

# Nutrition Guideline

## Healthy Infants and Young Children

### Prebiotics & Probiotics

*For Professional Reference Only*

Applicable to: Nurses, Physicians and Other Health Professionals

#### Recommendations

- Healthy infants and young children generally do not need prebiotic and/or probiotic supplements for optimal health.
- Food and supplement products containing prebiotics and/or probiotics available from internet sites or from other countries, but not for sale in Canada, are not recommended for infants and young children.
- Parents interested in providing their infant or young child prebiotics and/or probiotics should be encouraged to discuss this with the child's primary healthcare provider.

#### Prebiotics & Probiotics in Food

- Prebiotics naturally occurring in food (i.e. breastmilk, vegetables, fruits and grains) are considered safe.
- Some prebiotics may be added to foods in Canada, these are considered accepted dietary fibres and are safe to consume.
- Probiotics (*Lactobacillus* and *Bifidobacterium*) in foods consumed by healthy term infants and young children are generally considered safe.

#### Prebiotics & Probiotics in Infant formula

- Infant formulas (including those containing prebiotics and probiotics) are regulated in Canada by Health Canada. Use of unregulated infant formula (e.g. homemade, imported from another country) is not recommended.
- Commercial infant formulas available in Canada that are supplemented with prebiotics and/or probiotics are generally considered safe.
- In formula fed infants less than 6 month of age experiencing hard stools, trialing a prebiotic supplemented formula may help lead to softer stools.
- Probiotic supplemented formulas have not been found to improve stool consistency or frequency.

#### Probiotic Supplements

**Probiotic supplements** (strain specific) have been documented as safe. There is good evidence of effectiveness for the following probiotic supplements for healthy full term infants and young children:

- *Lactobacillus reuteri* DSM 17938 ( $1 \times 10^8$  colony forming units/day) given to exclusively breastfed infants under 3 month of age may decrease or prevent colic (defined as fussy crying that lasts  $\geq 3$  hours/day for  $\geq 3$  days/7 days).
- Infants and young children taking antibiotics may have a decreased risk of acquiring antibiotic associated diarrhea with the consumption of *Lactobacillus rhamnosus* GG ( $1 \times 10^{10}$  -  $2 \times 10^{10}$  colony forming units/day) or *Saccharomyces boulardii* (250 – 500 mg/day).
- Infants and young children experiencing acute gastroenteritis (diarrhea) may have a decreased duration of symptoms with the consumption of *Lactobacillus rhamnosus* GG ( $1 \times 10^{10}$  colony forming units/day) or *Saccharomyces boulardii* (250 – 750 mg/day).
- Currently *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii* products in Canada are for children over 1 year of age.

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#### Health Benefits

Prebiotics and probiotics are available in food and supplements; in some cases they are advertised to the general public for use by infants and young children. In 2014, a survey of 413 Albertan mothers of children under 2 years of age found that 51% had given their infant a probiotic.<sup>1</sup> Therefore, as parents are considering or offering their child a prebiotic or probiotic, this Nutrition Guideline (NG) can support health professionals to provide evidence based recommendations on appropriate use.

This NG provides an overview of evidence for prebiotics and probiotics in healthy full term infants and young children (birth to 2 years). Information within this NG is intended to provide health professionals with guidance on common questions regarding prebiotics and probiotics in infancy and young children, therefore not all foods and/or products are reviewed. The NG does not review evidence for preterm infants or infants/young children with acute/chronic medical conditions.

#### Definitions

**Prebiotics:** non-digestible food components that stimulate the growth and/or activity of bacteria in the colon which in turn confer a health benefit to the host.<sup>2</sup> Examples of prebiotics are: human milk oligosaccharides (in breastmilk), galactooligosaccharides (GOS), polydextrose (PDX), fructooligosaccharides (FOS), lactulose and inulin.

**Probiotics:** "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host."<sup>3</sup> Probiotics are labelled by genus, species, and strain.<sup>3</sup> Sometimes a subspecies is also defined within the probiotic name.

Effects of probiotics are strain specific, therefore only knowing the genus and species does not provide enough information to know whether the probiotic would be effective or not. Example: *Lactobacillus reuteri* DSM 17938 is a probiotic discussed in this NG. Lactobacillus is the genus; reuteri is the species; DSM 17938 is the strain.

**Synbiotics:** combination of pre- and probiotics.

#### Key Questions

|                             |
|-----------------------------|
| <b>What are prebiotics?</b> |
|-----------------------------|

Prebiotics like galactooligosaccharides (GOS), fructooligosaccharide (FOS), polydextrose (PDX) and inulin are non-digestible food components that change bacterial composition or activities within the gut that lead to a health benefit within humans.<sup>2,4</sup> Researchers have hypothesized that intestinal health is related to overall health (e.g. immunity, allergy). Therefore, researchers are investigating many potential health conditions which could be improved by the consumption of prebiotics.

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Breastmilk contains prebiotic oligosaccharides. These oligosaccharides are theorized to be the breastmilk component which supports the growth of healthy intestinal bacteria.<sup>5</sup> Studies have been conducted to examine the possibility of prebiotics in formula creating a microbiota which mimics that of a breastfed infant.<sup>6</sup> When prebiotics are studied in formula, breastfed infants are often used as the gold standard for the infant's intestinal bacteria.<sup>7,8,9,10</sup> Regardless of formula research, breastmilk still remains the optimal source of nutrition.<sup>11</sup>

Prebiotics are found in:

1. Foods – human milk oligosaccharides are a naturally occurring prebiotic found in breastmilk.<sup>12</sup> Other forms of prebiotics, such as inulin, are naturally present many in foods (vegetables, fruits and grains) and added to others (e.g. fortified cereals). A specific oligosaccharide, GOS, can be found naturally in fermented dairy products like yogurt, buttermilk and kefir.<sup>13</sup>
2. Infant formulas – there are two prebiotics currently added to infant formula in Canada: GOS and PDX. For information on which formulas contain prebiotics refer to the [Infant Formulas for Healthy Term Infants – Compendium](#).
3. Supplements – some prebiotics are available as a supplement and often marketed to adults (i.e. fibre supplements.) There are products for infants marketed online, however they are not for sale in Canada at this time.

#### Are prebiotics safe for infants and young children?

Prebiotics naturally occurring in food (i.e. vegetables, fruits and grains) are considered safe. Known prebiotics such as GOS, FOS, PDX, and inulin, are considered safe and may be added to foods as they are “accepted dietary fibres” in Canada.<sup>14</sup>

All commercial infant formulas must undergo a full safety and nutritional quality assessment before they can be sold in Canada.<sup>15</sup> Studies have demonstrated the safety of current formula supplemented with prebiotics (GOS and/or PDX).<sup>7,9,16,17,18,19</sup> Further safety testing of new prebiotic formulations or dosages is required before prebiotics in their entirety can be deemed safe. Health Canada cautions individuals against purchasing infant formula from internet sites or from other countries. Infant formulas that have not been approved by Health Canada pose a safety and nutritional risk, as they may not meet Health Canada safety and nutrition regulations.

In atopic child/adult populations, two small studies in Asia have identified allergy to GOS, but this has not been documented in North America or in children less than 5 years of age.<sup>20,21</sup>

#### Are there evidence based health benefits for infants or young children who consume a prebiotic?

The current evidence only supports prebiotic consumption for promoting softer stools in formula fed infants. Prebiotics studied for use in infant formula include GOS, FOS, PDX, inulin and lactulose, as well as various combinations of these products. However, for the purpose of this NG, only GOS and PDX studies are included as these are the only prebiotics available in commercial infant formula sold in Canada.

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Infants ( $\leq 6$  months old) fed formula with 4 – 5 g/L GOS or 4g/L PDX/GOS blend have been reported to have significantly improved stool consistency (i.e. softer stools) compared to infants fed formula without prebiotics.<sup>7,16,17,18</sup> In these studies, infants did not have a diagnosis of constipation;<sup>7,16,17,18</sup> therefore the studies were comparing stool characteristics of exclusively formula fed infants with and without prebiotics. While some prebiotic infant formulas in Canada have the recommended amount of prebiotic GOS or PDX/GOS blend added, some contain lower dosages. Lower dosages of GOS in formula (e.g. 2.9 g/L) have not been studied and therefore, it cannot be concluded if these formulas would also have the benefit of improved stool consistency. Formula fed infants not yet introduced to complementary foods (i.e. under 6 months of age) experiencing hard stools may benefit from consuming an infant formula supplemented with GOS (4 g/L) or PDX/GOS blend (2 g/L PDX and 2 g/L GOS).<sup>7,16</sup>

For information on amounts of GOS or PDX/GOS blend in specific formulas refer to the [Infant Formulas for Healthy Term Infants – Compendium](#).

#### Which prebiotic health claims are not supported for infants and young children?

Prebiotic supplemented formula may promote a healthy microbiota which is closer to that of a breastfed infant.<sup>7,10,18</sup> It has been theorized that a formula fed infant obtaining a microbiota similar to a breastfed infant could reduce the risk of infection and allergic manifestations; however research to date has not supported this hypothesis.<sup>17,18,22,23</sup>

Prebiotics have not been shown to prevent asthma, diarrhea or gassiness/fussiness.<sup>4,7,16,18,24</sup>

Results have been inconsistent on the benefit of prebiotic supplementation for:

- atopic dermatitis<sup>4,17,18</sup>
- food allergy<sup>18,25</sup>
- vomiting/regurgitation<sup>9,17,23</sup>
- antibiotic use<sup>18,24</sup>
- colic<sup>9,17,23</sup>

At this time no public health recommendations can be made on the use of prebiotics for these conditions.

Currently there is not enough evidence to support prebiotic supplementation to improve lipid blood levels (e.g. triglycerides, cholesterol) in infants.<sup>26</sup>

While food products in Canada may have GOS, FOS, PDX and/or inulin added, it is unknown if health benefits exist beyond the benefit of consuming dietary fibre due to limited research in infants and young children.<sup>14</sup>

#### What are probiotics?

Probiotics are microorganisms that:<sup>27</sup>

- are non-pathogenic and non-toxic, and yield a benefit to the host when consumed
- are able to induce a host response once they enter the intestine
- remain viable and stable until consumption

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In Canada, probiotic supplements (except for *Lactobacillus crispatus* and *Lactobacillus gallinarum*) are allowed to provide the following labels on their products:<sup>28</sup>

- 'Helps support intestinal/gastrointestinal health'
- 'Could promote a favourable gut flora'

While these claims may be on products marketed for infants and young children, it should not be inferred that a 'favourable gut flora' will provide specific health outcomes (e.g. immunity). The efficacy of a specific probiotic product cannot be expected unless specific identified strains are consumed at defined/specific doses.<sup>27,29</sup> Each probiotic strain has unique characteristics and provides different effects on the host.<sup>27</sup> Therefore, each strain must be backed by research and evaluated individually.<sup>27</sup> Research conducted on one particular strain cannot be applied to other strains.<sup>27</sup>

Foods and natural health products that contain probiotics are regulated under the Food and Drugs Act (FDA) and its associated regulations in Canada.<sup>30,31</sup> Parents who plan to provide their infant/child a probiotic should select a supplement labelled with an eight-digit Natural Product Number (NPN). The NPN indicates that the supplement has been assessed by Health Canada and has been found to be safe, effective and of high quality under its recommended conditions for use.<sup>32</sup> A natural health product not sold in Canada, but available online, cannot be recommended as it is unknown if it meets Canadian safety and quality regulations.<sup>33</sup>

Live bacterial cultures with a history of safe use can be added to foods in Canada.<sup>31</sup> Manufacturers are responsible for the safety, stability and viability of the probiotic culture in the food product so that the product delivers the declared level in a stated serving size throughout the product's shelf life.<sup>31</sup> A 2013 study which investigated probiotic (all bifidobacteria) stability of 24 fermented dairy products found that 23/24 and 22/24 met recommended probiotic bacteria counts at the time of store purchase and at the expiry date, respectively.<sup>34</sup> Yogurt, drinkable yogurts, non-yogurt drinks and kefir are food products which may have probiotics, however the strain(s) vary by manufacture/brand.

*Bifidobacterium animalis* subsp *lactis* (*B. lactis*) strain BB-12 (BB-12) (strain clarified in email from Laurie Berryman, Regional Manager Western Canada for Nestle Infant Nutrition, Sept 1 2016) is a probiotic currently available in some cow's milk infant formulas and cereals in Canada. *Lactobacillus rhamnosus* GG (LGG) is another probiotic currently available in an extensively hydrolyzed infant formula.<sup>35</sup> For information on which formulas contain probiotics refer to the [Infant Formulas for Healthy Term Infants – Compendium](#).

#### Are probiotics safe for infants and young children?

*Lactobacillus* and *Bifidobacterium* (the two most common probiotic genus) in foods (including infant formula) are generally classified as safe with minimal adverse effects reported in the literature.<sup>3,36,37,38,39,40</sup> However, adverse effects to probiotic consumption in research studies has been inconsistently monitored and reported.<sup>40</sup>

Infants born prematurely and people with immunocompromised health conditions (e.g. central venous catheter, short-gut syndrome, auto-immune disorders, cystic fibrosis, cancer, etc.) are at higher risk of a probiotic becoming opportunistic which can lead to fungemia or bacteraemia.<sup>40,41,42,43</sup> Therefore, parents of premature infants and immunocompromised infants/children should use caution with probiotics and consult their healthcare provider, to provide guidance based on risk/benefit.

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A blanket statement that all probiotic supplements are safe for infants/children cannot be made at this time; rather each strain must be looked at individually.<sup>40</sup> Although a probiotic strain may be deemed 'safe' there is always possibility (albeit rare) for it to become opportunistic and cause bacteraemia.<sup>40</sup>

Cow's milk proteins are a common growth substrate for some probiotics and very small quantities may be present in some probiotic supplements.<sup>29</sup> Therefore, the growth medium of particular probiotics should be checked, by reading the product label, prior to providing it to an infant/ child with a cow's milk protein allergy. LGG available in an extensively hydrolyzed casein formula is considered safe for infants with diagnosed cow's milk protein allergy.<sup>44,45,46,47</sup>

Probiotics are available without a prescription and therefore may be taken at parents' discretion. Parent should be encouraged to discuss all medications and natural health products, including probiotics, with the child's primary healthcare provider.

#### Are there health benefits for infants or young children who consume a probiotic?

Probiotic supplements are not necessary for all infants and young children. However, evidence supports that certain health conditions may be improved with the use of strain/dose specific probiotics. Table 1 provides health professionals with background information on conditions during infancy and childhood which may be improved with the use of a probiotic. Health professionals should encourage parents to read, and follow, manufacture duration instructions and considerations for use.

**Table 1. Conditions During Infancy and Childhood Which May Be Improved With the use of a Probiotic**

| Condition   | Potential benefit   | Probiotic strain and brands <sup>a</sup>   | Dose   |
|---|---|--|--|
| Colic (defined as fussy crying that lasts $\geq 3$ hours/day for $\geq 3$ days/ 7 days) <sup>48,49,50</sup> | May prevent or decrease colic in <u>exclusively breastfed</u> infants during the first three months of life <sup>48,49,50</sup> | <i>Lactobacillus reuteri</i> DSM 17938 (e.g. BioGaia®) <sup>48,49,50</sup>   | $1 \times 10^8$ (100 million) colony forming units (cfu)/day of <i>Lactobacillus reuteri</i> DSM 17938 <sup>48,49,50</sup>                                       |
| Antibiotic Associated Diarrhea (AAD) <sup>28,42,51</sup>  | May prevent AAD when taken when antibiotics are prescribed <sup>42,51</sup>   | <i>Lactobacillus rhamnosus</i> GG (LGG) <sup>42,51</sup> (e.g. Culturelle® Kids Probiotic*, Jamieson™ Digestive care kids*)<br>or<br><i>Saccharomyces boulardii</i> <sup>42,51</sup> (e.g. Florastor® Kids*) | $1 \times 10^{10} - 2 \times 10^{10}$ (10 – 20 billion) cfu/day of LGG <sup>28,51</sup><br><br>250 mg-500 mg/day of <i>Saccharomyces boulardii</i> <sup>51</sup> |
| Acute gastroenteritis (diarrhea) <sup>28,51</sup>   | Decrease duration of diarrhea by approximately 1 day (in addition to rehydration therapy) <sup>51</sup>                         | <i>Lactobacillus rhamnosus</i> GG (LGG) <sup>28,51</sup> (e.g. Culturelle® Kids Probiotic*, Jamieson™ Digestive care kids*)<br>or<br><i>Saccharomyces boulardii</i> <sup>51</sup> (e.g. Florastor® Kids*)    | $1 \times 10^{10}$ (10 billion) cfu/day of LGG <sup>28,51</sup><br><br>250 mg – 750 mg/day of <i>Saccharomyces boulardii</i> <sup>51</sup>                       |

<sup>a</sup> Known probiotics brands available as of August 2016 in Canada. AHS does not promote one specific brand, nor should this be considered a comprehensive list.

\* Currently LGG and *Saccharomyces boulardii* sold in Canada are for children  $\geq 1$  year old. Therefore, although research on the prevention of AAD and treatment of acute gastroenteritis is supported for infants and young children there are no products marketed for infants (less than 12 months old).

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#### Which probiotic health claims are not supported for infants and young children?

At this time, recommendations for probiotics cannot be made for the prevention or treatment of: atopic dermatitis, colic in formula fed infants, functional gastrointestinal disorders, gastrointestinal health and growth in formula fed infants, infections, or improvement to cow's milk allergy. Additionally, it has not been proven that infant formulas with probiotics have a health benefit compared to formulas without probiotics.

#### Atopic Dermatitis (Eczema)

Probiotics given in infancy have not been found to prevent atopic dermatitis in some meta-analysis, while others have found a protective effect.<sup>52,53,54</sup> Some evidence supports prevention of atopic dermatitis in infancy if probiotics are provided during gestation and then continued into infancy; however this is beyond the scope of this NG.<sup>52,53,55,56</sup>

There is insufficient evidence to conclude effectiveness of probiotics for food allergy, allergic rhinitis and conjunctivitis.<sup>53</sup>

#### Colic in Formula Fed Infants

Only two randomized control trials exist on probiotics to prevent or treat colic in formula fed infants. Indrio et al (2014) reported results to support *Lactobacillus reuteri* DSM 17938 in the prevention of colic in formula fed infants.<sup>49</sup> Sung et al (2014) reported that formula fed infants consuming *Lactobacillus reuteri* DSM 17938 had increased colic symptoms compared to the placebo group.<sup>57</sup> Therefore, based on the conflicting results of these two trials, recommendations cannot be made at this time for the role of probiotics to prevent or treat colic in formula fed infants.

#### Functional Gastrointestinal Disorders

A recent systematic review focused on probiotics and functional gastrointestinal disorders in children birth – 18 years yielded no studies on infants and young children (birth – 2 years old).<sup>58</sup> While their search included studies on probiotics that reported on gastrointestinal outcomes such as abdominal pain, stool frequency, stool consistency and bloating/flatulence, these studies did not include infants and young children. Therefore, as evidence is not available for infants and young children, no probiotics can be recommended to improve functional gastrointestinal disorders for those 2 years and under at this time.<sup>58</sup>

#### Gastrointestinal Health and Growth in Infant Formula

Formula with probiotics have not been found to make a significant difference in stool frequency or consistency, spitting up/vomiting, diarrhea, or growth compared to formula without probiotics.<sup>23</sup>

#### Improvement to Cow's Milk Allergy

Studies with small sample sizes have looked at extensively hydrolyzed casein formula with the addition of LGG to increase cow milk tolerance at 12 months of age. Preliminary findings have shown increased cow's milk tolerance at 12 months of age compared to children consuming same formula without LGG.<sup>44,45,59</sup> At this time, only one extensively hydrolyzed casein formula contains LGG in Canada. While it has been documented as safe in many studies, recommendations for choosing this formula over other extensively hydrolyzed casein formulas (without LGG) cannot be made until studies with larger sample sizes over longer duration are conducted.<sup>44,45,46,47,60</sup>

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#### Infections

A 2015 Cochrane review concluded that use of probiotics decreased the need for antibiotics to treat upper respiratory tract infections (URTI).<sup>61</sup> However, a specific probiotic strain/dose was not provided within their review and therefore does not allow for a public health recommendation.

At this time, evidence does not support LGG for the prevention of lower respiratory infections.<sup>62</sup> Infants and children consuming *B. lactis* BB-12 have not been shown to have significantly lower gastrointestinal infections compared to those consuming a placebo product.<sup>63,64,65</sup> Evidence is inconsistent on the effectiveness of probiotics for the treatment of acute otitis media.<sup>62,63,64,65</sup>

#### Is there evidence for use of a combination of pre and probiotics (synbiotics) for infants and young children?

Synbiotics refers to the combination of pre- and probiotics. Various strain combinations studied in research limits the ability to draw conclusions or recommendations. Additionally, many of the strain combinations tested in research do not appear within the Canadian market, which also limits the ability to make recommendations.

Synbiotic studies have reported conflicting results in regards to infant growth. In some studies, infants consuming synbiotics have grown the same as infants not consuming synbiotics;<sup>23,66,67</sup> however, another study found weight and head circumference significantly higher for infants consuming synbiotics.<sup>68</sup> Synbiotics are likely safe, however, each new strain combination needs to be tested.<sup>40</sup>

Due to limited research on specific synbiotic strains, recommendations for their use and potential benefits cannot be made. This includes areas that have some initial research such as synbiotics to:

- prevent atopic dermatitis<sup>69,70</sup>
- treat atopic dermatitis<sup>70</sup>
- treat colic<sup>71</sup>
- and treat acute infectious gastroenteritis<sup>47,72,73</sup>

Synbiotics in infant formula cannot be recommended due to limited research.<sup>23</sup> Currently, no Canadian commercial infant formulas contain synbiotics.

#### Do infants and young children need prebiotic or probiotic supplements?

Infants and young children generally do not need to be provided prebiotics and/or probiotic supplements for optimal health. Breastfeeding and offering a variety of complementary healthy foods, including vegetables, fruits, whole grains and fermented dairy products may promote intestinal health.

#### Are there any handouts on prebiotics or probiotics for infants and children that I can use with my clients?

No, not at this time. For other infant nutrition resources visit Nutrition Education Materials at <http://www.albertahealthservices.ca/nutrition/Page11115.aspx> and click on **Infants**.

For more information related to healthy infants and children see [Healthy Parents Healthy Children](#).

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