



PRACTICE ISSUE

Probiotic supplementation recommendations for the general public

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| Best Practice Issue (state as a question, PICO): | |
| What are probiotic supplementation recommendations for the general public? | |
| Member: | Site: |
| Kerri Cuthbert | River East/St. Vital |
| Lavonne Harms | Downtown |
| Date of Final Approval: | To be Reviewed: |
| Purpose: (goals, scope, intended users, settings, and patient/client groups) | |
| Increased use of probiotics and recent research on potential health benefits have led to this review. Is probiotic supplementation safe? Is there evidence to support recommending probiotic supplementation for the general population? | |
| Definitions: | |
| <p><u>Probiotic</u>: An oral supplement or a food product that contains a sufficient number of viable microorganisms to alter the microflora of the host and has the potential for beneficial health effects.</p> <p><u>Prebiotic</u>: Non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve host health.</p> <p><u>Live culture</u>: Refers to the living organisms such as <i>Lactobacillus bulgaricus</i> and <i>Streptococcus thermophilus</i> available in fermented dairy products and probiotic fortified foods</p> <p><u>Synbiotic</u>: Product which contains both prebiotics and probiotics.</p> <p><u>Supplement</u>: An encapsulated form of probiotics.</p> <p><u>Probiotic food product</u>: A food product which contains naturally occurring or added strains of probiotic bacteria.</p> | |
| Recommendations: | |
| <p>For the general population, the following is recommended for probiotic use:</p> <ul style="list-style-type: none"> • There is insufficient data to recommend the use of probiotic supplementation for overall health for the general public; however, commercially available probiotic strains (e.g. <i>Lactobacillus</i> and <i>Bifidobacterium</i> species) are safe for most general adult and pediatric populations. • There is sufficient evidence to recommend probiotic supplementation with specific strains in certain conditions; namely, infectious diarrhea, antibiotic associated diarrhea, inflammatory bowel disease and irritable bowel syndrome. • Due to possible benefits and the demonstrated safety profile of both supplements and probiotic food products, individuals may choose to take probiotic supplements or consume probiotic food products. • There is insufficient data to recommend the use of probiotic supplemented infant formula at this time, however, due to the lack of adverse effects, caregivers may choose supplemented formulas if desired. | |
| Evidence Review: (Please list type and grade of evidence reviewed) | |
| Probiotics | |
| a) Background | |
| By definition, a probiotic is live microorganisms, which when administered in a sufficient quantity, alter the microflora of | |

the host and have the potential for beneficial health effects. Probiotics can be ingested through oral supplements or food products. For a certain bacterial strain to be called probiotic, it must meet five criteria: the bacteria must be of human origin (meaning that it will survive in a human body), have a demonstrated safety profile, will survive transit through the gastrointestinal tract (will not be killed or digested by stomach acid or digestive enzymes), will colonize in the large intestine upon its arrival, and will provide a research-proven health benefit to the host.

Regarding nomenclature of probiotics, the bacteria will be written out by genus, species and strain, and one species or strain of probiotic cannot be assumed to have the same effects as another. For example, *Lactobacillus (genus) reuteri* (species) DSM 17938 (strain) is the probiotic ingredient of BioGaia, but a different species or strain of *Lactobacillus* may not have the same effects (19). It is the strain that determines how the probiotic produces the beneficial effect in the body, not the species. To add to the complexity, invented names are also used on package labels to market products containing probiotics. For example, *BL regularis* is a trade name that has been created to be more consumer friendly and the company (Activia) markets their product as promoting regularity. The scientific name of *BL regularis* is *Bifidobacterium lactis* DN-173 010, and is listed in the ingredient list.

Certain probiotic strains have been indicated for certain conditions:

| Condition | Effect of probiotics | Indicated probiotic strains | Grade level of evidence |
|--|---|---|-------------------------|
| Infectious diarrhea | Reductions in duration and severity of infectious diarrhea in infants and children with rehydration therapy | <i>L. casei</i> strain GG <i>S. Boulardii</i> <i>Enterococcus faecium</i> LAB SF68 | A |
| Antibiotic associated diarrhea | Reduction in antibiotic associated diarrhea in both children and adults | <i>L. casei</i> strain GG <i>S. Boulardii</i> <i>Lactobacillus acidophilus</i> CL128 <i>Lactobacillus casei</i> LBC80R <i>Lactobacillus casei</i> DN-114001 | A |
| Inflammatory Bowel Disease | Decrease pouchitis of mild activity Maintenance therapy while in remission | Multistrain (VSL#3® - dose of 3 packages/day) | A |
| Irritable Bowel Syndrome | Global improvement in Irritable Bowel Syndrome symptoms rather than specific improvement in bowel function | Multistrain (VSL#3® - 2 packages/day) <i>B. infantis</i> 35624 <i>B. Lactis</i> DM 173010 | A |
| <i>C. difficile</i> | May reduce the incidence of <i>C. difficile</i> infection in adults May prevent reoccurrence of <i>C. difficile</i> infection in combination with vancomycin | Unspecified | B |
| | | <i>S. Boulardii</i> | B |
| Inflammatory Bowel Disease | May maintain remission in mild-moderate Ulcerative Colitis with mesalamine. No benefits seen in induction of remission. Avoid in patients with severe Ulcerative Colitis. | Multistrain (VSL#3® - 1-3 packages/day) | B |
| <i>Helicobacter pylori</i> | Beneficial effects on <i>Helicobacter pylori</i> eradication rates and incidence of total side effects associated with triple therapy with other therapies for this infection | <i>L. casei</i> strain GG <i>S. Boulardii</i> <i>L. acidophilus</i> La5 <i>Bifidobacterium lactis</i> Bb12 <i>Lactobacillus casei</i> DN-114001 (children) | C |
| Upper Respiratory Tract Infection (URTI) | Preventing acute URIs in children attending daycare centres | <i>Lactobacillus casei</i> DN-114001 <i>L. casei</i> strain GG | C |

(19)

b) Mechanisms of action

Probiotics can affect a variety of systems in the body. Not all probiotics have the same mechanisms of action in the

body; the ways that probiotics function are thought to be strain specific (18). Two main mechanisms of action are 1) the inhibition of pathogenic colonization and 2) strengthening the immune system. Probiotics can inhibit pathogenic colonization by forming a protective barrier and competitively excluding unhealthy bacteria, which prevents pathogens from entering the body through the gastrointestinal tract (19). Up to seventy percent of immune cells are located within the gastrointestinal tract. Especially in infants, the immune system may need to be activated by the gut microflora to function properly. Probiotics can promote the development of a stronger immune system by influencing and stabilizing the gut microflora, enhancing resistance to potential pathogens, and modulating immune function parameters (20). It was not possible to determine for the purpose of this review whether or not, and in what amounts, the general population's bodies currently contain beneficial probiotic bacteria. It is known, however, that a number of factors can affect the probiotic content of the body, such as antibiotic therapy, stress, travel and diet (intake of high fat and high sugar foods versus a varied diet high in fruits and vegetables). Research examining these factors is ongoing (19, 20).

c) Dosage

Dosage is still an important area that needs to be addressed in future research. The dosage of a probiotic strain is measured in colony forming units (CFU), which is an indication of the number of live microorganisms present in a food or supplement (4). On average, dosages required to achieve beneficial effects are commonly reported to be above 100 million (10^8) CFU per day (9), but it is not possible to provide one dose for all probiotic foods and supplements found in the marketplace (4). For the greatest chance of effectiveness it is suggested to use the dosage and strains which have shown positive results in research (4). A larger dose does not always mean an enhanced effect and multiple strains do not necessarily equate to a more effective product (3). More research is needed to determine the optimal dosage and strains. The ingestion of probiotics does not lead to long-term colonization and survival in the digestive tract (1). Probiotics are transient microorganisms, therefore in order to maintain colonization they must be taken regularly (1). Even the most adherent strains will gradually be diluted out of the colon within one to two weeks of ingestion, unless there is continuous intake (13). The method of delivery of the probiotic has an impact on its effectiveness (7). For example, if the probiotic is consumed in a food product like yogurt versus a capsule there may be different effects due to viability of the strain. Combining a probiotic strain with a substrate which supports its growth (known as a prebiotic) has been shown to promote its survival and colonization in the bowel. The combination of probiotic and prebiotic is referred to as a synbiotic (17). Future research needs to focus on the how the probiotic is delivered to determine its efficacy.

d) Probiotic food products

The fastest growing market for probiotics is the food industry. A wide variety of probiotic strains are now being added to a variety of foods including juice, cereal, ice cream, gum, cheese, candy and chocolate. The availability of these food products varies greatly between countries. Many of the microorganisms that are either naturally found in food or that are added to food products have not necessarily undergone testing to demonstrate health benefits (10); therefore, it is not clear if the products can be labeled as being probiotic. Untested probiotic foods may have an effect, but cannot be recommended for any particular health benefit (7, 9).

Increasing in popularity are the 'daily dose' yogurt drinks (e.g. DanActive®). North Americans consume significantly fewer fermented dairy products (4-5 L/person/year) compared to Europeans (35-45 L/person/year) (3). These drinks range in size between 65-125 mL and are marketed as providing the consumer with an effective dosage of probiotics (3).

A fairly new category of probiotic-containing products includes infant formula. Infant formula companies are adding probiotics to infant formula to attempt to mimic the probiotic content of breast milk. Breast milk contains a number of bacteria; the most frequent are *Staphylococcus*, *Lactococcus*, *Enterococcus*, and *Lactobacillus*. Some of the *Lactobacillus* bacteria are of interest as they are potentially probiotic (21). There is still much to learn about the impact of these probiotic infant formulas on the composition of the intestinal flora and the impact that these infant formulas may have on the developing infant's immune system (11). There is insufficient data to recommend the use of probiotic supplemented infant formulas at this time (12).

No general recommendation can be given if probiotics from food or supplements are equally effective. Most health related effects of probiotics are thought to be strain specific, therefore efficacy cannot be determined unless the food or supplement has been appropriately tested in the form in which they are sold. It is not possible to generalize a minimum dose of probiotic as dosage varies for different probiotic strains and the health effect being investigated.

e) Safety

The majority of scientific studies completed to date have described a good tolerance to probiotic preparations and the

absence of significant adverse effects (2). Most commercially available probiotic strains are considered to be safe; however, the safety of one strain cannot be extrapolated to another. All known cases of bacteremia and fungemia related to administration of probiotics have occurred in individuals who were critically ill or severely immunocompromised (15). No reports of sepsis have occurred in healthy individuals. The *Lactobacillus* and *Bifidobacterium* species used in the food industry and in clinical trials are safe for the general adult and pediatric populations.

Probiotics, at the beginning of consumption, may cause bloating and flatulence (19). This will however dissipate with continued and consistent use.

Caution should be exercised if an individual is allergic to milk. Many strains of probiotics are grown on media containing milk protein and contamination from the culture medium may introduce an allergen into a non-milk based food or supplement (e.g. juice, candy, etc.), which has the potential to cause a serious allergic reaction (16). A milk-based probiotic is contraindicated for this population.

f) Storage

There are refrigerated food products containing probiotics, as well as freeze-dried supplements. The freeze-dried supplements do not have to be refrigerated, but as a cautionary measure some manufacturers recommend that they be refrigerated to assist in maintaining the viable counts. The shelf-life for refrigerated food products containing probiotics range from three to six weeks (5). The shelf-life of dried supplements is about twelve months. However, the viable counts of the probiotic micro-organisms may decrease significantly during this time (5).

g) Cost and availability

Probiotic food products and probiotic supplements, including those which have a proven health benefit and those that do not, have varying costs and availability. The below costing was completed September 15-22, 2014 in several grocery stores and pharmacies in the River East community area. Cost and availability of products and supplements may vary between community areas.

The most widely available probiotic food product on the market in Canada is likely probiotic yogurt. Many common brands of yogurt sell probiotic yogurts. Most conventional and probiotic yogurts have similar prices. Kefir is a fermented milk product rich in probiotic bacteria. Kefir is available in some large grocery stores, but may only be available at health food or organic grocery stores in some areas. Kefir may cost around \$5.00-6.00 per litre or around \$5.00 for 454ml of organic kefir. Other food products such as probiotic breakfast cereals and probiotic juice are available in Canada, but they may not be widely available and their cost could not be determined for this paper.

There are only a few probiotic food products available for infants. Probiotic supplemented infant formula is available, but not all brands of infant formula carry probiotic products. Gerber infant cereals have an added probiotic. There is not a significant price difference between this type of cereal and the standard non-probiotic infant cereals.

Probiotic supplements vary in cost and dosage. There are probiotic supplements available in most pharmacies, though the brands and varieties vary from store to store. These probiotic supplements often have unsupported health claims and may cost \$12.99-\$27.99 for 30-60 capsules. Many of the probiotic supplements which have evidence-based health claims may only be available online and are often more expensive than in-store varieties (19).

BioGaia is the only probiotic supplement marketed for infants and young children. This product is available in drops and in tablet form. The drops are widely available for sale at most large pharmacies. The cost for one bottle of drops (which would provide the supplement for one month) was found to vary between \$23.99 and \$33.89. BioGaia product tablets are not widely available.

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| Practice Implications: | |
| Communicate recommendations to other health care professionals. | |
| Recommendation for implementation: | |
| The authors of this Evidence Review have provided the information for health care practitioners to use as part of individual assessment, treatment planning and education only. | |
| These recommendations are being reviewed by: | |
| Name and Credentials | Date Review Complete |
| Public Health Dietitian Practice Council | January 6, 2015 |
| Primary Care Dietitian Practice Council | February 27, 2015 |
| PPH Nutrition Promotion Team | April 20, 2015 |
| FNS Nutrition Advisory Subcommittee | |