be used, a combination of mail and web surveys is optimum and should include a personalized cover letter. All survey invitations should be hand-delivered to the physician or physician's place of business, in an effort to increase response rate. Finally, a question could be added to the survey instrument to investigate the specific clinical applications for which physicians are using probiotics in patient care. This could further our understanding of physicians' practice patterns with regard to probiotics.

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APPENDICES

APPENDIX A: CHHS HSRC APPROVAL LETTER

EASTERN MICHIGAN UNIVERSITY
Education First

COLLEGE of HEALTH & HUMAN SERVICES
www.emich.edu/chhs

October 18, 2010

Anastasia Ensminger
c/o Rubina Haque
Eastern Michigan University
School of Health Sciences
Ypsilanti, Michigan 48197

Dear Anastasia Ensminger,

The CHHS Human Subjects Review Committee has reviewed the revisions to your proposal entitled: "Clinical Use of Probiotics: A Survey of Physicians' Belief and Practice Patterns" (CHHS 11-002).

The committee reviewed your proposal and its revisions and concluded that the risk to participants is minimal. Your study is approved by the committee.

Good luck in your research endeavors.

Sincerely,

[Signature Removed]

George Liepa, Ph.D.
Chair, CHHS Human Subjects Review Committee

303 Marshall Building, Ypsilanti, MI 48197 • 734.487.0077 • Fax: 734.487.8536

APPENDIX B: DRMC IRB RESPONSE TO PROPOSAL

YAHOO! MAIL Classic

RE: Proposal for IRB Tuesday, September 7, 2010 9:16 AM

From: "Wendy.Wagner

To:

Ms. Ensminger,

I have reviewed your proposal, the survey, and the Informed Consent. I took it to Dr. Leider, Chairman of our Institutional Review Board, and he does not feel that this proposal requires our review. Although the survey will be given to the physicians at DRMC, it has nothing to do with the hospital, or risk to the patients. I would be glad to send you a letter stating that fact.

From: anastasia ensminger
Sent: September 05, 2010 11:26 AM
To: Wagner Wendy
Cc: Jason Ensminger
Subject: Proposal for IRB

Ms. Wagner,

Attached are the research proposal documents I am submitting for the upcoming IRB meeting, which include the proposal, the informed consent form and the actual survey to be administered printed directly from Survey Monkey. If the IRB has any specific submission form that I am required to complete, please let me know as soon as possible so I can take care of this.

I would greatly appreciate if you could also send me an email confirming receipt of these documents and noting that my proposal will be reviewed by the IRB committee during the upcoming meeting on the 14th, as this is required by my university's Human Subjects Review Committee.

If you have any questions, please contact me.

Thank you,

Anastasia Ensminger

[Contact Removed]

APPENDIX C: INFORMED CONSENT FORM

Informed Consent Form

Project Title: Clinical Use of Probiotics: A Survey of Physicians' Beliefs and Practice Patterns

Investigator: Anastasia Ensminger, Eastern Michigan University
Co-Investigator: Rubina S. Haque, PhD, RD

Purpose of the Study: The objective of this research is to ascertain physicians' beliefs and practice patterns regarding the clinical use of probiotics, and the sources of information that drive them using an investigator-designed internet-based survey questionnaire. This study will help to determine how physicians view probiotics for clinical use and identify the sources of information that either prompted them to use probiotics in practice or that would potentially change their practice regarding probiotics. The results and subsequent publication(s) from the survey data will aid in assisting researchers in their efforts to reach physicians with current evidence and provide physicians with information about peer practice patterns.

Procedure: Participation in this study will involve a 14 question online survey about your demographic information, patient population, beliefs and current practices regarding the clinical use of probiotics using SurveyMonkey™ software. This survey will be accessible via the internet using the web link provided. The approximate total time to complete the survey should be about 10 minutes.

Confidentiality: Responses to the survey questions will remain anonymous. Only a unique computer generated code number will identify your survey responses. At no time will your personal information be associated with your responses to the survey. All data will be encrypted and stored in a password-protected electronic format. The results of this study will be used for scholarly purposes only.

Expected Risks: Participation in the survey does not place you, as the participant, at any foreseeable immediate nor future physical, psychological or emotional risk.

Expected Benefits: There will be no direct personal benefit to you, but your participation will contribute to our understanding of the clinical use of probiotics.

Voluntary Participation: Participation in this study is voluntary and uncompensated, monetarily or otherwise. You may choose not to participate. If you do decide to participate, you can change your mind at any time and withdraw from the study without negative consequences. Participation in the study is not connected to Danville Regional Medical Center and withdrawal or non-participation would not affect your standing at the hospital.

Use of Research Results: Results will be presented in aggregate form only. No names or individually identifying information will be revealed. Results may be presented at research meetings and conferences, in scientific publications, or as part of a doctoral dissertation being conducted by the principal investigator.

Future Questions: If you have any questions concerning your participation in this study now or in the future, or if you would like a copy of the study results, you can contact Rubina S. Haque, PhD, RD at 734-487-8538 or via e-mail at rhaque@emich.edu. This research protocol and informed consent document has been reviewed and approved by the Eastern Michigan University Human Subjects Review Committee for use from October 18, 2010 to October 18, 2011. If you have questions about the approval process, please contact Dr. George Liepa , Chair of CHHS HSRC, at 734-487-0077 or chhs_human_subjects@emich.edu.

APPENDIX D: SURVEY INSTRUMENT

Consent to Participate

* **Consent to Participate:**

I have read all of the information about this research study, including the research procedures and possible risks and benefits to me, as provided in the notification email. The content and meaning of this information has been explained, and I understand. All my questions, at this time, have been answered. By entering the survey and answering the questions, I hereby consent and do voluntarily offer to follow the study requirements and take part in the study. I realize that I may voluntarily withdraw from this study at any time.

- ○ Yes
- ○ No

Demographic Information

Please answer each of the following questions as accurately as possible by choosing the answer that best describes you.

1. Please indicate your gender.

- ○ Male
- ○ Female

2. Please indicate your age.

3. Please indicate the number of years you have been in practice.

- ○ Less than 5
- ○ 6 - 10
- ○ 11 - 15
- ○ 16 - 20
- ○ 21 - 25
- ○ 26 - 30
- ○ More than 30

4. What is your medical specialty?

5. Did you complete any of your specialty training outside of the United States?

- ○ Yes
- ○ No

Practice Characteristics

Please answer the following questions related to your practice.

6. Which of the following best describes your practice setting? (Choose all that apply)

- ☐ Private Practice
- ☐ Health Clinic
- ☐ Community Hospital
- ☐ Long Term Care Facility

7. Approximately what percentage of your patients are:

Pediatric (17 or younger)	
Adults (18 to 64)	
Geriatric (65 and older)	

8. Do you currently use electronic medical records in your practice?

- ○ Yes
- ○ No

9. Which of the following technological resources do you use in your practice? (Choose all that apply)

- ☐ Online Library Database (Cochrane, PubMed, Medline, etc.)
- ☐ Electronic Professional Journals
- ☐ Personal Digital Assistant or Smartphone Applications
- ☐ Other Internet Resources

Beliefs Regarding Probiotics

10. Do you know what constitutes a probiotic?

- ○ Yes
- ○ No
- ○ I would like to learn more about it

11. Please respond to each of the following statements by indicating the level of agreement that best represents your beliefs.

	Strongly Disagree	Disagree	Undecided	Agree	Strongly Agree
Probiotics have clinically beneficial effects.	○	○	○	○	○
There are minimal risks associated with the clinical use of probiotics.	○	○	○	○	○
Physiologic effects of probiotics vary by strain.	○	○	○	○	○
Matching the most beneficial probiotic strain to a specific indication is a barrier to recommending them to patients.	○	○	○	○	○
Lack of information regarding available probiotic supplements is a barrier to recommending them to patients.	○	○	○	○	○
I would benefit from education/training related to the use of probiotics in clinical practice.	○	○	○	○	○
More clinical evidence is needed to support the benefits of probiotics for my specialty.	○	○	○	○	○

Use of Probiotics

* 12. Do you currently recommend/use probiotics in clinical practice?

- Yes
- No

Information Regarding Probiotic Recommendation

13. What sources of information prompted your current or past recommendation/use of probiotics in clinical practice? (Choose all that apply)

- ☐ Continuing Medical Education
- ☐ Original Research Articles
- ☐ Review Articles
- ☐ Clinical Care Guidelines
- ☐ Peer Practice Patterns
- ☐ Internet Sources (UpToDate®, Cochrane database, Medline, etc.)

14. Have you seen a clinical benefit from the use of probiotics?

- ○ Yes
- ○ No
- ○ Yes, but placebo effect only

Information Regarding Not Recommending Probiotics

13. For what reasons do you choose not to recommend probiotics? (Choose all that apply)

- ☐ There are no clinical applications for probiotics in my specialty
- ☐ Not convinced of clinical benefit
- ☐ Costs
- ☐ Lack of prescriptive authority because not controlled by the U.S. Food and Drug Administration
- ☐ Fear of liability
- ☐ Negative experiences with prior use / adverse outcomes

14. What sources of information regarding the clinical use of probiotics would potentially change your practice patterns with regard to their recommendation/use? (Choose all that apply)

- ☐ Continuing Medical Education
- ☐ Original Research Articles
- ☐ Review Articles
- ☐ Clinical Care Guidelines
- ☐ Peer Practice Patterns
- ☐ Internet Sources (UpToDate®, Cochrane database, Medline, etc.)

Thank you for your participation! Your contribution is greatly appreciated!