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All about Gut Health: Understanding the Role of Prebiotics, Probiotics and Postbiotics

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October 26, 2021 | 2:00 PM EST

Learning Objectives

1

Describe the difference between live and active cultures, probiotics, prebiotics and postbiotics

2

Detail key factors one should consider when selecting probiotics for a specific benefit

3

Analyze three foods that contain prebiotics and discuss what clients should look for on food labels.

4

Describe how the gut and brain interact via our gut microbes

Microbiome Dictionary

Gut Microbiota

The microorganisms inhabiting the gastrointestinal tract. The composition of this microbial community is host specific.

Gut Microbiome

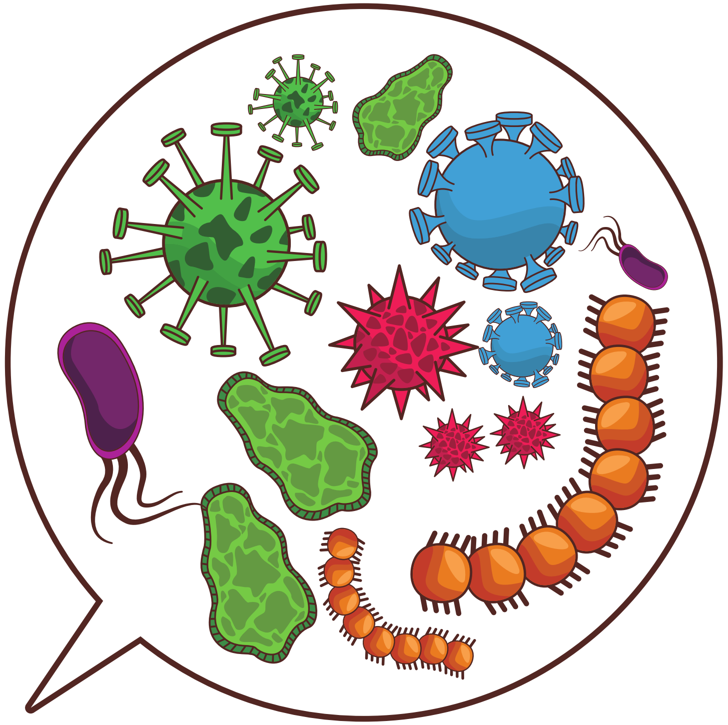
The entire collection of genes found in all of the microbial cells living in the gastrointestinal tract.

Metabolome

The specific metabolites in biological samples (tissues, cells, fluids, or organisms) under normal conditions in comparison with altered states promoted by disease, drug treatment, dietary intervention, or environmental modulation.

https://www.gutmicrobiotaforhealth.com/glossary-index/, Klassen A. et al. (2017) Metabolomics: Definitions and Significance in Systems Biology. In: Sussulini A. (eds) Metabolomics: From Fundamentals to Clinical Applications. Advances in Experimental Medicine and Biology, vol 965. Springer, Cham.

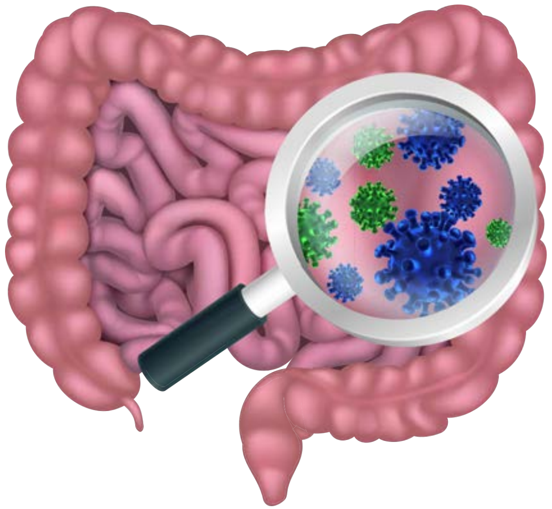
Gut Microbiome



- ✓ 100 trillion microbes
- ✓ Includes bacteria, viruses, fungi, archaea
- ✓ Influence human physiology, metabolism, nutrition (produce- riboflavin, folate and cobalamin) and immune function

Guinane CM, Cotter PD. *Therap Adv Gastroenterol*. 2013;6(4):295-308.

Functions of the Microbiome



- Pathogen protection-e.g competes for nutrients
- Maintenance of intestinal barrier-protects against increased intestinal permeability
- Nutrient + drug metabolism
- Immune modulation
- Produces and communicates with hormonal products as an endocrine-like organ
- Impacts brain function via gut-brain axis

Some examples: microbes are capable of producing SCFAs which are used as nutrients for colonocytes, create neurotransmitters potentially impacting mood, support cholesterol metabolism, and regulate various hormones involved in appetite.

Guinane CM, Cotter PD. *Therap Adv Gastroenterol*. 2013;6(4):295-308.
Dalton A, et al. *Gut Microbes*. 2019;10(5):555-568.

"Microbiota-modulating dietary interventions include many fermented foods and [fiber]-rich dietary regimens, as well as probiotics, prebiotics and synbiotics, some of which are available as drugs and medical devices, as well as foods."

Mills, S., et al. Precision nutrition and the microbiome, Part I: current state of the science. *Nutrients* **11**, 923 (2019). Salminen, S et al, *Nat Rev Gastroenterol Hepatol* **18,** 649–667 (2021).

Primer for "-biotics"

Probiotic: "Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host."

Prebiotics: "a substrate that is selectively utilized by host microorganisms conferring a health benefit."

Postbiotic: "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host."

Synbiotic: "a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host."

Swanson KS, et al Nat Rev Gastroenterol Hepatol. 2020 Nov;17(11):687-701
https://isappscience.org, SalminenS., et al.,*Nat Rev Gastroenterol Hepatol* 2021;**18:** 649–667.

Probiotics: It's in the Details

The word "probiotic" comes from Greek, and it means "for life"

- Probiotics include characterized strains with a scientifically demonstrated effect on health
- Probiotics are known by genus, species, and strain: for example, *Lactobacillus acidophilus* ABC
- Different strains of the same species may have different health effects
- Dose is important! A probiotic consumed at a higher dose may not necessarily have a > health benefit than one consumed at a lower dose
- Select dose shown in the research to confer a health benefit

Davani-Davari D, et al. *Foods*. 2019;8(3):92. Gibson GR et al. *Food Sci. Technol. Bull. Funct. Foods.* 2010;7:1–19. doi: 10.1616/1476-2137.15880. Salminen, S., *et al. Nat Rev Gastroenterol Hepatol* (2021). Swanson, K. S. et al.. *Nat. Rev. Gastroenterol. Hepatol.* **17**, 687–701 (2020). Markowiak P, Śliżewska K. *Nutrients*. 2017;9(9):1021. Published 2017 Sep 15.

Fermented Foods

Fermented foods are those made through desired microbial growth and enzymatic conversions of food components.

Live microbes present in traditional fermented foods and beverages such as kombucha, yogurt, sauerkraut, and kimchi ***typically do not meet the required evidence level for probiotics.***

https://isappscience.org/for-scientists/resources/fermented-foods/, https://isappscience.org/for-scientists/resources/probiotics/

Live Active Culture vs Probiotic

- Live active cultures are living microbes used to make fermented foods + beverages
- **Are cultures + probiotics the same?** Cultures provide technological benefits while probiotics provide health benefits. Sometimes a culture is also a probiotic + sometimes it is not
- **Where to find them:** Lactobacillus bulgaricus and Streptococcus thermophilus are widely used to ferment milk into yogurt to create unique nutritional and flavor benefits

Fermented Food

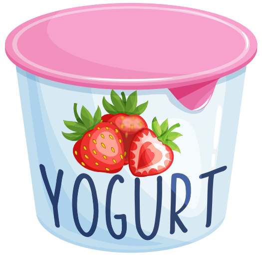
"Fermentation processes and products are believed to have been developed **9000 years ago** in order to preserve food for times of deficiency, improve flavor, and reduce poisonous effects"

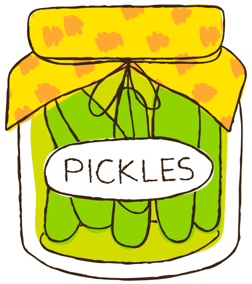
Contains live culture: fresh kimchi, water or cured olives, traditional salami, fresh sauerkraut

Does <u>not</u> contain live cultures: tempeh, most wine + beer, sourdough bread

https://isappscience.org

Why Consume Fermented Foods?





1. Enhanced taste and texture
2. Increased microorganism content that may improve gastrointestinal health, lowering the risk of type 2 diabetes and cardiovascular disease
3. Convert unsaturated fatty acids to conjugated linoleic acid, which has anti-inflammatory effects
4. Enhanced availability of B vitamins, Vitamin K, magnesium, and zinc
5. Creation of isoflavones genistein and daidzein from soy foods
6. Reduction of anti-nutrients such as phytates
7. Enhance polyphenols -- extracted out of the food by microbe fermentation (Polyphenols can function as prebiotics)
8. Increase gut microbial diversity and reduce inflammatory markers

Dennett, C The Facts About Fermented Foods. *Today's Dietitian* 2018;20(4): 24. Wastyk HC, et al Cell. 2021 Aug 5;184(16):4137-4153.e14.

RCT: Fermented Food vs High Fiber

N=36 healthy adults (18/arm) were randomly assigned to a 10-week diet that included either fermented (around 6 servings) or high-fiber (40 grams) diet

Combined with -omics measurements of microbiome and host, including extensive immune profiling

Results found diet-specific effects:

- High fiber diet noted to change microbiome function
- Fermented food (yogurt, kefir, fermented cottage cheese, kimchi and other fermented vegetables, vegetable brine drinks, and kombucha tea) led to an increase in overall microbial diversity
  - 4 types of immune cells showed less activation in the fermented-food group
  - The levels of 19 inflammatory proteins measured in blood samples decreased
  - One of these proteins, interleukin 6, has been linked to conditions such as rheumatoid arthritis, Type 2 diabetes and chronic stress

Wastyk HC, et al Cell. 2021 Aug 5;184(16):4137-4153.e14.

Selecting a Probiotic

Note: food and supplements may supply probiotics

Key factors to selection:

- Backed by science
- Provides effective dose
- Provides the benefit you are seeking
- Properly labeled with CFU* amount, GSS (genus, species, strain) dose and proper storage

https://isappscience.org

*Colony -Forming Units

Know the "G-S-S"

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BILLIONS OF LIVE AND ACTIVE PROBIOTICS

Bifidobacterium	animalis	DN-173 010
Genus	Species	Strain

*sub species=lactis

- Probiotics are known by genus, species, and strain
- Different strains of the same species may have different health effects
- The dosage consumed should match the level shown in an efficacy study to confer a benefit

https://isappscience.org/for-scientists/resources/probiotics/

Strain Specific Effects

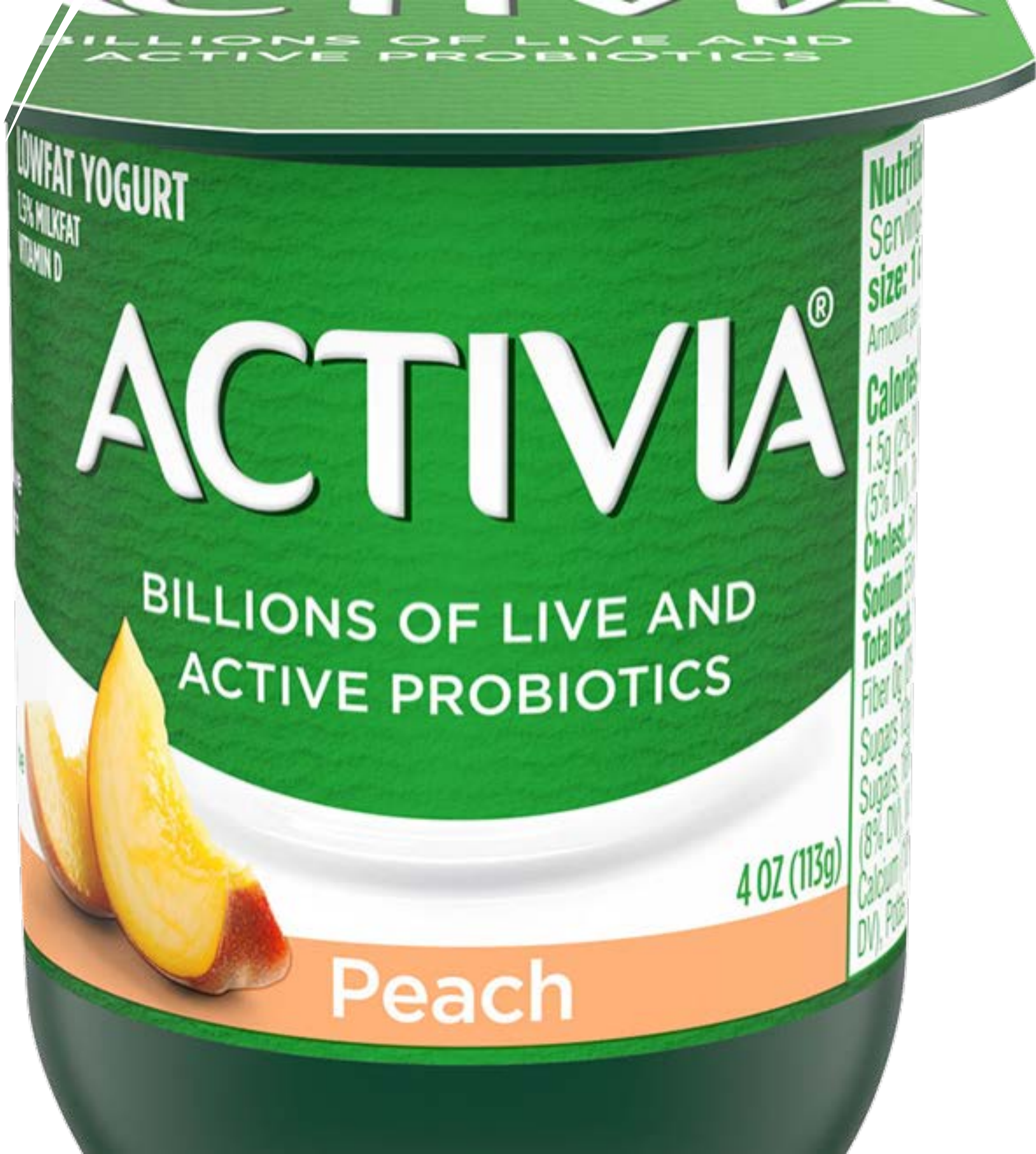
2 DBRCT studies combined, n=538 adult women with minor GI complaint

Primary endpoint: the effect of the consumption of a Fermented Milk Product (FMP) over 4 weeks on Subject's Global Assessment (SGA) of gastrointestinal well-being

Assessment of FMP with *Bifidobacterium animalis* subsp. *lactis* CNCM I-2494 and lactic acid bacteria 125 g BID compared to control (non-fermented dairy product without bacterial strains) has been shown to reduce the frequency of minor digestive symptoms(gas, rumbling, abdominal discomfort and bloating) when consumed twice a day for 2 and 4 weeks

This effect is not influenced by dietary fiber intake or physical activity at the start of study

Marteau P et al *Nutrients*. 2019; 11(1):92.



Probiotic Selection Resources

HTTPS://ISAPPSCIENCE.ORG
(INTERNATIONAL SCIENTIFIC ASSOCIATION FOR PROBIOTICS AND PREBIOTICS)

AEPROBIO: US PROBIOTIC GUIDE

Bear in mind: This guide is geared toward disease management. Not all probiotics are utilized to benefit disease specific symptomology but rather goal of prevention of disease or maintenance of health.

Prebiotics

Criteria are used to classify a compound as a prebiotic:

- The growth and/or activity of the intestinal microbes can be selectively stimulated by prebiotics and improve health
- Resistant to acidic pH of stomach
- Cannot be hydrolyzed by mammalian enzymes
- Should not be absorbed in the GI tract
- Most prebiotics are carbohydrates but NOT all!!

Gibson GR et al. *Food Sci. Technol. Bull. Funct. Foods.* 2010;7:1–19. doi: 10.1616/1476-2137.15880.

Prebiotics

- Majority are a subset of CHO groups—oligosaccharide carbohydrates:
  - GOS + Fructans→
- Others include non-carbohydrate prebiotics, such as cocoa-derived flavanols - e.g., Flavanols can stimulate lactic acid bacteria

Prebiotics You Might Find on a Food Label *or in Foods*

PREBIOTIC EXAMPLES	SOURCES
FOS, Oligofructose and Inulin	Onion, garlic, wheat, additives: chicory root extract, inulin, FOS
GOS	Legumes, nuts + seeds
Isomaltooligosaccharides- IMOs are a mixture of α-(1 → 6) and α-(1 → 4)-linked glucose oligomers, synthesized by an enzymatic reaction from starch (corn, tapioca).	Sweetener and bulking agent found in cereals, granola bars; IMOs naturally exist in honey, and fermented foods, such as soy sauce, miso, and sake.
Guar gum-polysaccharide extracted from endosperm of the plant Cyamopsis tetragonolobus.	Guar Gum is commonly used in dairy, bakery, cereal, and meat products.
RSs and maltodextrin (Resistant maltodextrin is highly water-soluble dextrin that is produced by treating cornstarch with numerous acid, enzymatic, and heating processes, and used in a variety of applications.)	RS-uncooked oats, cooked and cooled rice and potatoes, Hi-maize resistant starch is isolated from white, cornstarch with high amylose content, resists digestion in small intestine used in some products.
B-glucan	Oat and barley are the 2 highest sources of beta-glucans today in the diet.
Xylooligosaccharides	XOSs are commonly found in dairy products, cereals, bars, sports drinks, and isotonic beverages

Carlson JL,et al. *Curr Dev Nutr*. 2018;2(3):nzy005. Cloetens L et al. *Nutr Rev* 2012;70(8):444–58. Gourineni V, et al., *Nutrients*. 2018;10(3):301.

Health Benefits of Prebiotics

- Increase bioavailability of calcium
  - Calcium absorption is stimulated by the chemical changes and increases in acid fermentation of the prebiotic dietary fibers by various bacteria
- Reduction of potential deleterious metabolites (ammonia, indoles, sulfides)
  - Prebiotic intake with protein consumption reduces potential deleterious metabolites
- Reduction of pathogenic microbes
  - (e.g. E. coli, Salmonella ssp, Campylobacter) populations, via lowering colonic pH below pathogenic bacteria threshold, competition for limited nutrients, enhanced immune system, limited colonization sites
- Modulate immune function + improved intestinal permeability

Carlson JL, et al *Curr Dev Nutr*. 2018;2(3):nzy005.

Prebiotics: Chain Length Matters

- Certain microbes have the capacity of fermenting different carb chain length (DP*)
- Inulin (with DP of ≤60) can be fermented only by a few species, whereas a large number of microorganisms are able to degrade FOS (with DP of ≤10)
- Location of fermentation differs: FOS** are rapidly fermented in the proximal colon whereas inulin appears to have a more sustained fermentation profile that potentially enables protective effects in the distal colon

Scott K.P et al. *FEMS Microbiol. Ecol.* 2014;87:30–40. Franco-Robles E, López MG. *Scientific World Journal*. 2015;2015:289267.

*DP=degree of polymerization. **FOS=fructo-oligosaccharides

The *Newer* Kid on the Block: **Postbiotics**

Postbiotic: "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host"

- Effective postbiotics must contain inactivated microbial cells or cell components, with or without metabolites, that contribute to observed health benefits
- To qualify as a postbiotic, the microbial composition prior to inactivation must be characterized, and so preparations derived from undefined microorganisms are not included in the definition
  - Many traditional fermented foods are created with undefined, mixed cultures, and such a product could not be used for the preparation of a postbiotic

Salminen S, et al. *Nat Rev Gastroenterol Hepatol.* 2021 Sep;18(9):649-667.

CONSENSUS STATEMENT

OPEN

Check for updates

The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics

Seppo Salminen[1]✉, Maria Carmen Collado[2], Akihito Endo[3], Colin Hill[4,5], Sarah Lebeer[6], Eamonn M. M. Quigley[7], Mary Ellen Sanders[8], Raanan Shamir[9,10], Jonathan R. Swann[11,12], Hania Szajewska[13] and Gabriel Vinderola[14]

Abstract | In 2019, the International Scientific Association for Probiotics and Prebiotics (ISAPP) convened a panel of experts specializing in nutrition, microbial physiology, gastroenterology, paediatrics, food science and microbiology to review the definition and scope of postbiotics. The term 'postbiotics' is increasingly found in the scientific literature and on commercial products, yet is inconsistently used and lacks a clear definition. The purpose of this panel was to consider the scientific, commercial and regulatory parameters encompassing this emerging term, propose a useful definition and thereby establish a foundation for future developments. The panel defined a postbiotic as a "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host". Effective postbiotics must contain inactivated microbial cells or cell components, with or without metabolites, that contribute to observed health benefits. The panel also discussed existing evidence of health-promoting effects of postbiotics, potential mechanisms of action, levels of evidence required to meet the stated definition, safety and implications for stakeholders. The panel determined that a definition of postbiotics is useful so that scientists, clinical triallists, industry, regulators and consumers have common ground for future activity in this area. A generally accepted definition will hopefully lead to regulatory clarity and promote innovation and the development of new postbiotic products.

The past few decades have demonstrated unequivocally the importance of the human microbiota to both short-term and long-term human health. Early programming of the microbiota and immune system during pregnancy, delivery, breastfeeding and weaning is important and determines adult immune function, microbiome and overall health[1]. We have also seen rapid growth in the number of products that claim to affect the functions and composition of the microbiota at different body sites to benefit human health.

Improving human health through modulation of microbial interactions during all phases of life is an evolving concept that is increasingly important for consumers, food manufacturers, health-care professionals and regulators. Microbiota-modulating dietary interventions include many fermented foods and fibre-rich dietary regimens, as well as probiotics, prebiotics and synbiotics, some of which are available as drugs and medical devices, as well as foods[2]. The rich, diverse microbial ecosystems and immune cells inhabiting all mucosal and cutaneous surfaces provide targets for intervention, with the goals of reducing the risk of diseases and improving health status[2]. Consensus definitions of probiotics, prebiotics and synbiotics have been published previously. Probiotics are "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host"[3], whereas a prebiotic is a "substrate that is selectively utilized by host microorganisms conferring a health benefit"[4]. A synbiotic, initially conceived as a combination of both probiotics and prebiotics, has now been defined as "a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host"[5]. The concept of postbiotics is related to this family of terms and is emerging as an important microorganism-derived tool to promote health.

Probiotics are by definition alive and required to have an efficacious amount of viable bacteria at the

epsal@utu.fi
org/10.1038/
21-00440-6

Postbiotics

5 potential mechanisms postbiotics offer benefit:

1. modulation of the resident microbiota
2. enhancement of epithelial barrier functions
3. modulation of local and systemic immune responses
4. modulation of systemic metabolic responses
5. systemic signaling via the nervous system

Salminen S, et al. *Nat Rev Gastroenterol Hepatol.* 2021 Sep;18(9):649-667. Iwasaki, M. et al. Duodenal chemosensing of short-chain fatty acids: implications for GI diseases. *Curr. Gastroenterol. Rep.* **21**, 35 (2019).

Postbiotic Potential

- Molecules present in postbiotics, such as lactic acid and bacteriocins may provide direct antimicrobial activity
- Postbiotics could also modulate the microbiota indirectly by carrying lactic acid that can be consumed by some microbiota resulting in SCFAs and butyrate
- Postbiotics may also compete with resident microorganisms for adhesion sites
- SCFAs present in a postbiotics have the potential to modify epithelial barrier function and protect against negative lipopolysaccharide - induced changes

Salminen S, et al. *Nat Rev Gastroenterol Hepatol.* 2021 Sep;18(9):649-667.

Data with Postbiotics

Patients with IBS with diarrhea (*n* = 297)	Lacteol (inactivated *L. acidophilus* LB plus fermented culture medium), two capsules daily (no control)	1 month	Improved scores for pain, bloating, frequency of diarrhea and quality of life
Patients with recurrent respiratory tract infections (*n* = 160)	Lantigen B (Bruschettini Srl.), a suspension of bacterial antigens obtained from *S. pneumoniae* type 3, *S. pyogenes* group A, *B. catarrhalis*, *S. aureus*, *H. influenzae* type B and *K. pneumoniae* in oral drops vs placebo BID	4 weeks treatment followed by 2 weeks off followed by 4 weeks on and then followed for a further 6 weeks	Significant ($P < 0.05$) reduction in the number of acute infectious episodes and use of antibiotics in the active group
Patients with cancer and leukopenia following chemotherapy (*n* = 78)	DEODAN, an oral preparation, obtained from lysozyme lysates of *Lactobacillus bulgaricus* strain "I. Bogdanov patent strain Tumoronecroticance B-51" ATCC 21815 TID (no placebo)	Treated until resolution of leukopenia	Recovery of white blood count (>3,000/mm3) between days 3 and 5 in all patients
Preterm infants 30–35 weeks of gestational age, age 0–3 days (*n* = 58)	Preterm infant formula, heat-inactivated fermented formula with BB C50 and ST 065 vs preterm infant formula	During hospital stay; 2–5 weeks	Reduced incidence of abdominal distension in infants fed preterm fermented formula

Figure adapted from Salminen S, et al. *Nat Rev Gastroenterol Hepatol.* 2021 Sep;18(9):649-667.

Synbiotics

Define: “a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host”

2 subtypes:

Synergistic synbiotic

Complementary synbiotic

Swanson KS. *et al. Nat Rev Gastroenterol Hepatol* **17,** 687–701 (2020).

Synbiotics

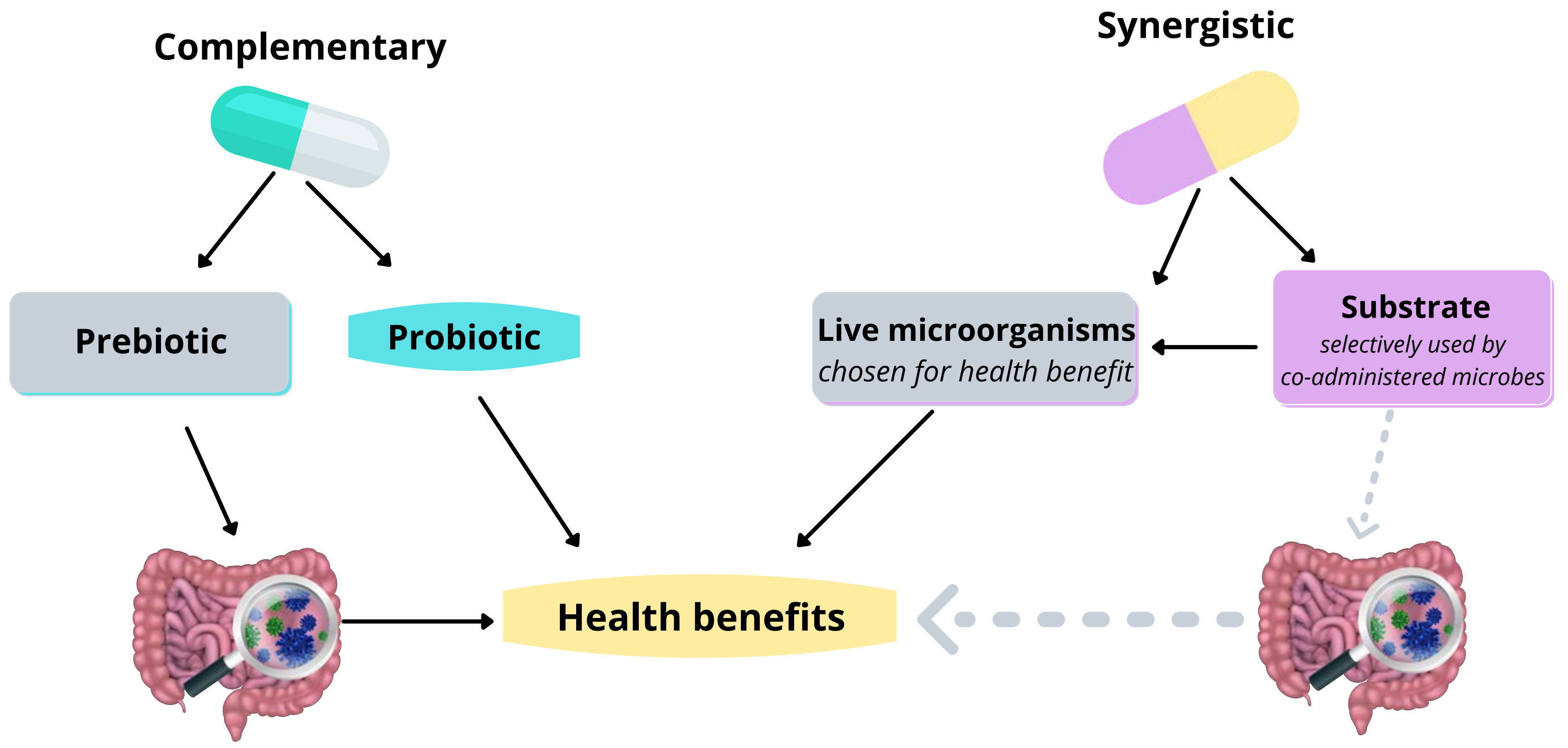
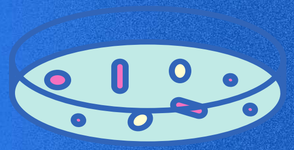


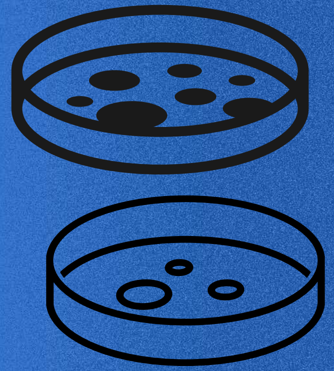
Figure adapted from Swanson KS. *et al. Nat Rev Gastroenterol Hepatol* **17,** 687–701 (2020).

The Shaping of Our Gut Microbiota

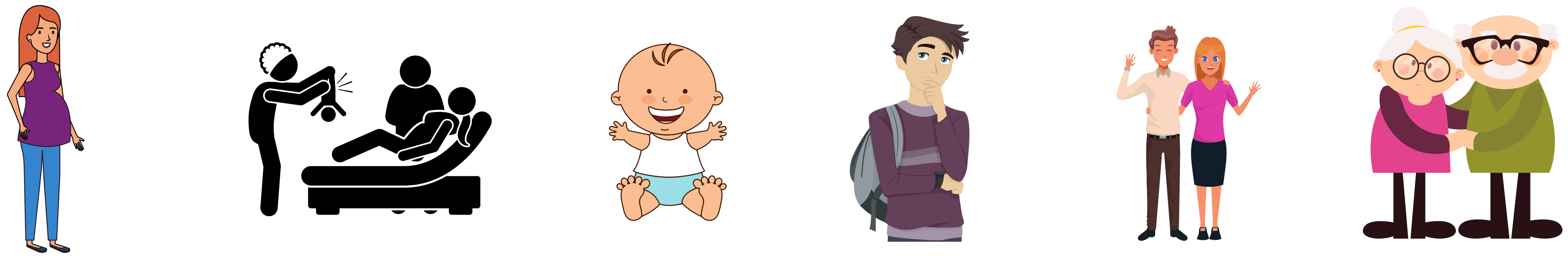
FETUS	BIRTH/FEEDING METHOD	WEANING	3 YRS-ADULT
uterine	c-section vs. vaginal birth Breast vs formula Antibiotic exposure	Solid foods	High fiber diet Western diet low fiber, high animal protein





Nagpal R, et al.. *Nutr Healthy Aging*. 2018;4(4):267-285. Figure adapted from Tanaka M, Nakayama J.. Allergol Int. 2017;66(4):515-522.



Factors that may impact gut microbiota composition + diversity during life stages

- Gestational health/DM
- Diet
- Antibiotics
- Probiotics + Prebiotics
- Bacteria in amniotic fluid
- Lifestyle
- Hygiene

- Mode of delivery
- Birth weight
- Environment
- Antibiotics
- Maternal flora
- Hospital flora

- Mode of feeding
- Fatty acids in breast milk
- Type of formula
- Siblings
- Pets
- Dust/hygiene
- Probiotics
- Antibiotics

- Diet
- Geography
- Hygiene
- Drugs
- Friends
- Malnutrition
- Allergies
- Pets
- Pro-Pre-biotics

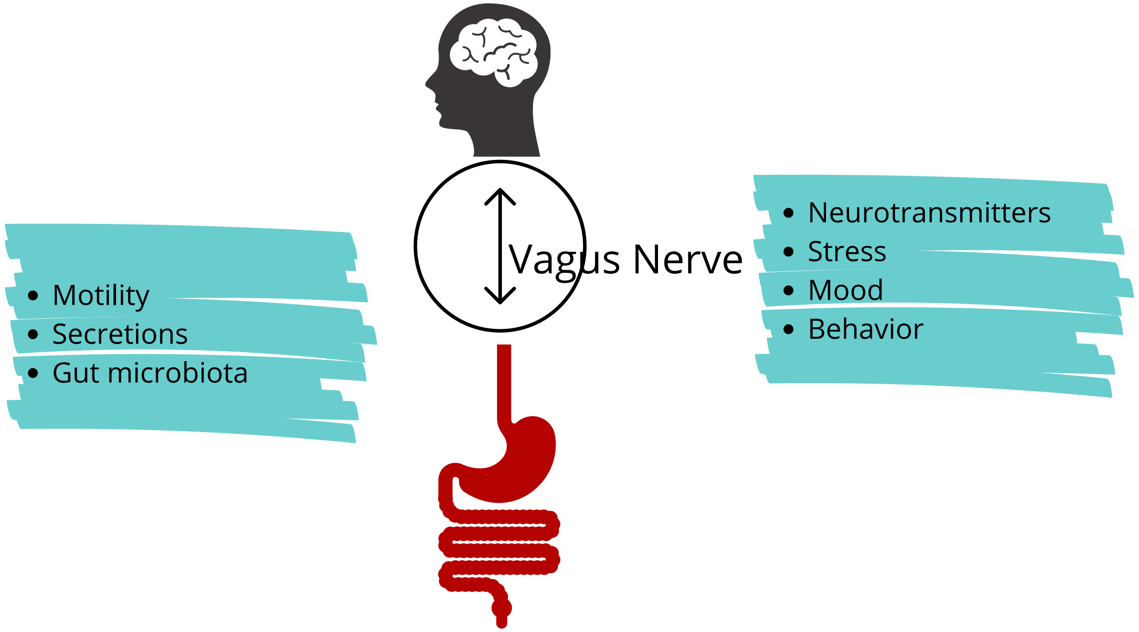
- Diet
- Lifestyle
- Antibiotics
- Probiotics
- Sleep
- Pregnancy
- Disease
- Travel

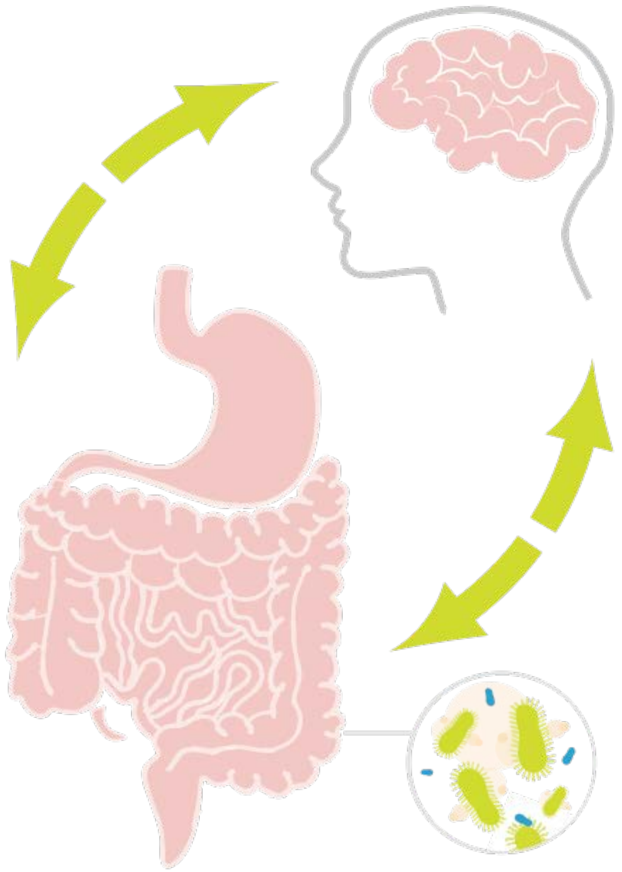
- Diet
- Lifestyle
- Age related illnesses
- Hospital stays
- Hygiene
- Menopause
- Drugs

Figure adapted from Nagpal R,, et al.. *Nutr Healthy Aging*. 2018;4(4):267-285.

The Brain-Gut Connection

- *Enteric nervous system + central nervous system highly linked*
- *Example: Stressful event—induces an emergent trip to the bathroom—or GI symptoms lead to anxiety*





Gut-Brain Axis (GBA)

- Gut microbiota regulates neurotransmitters/ brain chemicals such as: serotonin (alters precursors), GABA, dopamine
- When gut bacteria diversity diminishes, there are systemic consequences, such as GI and psychological distress

Dinan, TG, Cryan, JF The Microbiome-Gut-Brain Axis in Health and Disease Gastroenterol Clin N Am 2017;77-89., Del Toro-Barbosa M et al Nutrients. 2020;12(12):3896. Published 2020 Dec 19. Salminen, S *et al.* . *Nat Rev Gastroenterol Hepatol* **18,** 649–667 (2021).

Stress-Induced Gut Microbiome Changes

Stress exposure has been shown to change the composition of the gut microbiome and worsen intestinal inflammation

Stress exposure has a profound effect on microbiome diversity, multiple genera, and mucosal inflammation

Gut microbiota contribute to dysregulation of mucosal inflammatory responses during stress

Maltz RM, et al. *J Pediatr Gastroenterol Nutr*. 2019;68(4):533-540.

GI Tract, Microbes + Immune Response

- Colonization of gut microbes is necessary for normal immune system development, as indicated by the loss of immune function in germ-free mice
  - Microbiota stimulates immune cells through their metabolites. (e.g., SCFA + proliferation of T cells)
- Probiotic bacteria interact with the intestinal epithelial cells or immune cells associated with the lamina propria, through Toll-like receptors, and induce the production of different cytokines or chemokines
- Probiotics proposed to maintaining gut microbial balance - suppressing the growth of potential pathogenic bacteria in the gut

Maldonado Galdeano C, et al. Ann Nutr Metab. 2019;74(2):115-124, Tanaka M, Nakayama J. Development of the gut microbiota in infancy and its impact on health in later life. *Allergol Int.* 2017;66(4):515-522.

Gut Health, Immune Function, + Microbes

Specific probiotics influence the acquired and innate immune response by inducing phagocytosis and IgA secretion.

Specific probiotics alleviate intestinal inflammation and down-regulate hypersensitivity reactions.

Specific probiotics shown to inhibit growth of pathogenic microbes:
Lactobacillus rhamnosus strain GG can inhibit attachment of Escherichia coli in GI tract

Specific probiotics have been shown to strengthen intestinal barrier. Lactobacillus species increase mucin + increasing goblet cells which reinforce mucin layer.

Some microbes produce SCFA, e.g., butyrate, acetate which can suppress pro-inflammatory cytokines and bacteriocins which may reduce cancer risk + inflammation

Kechagia M, et al. *ISRN Nutr*. 2013;2013:481651.. Isolauri E, et al. *The American Journal of Clinical Nutrition* 2001; 73(2): 444s–450s. Smith PM,, et al. *Science*. 2013;341(6145):569–73.
Maldonado Galdeano C,et al. Ann Nutr Metab. 2019;74(2):115-124..

Attributes of a Healthy Gut Microbiome

- **Stability:** resist change in the setting of an ecologic stress (resistance) or to return to an equilibrium state following a stress-related perturbation (resilience)
- **Balance** of microbiota
  - Some microbial distributions may increase risk of infection or disease. E.g. antibiotics can put an individual at risk for *Clostridium difficile*
  - Microbiota can shift with changes in age, diet, geographical location, intake of food supplements and drugs
- Microbial **diversity**
  - The lack of sufficient diversity or evenness in a bacterial community structure appears to diminish its ability to withstand perturbation - e.g., obesity + IBD have reduced diversity

- Lifestyle factors can play a role in *positively* impacting these important gut microbiome attributes…

Bäckhed F et al. Cell Host Microbe. 2012 Nov 15;12(5):611-22.. PMID: 23159051. Tanaka M, Nakayama J. Allergol Int. 2017 Oct;66(4):515-522.

Exercise: Many Benefits

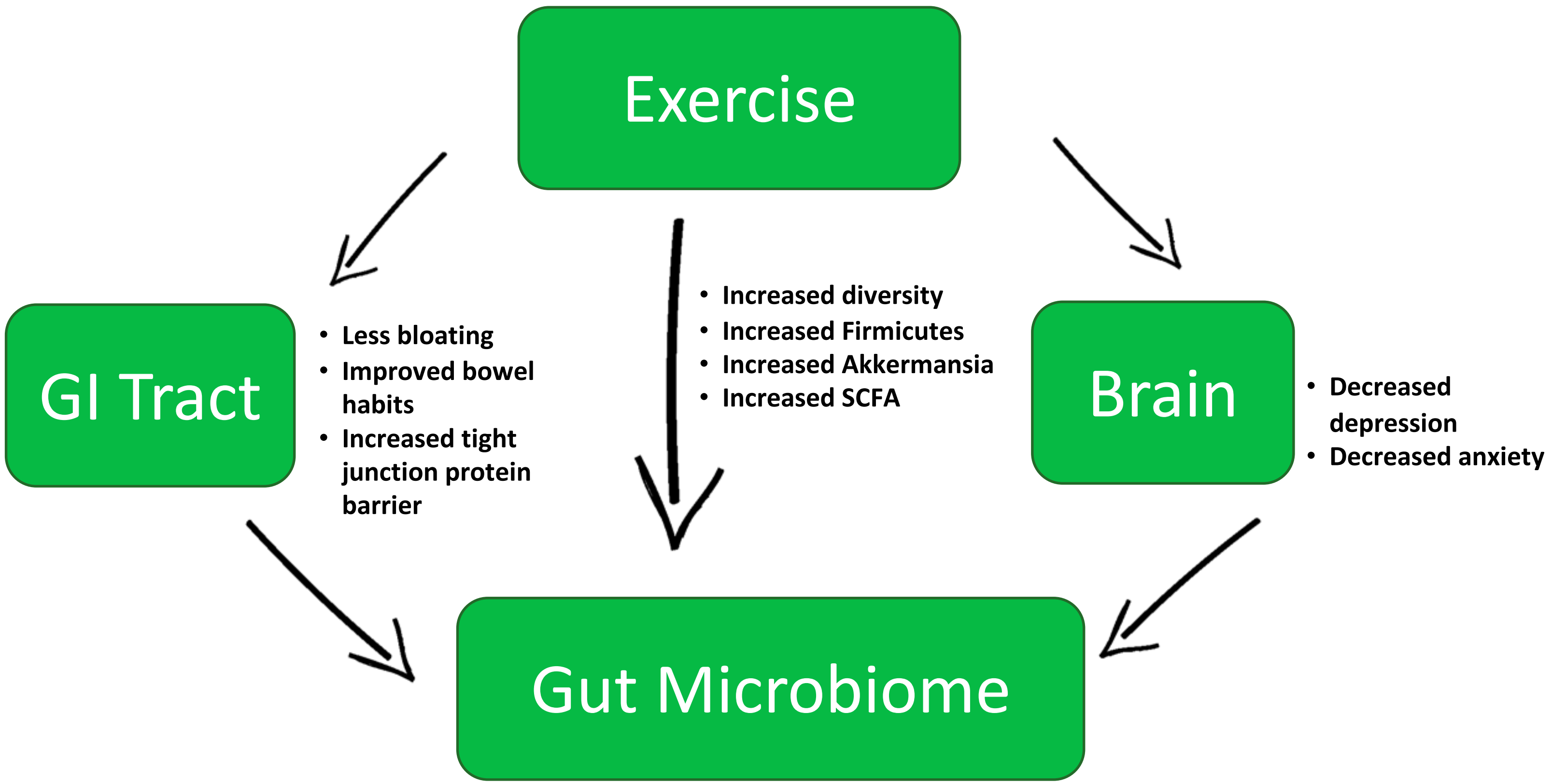


Figure adapted from Dalton A et al. *Gut Microbes*. 2019;10(5):555-568.

Exercise, Gut Microbiome, + Health

- Exercise increases gut microbial produced SCFA, butyrate
  - Study: active women + sedentary controls. Women who performed at least 3 h of exercise per week had increased levels of *Faecalibacterium prausnitzii*, *Roseburia hominis*, and *Akkermansia muciniphila*. *F. prausnitzii* and *R. hominis* are known butyrate producers
- Exercises reduces transit time—one way it may modulates the microbiome
- Reduces colon cancer risk -may be in part due to gut microbiome effects (e.g., increase in butyrate, transit effects)
- Many studies in athletes did not control for diet—major limitation in the research

Mailing, LJ et al, Exercise and Sport Sciences Reviews: 2019 ; 47 (2) 2:75-85.

Sleep

Small sleep and gut microbiome study n=26
Results: microbiome diversity was positively correlated with sleep efficiency, and total sleep time, and was negatively correlated with the sleep fragmentation.[1]

In humans, previous research has shown that partial sleep deprivation can alter the gut microbiome composition in as little as 48 hours.[2]

High sleep quality was associated with a gut microbiome containing a high proportion of bacteria from the *Verrucomicrobia* and *Lentisphaerae* phyla, and that this was associated with improved performance on cognitive tasks.[3]

1. Smith RP, et al.. *PLoS One*. 2019;14(10):e0222394, 2. Benedict C. et al.. *Mol Metab*. 2016;5(12):1175–86.
3. Anderson JR,, et al. *Sleep Med*. 2017;38:104–7.

Healthy Diet and Gut Microbiome

- Population-based study sample consisted of 4930 participants (ages 25–74; 53% women)- large, Finnish, population-based study sample
- Created a healthy food choices (HFC) score- A healthy food choices (HFC) score was formed by choosing and summing FPQ responses to food items that are recommended in the Nordic Nutrition Recommendations dietary guidelines
- **Plant- and fiber-rich dietary choices** (higher HFC score) are associated with a more diverse and compositionally distinct microbiota, and with a greater potential to produce SCFAs
- Known SCFA-producing species, *Faecalibacterium prausnitzii, Akkermansia muciniphila*, and *Roseburia intestinalis*, were all significantly elevated in individuals with a higher HFC score in this study

See corresponding editorial on page 420.

Associations of healthy food choices with gut microbiota profiles

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ABSTRACT

Background: Diet has a major influence on the human gut microbiota, which has been linked to health and disease. However, epidemiological studies on associations of a healthy diet with the microbiota utilizing a whole-diet approach are still scant.

Objectives: To assess associations between healthy food choices and human gut microbiota composition, and to determine the strength of association with functional potential.

Methods: This population-based study sample consisted of 4930 participants (ages 25–74; 53% women) in the FINRISK 2002 study. Intakes of recommended foods were assessed using a food propensity questionnaire, and responses were transformed into healthy food choices (HFC) scores. Microbial diversity (alpha diversity) and compositional differences (beta diversity) and their associations with the HFC score and its components were assessed using linear regression. Multiple permutational multivariate ANOVAs were run from whole-metagenome shallow shotgun–sequenced samples. Associations between specific taxa and HFC were analyzed using linear regression. Functional associations were derived from Kyoto Encyclopedia of Genes and Genomes orthologies with linear regression models.

Results: Both microbial alpha diversity (β/SD, 0.044; SE, 6.18×10^{-5}; $P = 2.21 \times 10^{-3}$) and beta diversity (R^2, 0.12; $P \leq 1.00 \times 10^{-3}$) were associated with the HFC score. For alpha diversity, the strongest associations were observed for fiber-rich breads, poultry, fruits, and low-fat cheeses (all positive). For beta diversity, the most prominent associations were observed for vegetables, followed by berries and fruits. Genera with fiber-degrading and SCFA-producing capacities were positively associated with the HFC score. The HFC score was associated positively with functions such as SCFA metabolism and synthesis, and inversely with functions such as fatty acid biosynthesis and the sulfur relay system.

Conclusions: Our results from a large, population-based survey confirm and extend findings of other, smaller-scale studies that plant- and fiber-rich dietary choices are associated with a more diverse and compositionally distinct microbiota, and with a greater potential to produce SCFAs. *Am J Clin Nutr* 2021;114:605–616.

Keywords: cross-sectional study, dietary score, epidemiology, healthy diet, metagenomics, microbiology, microbiota, nutrition

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The study was designed, implemented, analyzed, and interpreted independent of all the entities supporting the project.

Supplemental Figures 1–3, Supplemental Tables 1–6, and Supplemental Methods are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: ANOSIM, analysis of similarities; dbRDA, distance-based redundancy analysis; FPQ, food propensity questionnaire; HFC, healthy food choices; KO, Kyoto Encyclopedia of Genes and Genomes orthology; MaAsLin, multivariate association with linear models; PCA, principal coordinate analysis; PERMANOVA, permutational multivariate analysis of variance.

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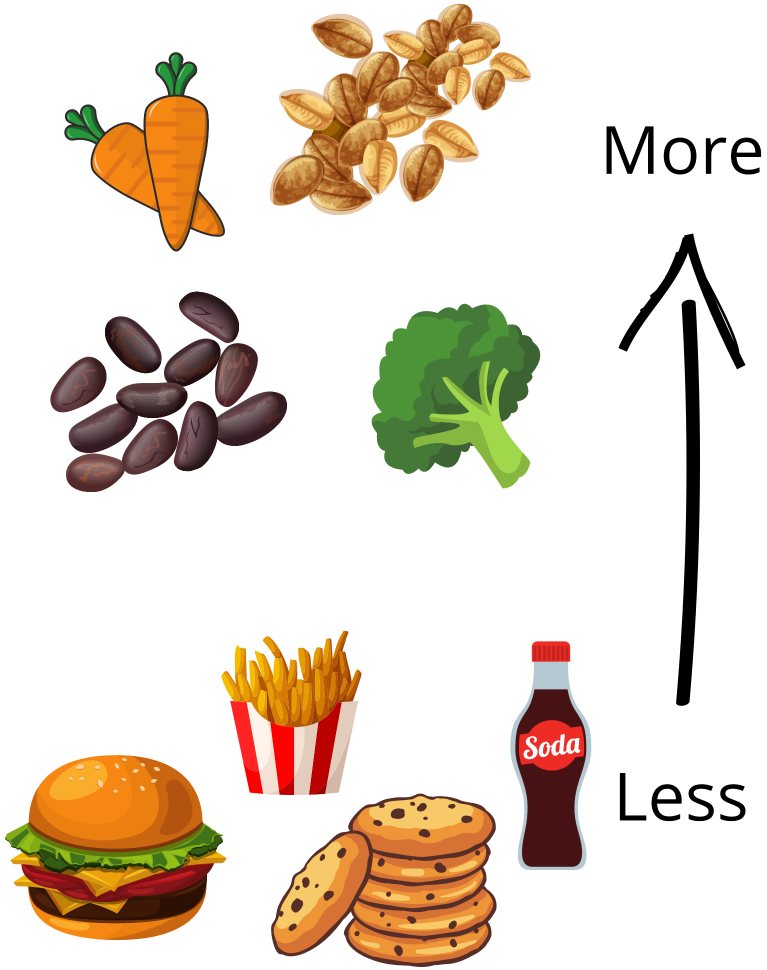
Koponen K, et al *The American Journal of Clinical Nutrition* 2021; 114 (2);605-616.

Eat More Plants!



Western diet + low-grade intestinal inflammation are implicated in a growing number of immune-mediated inflammatory diseases

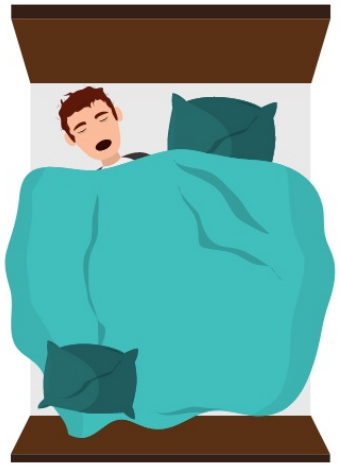
Higher intake of animal foods, processed foods, alcohol and sugar, associated with higher levels of intestinal inflammatory markers + corresponds to an inflammatory microbial environment

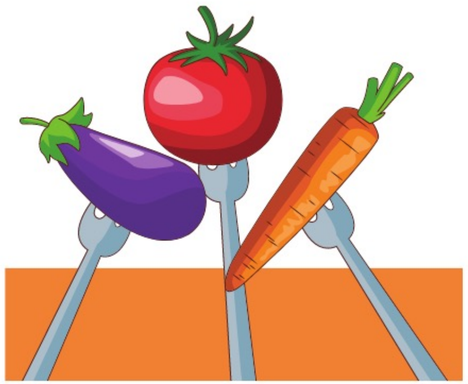
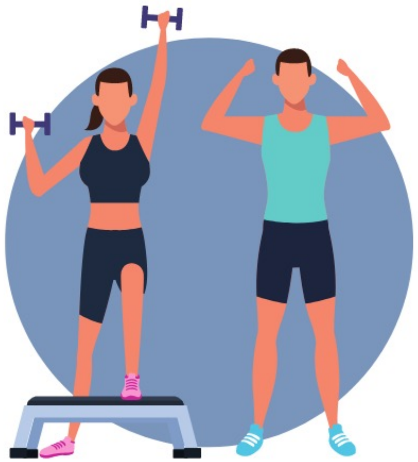
Plant-based foods are linked to short-chain fatty acid (SCFA)-producers, microbial metabolism of polysaccharides and a lower abundance of pathobionts

Bolte LA, et al. Gut. 2021 Jul;70(7):1287-1298.

Summary

- As the gut microbiome science is still in its infancy, the role of probiotics, prebiotics, synbiotics, and postbiotics will continue to evolve
- An individual's gut microbiome is as unique as their fingerprint—and individualized treatments will likely be key to success
- Beyond prebiotics, probiotics, synbiotics and postbiotics, lifestyle factors can impact our gut microbiome, such as:
    - Stress management
    - Sleep hygiene
    - Plant-rich diet
    - Exercise



Summary

- Probiotics -select strain specific data, proper dosing for symptomology reduction and/or desired health outcome
- The future: targeted treatments based on gut microbiome and personalized medicine
- Dietitian stay informed! Since diet, pro-pre-syn-biotics + fermented foods are a key modifiable factors influencing the composition of the gut microbiota, adjust clinical guidelines as dictated by the science!

Questions & Answers

Kate Scarlata MPH, RDN
www.katescarlata.com

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