Quality Assurance and Safety of Crops & Foods, 2016; 8 (4): 539-553

Wageningen Academic Publishers

Health benefits of fibre, prebiotics and probiotics: a review of intestinal health and related health claims

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Received: 23 October 2015 / Accepted: 24 March 2016

REVIEW ARTICLE

Abstract

Gastrointestinal health in regard to the gut microbiome is a rapidly emerging field and has many key components driving its emergence. Fibre, prebiotics and probiotics are all dietary components that can play a critical role in maintaining a healthy gut microflora. Fibre has long been appreciated for its influential role in cardiovascular disease, glycaemic control and weight management through various physiological mechanisms. Prebiotics have been shown to play an influential role in irritable bowel symptoms/disease, colon cancer, cardiovascular disease and overall digestive health. Together, various types of fibres and prebiotics have been targeted and synthesised to influence the gut microbiome, specifically *Lactobacillus* and *Bifidobacterium* populations. *Lactobacillus* spp. and *Bifidobacterium* spp. are common markers for gut health because they have been shown to down-regulate inflammation in the gastrointestinal tract, alleviate irritable bowel syndrome symptoms, stimulate immune functions, aid in mineral absorption and produce little, if any, gas or known carcinogenic substances. Probiotics have also been shown to display many of these pro-health components, and include many species of bacteria outside of the commonly utilised *Lactobacillus* and *Bifidobacterium* populations. How these dietary components are defined in the scientific and political arenas will play a critical role in the success of the gut health field moving forward. Key changes in administrative definitions and requirements of these dietary components will influence consumption, awareness and understanding of these key influential components. The purpose of this review is to provide current accepted definitions for fibre, prebiotics and probiotics, as well as introduce key scientific studies describing the health benefits of these components, as well as current health claims.

Keywords: fibre, gut health, prebiotic, probiotic

1. Introduction

The gut health field is one of the fastest emerging scientific fields in the public health community. Rapid innovation in the biotechnology field has allowed for novel insights into the gut microbiome and an understanding of the challenges that are associated with analysing this complex ecosystem (Sankar *et al.*, 2015). The gut microbiome plays a critical role in maintaining a healthy lifestyle, driving the necessity to thoroughly understand the dietary components that play an influential role in the development of the host's microflora throughout all stages of life (Wu *et al.*, 2011), and all critical pathways influenced in the body (Nicholson *et al.*, 2012).

As science emerges quickly on the influence of dietary components on microflora development, there is an increasing demand to accurately define the regulated definitions for fibre, prebiotics and probiotics (Hill *et al.*, 2014; Hutkins *et al.*, 2016; Slavin, 2013). Clear definitions in the scientific community, as well as for regulatory bodies, will play an influential role in a clear public understanding of these easily misunderstood definitions (Betz *et al.*, 2015; Oliver and Rasmussen, 2014). Accurate and expandable definitions will allow for clear categorisation and development of key dietary components that influence not only the gut microflora, but how the public views and understands these critical components and concepts.

The health benefits of consuming fibre, prebiotics and probiotics are extensive, and in some cases overlapping (Goldin, 1998; Slavin, 2013). Clear scientific studies have led to the development of authorised health claims for many of these dietary constituents under the jurisdiction of the largest regulatory bodies. The purpose of this review is to introduce and evaluate the definitions currently being used/proposed, the scientific studies and literature behind the health benefits of these dietary constituents (which have been extensively evaluated and reviewed elsewhere; Hauner *et al.*, 2012), health claims that are allowed by regulatory bodies, and involve adoption of a definition similar to the one proposed by the Institute of Medicine (IOM, 2002; i.e. total fibre; IOM, 2006b).

2. Fibre definition

Fibre definitions in the USA have been a highly debated topic over the past 30 years. Current changes for the 2015 USA dietary guidelines, according to the new proposal of the Food and Drug Administration (FDA), is looking to adapt a similar definition as the 2002 Institute of Medicine (IOM) definition of total fibre (IOM, 2006b). The Food and Nutrition Board's Dietary Reference Intake (DRI) Standing Committee put forth the panel on the definition of dietary fibre (Dietary Fibre Panel) in the FDA's proposed revision to the Nutrition and Supplemental Facts Label in March 2013 (FDA, 2014). According to the panel, the definition would include:

- Non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units) and lignin that are intrinsic and intact in plants.
- Isolated and synthetic non-digestible carbohydrates (with 3 or more monomeric units) that the FDA has granted to be included in the definition of dietary fibre, in response to a petition submitted to the FDA demonstrating that such carbohydrates have a physiological effect(s) that is beneficial to human health.
- Isolated and synthetic non-digestible carbohydrates (with 3 or more monomeric units) that are the subject of an authorised health claim.

According to the FDA's current regulations and guidance, there are only two isolated non-digestible carbohydrates meeting this definition: beta-glucan and barley beta-fibre. Although no guidance has been given for analytical methods or documentation required to display 'physiological effect(s) beneficial to human health, there is speculation that the FDA will provide an inclusive list categorising these components. Labelled fibre would then be quantified by the amount determined by the appropriate AOAC method, minus the amount of fibre not determined to have a 'physiological effect(s) beneficial to human health'. Currently, the FDA is proposing that manufacturers keep written records of all fibre that is contained in food products. The daily reference value that is used on the Nutrition Facts Panel is also proposed to increase from the current 25 to 28 g. The proposed increase will be affected both by fibre content and definition, potentially affecting health claims already in place for various fibres currently in market. This proposed change and definition was also introduced in the scientific advisory report of the 2015 Dietary Guidelines Committee (USDA, 2015).

The USA has shifted from the past definition of dietary fibre that was classified with basic ethanol dissolution assays, to the current international trend of basing this definition and classification to include many new synthetic fibres, largely taking into consideration their beneficial impact to the health of the consumer. No new approved analytical methods have been unanimously agreed upon, but many definitions for fibre outside the USA have adapted to these new trends. Proposed protocols to determine whether or not fibres display 'physiological effect(s) beneficial to human health' will need to be addressed.

In 2009, The World Health Organization (WHO), the United Nations Food and Agriculture Organization (FAO) and the Codex Alimentarius Commission (CODEX) have recently stated (Jones, 2014):

> Dietary fibre denotes carbohydrate polymers with 10 or more monomeric units that are not hydrolysed by the endogenous enzymes found in the small intestine of humans, belonging to the categories below.
> - Edible carbohydrate polymers naturally occurring in the consumed food.
> - Carbohydrate polymers that have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have physiological benefit to health, as demonstrated by generally accepted scientific evidence to competent authorities.
> - Synthetic carbohydrate polymers that have been shown to have a physiological benefit to health, as demonstrated by generally accepted scientific evidence to competent authorities.

Noting, this also includes lignin and others compounds quantified by AOAC 991.43 (AOAC International, 2016) and that the decision to include carbohydrates with 3-9 monomeric units should be left to the discretion of national authorities.

Currently, the European Food Safety Authority (EFSA) has accepted the most recent CODEX definition, along with Health Canada and Food Standards Australia and New Zealand. All three regulatory bodies also include the footnote to include substances with 3-9 monomeric units, and accept AOAC 2009.01 (AOAC International, 2016) as the method to correctly measure total dietary fibre with the CODEX definition. AOAC 2011.09 (AOAC

International, 2016) can also be used to measure CODEX total dietary fibre.

As the concept of dietary fibre merges with the notion of 'physiological effect(s) beneficial to human health', we must take into consideration how this will influence future definitions and distinctions of prebiotics and what they mean to consumer health and the food industry, both scientifically and politically. Definitions also need to be defined as flexible enough to take into consideration the improvements in the biotechnology and microbiology fields, so technological advances do not outpace current regulatory changes.

3. Prebiotic definition

The first active and published definition of the word 'prebiotic' was defined in 1995 as 'nondigestible 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, thus improving host health' (Gibson and Roberfroid, 1995), and eight years later changed to include, 'a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits' (Gibson *et al.*, 2004). In 2010 the International Scientific Association for Prebiotics and Probiotics widened that definition to include focus on the functionality of prebiotics, 'a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health' (Gibson *et al.*, 2010).

Important to note is that all prebiotics can be classified as fibre, although not all fibres are considered prebiotic (Brownawell *et al.*, 2012). Characteristics of functional prebiotics include: the ability to resist the low pH of the stomach, resist hydrolysis by mammalian enzymes, resist absorption in the upper gastrointestinal tract, the ability to be fermented by intestinal microbiota and selectively stimulate the growth and/or activity of intestinal bacteria associated with host health and overall well-being (Gibson and Roberfroid, 1995; Gibson *et al.*, 2004). It is generally accepted that beneficial bacteria includes bifidobacteria and also lactobacillus. Increased growth of lactobacilli due to stimulation of prebiotics is often less prevalent because of lower overall concentrations compared to bifidobacteria in the gastrointestinal tract.

The need to develop universal methods for specific, quantifiable results in clinical studies will result if fibre regulations need to show 'physiological effect beneficial to human health' in the USA. The general notion of beneficial stimulation of bifidobacteria and lactobacillus, as typically used to determine beneficial prebiotic capacity of molecules, will need quantifiable target ranges for stimulated populations of bacteria that are representative for universal populations in the USA.

4. Probiotic definition

The FAO/WHO defines probiotics as, 'live microorganisms that, when administered in adequate amounts, confer a health benefit to the host' which is a generally accepted definition (Hill *et al.*, 2014). In the USA, the FDA may define a probiotic as a drug, biological product, dietary supplement, food or food ingredient (Degnan, 2008). Both the FDA and EFSA have a similar stance, and have generally accepted the FAO/WHO definition for probiotics. Unlike Canada, the FDA and EFSA have yet to allow any health claim associated with probiotic products.

5. Health benefits of fibre

Cardiovascular disease

Dietary fibre, especially soluble fibre, has been consistently shown to protect against cardiovascular disease (CVD), but the exact functional components and mechanisms remain slightly unclear (Slavin, 2008). Soluble fibre has been shown to decrease serum cholesterol, primarily by decreasing low-density lipoprotein cholesterol (Anderson and Siesel, 1990). Bazzano *et al.* (2003) conducted an epidemiologic follow-up assessment study with an average time of 19 years of follow up, including 1,843 cases of coronary heart disease (CHD) and 3,762 cases of CVD and found that a higher intake of soluble fibre (5.9 g/d compared to 0.9 g/d) reduces risk of CHD. Bazzano *et al.* (2003) conducted a pooled analysis of ten prospective cohort studies in the USA and Europe and found that the consumption of dietary fibre from cereals and fruits is inversely associated with risk of CHD. Viscosity influences the protective effects against CVD and CHD, but other mechanisms include decreases in C-reactive protein (Ajani *et al.*, 2004; King and Egan, 2007; Ma *et al.*, 2006; Ning *et al.*, 2014) and decreases in blood pressure (Evans *et al.*, 2015; Streppel *et al.*, 2005; Whelton *et al.*, 2005) due to higher consumption of dietary fibre.

In the USA the FDA states that there is sufficient evidence for beta-glucans in oats and barley, and also psyllium husk, to authorise health claims to reduce the risk of heart disease for foods containing 0.75-1.7 g of soluble fibre (FDA 2002, 2003). EFSA has approved function health claims for beta-glucans from oat, oat bran, barley and barley bran for food products that contain at least 1 g of beta-glucans from these sources (pure or mixed), while informing the consumer that they must consume 3 g daily to contribute to the maintenance of normal blood cholesterol levels (EUR-Lex, 2012).

Glycaemic response and diabetes control

The relationship between fibre consumption and the development and control of type II diabetes includes many working theories and mechanisms. Mechanisms include increases in satiety cues that may lead to decreased caloric intake, thus, lesser weight gain, the ability of soluble, viscous fibres to attenuate glucose absorption rates, increase absorption and availability of nutrients and stimulate beneficial bacteria in the colon that may play an unknown role in the onset of type II diabetes.

Hopping *et al.* (2010) conducted a large-scale prospective multi-ethnic cohort study with 75,512 participants over a span of 14 years. Total dietary fibre intake was inversely associated with overall diabetes risk for all populations analysed (men: HR=0.75; 95% CI = 0.67, 0.84; $P<0.001$; and women: HR=0.95; 95% CI = 0.85, 1.06; $P=0.05$), and people who consumed greater than 15 g of fibre a day had significantly lower diabetes risk ($P<0.05$). Meyer *et al.* (2000) conducted a prospective cohort of 35,988 women for 6 years. Intakes of 17 g/d of insoluble fibre and 8 g/d of cereal fibre led to decreased risk of onset of type II diabetes ($P<0.0012$ and $P<0.0001$, respectively), while there was no positive association between soluble fibre intake. Schulze *et al.* (2004) conducted a similar cohort analysis of 91,249 young women for 8 years and found that low cereal fibre intake (<4.4 g/d) resulted in higher risk of developing type II diabetes.

Short-term intervention studies have displayed mixed results depending on dosage, fibre type and population analysed. A recent meta-analysis of 34 oat and barley fibre studies concluded that 3 g of beta-glucans from intact foods and 4 g of beta-glucans from processed foods is enough to significantly lower post-prandial glucose concentrations with 4 g of beta-glucans resulting in a decreased glycaemic response of 27±3 mmol•min/l. (Tosh, 2013). Analysis of many short-term studies found no correlations between fibre intake and post-prandial glucose concentrations (Mathern *et al.*, 2009). Mechanisms for fibre intake and type II diabetes prevention remain largely unclear with mixed results short-term, while long-term studies have found many positive associations between fibre intake and decreased risk of onset of type II diabetes.

Weight maintenance

Fibre intake and obesity prevention has been extensively reviewed (Slavin, 2005). It is generally recognised that dietary fibre intake supports weight loss and maintenance, although exact mechanisms remain unclear. Supported hypotheses include promotions in satiety cues (Pereira and Ludwig, 2001), alterations in absorption of select macronutrients (Gades and Stern, 2003), altering patterns and concentrations of gut hormones (Bourdon *et al.*, 2001, 1999; Burton-Freeman, 2002; Holt *et al.*, 2001; Nilsson *et al.*, 2015; Tseng *et al.*, 1996; Van Dijk and Thiele, 1999) and overall decreases in caloric intake. Heaton (1973) first introduced three primary hypothesised mechanisms of decreasing absorption efficiency in the small intestine, fibre displacing higher caloric nutrients in foods and promotion of saliva and gastric juice secretion due to increased mastication. Many mechanisms remain unclear and inconsistent at best. Cross-sectional observational studies have shown consistently an inverse relationship between fibre intake and BMI and body fat across many ages and populations (Alfieri and Pomerleau, 1995; Appleby and Thorogood, 1998; Ludwig *et al.*, 1999; Nelson and Tucker, 1996). Several observational studies have shown that obese adults have significantly lower dietary fibre intake (King *et al.*, 2012; Miller *et al.*, 1994).

USA fibre health claims

Currently, the FDA has allowed approved health claims for soluble fibres in foods from barley, psyllium and oats (Slavin, 2008). There are only twelve allowed health claims allowed on labels in the USA, with three of them (only two discussed) dedicated to dietary fibre (Table 1). Additional labelling describing quantities of fibre (nutrient content claims) on packages are allowed (FDA, 2013). To claim a product is 'high' in dietary fibre, the product must contain 20% or more of the daily value per reference amount customarily consumed, while a 'good source' claim requires 10-20%.

European fibre health claims

European health claims are covered by the Nutrition and Health Claims Regulation which includes: social media, print media, websites, presentations and product labels. The European Commission has overall authorisation. Allowable health claims are categorised as: general function (Article 13(1)), emerging science (Article 13(5)), disease risk reduction (Article 14(1)a), children's health (Article 14(1) b). Health claims are authorised for wheat, barley, oat, rye, sugar beet fibre and other dietary compounds (Table 2).

6. Health benefits of prebiotics

There is a wide range of health benefits associated with the consumption of prebiotics. Specifically looking at disease states that are affected by the prebiotic capacity of dietary constituents, inflammatory bowel disease, colon cancer and cardiovascular disease provide the most evidence for substantial influences from prebiotics.

Table 1. FDA authorised health claims regarding dietary fibre and disease.

Target of claim	Product requirements	Required terms	Model statement
Soluble fibre and risk of coronary heart disease	1. low saturated fat; 2. low cholesterol; 3. low fat; and must contain: whole oat/barley foods; or oatrim that contains 0.75 g beta-glucan/RACC; or psyllium husk that contains 1.7 g of soluble fibre/RACC[1]	heart disease' or coronary heart disease'; saturated fat; cholesterol; specify type of soluble fibre; and specify amount of soluble fibre/serving	Soluble fibre from foods such as (product), as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of (product) supplies (g) of the soluble fibre necessary per day to have this effect.
Beta-glucan soluble fibre (oat and barley sources)	1. oat bran; or 2. rolled oats; or 3. whole oat flour; or 4. oatrim; or 5. whole grain barley and dry milled barley; or 6. barley beta fibre; or 7. soluble fibre from psyllium husk with purity of <95%; and the amount of soluble fibre/RACC must be declared on nutrition label	'heart disease' or 'coronary heart disease'; 'saturated fat'; 'cholesterol'; specify type of soluble fibre; specify amount of soluble fibre/serving	Soluble fibre from foods such as (product), as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of (product) supplies (g) of the soluble fibre necessary per day to have this effect.

[1] Foods bearing a psyllium seed husk health claim must also bear a label statement concerning the need to consume them with adequate amounts of fluids. RACC = reference amount customarily consumed.

Inflammatory bowel disease

A recent randomised, double-blind, crossover study with twenty subjects with an ileal pouch-anal anastomosis receiving 24 g of inulin or a placebo for three weeks was conducted. After three weeks, subjects exhibited increased butyrate concentrations (11.7 mmol/g in placebo and 18.9 mmol/g in inulin group), decreased *Bacteroides fragilis* (7.68 cfu/g in placebo and 6.77 cfu/g in inulin group) and lowered concentrations of bile acids in the faeces (1.66 mmol/g in placebo and 1.42 mmol/g in placebo group), while reducing inflammation of the mucosa of the ileal reservoir under histological and endoscopical analysis (Welters *et al.*, 2002). A randomised, double-blind, placebo-controlled trial with 103 patients with active Crohn's disease fed a 15 g/d supplement of fructo-oligosaccharides (FOS) or placebo for four weeks was conducted, and found no significant differences in bifidobacteria or *Faecalibacterium prausnitzii*, concluding no significant clinical benefit to supplementation with 15 g/d of FOS (Benjamin *et al.*, 2011). Limited studies have shown consistent findings on alleviation of inflammatory bowel disease (IBD) symptoms with prebiotics. Many successful studies have utilised similar paired prebiotic and probiotic treatments with consistent success in lessening symptoms of IBD and related health issues (Ghouri *et al.*, 2014).

Colon cancer

Inulin, oligofructose, lactulose and resistant starch are all prebiotics that have been analysed for their role in colorectal cancer risk (Clark *et al.*, 2012). Roncucci *et al.* (1993) researched the effect of supplementing 209 adults who previously had polyps removed consuming 20 g/d of lactulose for three years. Significant reduction in adenoma recurrence was found at the end of the study, of 61 subjects analysed only 9 had recurrence while 61 saw no recurrence post-treatment, although no placebo or comparison group was included in this study. Langlands *et al.* (2004) conducted a 2-week study with 29 healthy adults, divided into an experimental and control group. Oligofructose (7.5 g) and 7.5 g of inulin were consumed daily in this study, with the control group not consuming a supplement. Bifidobacteria increased from 6.6 to 7.3 $\log_{10}$ cfu's (P<0.001) and lactobacilli increased from 3.0 to 3.7 $\log_{10}$ cfu's (P<0.02). MCM2 and Ki67 markers were measured for changes in cell proliferation, although no significant differences were found. Limburg *et al.* (2011) conducted a randomised, phase II chemoprevention trial with 85 subjects over 40 with previously resected colon cancer or multiple/advanced adenomas. No changes were seen for any measurements (aberrant crypt foci, Ki67 and caspase-3) for subjects consuming 12 g/d of oligofructose-enriched inulin. Many studies have researched

Table 2. Current EFSA requirements for health claims in the European Union.

Claim type	Nutrient	Claim summary	Health relationship
Article 13(1) (EUR-Lex, 2012)	Arabinoxylan from wheat endosperm	Consumption of arabinoxylan as part of a meal contributes to a reduction of the blood glucose rise after that meal	Reduction of post-prandial glycaemic responses
Article 13(5) (EUR-Lex, 2014)	Sugar beet fibre	Sugar beet fibre and increasing faecal bulk	Increasing faecal bulk
Article 13(1) (EUR-Lex, 2012)	Wheat bran fibre	Wheat bran fibre contributes to an increase in faecal bulk	Increase in faecal bulk
Article 13(1) (EUR-Lex, 2012)	Wheat bran fibre	Wheat bran fibre contributes to an acceleration of intestinal transit	Reduction in intestinal transit time
Article 13(1) (EUR-Lex, 2012)	Barley grain fibre	Barley grain fibre contributes to an increase in faecal bulk	Increase in faecal bulk
Article 13(1) (EUR-Lex, 2012)	Oat grain fibre	Oat grain fibre contributes to an increase in faecal bulk	Increase in faecal bulk
Article 13(1) (EUR-Lex, 2012)	Rye fibre	Rye contributes to normal bowel function	Changes in bowel function
Article 13(5) (EFSA, 2015)	Chicory root inulin	Chicory root inulin contributes to maintenance of normal defecation	Increasing stool frequency
Article 13(1) (EUR-Lex, 2012)	Beta-glucans	Beta-glucans contribute to the maintenance of normal blood cholesterol	Maintenance of normal blood cholesterol concentrations
Article 13(1) (EUR-Lex, 2012)	Beta-glucans from oats and barley	Consumption of beta-glucans from oats or barley as part of a meal contributes to the reduction of the blood glucose rise after the meal	Reduction of post-prandial glycaemic responses
Article 13(1) (EUR-Lex, 2012)	Guar gum	Guar gum contributes to the maintenance of normal blood cholesterol concentrations	Maintenance of normal blood cholesterol levels
Article 13(1) (EUR-Lex, 2012)	Pectins	Consumption of pectins with a meal contributes to the reduction of the blood glucose rise after that meal	Reduction of post-prandial glycaemic responses
Article 13(1) (EUR-Lex, 2012)	Pectins	Pectins contribute to the maintenance of normal blood cholesterol levels	Maintenance of normal blood cholesterol concentrations
Article 14(1) (EUR-Lex, 2012)	Barley beta-glucans	Barley beta-glucans has been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease	
	Chitosan		
Article 13(1) (EUR-Lex, 2012)	Hydroxypropyl methylcellulose	Consumption of hydroxypropyl methylcellulose with a meal contributes to a reduction in the blood glucose rise after that meal	Reduction of post-prandial glycaemic responses
Article 13(1) (EUR-Lex, 2012)	Hydroxypropyl methylcellulose	Hydroxypropyl methycellulose contributes to the maintenance of normal blood cholesterol levels	Maintenance of normal blood cholesterol concentrations
Article 13(1) (EUR-Lex, 2012)	Resistant starch	Replacing digestible starch with resistant starch in a meal contributes to a reduction in the blood glucose rise after that meal	Reduction of post-prandial glycaemic responses
Article 13(1) (EUR-Lex, 2012)	Alpha-cyclodextrin	Consumption of alpha-dextrin as part of a starch-containing meal contributes to the reduction of blood glucose rise after the meal	Reduction of post-prandial glycaemic responses

the potential influence of resistant starches on colorectal cancer. Worthley *et al.* (2009) conducted a randomised, double-blind, placebo-controlled 4-week crossover trial. No significant differences in epithelial proliferation or crypt height were noted for the subjects consuming 25 g/d of RS2. Wacker *et al.* (2002) found no effect on cell proliferation determined by bromodeoxyuridine labelling for the 12 volunteers consuming 50-60 g/d of RS in starchy foods during their two 4-week periods of a supplemented, controlled diet. Many studies with varying amounts of RS supplements have all found similar results (Burn *et al.*, 2011; Dronamraju *et al.*, 2009; Gorkom *et al.*, 2002; Grubben *et al.*, 2001). Prebiotics have displayed many potential protective effects against colorectal cancer in various animal models, but there has been limited evidence in human studies (Sunkata *et al.*, 2014). The current hypotheses include effects of short-chain fatty acids (SCFAs), stimulated immunity of the host and many anticarcinogenic pathways.

Table 3. Bacterial species with accepted non-strain-specific probiotic claims in foods in Canada (Gill and Prasad, 2008; Health Canada, 2009a,b; Picard *et al.*, 2005; Smug *et al.*, 2014).

Bacterial species	Eligible claims	Conditions	Substantiation requirements
Bifidobacterium adolescentis *Bifidobacterium animalis* subsp. *animalis* *Bifidobacterium animalis* subsp. *lactis* *Bifidobacterium bifidum* *Bifidobacterium breve* *Bifidobacterium infantis* *Bifidobacterium longum*	Probiotic that naturally forms part of the gut flora. Provides live microorganisms that naturally form part of the gut flora/contribute to healthy gut flora. Probiotic that contributes to healthy gut flora.	At least 1.0×10^9 colony forming units of one or more eligible microorganisms per serving. Must declare genus, species and strain in labelling. Recommended to include ATCC assigned number.	None
Lactobacillus acidophilus *Lactobacillus casei* *Lactobacillus fermentum* *Lactobacillus gasseri* *Lactobacillus johnsonii* *Lactobacillus paracasei* *Lactobacillus plantarum* *Lactobacillus rhamnosus* *Lactobacillus salivarius*			None
Bacteria not listed above	Claims need to be validated and wording of claim specific	Need strain-specific human efficacy evidence. Require genus, species and strain in labelling.	Strain-specific human efficacy evidence required

ATCC = American Type Culture Collection.

Cardiovascular disease

Causey *et al.* (2000) conducted a randomised, double-blind crossover study with twelve men with hypercholesterolemia divided into two controlled diets. One included a pint of ice cream with 20 g of inulin, and one a pint of ice cream with sucrose. Daily intake of 20 g of inulin significantly reduced serum triglycerides by 40 mg/dl (P<0.05), increased butyrate concentrations (0.91 mmol/l in control phase and 1.96 mmol/l in inulin phase) and did not significantly alter any change in transit time. Brighenti *et al.* (1999) researched the effects of inulin in ready-to-eat cereals in twelve healthy male volunteers. Volunteers consumed 50 g of rice-based cereal with 18% inulin daily for three periods throughout four weeks. They found no changes in faecal SCFAs or pH, but found plasma total cholesterol decreased significantly (P<0.05) and triacylglycerol decreased (P<0.05) and the end of each test period while bifidobacteria concentration increased (P<0.05). Gluconic acid, germinated barley, oligodextrans, lactose, glutamine, hemicellulose rich substrates and many types of resistant starches are all prebiotic compounds that have been targeted for their cholesterol-lowering effects. Although identified, no specific daily dosage has been established for these effects, resulting in conflicting study results (Ooi and Liong, 2010).

Prebiotic regulatory status

Authoritative governing branches have been strained to keep up with the rapidly growing field of prebiotics. In the USA, commonly consumed prebiotics include inulin, FOS and galacto-oligosaccharides primarily due to their tenure in the USA are being regarded as safe and effective (Kumar *et al.*, 2015), thus increasing their consumption. All foods and ingredients are regulated under the Food Drug and Cosmetic Act, which clearly states that the safety of introduced ingredients and foods is the responsibility of the company manufacturing the product. For items that are not generally recognised as safe, they are required to obtain FDA approval before products can be sold commercially. Although approval may be obtained for ingredients that act as what is generally defined as 'prebiotic', neither the FDA in the USA nor EFSA in the European Union have established a legal definition for a prebiotic (Loveren, 2012; IOM, 2006a). Cited above, EFSA currently used the FAO definition of a prebiotic, indicating the need to display a health benefit (Loveren, 2012; Pineiro *et al.*, 2008). Challenges exist for regulatory bodies in that the scientific community does not have a universally agreed upon definition for the term prebiotic, a key first step in addressing these regulatory issues (Hutkins *et al.*, 2016). Challenges will also be faced as fibres are required to display 'physiological effects beneficial to human health', as this may blend into the current opinions and definitions at stake.

7. Health benefits of probiotics

Currently, there are no health claims associated with probiotic products in the USA, or recommendations for probiotic consumption. In Europe, EFSA has taken a similar approach. Canada has accepted and regulated claims and health benefits for identified probiotics (Table 3), and have identified probiotic species known to promote health benefits in the gastrointestinal tract and body (Health Canada, 2009a; Smug *et al.*, 2014). Health impacts of probiotics have been well-documented (Table 3 and 4) and include the ability to reduce severity of symptoms of irritable bowel syndrome (IBS) (Hoveyda *et al.*, 2009; Moayyedi *et al.*, 2010; Nikfar *et al.*, 2008), preventing and reducing various types of diarrhoea (Hempel *et al.*, 2012; McFarland, 2006, 2007), improving overall lipid profiles (Guo *et al.*, 2011) and many more (Sanders *et al.*, 2014). Commonly used microorganisms as probiotics usually belong to the *Lactobacillus* and *Bifidobacterium* genera (Table 5), but many others are commonly used, including: *Streptococcus thermophilis*, *Streptococcus diacetylactis* *Streptococcus intermedius*, *Lactococcus lactis*, *Leuconstoc mesenteroides*, *Saccharomyces bourlardii*, *Saccharomyces cerevisae* and *Escherichia coli* strain *Nissle.*

Table 5. *Lactobacillus* and *Bifidobacterium* microorganisms most commonly used as probiotic supplements worldwide.

Bifidobacterium	***Lactobacillus***
B. adolescentis	*L. acidophilus*
B. animalis	*L. casei*
B. animalis subsp. animalis	*L. crispatus*
B. animalis supsp. lactis	*L. fermentum*
B. bifidum	*L. gasseri*
B. breve	*L. johnsonii*
B. infantis	*L. plantarum*
B. lactis	*L. reuteri*
B. longum	*L. rhamnosus*
B. thermophilum	*L. salivarius*

Table 4. Probiotic health claim criteria for natural health products.

Species	Eligible claims/purposes	Conditions
Bifidobacterium adolescentis *Bifidobacterium animalis* subsp. *animalis* *Bifidobacterium animalis* subsp. *lactis* *Bifidobacterium bifidum* *Bifidobacterium breve* *Bifidobacterium infantis* *Bifidobacterium longum* *Lactobacillus acidophilus* *Lactobacillus casei* *Lactobacillus fermentum* *Lactobacillus gasseri* *Lactobacillus johnsonii* *Lactobacillus paracasei* *Lactobacillus plantarum* *Lactobacillus rhamnosus* *Lactobacillus salivarius*	Probiotic that forms/contributes to a natural healthy gut flora. Probiotic to benefit health and/or to confer a health benefit. Provides live microorganisms that form part of a natural healthy gut flora/that contribute to a natural healthy gut flora/ benefit health/confer a health benefit.	1.0×10^7 to 1.0×10^{11} colony forming units of one or more eligible microorganisms per day
Lactobacillus rhamnosus GG	Helps to manage acute infectious diarrhoea	6.0×10^9 to 1.2×10^{10} colony forming units/day
	Helps to manage/reduce antibiotic-associated diarrhoea	1.0×10^{10} to 2.0×10^{10} colony forming units/day
Lactobacillus johnsonii La1/Lj1/NCC533	An adjunct to physician-supervised antibiotic therapy in patients with *Helicobacter pylori* infections	1.25×10^8 to 3.6×10^9 colony forming units/day
Saccharomyces boulardii *Saccharomyces cerevisiae*	Helps to reduce the risk of antibiotic-associated diarrhoea	1.0×10^{10} to 3.0×10^{10} colony forming units/day

8. Fibre, prebiotic and probiotic consumption

Fibre consumption in the USA and other countries is typically half of what is recommended by governing regulating bodies. In the USA current intake of fibre is typically around 17 g/d, while recommendations are 25 and 38 g/d for women and men, respectively. Similar consumption patterns are seen in Europe and other industrialised countries (Threapleton *et al.*, 2013). Fortified foods have evolved to help bridge the gap between consumption and recommendations, but further progress needs to be made. Changes in definitions and analytical methods have also been suggested as a means to address the 'fibre gap' in many countries (Jones, 2014).

Inulin is a prebiotic that occurs naturally in leeks, asparagus, onions, wheat, garlic, chicory, oats, soybeans and Jerusalem artichokes. Estimated consumption in USA and European diets is several grams a day for naturally occurring prebiotics (inulin and FOS) (Loo *et al.*, 1995; Moshfegh *et al.*, 1999). At this dosage, it may be improbable that naturally-occurring prebiotics may have any beneficial effect. Without universal definitions of prebiotics and inclusive lists of ingredients included, epidemiological tracking of prebiotic consumption patterns will be difficult to obtain.

Probiotic consumption is hard to quantitate due to its diverse origin across many food categories. Probiotic milk products, a common subset of probiotic products, are very widely consumed (Ozen *et al.*, 2012). In Finland, sour milk is reportedly consumed by over 90% of respondents (Lahtl-Koski *et al.*, 2002). Japan and Belgium have much lower consumption rates, with less than 5% of respondents consuming fermented dairy products (Iso *et al.*, 2005; Mullie *et al.*, 2009).

9. The evolution of intestinal health

Microbiome composition

Many ecosystems co-exist throughout the human gastrointestinal tract. Outside of the distal intestine, diverse ecosystems exist on the skin, parts of the oral cavity and also the urogenital tract. The oral cavity microbiota contains over 500 diverse bacterial species (Moore and Moore, 1994). Depending on exposure and quality of hygiene, evidence suggests that these bacteria are responsible for a wide array of systemic diseases (Gendron *et al.*, 2000). The stomach also contains between 10^2 to 10^3 cfu/ml of stomach contents, primarily due to the low pH of the stomach (Holzapfel *et al.*, 1998). The distal intestine is the primary home of the human gut microbiome, a diverse and complex ecosystem containing between 10^{10} to 10^{12} cfu/g of cells, belonging to hundreds of species of bacteria (Finegold *et al.*,1975; Hentges, 2012; Holdeman *et al.*, 1976). It is estimated that up to 30 g of bacteria are produced for every 100 g of carbohydrate fermented in the distal intestine (Slavin, 2013). By volume, bacteria compose 30% of the human colon (Salyers, 1979). There are many abundant genera of bacteria in the distal intestine, including: bacteroides, eubacteria, fusobacteria, bifidobacteria, peptostreptococci, clostridia, lactobacilli and streptococci (Salminen *et al.*, 2007). The gut microflora serves as the primary, interchangeable interface between the diet and the host's health, and has recently been associated with many diseases and conditions (Kinross *et al.*, 2011). Advances in clinical studies and biotechnology are leading the way to successful modulation of the gut microflora, improving knowledge of many disease states and pioneering diets and functional foods that will continue to aid in health promotion.

Influences on the gut microbiome and intestinal health

Establishment of a healthy gut microbiota starts immediately at birth, although this progression is highly debated, partly due to the complexity of defining what a 'healthy microbiome' entails. It is well-established that fibre and other non-digested food contents play a large role in the influence and development of the host's microflora (Holscher *et al.*, 2015). Other influential factors include: age, stress, infection, geography and many other environmental components (Claesson *et al.*, 2011; Maslowski and Mackay, 2011; Maslowski *et al.*, 2009; Tap *et al.*, 2009; Yatsunenko *et al.*, 2012). Independent of the geography of populations, specific species of bifidobacteria have been shown to decrease with increasing age (Yatsunenko *et al.*, 2012). Stress has also been shown to influence certain bacteria over extended periods of time (Holdeman *et al.*,1976). Differences in delivery be either caesarean section or the vaginal canal play a critical role in the early development of the microbiota (Orrhage and Nord, 2007; Palmer *et al.*, 2007; Penders *et al.*, 2006), and leads to both changes in bacterial composition and also the timing of advanced colonisation (Bennel and Nord, 1987; Hällström *et al.*, 2004; Neut *et al.*, 1987; Penders *et al.*, 2006). At ages 1-3, most individuals have colonisation most similar to adult populations (Costello *et al.*, 2013; Palmer *et al.*, 2007). Studies have shown that breast-fed infants have a microflora dominated by bifidobacteria populations (Favier *et al.*, 2002; Penders *et al.*, 2006; Stark and Lee, 1982), while other studies have shown bifidobacteria to be much less prevalent (Hall *et al.*, 1990; Hopkins *et al.*, 2005). Extreme biodiversity exists among individuals, making identifying a healthy microbiome difficult. As dietary constituents continue to aim at improving gut health, continued research is needed to examine the full effects of exogenous factors on host development.

Influential roles of lactobacilli and bifidobacteria

Because of the many health-promoting properties of these genera of bacteria they are commonly used markers of microflora health, and common targets for dietary stimulation. Lactobacilli have been shown to down-regulate mucosal inflammation in the gastrointestinal tract (Borruel, 2002). Lactobacilli play a role in helping digest lactose for lactose-intolerant individuals, alleviate constipation, improve IBS symptoms and potentially help prevent traveller's diarrhoea (Salminen *et al.*, 1993). Bifidobacteria and lactobacilli also inhibit the growth of harmful bacteria, stimulate immune functions throughout the body, aid in mineral absorption and help in the synthesis of vitamins. (Gibson and Roberfroid, 1995). Bifidobacteria reside naturally in the gastrointestinal tract of healthy human adults and have a strong affinity to ferment select oligosaccharides, making them a common marker for prebiotic capacity. Bifidobacteria are a unique genus of bacteria in that no gas is formed as an end product of metabolism (Buchanan and Gibbons, 1974). Similar to the *Lactobacillus* genera, these bacteria are saccharolytic, an often used marker for beneficial bacteria (Salyers, 1979). Bifidobacteria also do not produce any known carcinogenic substances *in vivo*. Bifidobacteria concentrations have been negatively associated with obesity and weight gain (Collado *et al.*, 2008; Kalliomäki *et al.*, 2008; Santacruz *et al.*, 2010; Schwiertz *et al.*, 2010). Specific species might play a critical role in this association, as not all species of bifidobacteria may have identical influence (Yin *et al.*, 2010). Decreased levels of bifidobacteria and lactobacilli have been positively associated with the development of allergy diseases in the first five years of life (Kalliomäki *et al.*, 2001; Sjögren *et al.*, 2009). Decreases in bifidobacteria, along with decreases in bacterial diversity, have been associated with higher inflammation and IBS (Hansen *et al.*, 2010; Joossens *et al.* 2011). The mechanisms behind disease states and lactobacilli and bifidobacteria are unclear, but sufficient studies show these bacteria are highly associated with improved health.

10. Conclusions

Fibre, prebiotics and probiotics have all been shown to play an influential part in developing and maintaining a healthy microbiota throughout all stages of life. As gut microbiome research continues to advance our understanding of the significance and importance of this diverse ecosystem, critical importance should be placed on public awareness of this topic. Categorisation and definitions of these critical dietary components will be influential in advancing the understanding of the gut microbiome. Health claims should continue to place importance on the roles that these dietary components can play in maintaining a healthy lifestyle and their importance in various diseases and conditions. As science advances our understanding of the critical components that influence the gut microbiome through the diet, regulation of these dietary components will play a critical role in the perception and consumption of fibre, prebiotics and probiotics.

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