The microbes we eat (or should be eating)

Bob Hutkins

April 21, 2023

Nebraska Academy of Nutrition & Dietetics

NAND
Nebraska Academy of Nutrition and Dietetics
eat right. an affiliate of the Academy of Nutrition and Dietetics

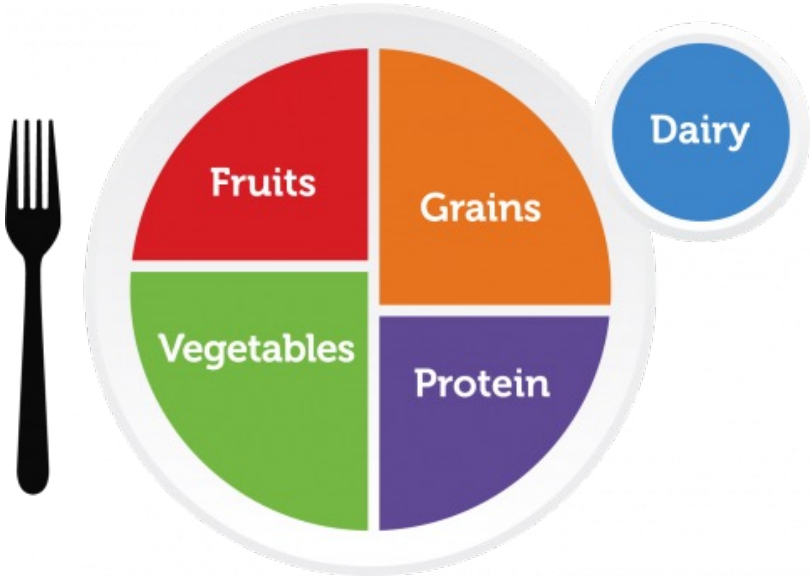
Food Science and Technology Department
Impacting the World Three Times a Day

NEBRASKA FOOD FOR HEALTH CENTER
at the University of Nebraska

University of Nebraska Lincoln

Disclosures: *Recipient of grants from food and supplement companies and founding partner of Synbiotic Health*

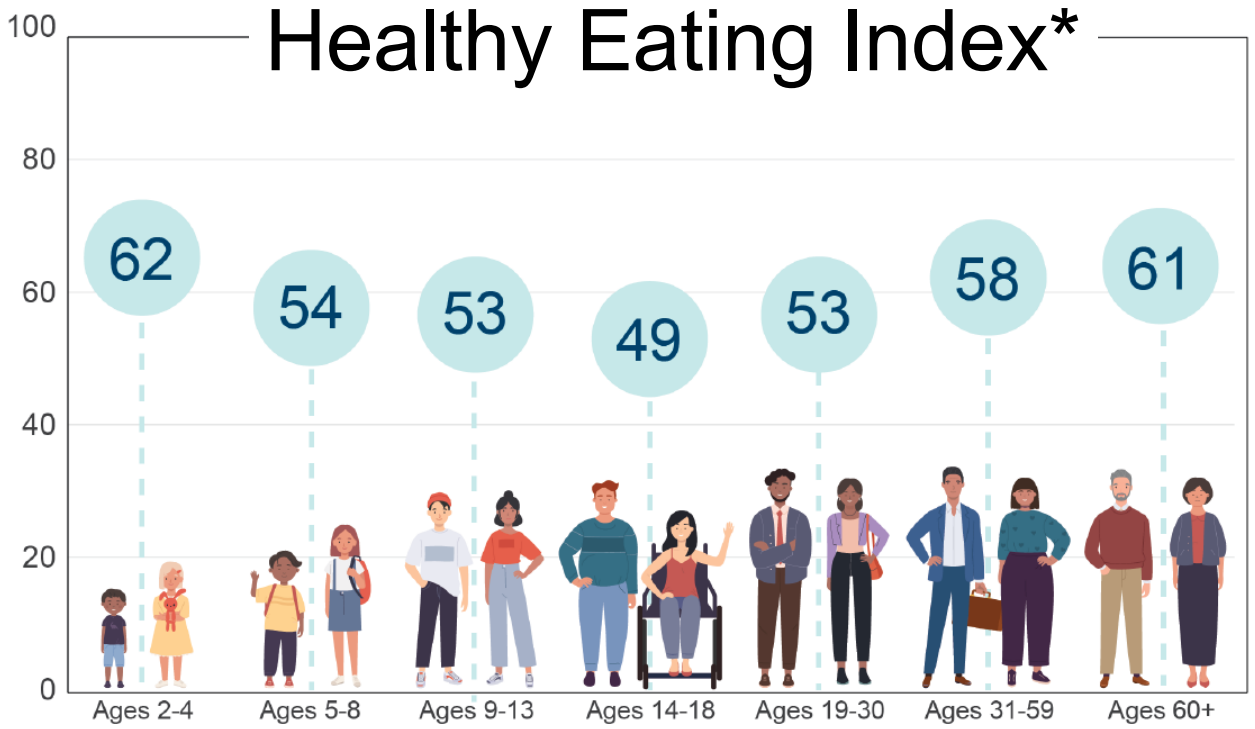
What are Americans eating in 2023?



The Western Diet
(what many, if not most Americans eat)

The American diet scores only 58% based on nutrient quality

HEI Score
(maximum = 100)



* From WWEIA/NHANES 2017-2018 and the *Dietary Guidelines* recommendations

The Bob Diet
(what few Americans eat)

Yogurt with Granola for Breakfast

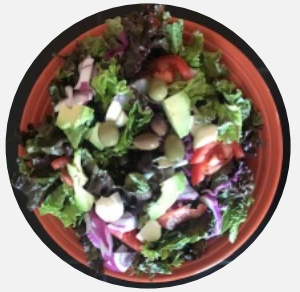
Salad for Lunch

Fresh Fruit for Snack

Tempeh Reuben For Dinner

Apart from sugar, fat, salt, calories, and other macro- and micro-nutrients, what's the main difference between these diets?

Live microbes + prebiotic fibers



The importance of live microbes in the human diet

1. What is the rationale for eating live microbes?

2. If so, which foods are good sources?

3. Does is matter **which** microbes we eat
   (i.e., is one microbe just as good as another?)

4. What is the evidence to support the hypothesis?

It’s a microbial world

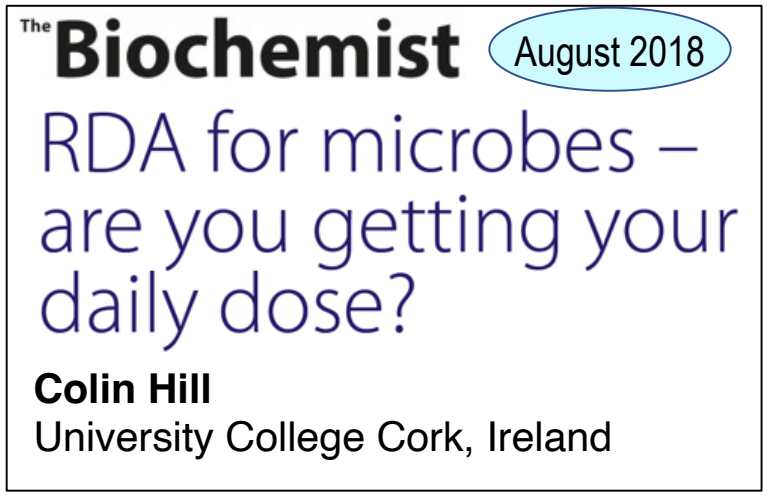
“If you don’t like bacteria, you’re on the wrong planet. This is the planet of the bacteria”

Craig Venter, American geneticist, as reported in a Los Angeles Times interview, November 2007.

Indeed, there are as many live bacteria in a cup of yogurt as there are humans on the planet (ca. 8B)

=

The premise is simple: Consuming live microbes in foods may benefit human health



… in addition to RDAs for nutrients and vitamins, dietary guidelines should also advise consumers to include ***safe*** *microbes in their diets … by recommending increased* ***consumption of fermented foods”***

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS

Goals of the Live Microbe Panel

1. Estimate consumption of foods containing live microbes
2. Model consumption with disease risk.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Rationale, justification, and planning

The Journal of Nutrition
Nutritional Epidemiology

December 2020

Should There Be a Recommended Daily Intake of Microbes?

Maria Marco, Colin Hill, Robert Hutkins, Joanne Slavin, Daniel Tancredi, Daniel Merenstein, Mary E Sanders

Results, Part 1. Consumption of live dietary microbes

The Journal of Nutrition
Nutritional Epidemiology

July 2022

A Classification System for Defining and Estimating Dietary Intake of Live Microbes in US Adults and Children

Maria Marco, Robert Hutkins, Colin Hill, Victor L Fulgoni, III, Christopher Cifelli, Jaime Gahche, Joanne Slavin, Daniel Merenstein, Daniel Tancredi, Mary E Sanders

1. Why should we be eating live microbes?

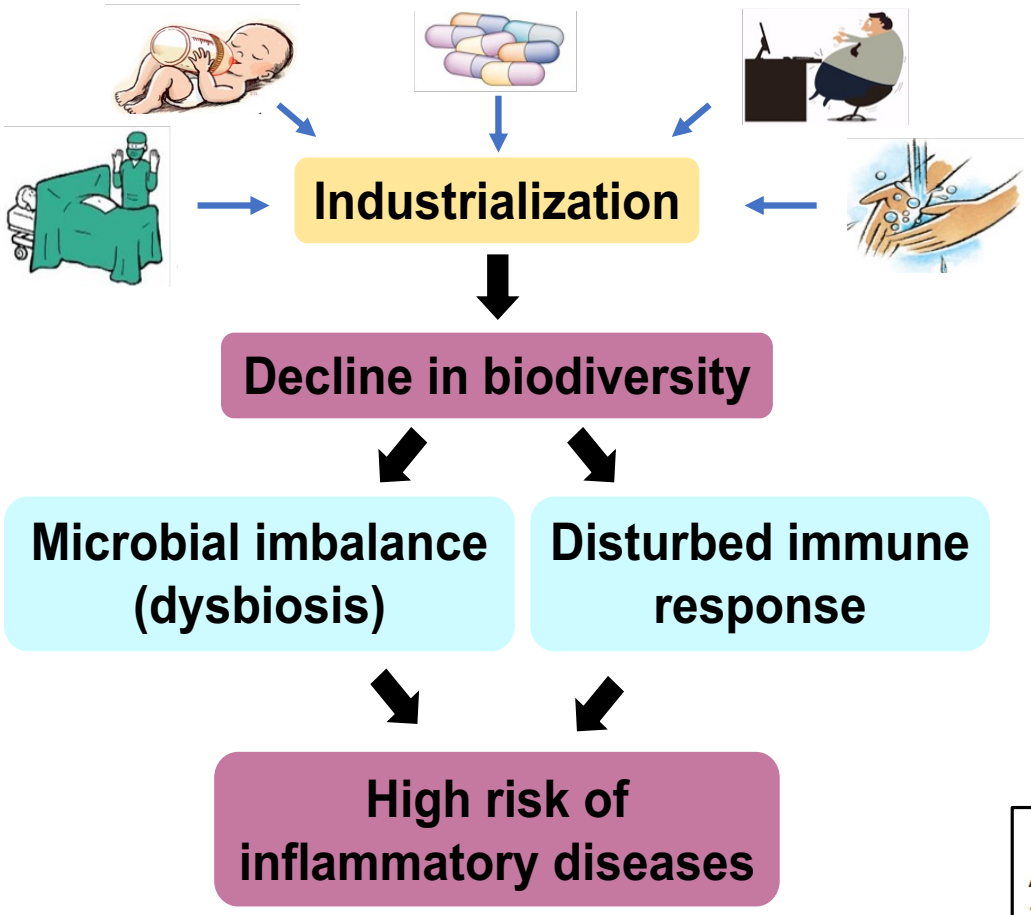
The New England Journal of Medicine 2002

EAT DIRT — THE HYGIENE HYPOTHESIS AND ALLERGIC DISEASES

*"Eating dirt or moving to a farm are **theoretical** rather than practical ...*

However, supplementation with Lactobacillus, a dog in the home, attendance at day care are factors that protect against development of allergies"

Old Friends Hypothesis (aka the **Biodiversity Hypothesis)**



A Darwinian View of the Hygiene or "Old Friends" Hypothesis

When urban living reduced contacts of humans with microbes and worms, it increased our risk for chronic inflammatory disorders

Graham A. W. Rook Microbe, 2012, 7

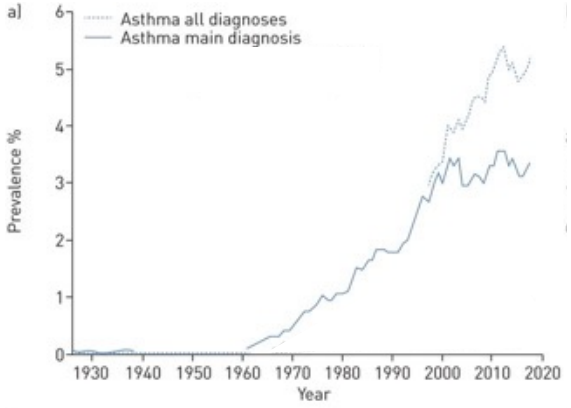
Allergy 2019;74:1445–1456

A biodiversity hypothesis

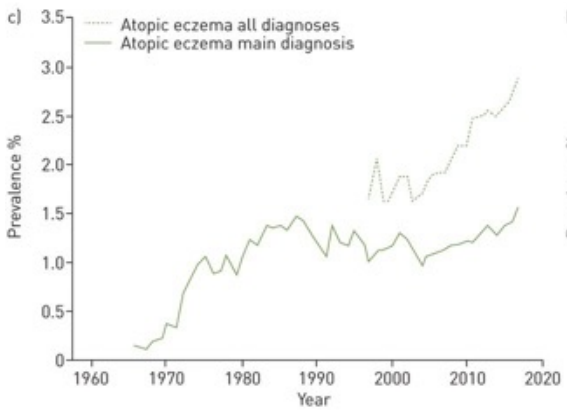
Tari Haahtela

Prevalence of allergic diseases in Finnish men: **From non-existent in 1960 to major health burden**

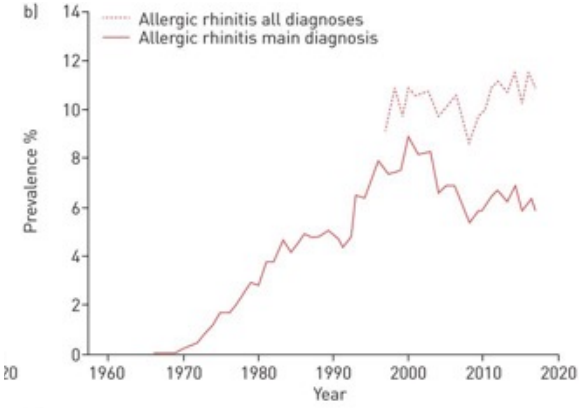
Asthma



Atopic eczema



Allergic rhinitis



Long-term trends of asthma, allergic rhinitis and atopic eczema in young Finnish men: a retrospective analysis, 1926–2017

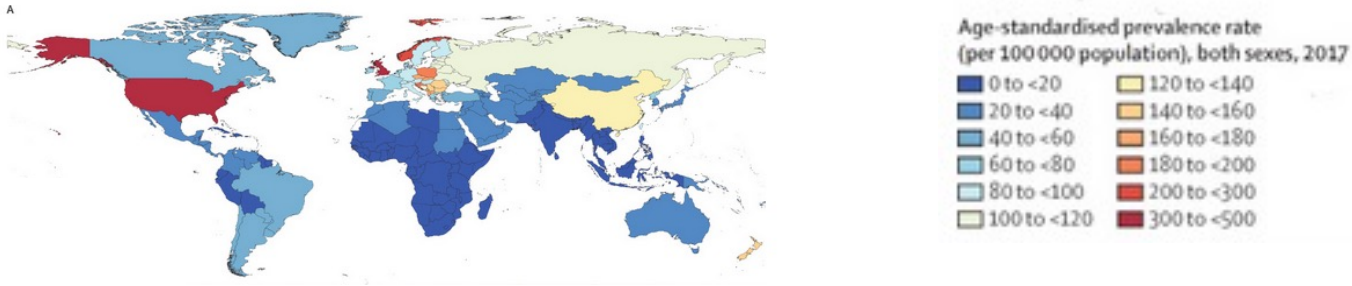
Jere Reijula[1,2], Jari Latvala[3], Mika Mäkelä[4], Simo Siitonen[5], Mari Saario[5] and Tari Haahtela[4]

Eur Respir J 2020; 56: 1902144

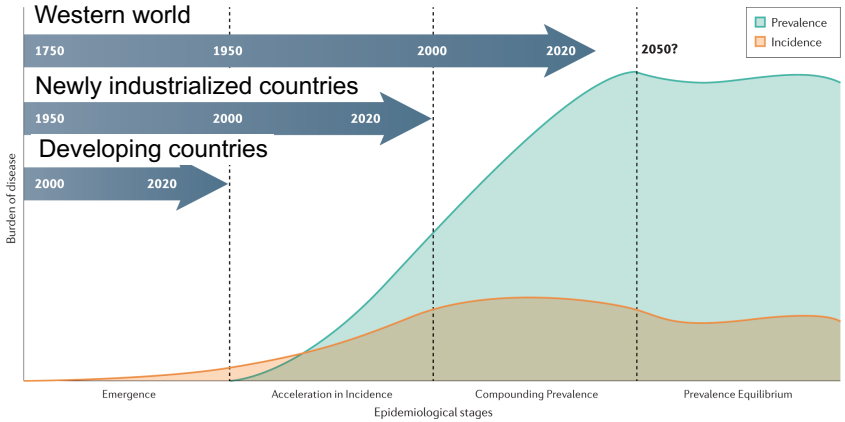
"The changes in environment and lifestyle, affecting microbial exposure and immune regulation, seem to play a major role in the so-called post-war allergy epidemic"

Global incidence of Inflammatory Bowel Diseases (IBDs)

Prevalence rate (per 100,000 population) of IBD in 2017



Epidemiological trajectory of IBD

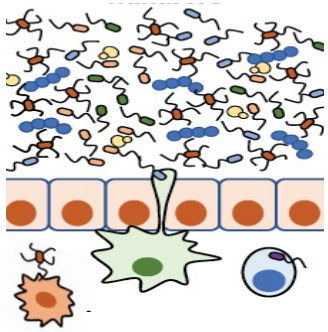


"… risk factors include urbanisation, hygienic environments, and diets low in dietary fibre …"

Lancet Gastroenterol. Hepatol, 2020, 5, 17-30 and Nature Rev Gastroenterol Hepatol 2021, 18, 56-66

Early human diet

High diversity



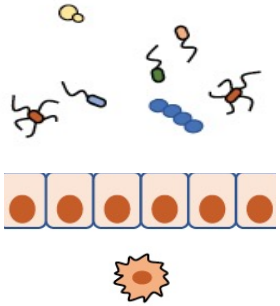
Trained immune system

Tolerance

Adaptation to modern life

Industrialized diet

Low diversity



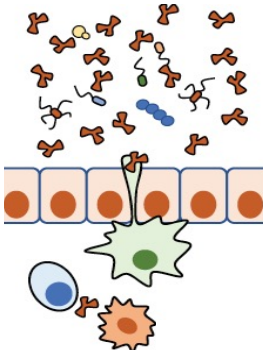
Untrained immune system

Inflammation

Exposure to safe microbes

Microbe-rich diet

Restored diversity

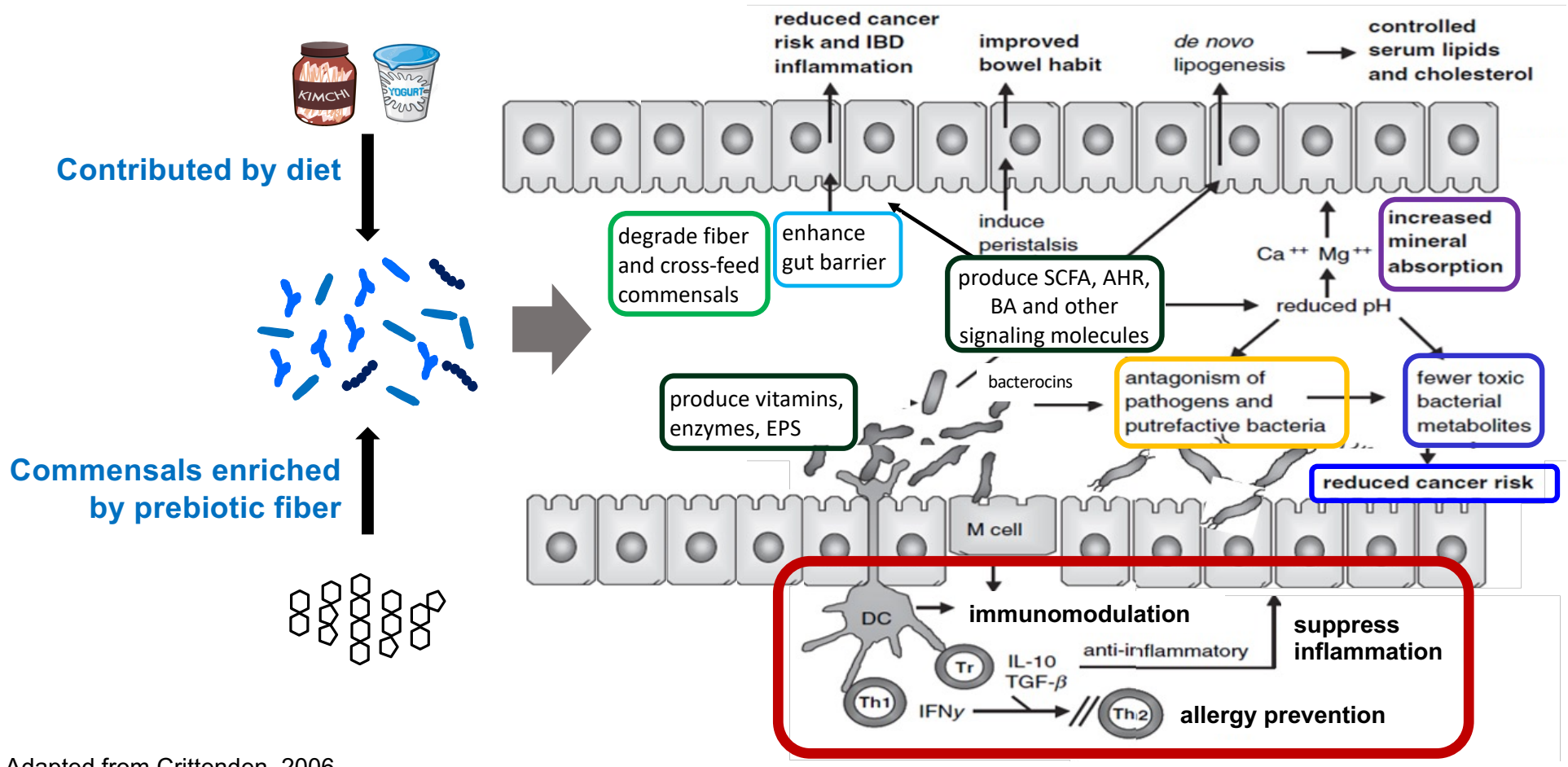


Re-trained immune system

Tolerance

Adapted from Marco et al., 2020

The role of beneficial live microbes in the gut



Adapted from Crittenden, 2006.

First a caveat: Industrialization has plenty of positives

- Prior to pasteurization, raw milk (among other foods) carried *M. tuberculosis, Salmonella*, and other pathogens
- Food processing made foods safe, with enhanced shelf-life and year-round availability.
- Nonetheless, many dietary microbes have been lost due to processing and improved hygiene, reducing microbial diversity

1. Why should we be eating live microbes?

2. If so, which foods are good sources?

What food consumption data base to use?

National Health and Nutrition Examination Survey

- Cross-sectional survey of adults and children for diet, exercise, and health status
- Large number of participants (> 70,000)
- Data is based on 24-hour recall, collected every other year.
- Using NHANES data, it is possible to correlate food consumption to health status

Step 1. Estimating live microbes in foods

- The NHANES database has **9,388** food codes for individual products
- These were divided roughly in half among **two teams of experts (two per team)**
- Each team ranked each product for microbe content where:

Low < 10^4 CFU/g

Medium = 10^4 – 10^7 CFU/g

High > 10^7 CFU/g

Arbitrary categories, but it was not possible to be more precise

- Experts worked independently, reconciling differences when needed
- Experts relied on published literature, including primary studies and reviews

Lots and lots of foods to assess mostly Lo

Foodcode	Description	Assigned category
58106705	Pizza with meat and vegetables, fro	Lo
58106710	Pizza with meat and vegetables, NS	Lo
58106720	Pizza with meat and vegetables, fro	Lo
58106725	Pizza with meat and vegetables, fro	Lo
58106730	Pizza with meat and vegetables, fro	Lo
58106733	Pizza with extra meat and extra veg	Lo
58106734	Pizza with extra meat and extra veg	Lo
58106735	Pizza with extra meat and extra veg	Lo
58106736	Pizza with extra meat and extra veg	Lo
58106737	Pizza with extra meat and extra veg	Lo
58106738	Pizza with extra meat and extra veg	Lo
58106740	Pizza with meat and fruit, NS as to	Lo
58106750	Pizza with meat and fruit, thin crust	Lo
58106755	Pizza with meat and fruit, medium c	Lo
58106760	Pizza with meat and fruit, thick crus	Lo
58106780	Pizza with meat and vegetables, pr	Lo
58106820	Pizza with beans and vegetables, th	Lo
58106830	Pizza with beans and vegetables, th	Lo
58106910	Pizza with seafood, thin crust	Lo
58106915	Pizza with seafood, regular crust	Lo
58106920	Pizza with seafood, thick crust	Lo
58107030	Pizza, no cheese, NS as to type of	Lo
58107050	Pizza, no cheese, thin crust	Lo
58107060	Pizza, no cheese, regular crust	Lo
58107100	Pizza, no cheese, thick crust	Lo
58107205	White pizza, cheese, thin crust	Lo
58107210	White pizza, NS as to type of crust	Lo
58107212	White pizza, cheese, with vegetable	Lo
58107220	White pizza, thin crust	Lo
58107222	White pizza, cheese, with meat, thi	Lo
58107224	White pizza, cheese, with meat, thi	Lo
58107225	White pizza, regular crust	Lo
58107230	White pizza, thick crust	Lo

Foodcode	Description	Assigned category
63201800	Blackberries, frozen, sweetened, N	Lo
63203110	Blueberries, canned	Lo
63203120	Blueberries, cooked or canned, uns	Lo
63203130	Blueberries, cooked or canned, in h	Lo
63203700	Blueberry pie filling	Lo
63207000	Cranberries, NS as to raw, cooked,	Lo
63207110	Cranberry sauce	Lo
63219110	Raspberries, cooked or canned, NS	Lo
63219120	Raspberries, cooked or canned, un	Lo
63219130	Raspberries, cooked or canned, in	Lo
63223110	Strawberries, canned	Lo
63223120	Strawberries, cooked or canned, un	Lo
63223130	Strawberries, cooked or canned, in	Lo
63301010	Ambrosia	Lo
63307010	Cranberry-orange relish, uncooked	Lo
63307100	Cranberry-raspberry Sauce	Lo
63311110	Fruit cocktail, canned, NFS	Lo
63311120	Fruit cocktail, cooked or canned, un	Lo
63311130	Fruit cocktail, cooked or canned, in	Lo
63311140	Fruit cocktail, canned, in syrup	Lo
63311145	Tropical fruit cocktail, cooked or ca	Lo
63311150	Fruit cocktail, cooked or canned, dr	Lo
63311170	Fruit cocktail, canned, juice pack	Lo
63401060	Apple, candied	Lo
63401070	Fruit, chocolate covered	Lo
63401990	Banana, chocolate-covered with nu	Lo
63402045	Fried dwarf banana, Puerto Rican s	Lo
63402990	Fruit salad, including citrus fruits, w	Lo
63403000	Fruit salad, excluding citrus fruits, w	Lo
63403100	Fruit dessert with cream and/or puc	Lo
63406010	Guacamole with tomatoes	Lo
63406200	Guacamole with tomatoes and chili	Lo
63409010	Guacamole, NFS	Lo

Foodcode	Description	Assigned category
41103020	Lima beans, dry, cooked, fat not ad	Lo
41103050	Pink beans, dry, cooked, NS as to f	Lo
41103060	Pink beans, dry, cooked, fat not ad	Lo
41103070	Pink beans, cooked	Lo
41103090	Pink beans, canned, drained, fat ac	Lo
41103100	Pink beans, canned, drained, fat no	Lo
41103990	Pinto beans, NFS	Lo
41104000	Pinto, calico, or red Mexican beans	Lo
41104010	Pinto beans, from dried, fat added	Lo
41104011	Pinto, calico, or red Mexican beans	Lo
41104012	Pinto, calico, or red Mexican beans	Lo
41104013	Pinto, calico, or red Mexican beans	Lo
41104020	Pinto beans, from dried, no added f	Lo
41104030	Pinto, calico, or red Mexican beans	Lo
41104040	Pinto beans, from canned, fat adde	Lo
41104050	Pinto, calico, or red Mexican beans	Lo
41104060	Pinto, calico, or red Mexican beans	Lo
41104080	Pinto beans, from canned, no adde	Lo
41104110	Pinto beans, from canned, reduced	Lo
41104120	Pinto, calico, or red Mexican beans	Lo
41104200	Pinto beans, from fast food / restau	Lo
41104250	Pinto beans with meat	Lo
41105990	Kidney beans, NFS	Lo
41106000	Red kidney beans, dry, cooked, NS	Lo
41106010	Kidney beans, from dried, fat added	Lo
41106011	Red kidney beans, dry, cooked, ma	Lo
41106012	Red kidney beans, dry, cooked, ma	Lo
41106013	Red kidney beans, dry, cooked, ma	Lo
41106020	Kidney beans, from dried, no added	Lo
41106040	Kidney beans, from canned, fat add	Lo
41106050	Red kidney beans, canned, drained	Lo
41106080	Kidney beans, from canned, no add	Lo
41106100	Red kidney beans, canned, drained	Lo
41106110	Kidney beans, from canned, reduce	Lo

Lo

Foodcode	Description	Assigned category
11100000	Milk, NFS	Lo
11111000	Milk, whole	Lo
11111100	Milk, low sodium, whole	Lo
11111150	Milk, calcium fortified, whole	Lo
11111160	Milk, calcium fortified, low fat (1%)	Lo
11111170	Milk, calcium fortified, fat free (skim	Lo
11112000	Milk, cow's, fluid, other than whole,	Lo
11112110	Milk, reduced fat (2%)	Lo
11112210	Milk, low fat (1%)	Lo
11113000	Milk, fat free (skim)	Lo
11114300	Milk, lactose free, low fat (1%)	Lo
11114320	Milk, lactose free, fat free (skim)	Lo
11114330	Milk, lactose free, reduced fat (2%)	Lo
11114350	Milk, lactose free, whole	Lo
11116000	Goat's milk, whole	Lo
11120000	Milk, dry, reconstituted, NS as to fa	Lo
11121100	Milk, dry, reconstituted, whole	Lo
11121210	Milk, dry, reconstituted, low fat (1%	Lo
11121300	Milk, dry, reconstituted, fat free (ski	Lo
11210000	Milk, evaporated, NS as to fat conte	Lo
11210050	Milk, evaporated, NS as to fat conte	Lo
11210100	Milk, evaporated, NS as to fat conte	Lo
11211000	Milk, evaporated, whole, NS as to c	Lo
11211050	Milk, evaporated, whole	Lo
11211100	Milk, evaporated, whole, undiluted	Lo
11211200	Milk, evaporated, whole, diluted	Lo
11211400	Milk, evaporated, reduced fat (2%)	Lo
11212000	Milk, evaporated, skim, NS as to di	Lo
11212050	Milk, evaporated, fat free (skim)	Lo
11212100	Milk, evaporated, skim, undiluted	Lo
11220000	Milk, condensed, sweetened	Lo
11220100	Milk, condensed, sweetened, undilu	Lo

Lo

Foodcode	Description	Assigned category
21304000	Beef, shortribs, cooked, NS as to fa	Lo
21304110	Beef, shortribs, cooked, lean and fa	Lo
21304120	Beef, shortribs, cooked, lean only e	Lo
21304200	Beef, shortribs, barbecued, with sa	Lo
21304210	Beef, shortribs, barbecued, with sa	Lo
21304220	Beef, shortribs, barbecued, with sa	Lo
21305000	Beef, cow head, cooked	Lo
21401000	Beef, roast, roasted, NS as to fat e	Lo
21401110	Beef, roast, roasted, lean and fat e	Lo
21401120	Beef, roast, roasted, lean only eate	Lo
21401400	Beef, roast, canned	Lo
21407000	Beef, pot roast, braised or boiled, N	Lo
21407110	Beef, pot roast, braised or boiled, le	Lo
21407120	Beef, pot roast, braised or boiled, le	Lo
21410000	Beef, stew meat, cooked, NS as to	Lo
21410110	Beef, stew meat, cooked, lean and	Lo
21410120	Beef, stew meat, cooked, lean only	Lo
21416000	Corned beef, cooked, NS as to fat	Lo
21416110	Corned beef, cooked, lean and fat	Lo
21416120	Corned beef, cooked, lean only eat	Lo
21416150	Corned beef, canned, ready-to-eat	Lo
21417100	Beef brisket, cooked, NS as to fat e	Lo
21417110	Beef brisket, cooked, lean and fat e	Lo
21417120	Beef brisket, cooked, lean only eats	Lo
21420100	Beef, sandwich steak, flaked, forme	Lo
21500100	Ground beef, cooked	Lo
21500110	Ground beef, meatballs, meat only,	Lo
21500200	Ground beef or patty, breaded, coo	Lo
21500300	Ground beef patty, cooked (for fast	Lo
21500310	Ground beef patty, cooked	Lo
21501000	Ground beef, less than 80% lean, c	Lo
21501200	Ground beef, 80% - 84% lean, cook	Lo
21501300	Ground beef, 85% - 89% lean, cook	Lo

Lo

Foodcode	Description	Assigned category
26118023	Halibut, baked or broiled, no added	Lo
26118024	Halibut, baked or broiled, made wit	Lo
26118030	Halibut, coated, baked or broiled, n	Lo
26118050	Halibut, steamed or poached	Lo
26119100	Herring, raw	Lo
26119110	Herring, cooked, NS as to cooking	Lo
26119120	Herring, baked or broiled, fat added	Lo
26119121	Herring, baked or broiled, no added	Lo
26119130	Herring, coated, baked or broiled, fa	Lo
26119131	Herring, coated, baked or broiled, n	Lo
26119140	Herring, coated, fried	Lo
26119160	Herring, pickled, in cream sauce	Lo
26119180	Herring, pickled	Lo
26119190	Herring, smoked, kippered	Lo
26121100	Mackerel, raw	Lo
26121110	Mackerel, cooked, NS as to cookin	Lo
26121120	Mackerel, baked or broiled, fat adde	Lo
26121121	Mackerel, baked or broiled, no adde	Lo
26121140	Mackerel, coated, fried	Lo
26121160	Mackerel, pickled	Lo
26121180	Mackerel, canned	Lo
26123120	Mullet, baked or broiled, fat added	Lo
26123121	Mullet, baked or broiled, no added f	Lo
26123140	Mullet, coated, fried	Lo
26123160	Mullet, steamed or poached	Lo
26125110	Ocean perch, cooked, NS as to coo	Lo
26125120	Ocean perch, baked or broiled, fat a	Lo
26125121	Ocean perch, baked or broiled, no a	Lo
26125130	Ocean perch, coated, baked or broi	Lo
26125140	Ocean perch, coated, fried	Lo
26125150	Ocean perch, battered, fried	Lo
26125160	Ocean perch, steamed or poached	Lo
26127110	Perch, cooked, NS as to cooking m	Lo

Med

Foodcode	Description	Assigned category
63123020	Grapes, American type, slip skin, ra	Med
63125010	Guava, raw	Med
63129020	Mango, pickled	Med
63131010	Nectarine, raw	Med
63135010	Peach, raw	Med
63135610	Peach, frozen, NS as to added swe	Med
63135620	Peach, frozen	Med
63135630	Peach, frozen, with sugar	Med
63137010	Pear, raw	Med
63137050	Pear, Asian, raw	Med
63139010	Persimmon, raw	Med
63143010	Plum, raw	Med
63143650	Plum, pickled	Med
63200100	Berries, NFS	Med
63200200	Berries, frozen, NFS	Med
63201010	Blackberries, raw	Med
63201600	Blackberries, frozen	Med
63203010	Blueberries, raw	Med
63203550	Blueberries, frozen, sweetened	Med
63203570	Blueberries, frozen, NS as to sweet	Med
63203600	Blueberries, frozen	Med
63205010	Boysenberries, raw	Med
63205600	Boysenberries, frozen	Med
63207010	Cranberries, raw	Med
63214000	Huckleberries, raw	Med
63215010	Loganberries, raw	Med
63217010	Mulberries, raw	Med
63219000	Raspberries, raw	Med
63219020	Raspberries, red, raw	Med
63219600	Raspberries, frozen, NS as to adde	Med
63219610	Raspberries, frozen	Med
63219620	Raspberries, frozen, with sugar	Med
63223020	Strawberries, raw	Med

Med

Foodcode	Description	Assigned category
75107000	Cauliflower, raw	Med
75109000	Celery, raw	Med
75109010	Fennel bulb, raw	Med
75109400	Basil, raw	Med
75109500	Chives, raw	Med
75109550	Cilantro, raw	Med
75109600	Corn, raw	Med
75111000	Cucumber, raw	Med
75111200	Eggplant, raw	Med
75111800	Jicama, raw	Med
75112000	Kohlrabi, raw	Med
75112500	Leek, raw	Med
75113000	Lettuce, raw	Med
75113060	Lettuce, Boston, raw	Med
75113080	Lettuce, arugula, raw	Med
75114000	Mixed salad greens, raw	Med
75115000	Mushrooms, raw	Med
75117010	Onions, green, raw	Med
75117020	Onions, raw	Med
75119000	Parsley, raw	Med
75120000	Green peas, raw	Med
75121000	Pepper, hot chili, raw	Med
75121400	Pepper, poblano, raw	Med
75121500	Pepper, Serrano, raw	Med
75122000	Pepper, raw, NFS	Med
75122100	Pepper, sweet, green, raw	Med
75122200	Pepper, sweet, red, raw	Med
75124000	Pepper, banana, raw	Med
75125000	Radish, raw	Med
75127000	Rutabaga, raw	Med
75127500	Seaweed, raw	Med
75127750	Snowpeas, raw	Med
75128000	Summer squash, yellow, raw	Med

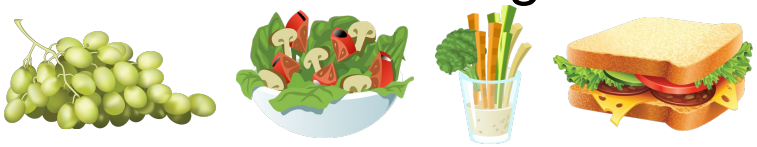
Hi

Foodcode	Description	Assigned category
11435020	Yogurt, Greek, low fat milk, flavors	HI
11435030	Yogurt, Greek, nonfat milk, flavors	HI
11435100	Yogurt, Greek, with oats	HI
11436000	Yogurt, liquid	HI
11440010	Chipotle dip, yogurt based	HI
11440020	Dill dip, yogurt based	HI
11440040	Ranch dip, yogurt based	HI
11440050	Spinach dip, yogurt based	HI
11440060	Tzatziki dip	HI
11440070	Vegetable dip, yogurt based	HI
11445000	Yogurt, fruit and nuts, lowfat milk	HI
11446000	Yogurt parfait, low fat, with fruit	HI
11480010	Yogurt, whole milk, baby food	HI
11480020	Yogurt, whole milk, baby food, with	HI
11480040	Yogurt, whole milk, baby food, with	HI
12310100	Sour cream, regular	HI
12310300	Sour cream, reduced fat	HI
12310350	Sour cream, light	HI
12310370	Sour cream, fat free	HI
12320100	Sour cream, imitation	HI
14010000	Cheese, NFS	HI
14100100	Cheese, natural, NFS	HI
14101010	Cheese, Blue or Roquefort	HI
14102010	Cheese, Brick	HI
14103010	Cheese, Camembert	HI
14103020	Cheese, Brie	HI
14104100	Cheese, Cheddar	HI
14104110	Cheese, Cheddar, reduced fat	HI
14104115	Cheese, Cheddar, nonfat or fat free	HI
14104200	Cheese, Colby	HI
14104250	Cheese, Colby Jack	HI
14104400	Cheese, Feta	HI
14104600	Cheese, Fontina	HI
14104700	Cheese, goat	HI

Results: Estimates of live microbes in 9,388 foods

Low: $<10^4$ CFU/g — Processed/heated foods — **8,998 (96%)**

Medium: 10^4 - 10^7 CFU/g — Fresh fruits and vegetables — **284 (3%)**

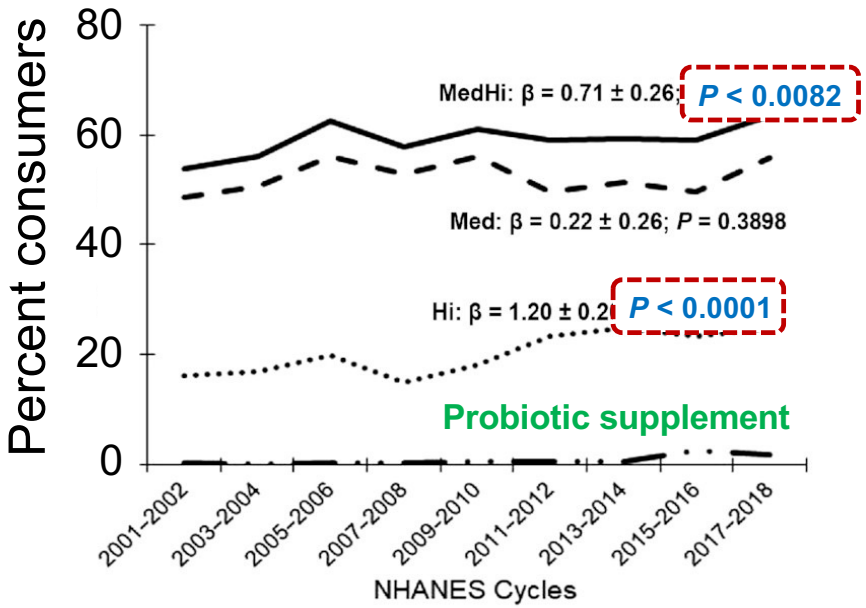


High: $>10^7$ CFU/g — Unheated fermented foods — **106 (1%)**

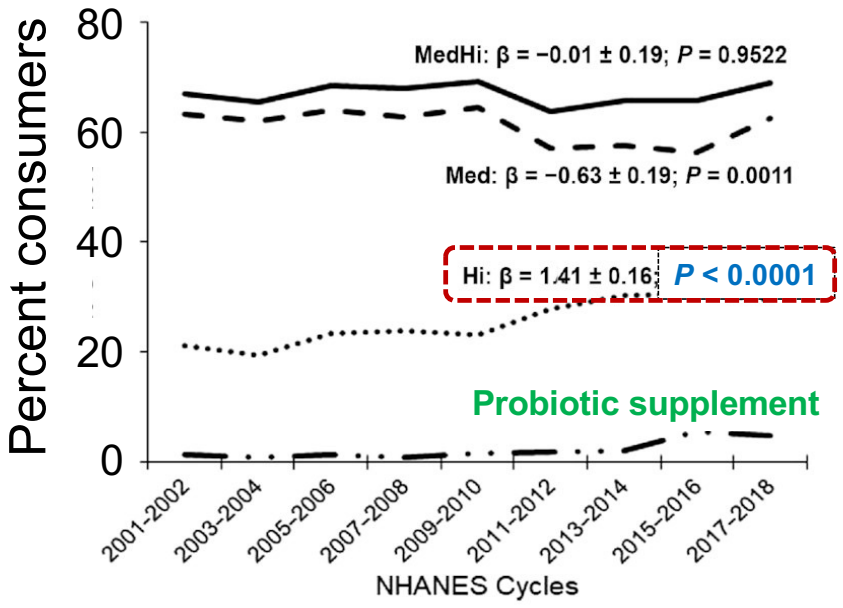
Observation #1. About 2/3 of the population are consumers of microbe-containing foods (**but 1/3 are not**)

Note, probiotic supplement consumption is less than 3%

Children and adolescents (age 2-18 y)



Adults (≥ 19 y)

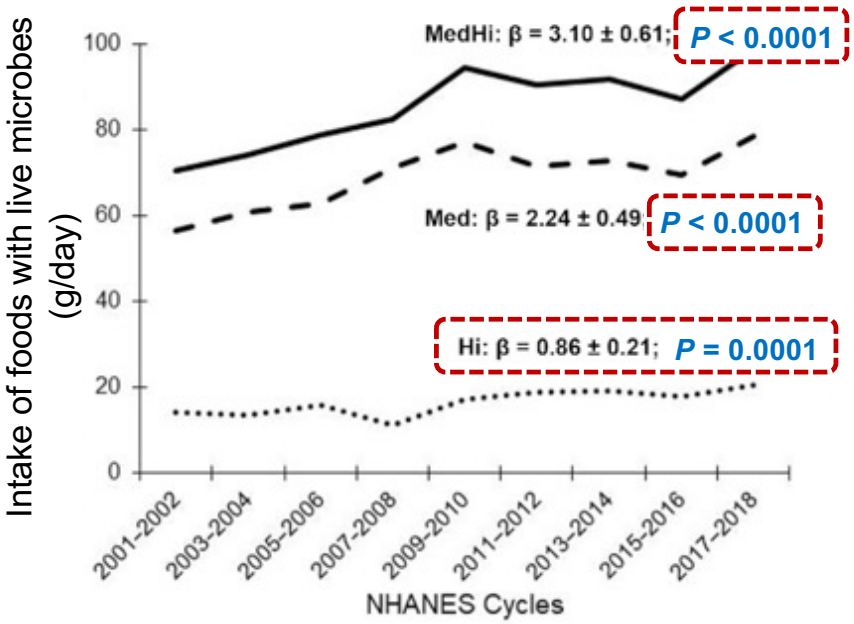


Marco et al., J Nutrition 2022, 152, 7, 1729–1736

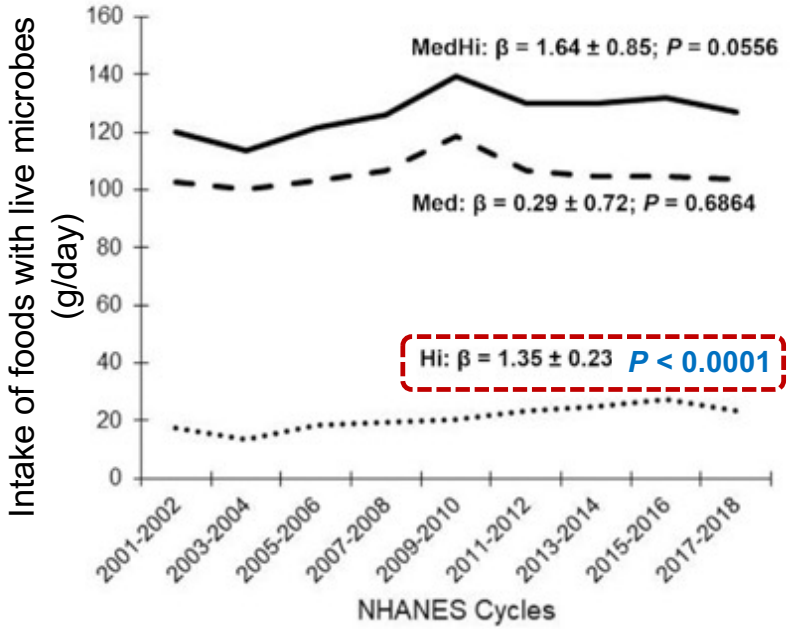
Observation #2. We eat 90 g/day (children and adolescents) to 120 g/day (adults) of microbe-containing foods

Note, that's < 25% of the total amount of food consumed/day

Children and adolescents (age 2-18 y)



Adults (≥ 19 y)



Marco et al., J Nutrition 2022, 152, 7, 1729–1736

Observation #3. Consumers of live microbe foods consume more than **10^8 (100 million) microbes/day**

Most (>90%) are from fermented foods

Per capita consumption of live-microbe foods*

Age, y	*n*	Percent consumers	Consumption (g/day)	Live microbes (CFU/day)
2 - 8	11,626	63	89	> 2.7 x 10^8
9 - 18	**16,749**	**56**	**83**	> 2.0 x 10^8
19 - 50	25,071	65	119	> 2.9 x 10^8
≥ 51	**21,020**	**70**	**139**	> 2.9 x 10^8

* In the MedHi aggregated category

Marco et al., J Nutrition 2022, 152, 7, 1729–1736

Comparing our results with other values in the literature

Trends in Microbiology June 2015, 23

Fate, activity, and impact of ingested bacteria within the human gut microbiota

Muriel Derrien and Johan E.T. van Hylckama Vlieg*

estimated

*"orally ingested strains from fermented foods and probiotics ranges between **10^8 and 10^{12}** CFU per day."*

International Journal of Food Microbiology 2015, 213, 139

Maintaining gut ecosystems for health: Are transitory food bugs stowaways or part of the crew?

Coline Plé, Jérôme Breton, Catherine Daniel, Benoît Foligné *

estimated

*"Transient microorganisms, provided mostly through food, can reach **10^{10} to 10^{11}** viable bacteria ingested per day,*

PeerJ 2014, 2:e659

The microbes we eat: abundance and taxonomy of microbes consumed in a day's worth of meals for three diet types

Jenna M. Lang[1], Jonathan A. Eisen[2] and Angela M. Zivkovic[3,4]

calculated

The **typical American diet** provides only **10^6 CFU per day**: the "USDA" diet plan provides **10^9 CFU per day**

Ultimately, the number and types of microbes we consume depends on diet and provenance

Product	Country	Per capita consumption (kg/person/year)	Daily consumption	Microbes consumed/day (est.)
yogurt	Netherlands	36	100 g	$10^{10\text{-}11}$
cheese	France	27	75 g	$10^{8\text{-}9}$
olives	Albania	11	30 g	$10^{8\text{-}9}$
fermented meats	Germany	5	14 g	$10^{7\text{-}8}$
kimchi	Korea	35	96 g	$10^{9\text{-}10}$
miso	Japan	5	14 g	$10^{7\text{-}8}$

Rezac, Kok et al., 2018, Front. Microbiol. 9, 1785

Thus, the “high microbe” diet (e.g., a Bob-type diet) could deliver more than 10 billion microbes

Food	Live microbes
Yogurt 120 g @ 10^8 CFU/g	10^{10} CFU
Salad, 150 g @ 10^6 CFU/g	10^8 CFU
Fresh fruit, 150 g @ 10^6 CFU/g	10^8 CFU
Reuben w/50 g sauerkraut @ 10^8 CFU/g	10^9 CFU
Daily amount consumed:	**> 10^{10} CFU**

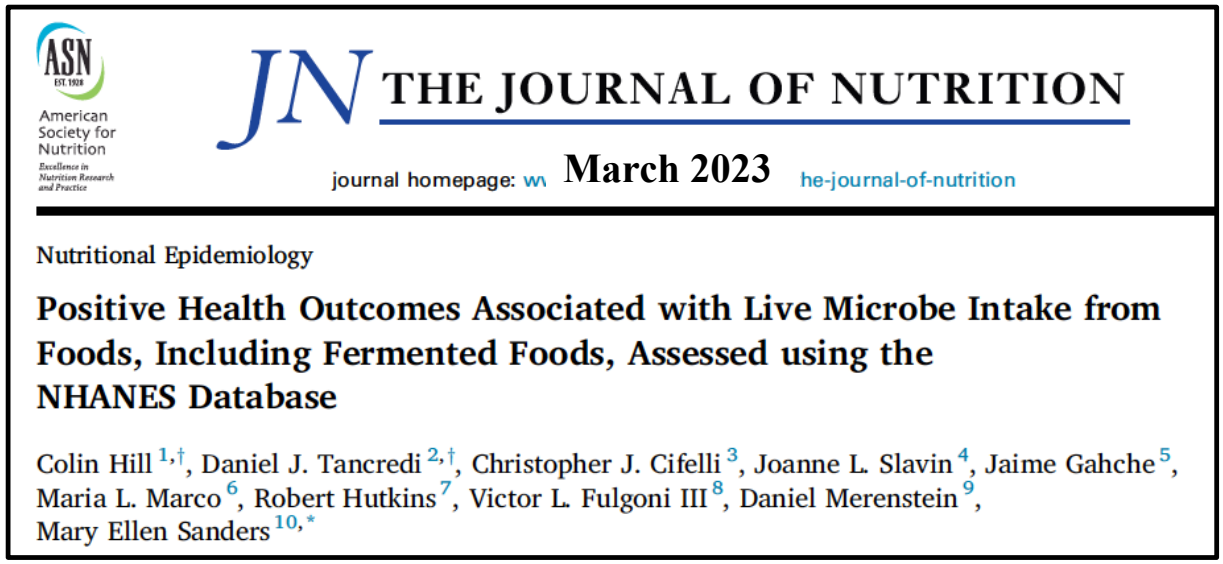
Can microbe-rich diets affect human health?

National Health and Nutrition Examination Survey

- Cross-sectional survey of US adults and children
- Large number of participants (> 70,000)
- Data is based on 24-hour recall
- Using NHANES data, it's possible to correlate food consumption to health status
- **The survey also includes interviews, physical exams, and health assessment data**

Diseases and health indicators:

- Anemia
- Cardiovascular disease
- Diabetes
- Environmental exposures
- Eye diseases
- Hearing loss
- Infectious diseases
- Kidney disease
- Nutrition
- Obesity
- Oral health
- Osteoporosis
- Physical fitness
- Reproductive history
- Respiratory disease
- Sexually transmitted diseases
- Vision



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JN THE JOURNAL OF NUTRITION

journal homepage: ww March 2023 he-journal-of-nutrition

Nutritional Epidemiology

Positive Health Outcomes Associated with Live Microbe Intake from Foods, Including Fermented Foods, Assessed using the NHANES Database

Colin Hill [1,†], Daniel J. Tancredi [2,†], Christopher J. Cifelli [3], Joanne L. Slavin [4], Jaime Gahche [5], Maria L. Marco [6], Robert Hutkins [7], Victor L. Fulgoni III [8], Daniel Merenstein [9], Mary Ellen Sanders [10,*]

Conclusions: To our knowledge, this study is the first to quantify, in a nationally representative data set of American adults … associations of dietary intakes of live microbes with a variety of outcomes…. **Our findings suggest that foods with higher microbial concentrations are associated with modest health improvements across a range of outcomes.**

Statistical Analysis

(Developed and implemented by Prof. Dan Tancredi, UC Davis, and Dr. Vic Fulgoni, Nutrition Impact, LLC)

Regression analyses were used to assess the relationship between consumption of foods with live microbes with physiological parameters.

Two covariate sets were utilized for each analysis:

Covariate set 1 included age, gender, ethnicity, physical activity, poverty income ratio, smoking status, and alcohol intake.

Covariate set 2 was the same but also included the anthropometric variables (BMI, waist circumference, and weight), switching them from being outcomes to being covariates

Adjusted associations of dietary intake (**per 100 g**) of **foods with medium or high** microbial concentrations with physiological parameters in adults

Outcome	N	Regression Coefficient (95% CI)	p-value
BP diastolic (mean rdg mm hg)	40,898	-0.131 (-0.228, -0.034)	**0.009**
BP systolic (mean rdg mm hg)	41,077	-0.405 (-0.523, -0.287)	**<0.001**
Body Mass Index (kg/m**2)	41,697	-0.217 (-0.273, -0.160)	**<0.001**
C-reactive protein (mg/dL)	31,439	-0.017 (-0.023, -0.012)	**<0.001**
Glucose, plasma (mg/dL)	18,509	-0.535 (-0.780, -0.291)	**<0.001**
HDL-cholesterol (mg/dL)	40,313	0.578 (0.425, 0.732)	**<0.001**
Insulin (uU/mL)	18,163	-0.428 (-0.563, -0.294)	**<0.001**
Triglyceride (mg/dL)	18,327	-2.068 (-3.374, -0.762)	**0.002**
Waist Circumference (cm)	40,804	-0.554 (-0.679, -0.428)	**<0.001**
Weight (kg)	41,847	-0.440 (-0.604, -0.275)	**<0.001**

Hill, Tancredi, et al, 2023. Results adjusted for covariate set 1.

Adjusted associations of dietary intake (**per 100 g**) of **fermented foods** with with physiological parameters in adults

Outcome	N	Regression Coefficient (95% CI)	p-value
BP systolic (mean rdg mm hg)	41,077	-0.768 (-1.136, -0.399)	**<0.001**
Body Mass Index (kg/m**2)	41,697	-0.309 (-0.465, -0.154)	**<0.001**
HDL-cholesterol (mg/dL)	40,313	0.696 (0.294, 1.098)	**<0.001**
Insulin (uU/mL)	18,163	-0.644 (-0.995, -0.292)	**<0.001**
Triglyceride (mg/dL)	18,327	-4.844 (-7.674, -2.014)	**<0.001**
Waist Circumference (cm)	40,804	-0.793 (-1.166, -0.421)	**<0.001**
Weight (kg)	41,847	-0.621 (-1.156, -0.087)	**0.023**

Hill, Tancredi, et al, 2023. Results adjusted for covariate set 1.

Main outcomes and caveats

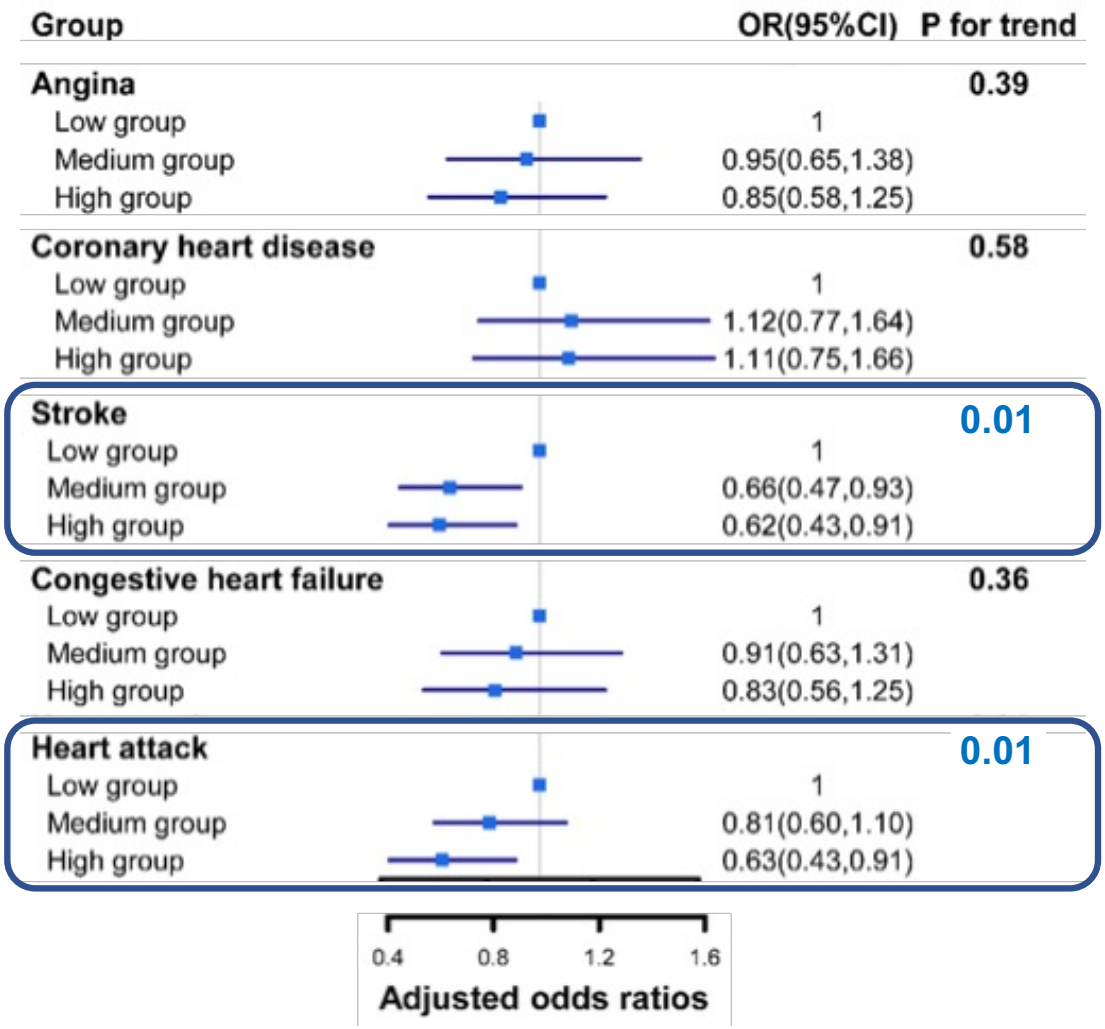
- Consumption of foods that contain high levels of live microbes is associated with a range of improved health benefits
- Health benefits can be achieved by modest changes in diet, i.e., adding servings of yogurt and fresh fruits and vegetables
- Many live microbe foods are also good sources of vitamins, minerals, fibers, phytochemicals, and other nutrients
- This study does not prove causality, RCTs are needed

Nutrients, Han and Wang, 2022

Association of Dietary Live Microbe Intake with Cardiovascular Disease in US Adults: A Cross-Sectional Study of NHANES 2007-2018

Main Result:

High dietary live microbe intake was associated with reduced prevalence of stroke and heart attack.



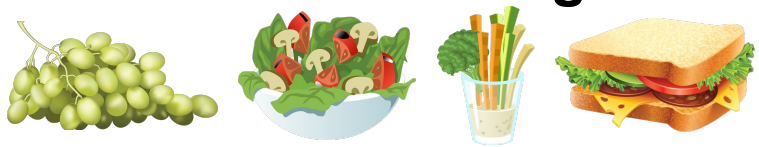
Reminder: Which foods contained live microbes?

Low: $<10^4$ CFU/g

Processed/heated foods

Medium: 10^4 - 10^7 CFU/g

Fresh fruits and vegetables

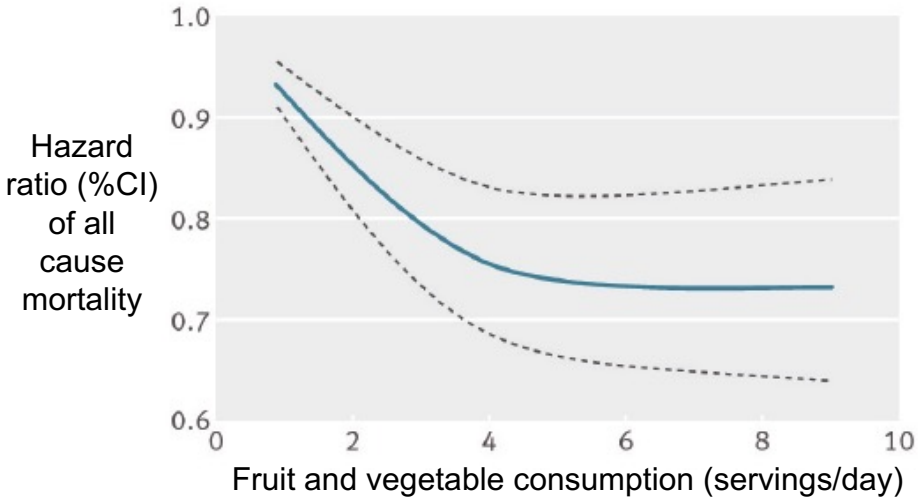


High: $>10^7$ CFU/g

Unheated fermented foods

News Flash: Fruits and vegetables are good for health

More fruits and vegetable are consumed, the longer you live

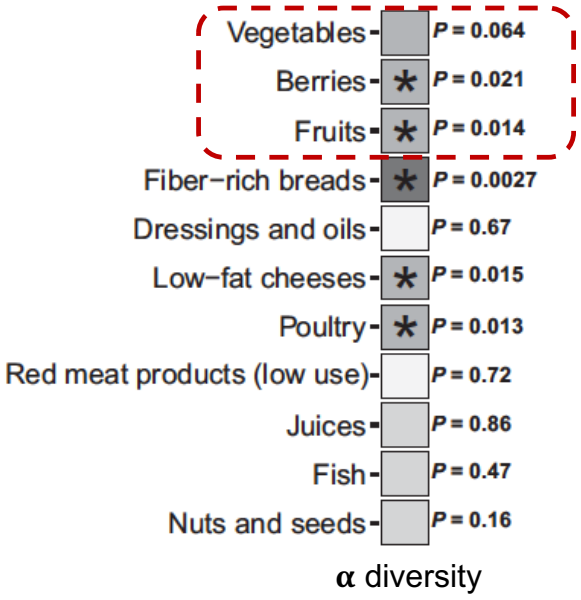


BMJ 2014;349:g4490

Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies

Xia Wang, Yingying Ouyang, Jun Liu, Minmin Zhu, Gang Zhao, Wei Bao, Frank B Hu

Diets rich in fruits and vegetables also increase microbial diversity



Am J Clin Nutr 2021;114:605–616

Associations of healthy food choices with gut microbiota profiles

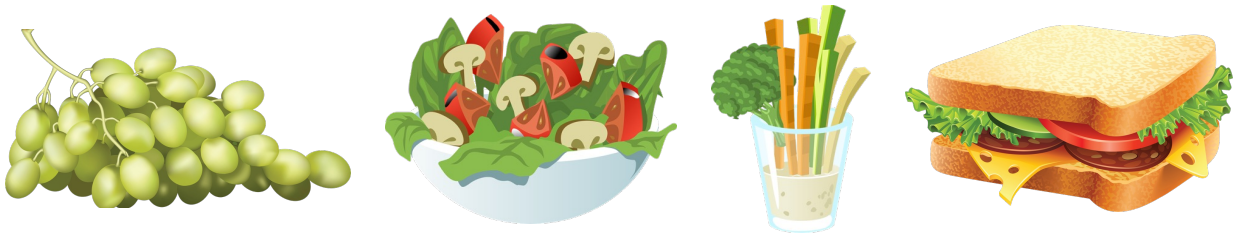
Kari K Koponen,[1,2] Aaro Salosensaari,[3,4] Matti O Ruuskanen,[2,5] Aki S Havulinna,[2,6] Satu Männistö,[2] Pekka Jousilahti,[2] Joonatan Palmu,[2,3,5] Rodolfo Salido,[7] Karenina Sanders,[7] Caitriona Brennan,[7] Gregory C Humphrey,[7] Jon G Sanders,[7,8] Guillaume Meric,[9,10] Susan Cheng,[11,12,13] Michael Inouye,[10,14] Mohit Jain,[15] Teemu J Niiranen,[2,3,5] Liisa M Valsta,[2] Rob Knight,[7] and Veikko V Salomaa[2]

Outstanding challenges to address

1. How to distinguish between the contribution of live microbes versus those nutrients ordinarily present in the food matrix?

Fresh fruits and vegetables

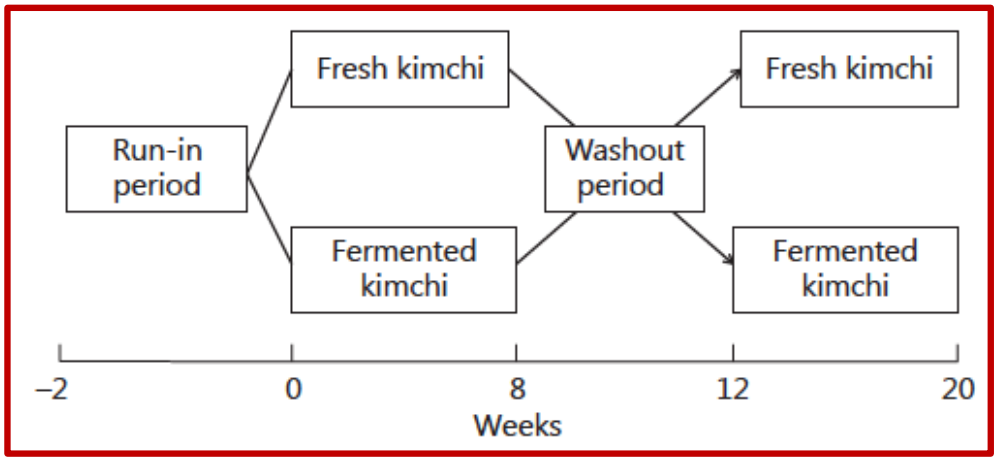
(Medium: 10^4 - 10^7 CFU/g)



- These foods are rich sources of vitamins, minerals, protein, and fiber, and their consumption is associated with positive health outcomes.
- **How to assess health benefits derived from the live microbes?**

Designing RCTs with suitable controls:

Directly compare **fermented** foods to **non- fermented** versions (or heat processed)



Mol. Nutr. Food Res. 2015, 59, 1004–1008

Contrasting effects of fresh and fermented kimchi consumption on gut microbiota composition and gene expression related to metabolic syndrome in obese Korean women

Kyungsun Han[1], Shambhunath Bose[2], Jing-hua Wang[1], Bong-Soo Kim[3], Mi Jeong Kim[4], Eun-Jung Kim[5] and Hojun Kim[1]

Ann Nutr Metab 2013;63:111–119

Beneficial Effects of Fresh and Fermented Kimchi in Prediabetic Individuals

So-Yeon An[a] Min Suk Lee[a] Ja Young Jeon[a] Eun Suk Ha[a] Tae Ho Kim[c]
Ja Young Yoon[b] Chang-Ok Ok[b] Hye-Kyoung Lee[b] Won-Sun Hwang[b]
Sun Jung Choe[b] Seung Jin Han[a] Hae Jin Kim[a] Dae Jung Kim[a] Kwan-Woo Lee[a]

Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients

Eun Kyoung Kim[a,1], So-Yeon An[a,1], Min-Seok Lee[a,1], Tae Ho Kim[b], Hye-Kyoung Lee[c], Won Sun Hwang[c], Sun Jung Choe[c], Tae-Young Kim[d], Seung Jin Han[a], Hae Jin Kim[a], Dae Jung Kim[a], Kwan-Woo Lee[a,*]

Nutrition Research 31 (2011) 436–443

Food Funct., 2018, 9, 5323–5335

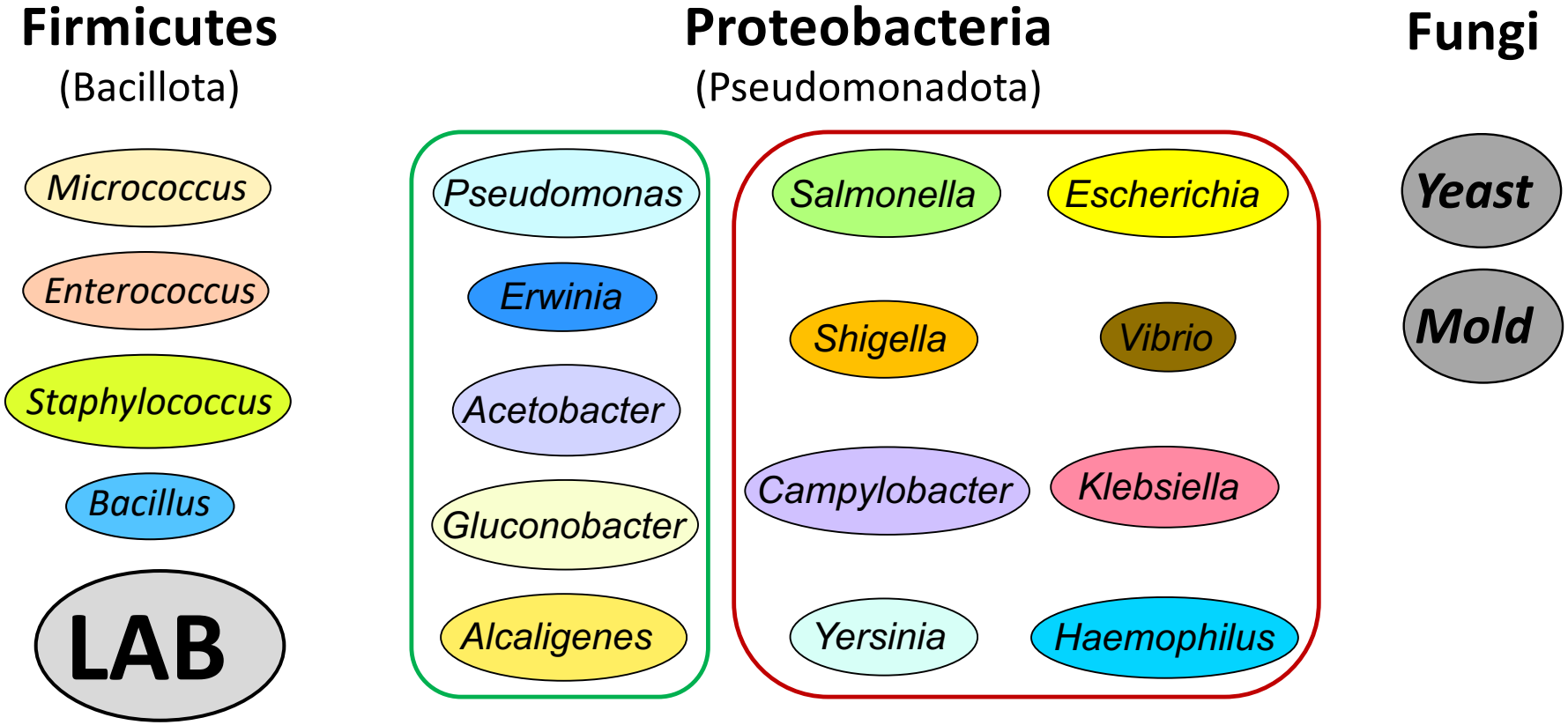
Lacto-fermented sauerkraut improves symptoms in IBS patients independent of product pasteurisation – a pilot study†

Elsa Sandberg Nielsen,[a] Eirik Garnås,[a] Kathrine Juul Jensen,[a] Lars Hestbjerg Hansen,[b] Peder Sandvold Olsen,[c] Christian Ritz,[d] Lukasz Krych[a] and Dennis Sandris Nielsen[*a]

1. Why should we be eating live microbes?
2. If so, which foods are good sources?
3. **Does is matter which microbes we eat (i.e., is one microbe just as good as another?)**

The microbes we eat

Good, Bad, and Very Bad



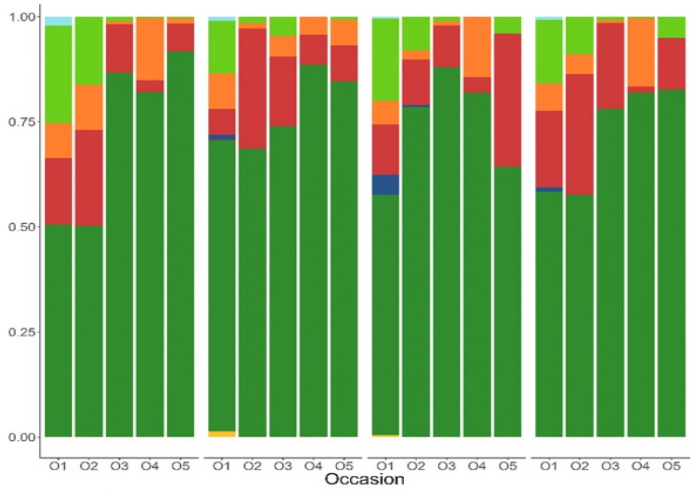
Lactic acid bacteria are often out-numbered > 1000 to 1 in fresh vegetables

		Aerobic Mesophiles (CFU/g)		Psychrotrophs (CFU/g)		LAB (CFU/g)	
	n	Range[b]	Mean[b]	Range[b]	Mean[b]	Range[b]	Mean[b]
Fresh-cut vegetables	**236**	**4.3–8.9**	**7.0**	**4.3–8.9**	**7.0**	**<1.0–8.5**	**4.2**
Arugula	5	6.7–8.0	7.5	5.7–8.2	7.3	3.0–5.9	4.0
Carrot	18	6.5–8.9	7.8	6.6–8.9	7.9	4.3–7.6	5.9
Corn salad	21	6.4–7.8	7.1	5.9–7.8	7.0	<1.0–4.0	2.2
Endive	21	4.3–7.2	6.2	4.3–7.1	6.1	<1.0–4.6	2.7
Lettuce	29	4.9–7.6	6.3	4.9–7.8	6.4	1.7–6.3	3.8
Spinach	10	6.2–8.0	7.4	6.1–8.1	7.4	3.7–6.9	5.1
Mixed salads	132	5.4–8.5	7.1	5.2–8.5	7.1	<1.0–8.5	4.5
Fresh-cut fruit	**21**	**2.0–7.1**	**3.8**	**1.7–7.1**	**3.6**	**1.7–4.8**	**3.0**
Sprouts	**15**	**7.1–9.2**	**7.9**	**6.3–8.9**	**7.3**	**3.4–7. 5**	**5.5**
Whole vegetables	**28**	**2.7–8.0**	**5.9**	**3.0–7.8**	**5.8**	**<1.0–3.3**	**1.6**
Iceberg	5	3.3–5.9	4.6	3.2–5.9	4.6	<1.0–1.2	1.0
Lettuce hearts	3	2.7–5.3	4.4	3.0–5.2	4.4	<1.0–2.0	1.3
Oakleaf	5	5.8–8.0	6.7	5.8–7.8	6.6	<1.0–2.8	1.7
Trocadero	5	5.1–7.3	6.2	5.2–6.7	6.0	<1.0–3.3	1.9
Romaine	5	5.4–6.6	6.0	5.3–6.5	5.9	<1.0–1.9	1.2
Endive	5	6.7–7.2	7.0	6.2–7.2	6.8	1.7–2.7	2.2

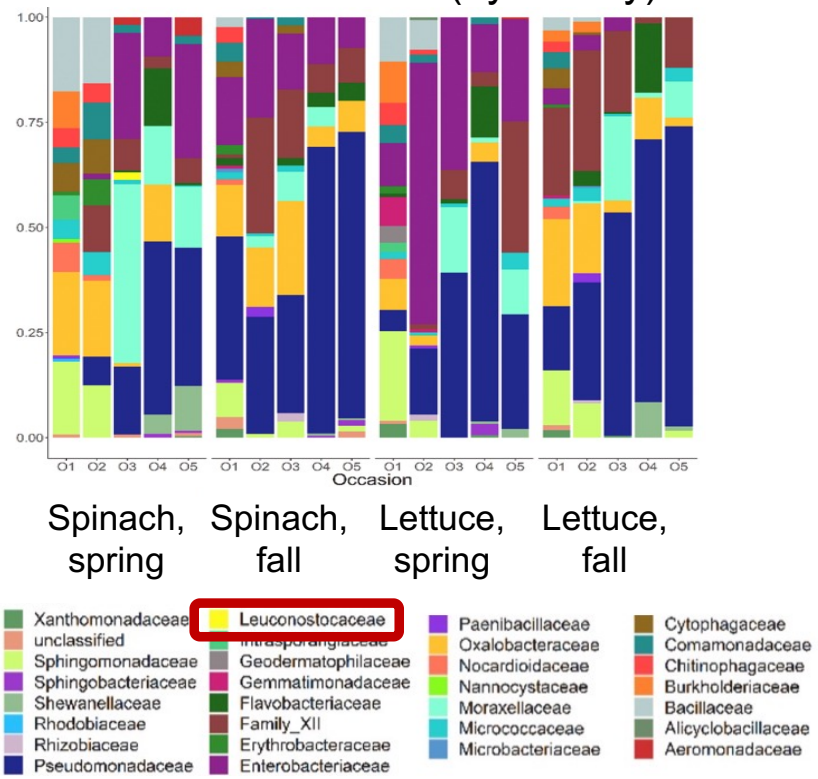
Abadias, M., et al., 2008. Int. J. Food Microbiol. 123, 121–129.

Microbes in spinach and lettuce:
Mostly Pseudomonadota and Bacillota, with **relatively few LAB**

Relative abundance (by Phylum)



Relative abundance (by Family)



Rosberg et al., 2021. Food Microbiol. 94, 103667.

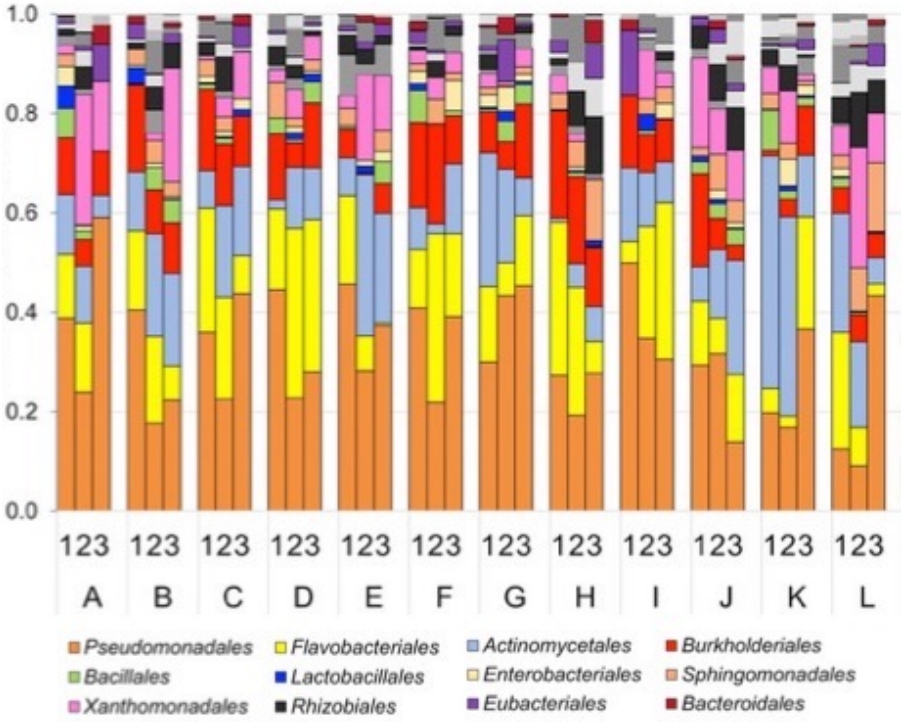
Microbiology Spectrum 2023

Ready-To-Eat Rocket Salads as Potential Reservoir of Bacteria for the Human Microbiome

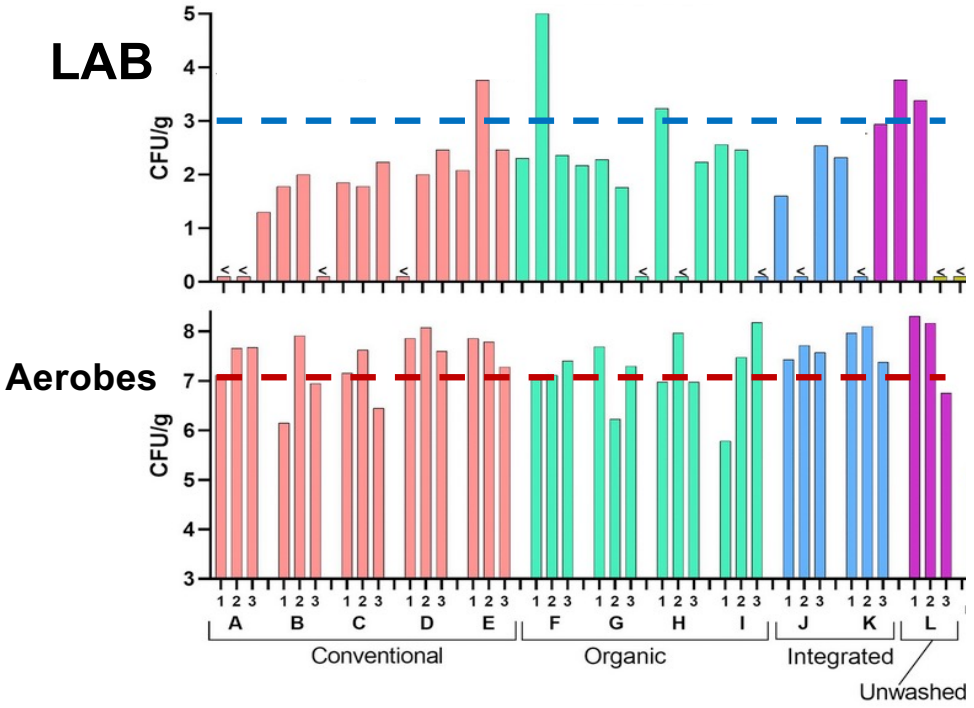
Giacomo Mantegazza[a], Giorgio Gargari[a], Robin Duncan[a], Fabio Consalez[a], Valentina Taverniti[a], Patrizia Riso[b], Simone Guglielmetti[a]

The live microbes in salad greens are typical phyllosphere-associated microbes (epiphytes)

Relative abundance (by Family)



Live microbes by plate counting

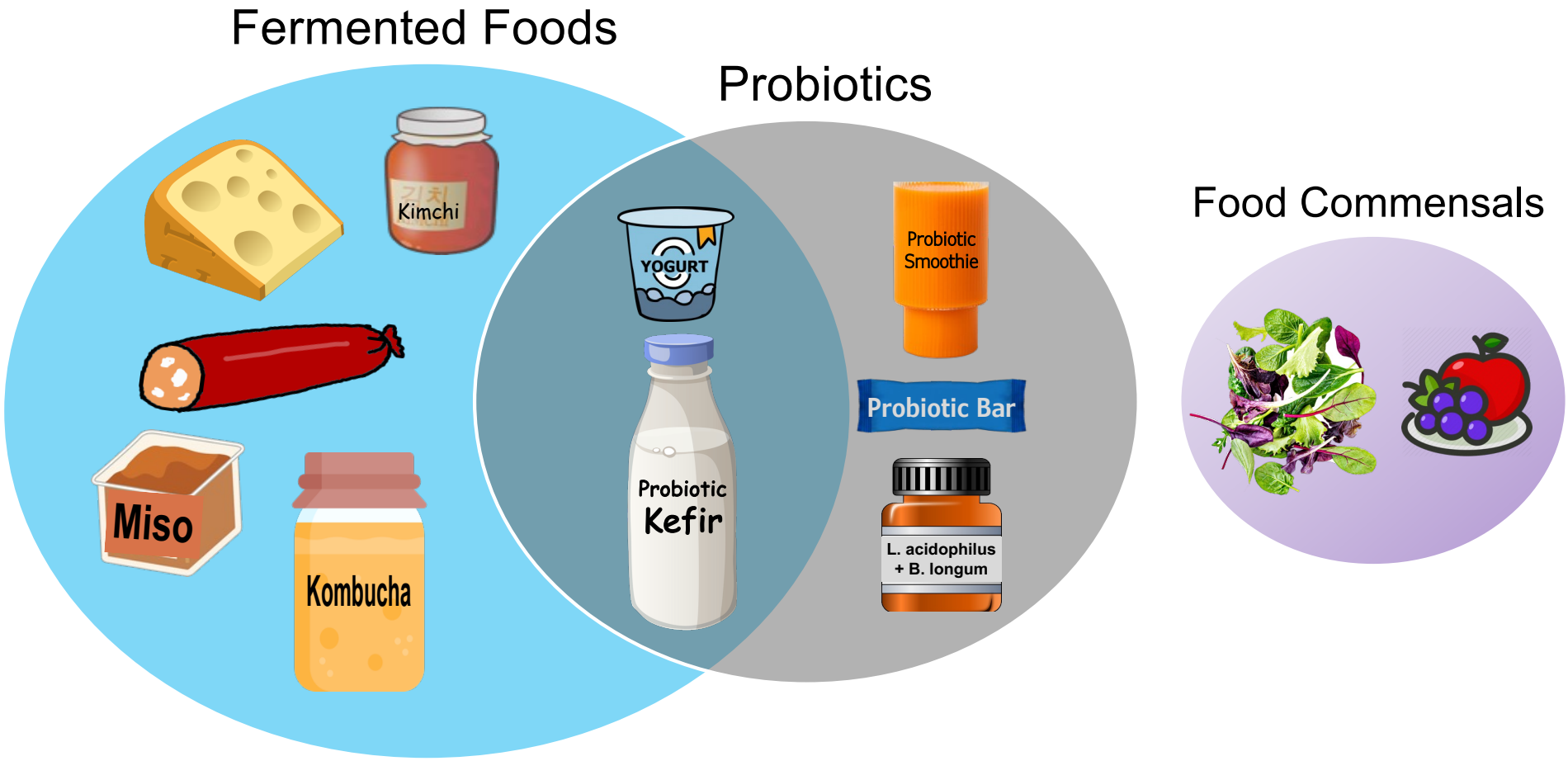


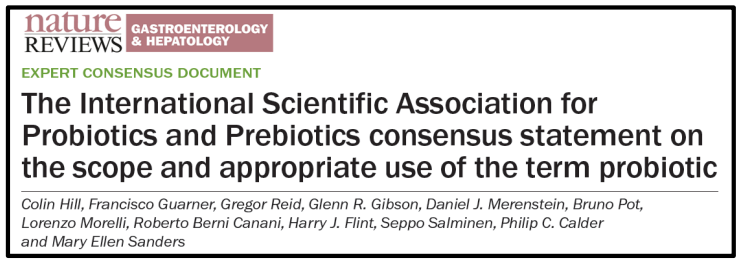
Role of the ‘Medium’ category microbes

- Salad greens contain about 10^6 - 10^7 microbes/g
- Most are common plant-associated microbes
- Unclear if these live plant microbes influence gut health
- Indeed, many don’t even make it into the GI tract

But this does not preclude an immunological impact

Sources of Live Dietary Microbes





Q. What is the difference between fermented foods and probiotics?

*By definition, "the term 'probiotic' should only be used when there is a **demonstrated health benefit** on the host that is conferred by **well-defined and characterized live microbes.**"*

*In contrast, fermented foods often contain **uncharacterized, undefined** microbes, for which a health benefit has **not** been established*

Fermented Foods ≠ Probiotics

Implications

- Except for fermented foods, LABs are not numerically dominant in Med foods
- Indeed, the main microbes in non-fermented fresh foods include non-LAB firmicutes, proteobacteria, yeast and molds,
- Any potential role for these plant and environmental commensal microbes in human health is not clear and needs further study

Coming attractions and opportunities

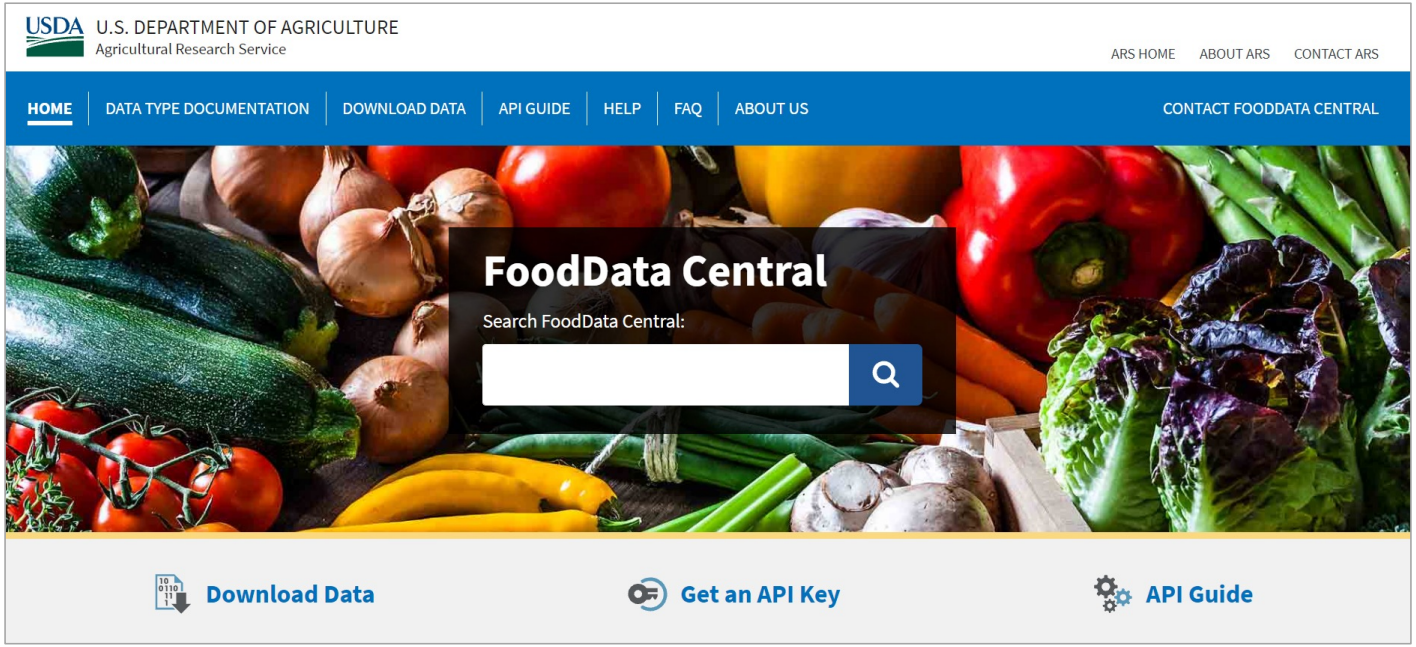
- More RCTs are needed to address the role of live microbes on health
- Need to distinguish between nutrients and microbes
- Epidemiologic data can still be very useful. Remember that fiber recommendations were initially developed based on these studies
- Such studies can lead to consumer awareness of the benefits of live microbes as well as dietary recommendations for live microbe intake

Institute for the Advancement of Food and Nutrition Sciences

Live Microbes: A *New* USDA Global Branded Food Products Database Product Attribute

The Branded Foods Database is Part of USDA's FoodData Central

Location: fdc.nal.usda.gov



Foundation Foods (159) | SR Legacy Foods (7,793) | Survey Foods (FNDDS) (7,083) | **Branded Foods (381,524)** | Experimental Foods (16)

Live Microbe Fields are Now Available to Populate

- Fields made available in October 2021
- The Partnership will be holding an instructional webinar in 4Q 2022 to address detailed questions – open to all.

Offers a non-competitive, objective, and transparent mechanism for stakeholders to understand live microbe intake and eventually link intake to health outcomes!

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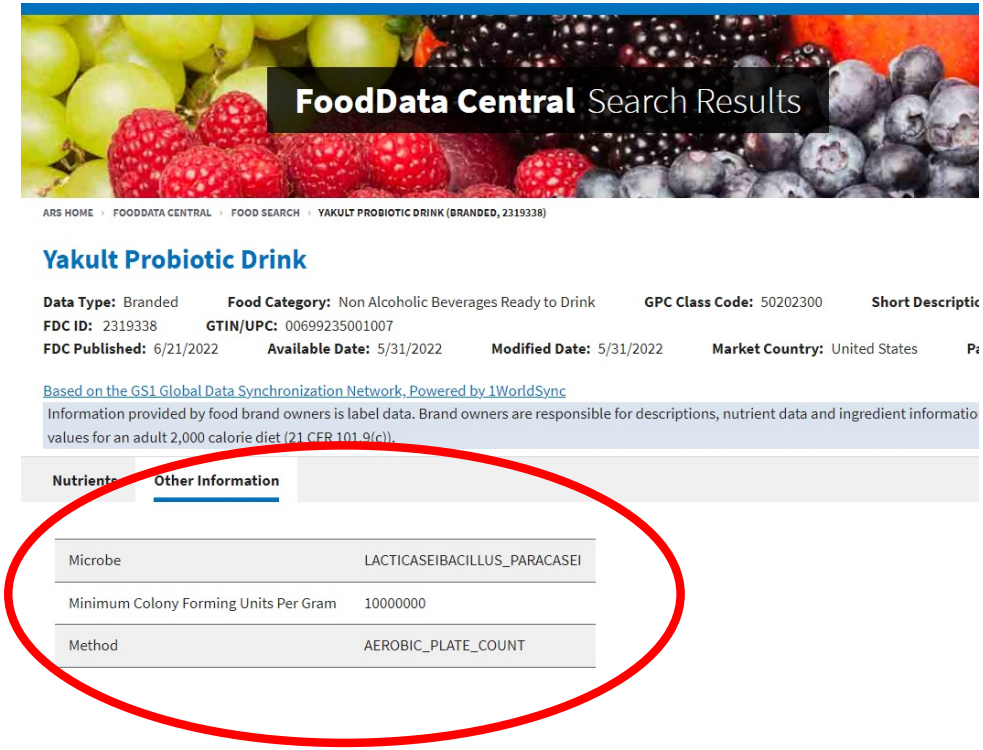
Entering data into FoodData Central

Live Microbes Attribute Inputs

- Total live microbes, minimum value (CFU/g)*
- Total live microbes, maximum value (CFU/g)*
- Live Microbes Method of Analysis
  - *Aerobic plate count, flow cytometry, other*
- Contains Microbes
  - *Select all that apply from list**



**Database submission instructions include thresholds to indicate for Min and Max values for those wanting to indicate a generic "High," "Medium," or "Low" number of live microbes in their products.*

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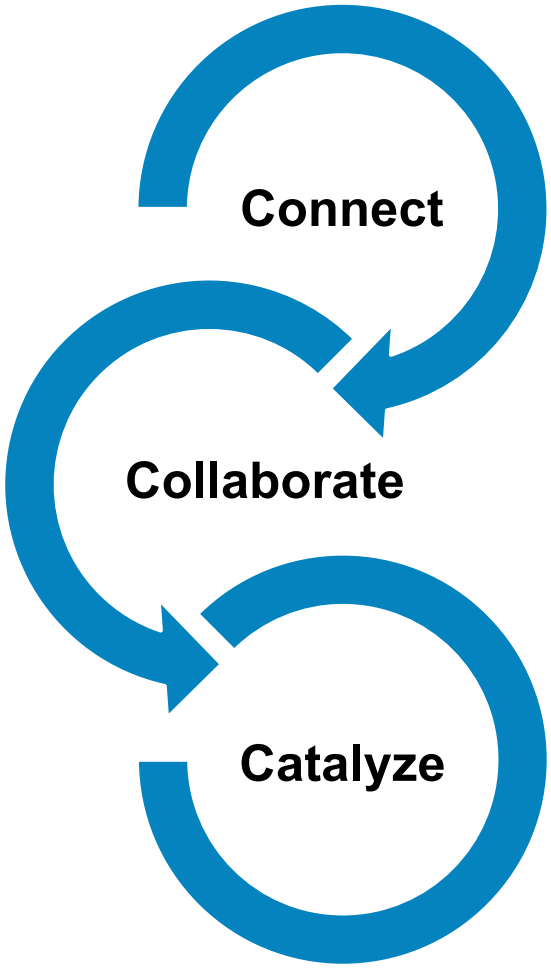

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- IAFNS advances food and nutrition science for public benefit - through collaboration
- Questions about the Gut Microbiome Committee, the Live Dietary Microbes Subcommittee or the USDA Database?

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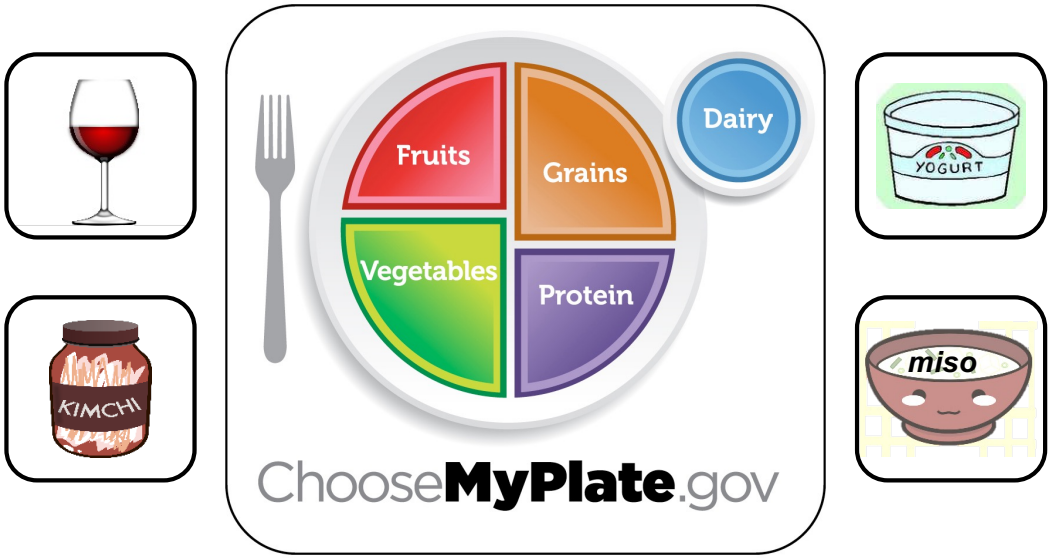
https://www.linkedin.com/company/iafns-science

Maybe we're not far from the following:

"Fermented foods, including those that contain live microorganisms, should be included as part of a healthy diet"



Adapted from Hutkins 2021, Microbiology and Technology of Fermented Foods

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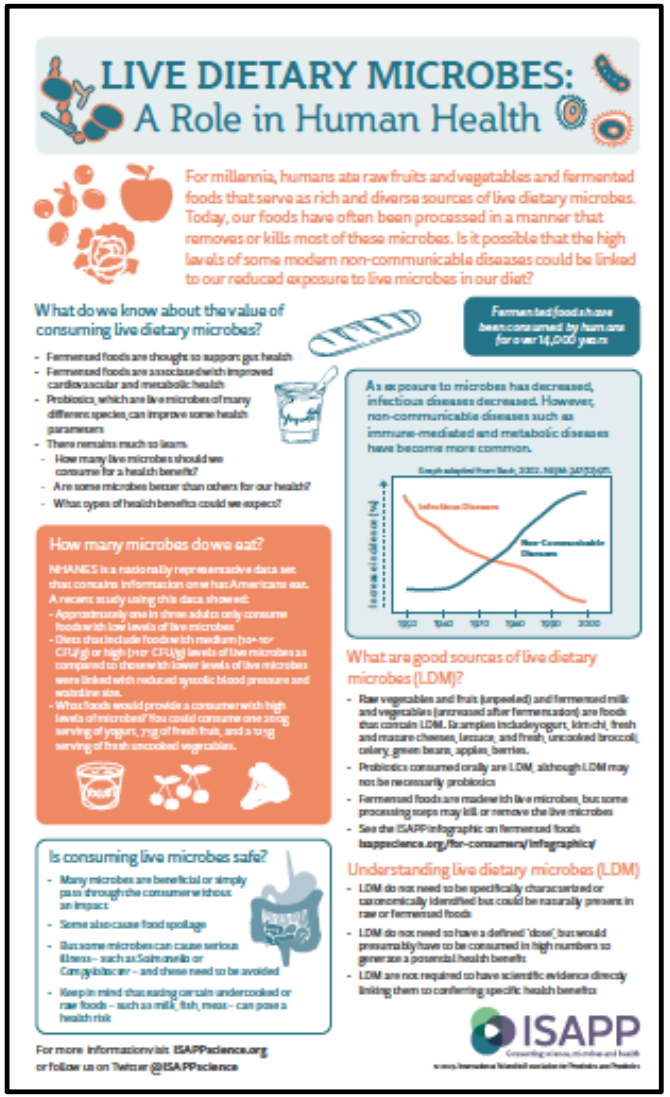

LIVE DIETARY MICROBES:
A Role in Human Health

For millennia, humans ate raw fruits and vegetables and fermented foods that serve as rich and diverse sources of live dietary microbes. Today, our foods have often been processed in a manner that removes or kills most of these microbes. Is it possible that the high levels of some modern non-communicable diseases could be linked to our reduced exposure to live microbes in our diet?

What do we know about the value of consuming live dietary microbes?

- Fermented foods are thought to support gut health
- Fermented foods are associated with improved cardiovascular and metabolic health
- Probiotics, which are live microbes of many different species, can improve some health parameters
- There remains much to learn.
  - How many live microbes should we consume for a health benefit?
  - Are some microbes better than others for our health?
  - What types of health benefits could we expect?

Fermented foods have been consumed by humans for over 14,000 years

As exposure to microbes has decreased, infectious diseases decreased. However, non-communicable diseases such as immune-mediated and metabolic diseases have become more common.

How many microbes do we eat?

NHANES is a nationally representative data set that contains information on what Americans eat. A recent study using this data showed:

- Approximately one in three adults only consume foods with low levels of live microbes
- Diets that include foods with medium (10⁴–10⁷ CFU/g) or high (>10⁷ CFU/g) levels of live microbes as compared to those with lower levels of live microbes were linked with reduced systolic blood pressure and waistline size.
- What foods would provide a consumer with high levels of microbes? You could consume one 200g serving of yogurt, 75g of fresh fruit, and a 10g serving of fresh uncooked vegetables.

What are good sources of live dietary microbes (LDM)?

- Raw vegetables and fruits (unpeeled) and fermented milk and vegetables (unpressed after fermentation) are foods that contain LDM. Examples include yogurt, kimchi, fresh and mature cheeses, lassi, and fresh, uncooked broccoli, celery, green beans, apples, berries.
- Probiotics consumed orally are LDM, although LDM may not be necessarily probiotics
- Fermented foods are made with live microbes, but some processing steps may kill or remove the live microbes
- See the ISAPP infographic on fermented foods isappscience.org/for-consumers/infographics/

Is consuming live microbes safe?

- Many microbes are beneficial or simply pass through the consumer without an impact
- Some also cause food spoilage
- But some microbes can cause serious illness – such as Salmonella or Campylobacter – and these need to be avoided
- Keep in mind that eating certain undercooked or raw foods – such as milk, fish, meats – can pose a health risk

Understanding live dietary microbes (LDM)

- LDM do not need to be specifically characterized or taxonomically identified but could be naturally present in raw or fermented foods
- LDM do not need to have a defined "dose", but would presumably have to be consumed in high numbers to generate a potential health benefit
- LDM are not required to have scientific evidence directly linking them to conferring specific health benefits

For more information visit: ISAPPscience.org
or follow us on Twitter @ISAPPscience

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