

Could we create a category of “dietary microbes” in analogy with “dietary fibres”?

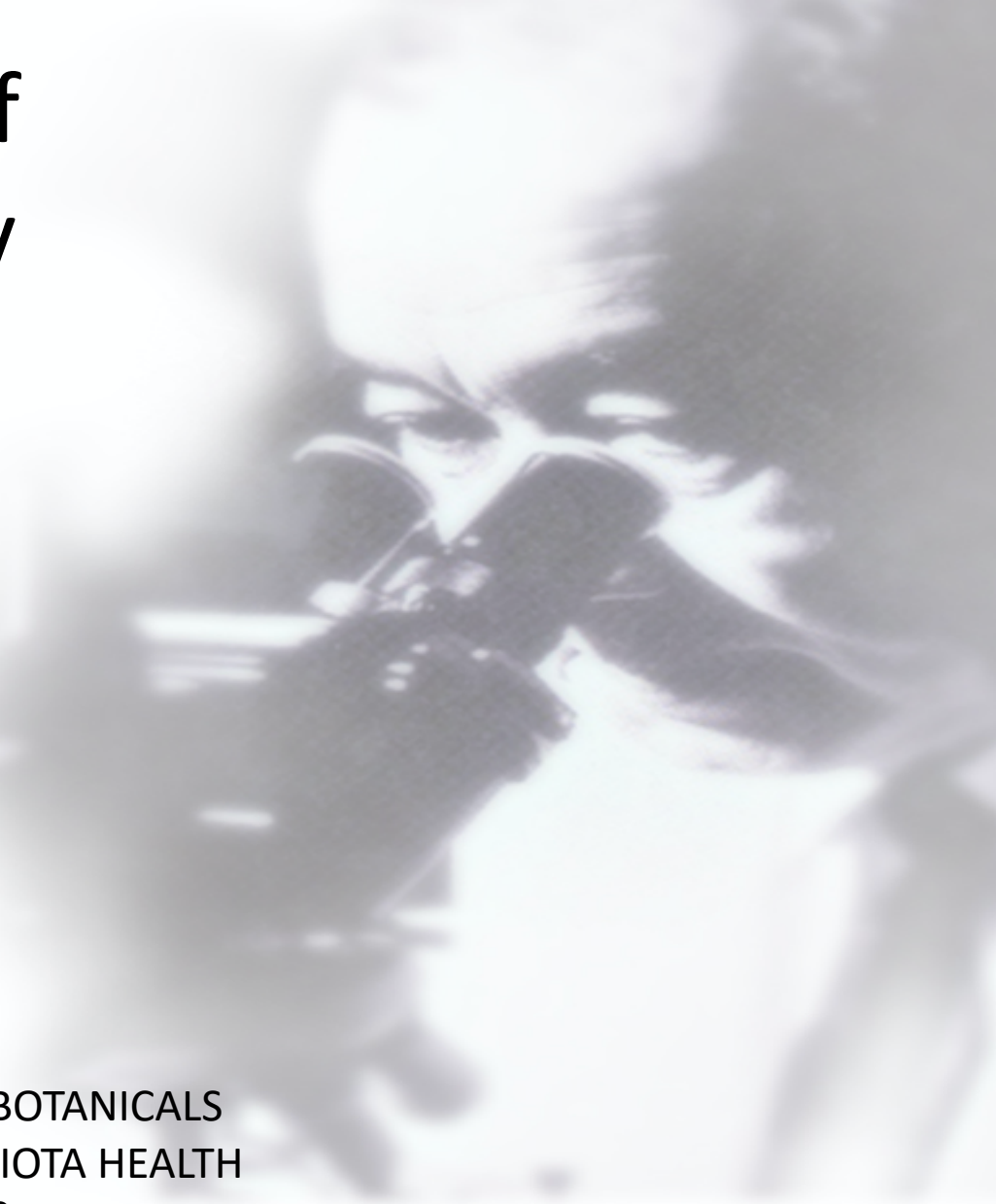
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PROBIOTICS, PREBIOTICS
NEW FOODS, NUTRACEUTICALS AND BOTANICALS
for NUTRITION & HUMAN and MICROBIOTA HEALTH
ROME, SEPTEMBER 9, 2020

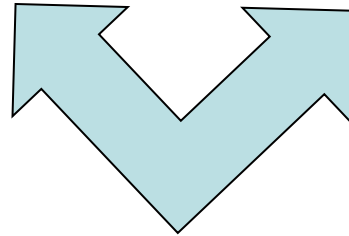
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science for health 



The current situation in Europe

- Because of the 2001 FAO/WHO definition, the terms “probiotic” and “prebiotic” can not be used in communication to the consumer.
- The European Commission has also rejected the term “probiotic” as a generic descriptor.



Consequence:

- The consumer has no means to learn from the producers on the possible health benefits of all these products in the market
- Because of the known health aspect, the word probiotic is increasingly being abused, without any consequence, e.g. in a non-food context (mattresses, air-conditioning cleaners, cleaning products, ...), contributing even more to the consumer’s confusion

- It is generally accepted that some probiotics can positively impact on the microbiota (prophylactically: e.g. in case of antibiotic intake or therapeutically: e.g. in case of *C. dif* infection).
- Multiple nutri-economic studies have calculated the financial benefits of general probiotic consumption on national health care budgets.
- Western diets, poor in fermented foods, have been linked to increasing frequencies of non-communicable diseases (obesity, diabetes, allergy)
- Probiotics are abundantly present in the market as foods or as food supplements, some as medical device, others as drugs (national authorisation only).

Communication on foods is important

The importance of this communication shouldn't be underestimated

- Consumers know the risks for health of
 - Too much salt
 - Too much sugar
 - Too much alcohol
 - ...

- Consumers know the importance for health of:
 - Vitamins
 - Minerals
 - Water
 - Fibres
 - ...

- Thanks to the existence of national guidelines and recommended daily doses

The current “ fibre ” situation in Europe

- On <https://ec.europa.eu/jrc/en/health-knowledge-gateway/promotion-prevention/nutrition/fibre>
→ Fibres are actively promoted.

The screenshot shows the EU Science Hub website. The header includes the European Commission logo and the text "EU SCIENCE HUB The European Commission's science and knowledge service". A search bar is located in the top right corner. The main navigation menu includes "About Us", "Research", "Knowledge", "Working With Us", "Procurement", "News & Events", and "Our Communities". The breadcrumb trail reads: "European Commission > EU Science Hub > Health Promotion and Disease Prevention Knowledge Gateway > Health Promotion and Disease Prevention > Nutrition > Fibre".

The left sidebar contains a navigation menu with the following items: Home, About, Methodology, Health Promotion & Disease Prevention, Nutrition, Fibre (highlighted), Protein, Salt, Fruit and Vegetables, Sugars and Sweeteners, Water, Whole Grain, Food-Based Dietary Guidelines in Europe, Physical activity and sedentary behaviour, Alcoholic beverages, Other policy areas, Food and non-alcoholic beverage marketing to children and adolescents, and Societal Impacts.

The main content area features a banner for "Health Promotion and Disease Prevention Knowledge Gateway" with an illustration of various health-related icons. Below the banner is the section "Dietary Fibre" with a "Table of Contents" listing seven items:

1. Defining dietary fibre
2. Labelling of fibre in the EU
3. Fibre intake: effects on health
4. Recommended intake of fibre
5. Fibre intake across European countries
6. Disease burden related to low intake of fibre
7. Implemented policies addressing fibre intake

Two red arrows point to item 3 and item 6 in the table of contents.

The current “ fibre ” situation in Europe

- Also: the societal impact is discussed extensively.

Cost of Non-Communicable Diseases in the EU

Table of Contents

1. Measuring the cost of non-communicable diseases

1.1 Healthcare costs

1.2 Non-healthcare costs

1. Measuring the cost of non-communicable diseases

Depending on the perspective adopted in an economic evaluation, e.g. public spending on health care or a wider societal perspective, the cost of disease can be estimated from costs associated with the delivery of healthcare and the non-healthcare costs, which also reflect productivity losses due to morbidity or mortality and also costs of informal care. The economic burden of non-communicable diseases (NCDs) is on the rise and is projected to show steeper increases in the future, especially in less developed economies and among the poor in middle- and high-income countries. Rising mortality rates (even in age groups contributing to increasing life expectancy), however, decreasing mortality at the expense of increasing morbidity means more years spent with chronic illnesses (IC 2013). The key drivers associated with the high socioeconomic cost of NCDs are detailed below at 3 different levels (WHO 2012):

- Costs at the level of individuals and households: increased disabilities and premature deaths, decreased household income, increased expenditures, including out-of-pocket payments for health, and loss in savings and assets, and reduced opportunities;
- Health care delivery costs: more people living with NCDs leading to increased use of NCD-related healthcare services, high medical treatment costs and the demand for more expensive treatments;
- Costs to national economies: including reduced labour supply, reduced labour output (e.g. absenteeism, lower tax revenues and lower return on human capital investments).

Public health expenditure is among the largest and fastest growing spending items for governments. In 2015, public expenditure on health was 7.9% of GDP in the EU as a whole, with more than 70% of expenditure funded by the public sector in low levels of Member States (IC 2017). In 2011, premature deaths due to major NCDs (cardiovascular diseases, cancer, respiratory diseases and diabetes) cost the economies 0.8% of GDP (WHO IC 2014), with further losses incurred due to the lower productivity and employment rates of people living with chronic health problems. Due to population aging, chronic diseases and the diffusion of new diagnostic and therapeutic technologies, the share of GDP spending on health is projected to increase in the coming years (IC 2014, WHO IC 2015). In most high and middle-income countries, non-communicable diseases are responsible for the biggest share of both healthcare costs (IC 2014).

1.1 Healthcare costs

Cost-of-illness studies have estimated the cost to EU health care systems from cardiovascular disease (CVD) and cancer. The estimates include costs due to primary care, specialist care, accident and emergency, inpatient care and rehabilitation. The healthcare costs for CVD and cancer have been estimated as follows:

- CVD cost EU health care systems just under €113 billion in 2015, approximately €29 billion due to ischaemic heart disease (IHD) and €29 billion due to stroke (€9.9 billion). Other costs such as hospitalisation and other forms of health care may account for a significant portion of these costs (Lau et al., 2016).
- Cancer cost the EU €31 billion in 2009 (Luengo-Fernandez 2012).

(Ischaemic heart disease and stroke) and cancer are

€110 and cardiovascular disease) and cancer in

adult population (aged 20-79 years) have also been national children reduction European Region (€7.5 billion international dollars.

It, for example productivity losses due to morbidity (these costs are as follows:

€6 with CVD cost the EU €24 billion in 2015 and the EU €15 billion (€9.9 billion 2017).

- Cancer cost over €30 billion in productivity losses due to mortality and morbidity in 2009 and over €29 billion in informal/family care spending (Luengo-Fernandez 2012).

These country-based non-healthcare costs are reported in Table 2.

Table 2: Estimated country-based non-healthcare costs (in billion €) of CVD (IHD, stroke and cardiovascular disease) and cancer, for the years 2014 and 2009 respectively.

Approximate costs € per capita of Cardiovascular Disease in the EU (including Ischaemic Heart Disease and Cardiovascular Disease) in 2015. Click to see graph.



Societal Impacts

In this section of the Knowledge Gateway you will find Briefs related to societal impacts of non-communicable diseases and its dietary and physical activity-related determinants:

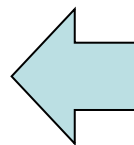
EU burden from non-communicable diseases and key risk factors

Health inequalities: dietary and physical activity-related determinants

Cost of non-communicable diseases

Focus:

- CVD
- Cancer



“Dietary Fibre” has a formal definition at EU and USA level

In the EU, regulation 1169/2011 ([EU 2011](#)) on the provision of **food information to consumers**, defines fibre as:

Carbohydrate polymers with *three or more monomeric units*, which are neither digested nor absorbed in the human small intestine and belong to the following categories:

- edible carbohydrate polymers **naturally** occurring in the food as consumed,
- edible carbohydrate polymers which have been **obtained from** food raw material by physical, enzymatic or chemical means and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence,
- edible **synthetic carbohydrate polymers** which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.

Similar to the EU, **the United States (US)** Food and Drug Administration (FDA) definition ([FDA 2016](#)) refers to:

Non-digestible soluble and insoluble carbohydrates (with *3 or more monomeric units*), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health.

Let's consider this “dietary fibres” definition in detail (looking with a “dietary microbes” eye)

Carbohydrate polymers with *three or more monomeric units*

This is a very broad definition, covering

- Many different chemical compounds
- Sugars and molecules linked in different chemical ways
- In different ratios and concentrations
- Prepared in different ways
- And packed into different foods or food supplements
- Consumed in different doses, by the total population, in combination or not with other food (compounds)

Dietary microbes are also diverse, covering

- Many different species and strains
- With different metabolisms...
- and different chemical structures (cell walls, pilli, etc...)
- Prepared in different ways
- And packed into different foods or food supplements
- Consumed in different doses, by the total population, in combination or not with other food (compounds)

Let's consider this definition in detail

Carbohydrate polymers with *three or more monomeric units*, **which are neither digested nor absorbed in the human small intestine** and belong to the following categories:

- edible carbohydrate polymers naturally occurring in the food as consumed,
- edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence,
- edible synthetic carbohydrate polymers which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.

which are neither digested nor absorbed in the human small intestine

- **Dietary Fibers are not *absorbed* by the host**
- **They remain in the human intestinal tract until they are metabolized and have their impact on the microbiome and the host through bacterial fermentation activity**

- **Dietary Microbes are not *absorbed* by the host**
- **They remain in the human intestinal tract where they are metabolically and immunologically active and have their impact on the microbiome and the host, mainly through bacterial activity**

Let's consider this definition in detail

Carbohydrate polymers with *three or more monomeric units*, which are neither digested nor absorbed in the human small intestine and **belong to the following categories**:

- edible carbohydrate polymers naturally occurring in the food as consumed,
- edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence,
- edible synthetic carbohydrate polymers which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.

belong to the following categories

- edible carbohydrate polymers **naturally occurring** in the food as consumed
 - **Dietary microbes naturally occurring** in many fermented food as consumed,
- edible carbohydrate polymers which have been **obtained from food raw material by physical, enzymatic or chemical means** and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence
 - **Dietary microbes** which have been **obtained from food raw material by microbiological means (resulting in pure or mixed cultures that are taxonomically characterized at the species level and identifiable at the strain level)** and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence
- **edible synthetic carbohydrate polymers** which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.
 - → **Genetically modified or engineered microbes** are currently **not allowed** in food, unless approved as Novel Food.

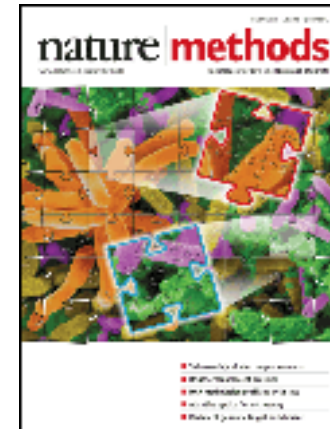
Let's consider this definition in detail

Carbohydrate polymers with *three or more monomeric units*, which are neither digested nor absorbed in the human small intestine and **belong to the following categories**:

- edible carbohydrate polymers naturally occurring in the food as consumed,
- edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and **which have a beneficial physiological effect demonstrated by generally accepted scientific evidence**,
- edible synthetic carbohydrate polymers **which have a beneficial physiological effect demonstrated by generally accepted scientific evidence**.

With beneficial physiological effect...

- edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and **which have a beneficial physiological effect demonstrated by generally accepted scientific evidence**
- **Dietary microbes** have been obtained from food raw material by microbiological means and **can have a beneficial physiological effect as can be demonstrated by generally accepted scientific evidence**



This brings us to the terms **Pro- and Pre-biotics** in particular...

- Both terms can be used ONLY in consumer communication if indeed a **beneficial physiological effect** has been demonstrated by, generally accepted scientific evidence, and **approved by EFSA**.
- For Prebiotics examples are:
 - Reduction of post-prandial glycaemic responses*
 - Increase in faecal bulk**
 - Changes in bowel function**
 - Reduction in intestinal transit time**
- For Probiotics an example is:
 - Alleviation of lactose intolerance by yoghurt

CONDITIONS OF USE

* The claim may be used only for food in which digestible starch has been replaced by resistant starch so that the final content of resistant starch is at least 14 % of total starch.

* In order to bear the claim, glucose and/or sucrose should be replaced by fructose in sugar-sweetened foods or drinks so that the reduction in content of glucose and/or sucrose, in these foods or drinks, is at least 30%.

* The claim may be used only for food which contains at least 4 g of beta-glucans from oats or barley for each 30 g of available carbohydrates in a quantified portion as part of the meal. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained by consuming the beta-glucans from oats or barley as part of the meal.

* Depending on the fibre, other conditions may apply (Table 7)

** The claim may be used only for food which is high in that fibre as referred to in the claim HIGH FIBRE as listed in the Annex to Regulation (EC) No 1924/2006 (Table 7)

Both categories have a large set of *unapproved* health claims ...

For ***Prebiotics*** examples are:

- Contribution to immune defence against pathogens
- Increase in the frequency of daily bowel movements
- Defence against upper respiratory tract infections
- Decreasing potentially pathogenic gastro-intestinal microorganisms
- Changes in bowel function
- Reduction of gastro-intestinal discomfort
- Changes in short chain fatty acid (SCFA) production and pH in the gastro-intestinal tract
- Increasing calcium and/or magnesium absorption leading to an increase in magnesium and/or calcium retention
- Increasing the number of gastro-intestinal microorganisms
- Maintenance of normal blood cholesterol concentrations
- Antioxidant activity, antioxidant content, and antioxidant properties
- Growth or maintenance of muscle mass
- Maintenance of tooth mineralisation

For ***Probiotics*** examples are:

- Protection of the skin from UV-induced damage
- Stimulation of immunological responses
- Reduce the daily number of bowel movements; Improve the consistency of faeces in adult subjects reporting acute diarrhoea
- Decreasing potentially pathogenic gastro-intestinal microorganisms
- Changes in bowel function, and digestion and absorption of nutrients
- Relief of abdominal discomfort and bloating; relieve symptoms typically associated with Irritable Bowel Syndrome (IBS), especially diarrhoea-predominant IBS

→ **This has not been a problem for the recognition of the dietary fibre category**

The type of health claims, moreover overlap to a large extent

For **Prebiotics** examples are:

- Contribution to **immune defence against pathogens**
- Increase in the frequency of **daily bowel movements**
- Defence against upper respiratory tract infections
- **Decreasing potentially pathogenic gastro-intestinal microorganisms**
- **Changes in bowel function**
- **Reduction of gastro-intestinal discomfort**
- Changes in short chain fatty acid (SCFA) production and pH in the gastro-intestinal tract
- Increasing calcium and/or magnesium absorption leading to an increase in magnesium and/or calcium retention
- Increasing the number of gastro-intestinal microorganisms
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For **Probiotics** examples are:

- Protection of the skin from UV-induced damage
- Stimulation of **immunological responses**
- Reduce the **daily number of bowel movements**; Improve the consistency of faeces in adult subjects reporting acute diarrhoea
- **Decreasing potentially pathogenic gastro-intestinal microorganisms**
- **Changes in bowel function**, and digestion and absorption of nutrients
- **Relief of abdominal discomfort** and bloating; relieve symptoms typically associated with Irritable Bowel Syndrome (IBS), especially diarrhoea-predominant IBS

→ **This may have to do with the complexity of the applications: multiple interactions with (amongst others) the individual microbiota, host factors and complex intestinal metabolism**

Wat other homologies ? *Dietary fibre versus Dietary microbes*

Nutrition claim!

According to Regulation (EC) No 1924/2006 (EC 2006), **nutrition claims are permitted** for fibre as below:

- **Source of fibre:** 'A claim that a food is a source of fibre, and any claim likely to have the same meaning for the consumer, can only be made where the product contains at least 3 g of fibre per 100 g or at least 1.5 g of fibre per 100 kcal'
- **High in fibre:** 'A claim that a food is high in fibre, and any claim likely to have the same meaning for the consumer, can only be made where the product contains at least 6 g of fibre per 100 g or at least 3 g of fibre per 100 kcal'

Source of live microorganisms

Contains $X.Y \times 10^Z$ live microorganisms

As a Nutrition claim linked to the category.

Wat other homologies ? *Dietary fibre versus Dietary microbes*

Disease burden related to low intake!

Fibre is not an indispensable component in human diets; however as detailed in Table 2, poor fibre intake is a risk factor for ill health.

The most recent Global Burden of Disease study (GBD) (GBD Study 2017) estimated that in the EU diets low in fibre account for approximately 97,000 deaths and more than 1440000 Disability Adjusted Life Years (DALYs), mainly caused by ischaemic heart disease (approx. 75,000 deaths and 1,077,000 DALYs) and colon and rectum cancer (22,000 deaths and 366,000 DALYs) (GBD tool 2017).

In the GBD study, exposure to diet low in fibre is defined as average daily consumption of less than 23.5 grams per day of than fibre from all sources including fruits, vegetables, grains, legumes and pulses.

Dietary microbes are not an indispensable component in human diets; however, a dysbiotic microbiota has been linked to many disease risks and the depletion of microbiota diversity has been linked to many NCD (obesity, metabolic diseases, IBD, IBS, neurological disorders).

Can we substantiate the “old friend’s” hypothesis” through epidemiological work?

There is no GBD available (to my knowledge) but there are several nutri-economic studies for probiotics.

Wat other differences ? *Dietary fibre versus Dietary microbes*

Recommended intake!

In adults, the recommended amounts of dietary fibre for promotion of adequate laxation and for **prevention of NCDs such as diabetes type 2, colorectal cancer, CVD or of overweight and obesity range from 25 to 38 grams/day.**

In children, recommended amounts vary according to the energy requirements of different age groups. Recommended intake values are expressed in the majority of the cases as adequate intakes (AI) of AOAC fibre unless differently stated; some public health organisations also recommend fibre intakes on per energy requirements basis (grams fibre per MJ or grams per 1000 kcal).

The majority of food and health-related organisations encourage meeting the recommendations through a diet rich in vegetables, fruit and whole grain cereals.

To be developed based on epidemiological and clinical data for specific non-communicable diseases.

The recommendation could include the consumption of sufficient amounts of non-sterilised/pasteurized fermented foods, high in live micro-organisms.

Wat differences ? *Dietary fibre versus Dietary microbes*

(Inter)national policies addressing fibre intake.

A number of policies have the aim of improving diets and nutrition in the population and among these, some include explicit indications on how to achieve recommended fibre intakes.

Table 4 lists implemented policies across the globe that address fibre intake and include explicit indications to meet the recommended intakes.

Policies targeted at **increasing fruit and vegetables** and **whole grain** foods consumption can also increase dietary fibre intake.

Very few official recommendations currently promote the intake of live micro-organisms or probiotics.

However:

In many countries specific probiotic health claims have approved (Switzerland, Canada, Japan, Italy, ...).

Many nutri-economic studies show/calculate the possible economic impact of more general probiotic use (reduced absence at work and school, reduced health care costs, improved life expectancy, improved QOL, ...)

Policies targeted at **increased intake of fermented food** would also increase dietary microbes intake.

Conclusion

- Homology between the two food categories is high in terms of
 - Definition
 - Compositional diversity of these food ingredients
 - Health impact or disease risk at low consumption levels (for a large variety of diseases)
 - Targeting a complex ecosystem with high inter- and intra-individual variation, depending on host (epi)genetics, diet, environment, age, ...
 - Labelling
 - Dose recommendations (daily intake)
- While the “dietary fibre” category is almost universally recognized, the “dietary microbes” category needs still to be “invented”
- Clearly, this would allow to communicate to the consumer about possible health benefits (through nutrition claims) of these foods.
- The terms “prebiotic” and “probiotic” could then be considered special, documented cases (with an approved HEALTH claim) of “dietary fibres“ and “dietary microbes” respectively.

Open questions for the discussion

- **What are we missing to create this “dietary microbes” category?**
- **What needs to be done?**
 - **SCIENTIFICALLY**
 - **Medical**
 - **Nutritional**
 - **Microbiological**
 - **...**
 - **From the regulatory point of view**
- **What with probiotics for the skin, vagina?**

- **Let’s discuss at the end of this session !**

Thank you for your attention!

***Probiotics are our
invisible friends!***

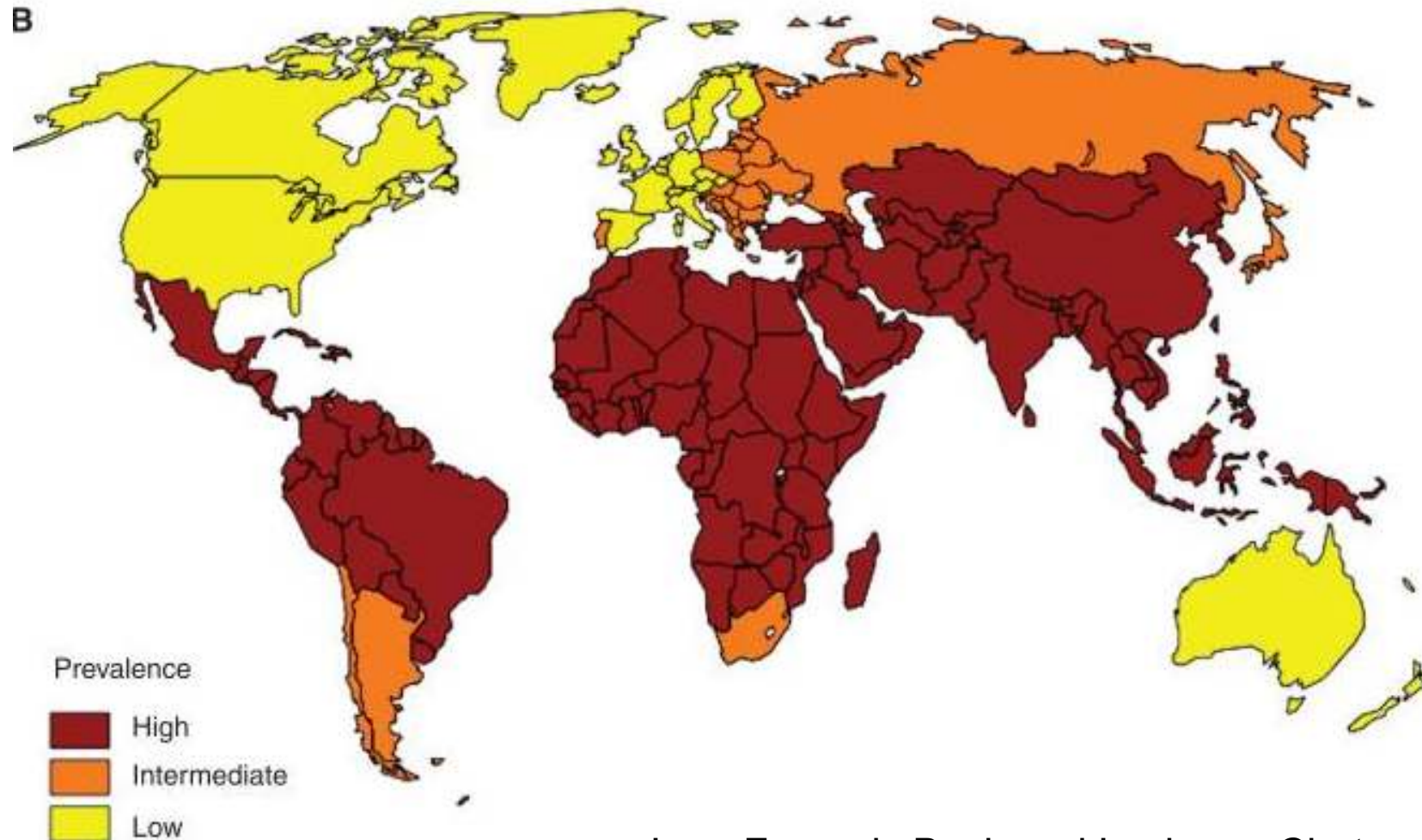
***That's maybe why
they are difficult to study!***

***But they do deserve a
proper regulatory framework!***

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Incidence of childhood diarrrheal diseases



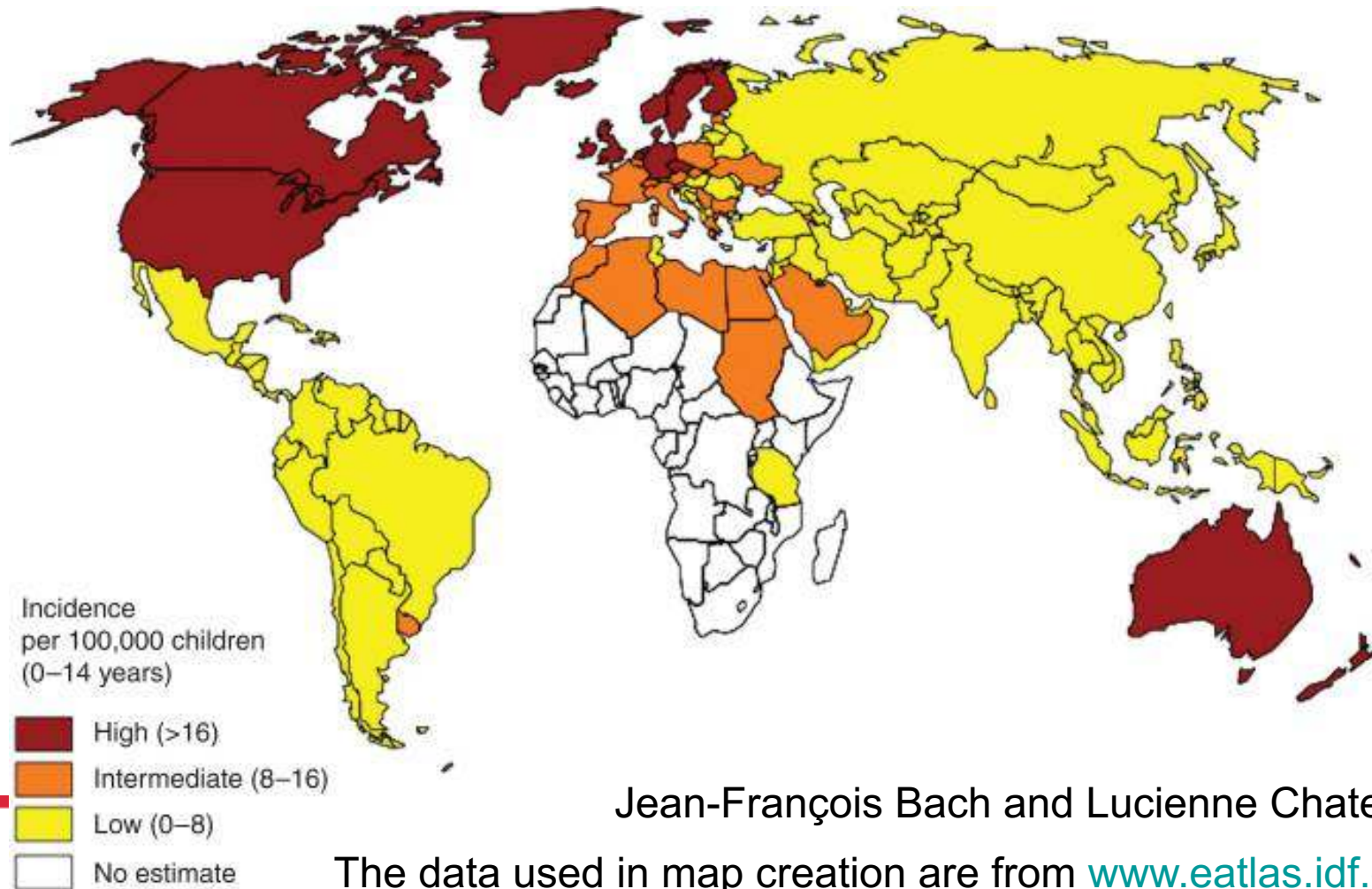
Jean-François Bach and Lucienne Chatenoud

(the data used in map creation are from

www.cdc.gov)

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Frequency of Type 1 diabetes (children 0–14 yr)



Jean-François Bach and Lucienne Chatenoud

The data used in map creation are from www.eatlas.idf.org



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