# Ethical and governance issues in microbiome research and symbiosis monitoring

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# Executive summary

During past decades, life sciences research has profoundly affected our view of ourselves as human beings. WP7 is dedicated to assessing the societal and ethical dimensions of microbiome research in general and the work within the IHMCSA consortium in particular. In Chapter 1, we will address the implications for microbiome research for our self-understanding as humans from a philosophical anthropological angle. This entails a mutual exposure or confrontation between microbiome research and philosophical anthropology, building on the holobiont concept. In Chapter 2, building on this, we will zoom in on the interaction of task 7.1 with other tasks and work-packages, e.g., on mutual learning between microbiome research and the humanities. Chapter 3 outlines important ethical and governance aspects of microbiome research and its applications, such as responsible promise management and the challenge of defining a healthy microbiome. The latter is taken up in Chapter 4. An important aspect of microbiome research and its ethical implications amounts to defining a "healthy" or "normal" microbiome, but while it may seem obvious that microbiome self-management and self-care strive to improve the health of our microbiome, the question how to define and determine microbiome health proves a challenge. We outline an understanding of microbiome health which moves beyond a compositional approach (adopted in most diagnostic tools for consumers) towards an understanding in terms of function, care, and relationship, in line with the holobiont concept introduced in Chapter 1. Informed by these insights, Chapter 5 (the most extensive chapter) zooms in on ethical issues of microbiome self-management. Here we will notably present and discuss the results of a mutual learning workshop entitled *Our Microbial Selves* organised in September 2022 (IHMCSA Milestone 14). Finally, we will recapitulate our results as input for task 7.2: the regulatory challenges of self-management tools addressed in more detail in D7.2.

# Introduction

## The microbiome and us

During past decades, life sciences research has profoundly affected our view of ourselves as human beings. WP7 is dedicated to assessing the societal and ethical dimensions of microbiome research in general and the work within the IHMCSA consortium in particular. In D7.1 we will zoom in on the ethical aspects entailed in microbiome research. Here, we encounter the expectation that life sciences research (especially -omics fields) in general and microbiome research in particular may offer a plethora of tools for fostering self-management and self-care. There is the prospect that scientific insights will allow humans to become the stewards of their own health in an evidence-based manner, resulting in, among other things, improved lifestyles, and prevention of disease.

In fact, a range of support tools is already available on the market. This raises numerous issues such as validation, standardisation, regulation (governance) and critical assessment. But it also raises a series of ethical questions. While regulatory challenges are mainly addressed in D7.2, D7.1 will focus on the ethical challenges involved, thereby providing input for D7.2 and subsequent deliverables. Will these options really empower individuals to take responsibility for their own health, or will information provided be too unspecific or unreliable to be of much help? And what about expectation management and overpromising? Are the claims made by researchers in their research proposals, or by producers of microbiome products, trustworthy? As the evidence for self-management tools is often fragile, there is a need to bring scientific expertise from various disciplines and clinical evidence into the landscape so as to distinguish realistic scenarios from hype.

Against this backdrop, D7.1 takes a societal and philosophical perspective. What would be needed to develop robust self-management tools for health professionals and citizens? What are the expectations, questions, and concerns from various stakeholders? How to align lab developments with societal needs to foster translation into daily practice?

As will be argued below, moreover, ethical questions and deliberations should be developed against the backdrop of a broader understanding of emerging microbiome research, resulting in a more comprehensive philosophical assessment or diagnostic. The impact of microbiome research goes much deeper than merely the availability of new lifestyle products on the market of health and wellness. First and foremost, microbiome research challenges long-standing views about ourselves. In terms of our self-image, notably in the West, and notably supported by worldviews such as

Enlightenment and Liberalism, much emphasis has been placed on human autonomy, independence, and self-determination, while challenges to this self-image amount to a narcissistic offence (Freud 2017). Yet, microbiome research emphasises that we are part of nature, not only in the sense that we are embedded in and dependent on our external environment, but also in the sense that we are ecosystems ourselves, inhabited by millions of organisms who are part of our physical selves. We *have* a microbiome, but at the same time our microbiome is part of who we *are* as "microbial selves". Therefore, to convincingly address the ethical quandaries and challenges involved, a reflection on the broader implications of microbiome research on our understanding of ourselves as autonomous beings (who may be less autonomous than we think) is an important requirement. For, evidently, before addressing issues of self-management, we first have to ask ourselves how we see concepts such as "self" and "management" in the light of microbiome research.

The question how to understand ourselves as human beings is central to a philosophical research field known as *philosophical anthropology*. It is a discipline within philosophy which aspires to learn from and critically reflect on scientific investigations in more empirical research areas such as biology and psychology, in order to understand ourselves as human beings in relationship to our social, cultural and natural environment. Therefore, ethical issues raised by microbiome research are closely entangled with reflections of a philosophical anthropological nature.

The design of this deliverable is as follows. First (in Chapter 1), we will address the implications for microbiome research for our self-understanding as humans from a philosophical anthropological angle. Here, our methodology has been to organise a mutual exposure or confrontation between microbiome research and philosophical anthropology, indicating how self-understandings are challenged by microbiome research insights while philosophical anthropology allows us to question and determine more precisely the meaning of microbiology for human self-understanding. This part of the deliverable will present the results of desk research acquired during the first months of the project, resulting in a first academic paper (Zwart 2023), while the insights gained form desk research will be further developed, informed, and fine-tuned via a series of interactive lectures and deliberations.

Subsequently (in Chapter 2), building on this, we will zoom in on the interaction of this task (7.1) with other tasks and work-packages, e.g., on mutual learning between microbiome research and the humanities. This will prepare the ground for zooming in on important ethical and governance aspects of microbiome research (in Chapter 3), such as responsible promise management and the challenge of defining a healthy microbiome. An important aspect of

microbiome research and its ethical implications amounts to defining a “healthy” or “normal” microbiome, an issue which is notably addressed by WP4 (“Defining a Healthy Microbiome”). It may seem obvious that microbiome self-management and self-care strive to improve the health of our microbiome, but how to define and determine microbiome health? At closer inspection, concepts such as microbiome health or microbiome normalcy prove challenging and questionable in the sense that multiple questions are raised in the context of this endeavour. Should quantitative indicators and biomarkers be developed to determine and monitor microbiome health? Or is health rather a functional, relational, and dynamical concept, so that self–care is rather a question of interaction: developing a health relationship with your microbiome? Chapter 4 offers a philosophical assessment of these issues.

Next (in Chapter 5), building on and informed by these insights, the focus of D7.1 will zoom in on ethical issues of microbiome self-management. Here we will notably present and discuss the results of a mutual learning workshop entitled *Our Microbial Selves* organised in September 2022 (IHMCSA Milestone 14).

Finally (Chapter 6), we will summarise our points of attention as input for D7.2 while outlining the next steps, building on our work so far, but preparing the ground for D7.3, which aims to link reflections on microbiome research and self-management to the broader issue of *responsible research*.

## Bullet points

- The availability of microbiome diagnostic support tools for self-management on the market raises numerous ethical and governance issues such as validation, standardisation, regulation (governance). To address these issues in depth, however, a more comprehensive assessment is required of the implications of microbiome research for how we see ourselves as human beings.
- Besides issues such as expectation management and promise management, microbiome research challenges us to reconsider our conception of health. In order to care for or manage our microbial health, the question emerges how to determine microbiome health, but this proves a challenging issue. Beside microbiome research, also philosophical and societal reflections may contribute to this.
- An important aspect of self-management is how we see our relationship with our microbiome and which sources of knowledge and insight inform practices of microbiome self-care.

# Chapter 1. The microbiome and us

## Towards a more inclusive and holistic view on human identity (literature review)

As indicated, during the past decades, research in the life sciences has had a tremendous impact on the way we see ourselves. A paradigmatic example of this has been the *Human Genome Project* (HGP), whose draft result was proudly presented by President Bill Clinton and scientists Francis Collins and Craig Venter during a White House press conference in June 2000. From a philosophical perspective, the basic message of this press conference was that we now finally know ourselves. The ancient adage *Know Thyself* was finally brought to a conclusion. Others (life scientists as well as philosophers) soon pointed out, however, that, while not denying the importance and relevance of the HGP as such, the claim concerning self-knowledge was both exaggerated and one-sided (Zwart 2007). Its philosophical anthropology was flawed if you like. On the one hand because the press conference celebrated genetic determinism, i.e., the claim that we basically *are* our genome. This evidently underestimated and obfuscated the complexity of life and the importance of environmental factors (Collins 2010). Another problematic issue was its anthropocentric penchant. Although the genomes of other species were sequenced as well, the focus was on decoding and deciphering human DNA. An important message of contemporary life sciences research, however, is that, to understand ourselves, we should broaden our scope (Venter 2010). We are not fully autonomous, isolated, and solipsistic beings, but embedded, interactive and dependent. Human existence is shaped via interactions with myriads of accompanying species.

We have always known this, of course, but sometimes we seem to forget this, and microbiome research counteracts this forgetfulness. While the HGP was basically an anthropocentric research endeavour, microbiome research entails a much more interactive and symbiotic view of human existence, seeing human beings as *holobionts*, a term coined by Lynn Margulis to emphasise the interconnectedness, inter-dependence, and multiplicity of organisms. Both in science (Margulis and others) and in philosophy, authors aim to supersede the ontological divide between self and other, between humans and microbes, and to incorporate the microbiome as a crucial dimension of human existence, not only corporally, but also in terms of mood and cognition. This reflection is important to emphasize, because it helps us to subsequently address issues of a more ethical and practical nature. As indicated, microbiome insights promise to offer opportunities for self-care and

self-management, allowing us to consciously interact with our microbiome so as to foster wellness and health. How to distinguish realistic scenarios from hype? Here again, an interactive approach will be adopted, arguing that practices of the self should result from mutual learning between laboratory research and life-world experience.

Since the HGP press conference in June 2000, owing to multiple research endeavours, including the Human Microbiome Project (HMP)—a metagenomic initiative to sequence the genomes of all microbiological entities collected from a variety of body sites—we became increasingly aware of the vital role played by the indigenous microbial metagenome in human physiology (Juengst, 2009; Parry and Dupré, 2010). Seen from this perspective, the human body is basically an ecosystem, containing multiple ecological niches and habitats in which a wide variety of cellular species collaborate and compete. Human beings are redefined as superorganisms that incorporate a plethora of symbiotic multiple-species consortia. This challenges traditional views on human identity and individuality as we have argued. As Rees, et al. (2018) explained, the three classical biological explanations of the individual self—the immune system, the brain, and the genome—are all challenged by microbiome research. Our resident microbes not only orchestrate the immune system, but they also influence mood and cognition. The realization that humans are not insulated entities, but rather the outcome of multiple interactions with microorganisms, both indigenous and external, has consequences beyond biological disciplines. Our traditional self-image, as autonomous human individuals, is under siege.

The question whether we, as organisms, are 'one' or 'many,' and whether we are 'autonomous' or 'dependent,' entails a false dichotomy; for evidently, as hosts to our microbiome, we are both. We are the outcome of a dialectical interplay between autonomy and dependence, singularity and multiplicity, immunisation and receptivity, as moments of a more comprehensive interactive system. In philosophical terms, what is required is a dialectical understanding of life. And this is not only the conviction of philosophers, for such a dialectical approach has also been advocated in modern biology by authors such as Levins and Lewontin (1985), Gould (2002, pp. 745-757), and Gilbert and Tauber (2016).

Notably, the recognition of the ubiquity of symbiosis has challenged traditional notions of biological individuality. Although it is often claimed that "we" are all Darwinians (Caporael and Brewer, 1990), microbiome research shows that our view of life and evolution are rapidly evolving. Rather than seeing nature in terms of struggle and competition, authors such as Lynn Margulis emphatically acknowledged the importance of collaboration and mutual dependence: seeing individuals as "holobionts" (1991), as collections of closely associated and interacting species, and as

components of a web of life (Margulis and Sagan, 1986, 2002). In various publications, Margulis and her co-authors argued that life on earth depend on a worldwide microbial superorganism, maintaining the conditions that sustain life. Earth is basically a microbial planet. Microbes created the atmosphere. As recyclers, they support the global metabolism. And nearly all metabolic processes were developed by them. They are cyclical beings. Moreover, microbes not only dominate our external environment, they steer our internal environment as well. They are our "forgotten organ," our "collective unconscious" (Dinan, et al., 2015), affecting human health, mood and cognition. Although initially organisms and their microbial parasites are antagonistic (antithetical), eventually organisms may join forces with their microbes, living better while being hardened by them (Serres, 1982, p. 68).

Thus, increasingly, 'individuals' are understood as symbiotic consortia of hundreds of species: as composite organisms, as 'holobionts' whose physiology entails co-metabolism between host and microbiome (Gilbert and Tauber, 2016, p. 840). Rather than being a mere paradigm shift, this conceptual rethinking of individuality entails a change in terms of our ontological understanding of living beings, displacing the self-centred individual as a governing concept and paying due attention to the beneficial interaction between organisms and their internal and external milieus. Symbiosis is a decisive signature of life on earth.

## Bullet points

- Microbiome research urges us to move away from anthropocentric views of ourselves towards a more relational and embedded understanding of human existence. The microbiome affects not only physiological well-being, but also mood and cognition, in short: human agency as such. Human health is the outcome of multiple interactions with myriads of organisms.
- Therefore, before addressing ethical and governance issues, a philosophical anthropological reflection on the implications of microbiome research is required.
- The holobiont concept coined by biologist Lynn Margulis can help us to rethink this dynamical dimension of human existence.

# Chapter 2. Mutual learning between microbiome research and the humanities

The *International Human Microbiome Coordination and Support Action* is an interdisciplinary endeavour. Rather than as "philosophy of" microbiome research, we would rather see our philosophical contributions in tasks 7.1 and 7.4 as philosophy *in* microbiome research: philosophy not as hands-off reflection, but as interactive dialogue across disciplines, a mutual learning process involving microbiome research in combination with other sources of insight (e.g., public intelligence and practical existence, including practices of the self). In such a context, and as explained in the previous chapter, if we want the life sciences – humanities dialogue to work, it is important not to limit philosophical contributions to applied ethics or public engagement in the traditional sense of the term, but to address a broader and more comprehensive spectrum of questions.

From a philosophical perspective, a plethora of philosophical issues is at stake in microbiome research, albeit often in an implicit and abstract manner, awaiting further explanation. For instance, as indicated above, microbiome research entails a basic view of nature, emphasising collaborative networks and mutual dependencies rather than selfish and competitive entities. And notwithstanding the impact of Darwinism, microbiome research urges us not see nature in terms of struggle and competition, but first and foremost in terms of collaboration and mutual dependence (a web of life). The microbiome is our forgotten, extimate organ, 'extimate' in the sense that it represents both intimacy and otherness. It is internal and embedded, and yet foreign. Such questions help us to make our ethical question more specific and precise and to add important points of attention to deliberations in the public realm. Microbes are everywhere, and the whole human organism is involved in host-microbiome interactions. As a result, microbiome research is itself an interactive field, involving multiple forms of interdisciplinary collaboration. Microbiome research not only *studies* processes of interaction, but is also itself the result of interaction across sub-disciplines.

The humanities contribute to this. In a publication written during the first months of the project (Zwart 2022), we used a letter written by Vincent van Gogh as an example. At the time of writing, Van Gogh was a patient in a mental hospital and he wrote his letter to his sister Wilhelmina, on April 30, 1889: "When I suffer from attacks of melancholy and atrocious remorse, I tell myself that all these things might possibly be caused by microbes too, like love". Apparently, a physician –

"the junior doctor here" who, according to the same letter, was telling that "love is a microbe" –, had informed him about some recent developments in microbial research and their implications for human self-understanding (Martin 2008, 2010). This epistolary exchange indicates the awareness that the impact of "our" microbes exceeds metabolism and digestion. It affects mood, cognition and self-reflection.

Vincent would probably have been interested to hear about the gut-brain axis (GBA), which refers to the bidirectional communication between the central and the enteric nervous system, linking emotional and cognitive centres of the brain with peripheral intestinal functions (Carabotti et al. 2015). As indicated, the interaction between microbiota and the GBA is bidirectional, so that it involves signalling from gut-microbiota to the brain and back (Zmora et al. 2019), thereby confirming the proverbial saying that we are what we eat. Physicians treating cancer patients with cytostatic therapies, resulting in the elimination of gut biota (therefore requiring microbiome transplants), noticed that the latter could give rise to physical and mental changes. Our intestines are more intelligent than we tend to think: they contain huge amounts of neurons and interact with the brain through multiple pathways and two-way contact.

Although the bidirectional communication between gut microbes and the brain occurs via a number of routes (Dinan et al. 2015), the *nervus vagus* (i.e., the vague or wandering nerve) plays a fundamental role in enabling signals to travel from brain to gut and vice versa. Intestinal nerves influence production of neurotransmitters in the brain, but this proves to be a circular process, a cycle of cycles, involving multiple feed-back loops. In their comprehensive analysis Dinan et al. (2015) conclude that gut microbiota play an important role in brain development, cognitive function and fundamental behaviour patterns, such as facilitating social interaction and effectively coping with environmental stressors. Other authors add that the microbiome also plays a major role in psychic ailments, mentioning autism, anxiety disorders and depression as examples, so that microbiome research may necessitate a "paradigm shift" in neuroscience (Mayer et al. 2014). Huang et al. (2019) likewise argue in their review article that the gut microbiome plays an important role in the bidirectional communication between the gut and the central nervous system, and that the microbiome may notably have an impact on mood and mood disorders, through the gut-brain microbiota axis. Their focus is clinical, arguing that the gut-brain axis emerges as a promising target for disease diagnosis and therapeutic interventions in the future. Although critics point out that it remains a difficult challenge to separate hype from robust and validated connections between microbes and mental health, a promising program of research is evidently opened up (O'Malley 2014; Morgan et al 2018; Faintuch and Faintuch 2019).

Beyond clinical applications, these research findings are also relevant on a more everyday level, providing opportunities for self-management, giving rise to “practices of the self” (Foucault 1984; Sloterdijk 2009), allowing humans to consciously interact with and care for their microbiome via food, diet, exercise, life-style, and so on. Again, this points to opportunities for superseding the divide between the natural and the human sciences. At the same time, as will be argued in the next chapters, this convergence must be carefully worked out and thought through. Otherwise, this budding research arena may easily become the target for unfounded claims. Here again, the challenge is to distinguish hype from validated insight.

Microbiome research entails the expectation that individuals may be empowered to take responsibility for their own health and become the stewards or managers of their own health. To assess the meaning, validity and implications of these claims, an understanding of the concept of health seems an inevitable requirement. Here, however, we encounter the problem that “health” is notoriously difficult to define. Therefore, in the next two chapters, we will zoom in on the problem of defining microbiome health.

## Bullet points

- Although microbiome research is a relatively recent development, it builds on a longer history of interest in the relationship between subjective experience, mental health, mood and cognition on the one hand and the role of microbes.
- Notably research concerning the so-called gut-brain axis emphasises that our microbiome not only determines physiological health and well-being, but also mood and cognition.
- These insights concerning the pervasive impact of the microbiome as a dimension of human existence must inform ethical and societal deliberations concerning self-management and practices of the self in the lifeworld. This requires a science – humanities mutual learning dialogue.

# Chapter 3. Microbiome health

## A first exploration

A plethora of websites can be found on the Internet where the implications of microbiome research are discussed and microbiome products are offered. In this chapter we have selected one of those websites, more or less at random, to explore how microbiome health is discussed, before addressing the issues involved more in depth in the next chapter. The website we have chosen as an introductory example is devoted to microbiome health in human and their pets, and therefore entitled kittybiome.com.[1] This website contains the following section:

> "New discoveries continue to expand our understanding of the gut microbiome - that diverse community of bacteria and other tiny organisms that live in the digestive tract. Every year we learn more about how the microbiome affects the health of humans, animals, and the environment. For World Microbiome Day, we highlight some of the latest happenings in the exciting field of microbiome studies, where the complex ecosystem of the gut is proving to be a source of promising new treatments for humans and pets alike. The trillions of bacteria in the digestive tract not only help break down the components of the host's diet (such as protein and carbohydrates); they also produce a variety of substances that actively participate in the body's many life-sustaining chemical processes (metabolism)."

The microbiome is described as a "drug factory", because the microbiome produces many different substances that have physiological effects on the body, while pharmaceutical drugs such as antibiotics have a detrimental impact on the microbiome, because, along with the "bad" bacteria responsible for the infection being treated, "antibiotics also kill off a lot of beneficial bacteria in both humans and animals". The website subsequently explains how microbiome research can help to improve health:

> "Our ability to monitor gut health (in both humans and animals) keeps improving. Better diagnostics are evolving to detect chronic inflammation. Individualized diets can be designed to promote healthy bacterial communities. New probiotics can be tailored to specific individuals and conditions. And both humans and their pets can benefit from interventions like FMT [faecal microbiota transplantation] to restore the microbiome's healthy diversity and balance. With microbiome science innovation, the future promises new solutions as we

[1] https://kittybiome.com/expert-advice/here-are-the-latest-advancements-in-microbiome-health/?gclid=CjwKCAjw586hBhBrEiwAQYEnHW9Y9PzkE6d9D5JsCx4I9EiKd53LSfY00dRRqdwVVmJ_pbJqmY8RiRoCO-kQAvD_BwE

> continue to learn more ways to help the gut microbiome help the whole body toward better health.

If we read this website carefully, from a philosophical perspective, our focus is not on the scientific or technical details, but rather on the basic concepts, the basic logic if you like, and the basic claims that are made. In essence, the logical argument can be summarised as follows: more knowledge about the microbiome will lead to applications that empower consumers to improve the health of their pets and themselves by using certain marketed products, some of which are already available. Although this argument seems plausible, some questionable elements can nonetheless be pointed out.

First of all, the trajectory (the translation) from basic research (devoted to deepening our understanding of the basic mechanisms of microbiome functioning) to effective and evidence-based applications is a hazardous one and the challenges of translational biomedical research have been analysed in numerous publications. The process of taking a laboratory idea all the way to pharmaceutical options that benefit patients is a laborious and sinuous pathway that may last up to twenty years and has a success rate lower than one percent (Austin 2021). In fact, translational biomedicine suffers from a very low success rate and according to some authors, less than one percent of all scientific inventions ends up in effective, validated, and trustworthy applications, so that the gap between basic (curiosity-driven) research and application is sometimes referred to as the valley of death (Seyhan 2019). Thus, although microbiome science has reached a point of maturity where it can reasonably be expected to impact preventive nutrition and medicine via translational therapeutic developments (Wilkinson et al 2021),[2] we should not underestimate the practical challenges involved. Responsible promise management is required, especially in this area. Since the emergence of genomics, notably its highly visible flagship endeavour the *Human Genome Project* (HGP), a whole series of new research fields have emerged. As a rule, these research endeavours tend to give rise to quite substantial promises and expectations for society. Yet, promissory discourse ('promisomics', Zwart & Chadwick 2013) runs the risk of becoming inflated and may entail loss of credibility for the research fields involved. Thus, as will be argued more extensively in D7.3, responsible promise management (the articulation of feasible promises and expectations) should be part of responsible research, and the outcome of an on-going dialogue between science and society.

[2] IHMCSA MS2: Determining factors that influence the microbiome and map of the degree of their contribution to health.

In this deliverable, however, we want to highlight another problematic aspect. Although the word “health” is used repeatedly on this website, and even occurs in the title, the term “health” is not explained, or only indirectly, namely by referring to diseases or side-effects (e.g., of antibiotics), that is, the website adopts a *via negativa*, outlining health by referring to instances of ill health. Apparently, the meaning of the word health is taken for granted. In our deliverable, however, the challenge of defining health cannot be by-passed.

We have already pointed out above that microbiome research entails the expectation that individuals may be empowered to take responsibility for their own health and become the stewards or managers of their own health. To assess the meaning, validity and implications of these claims, an understanding of the concept of health seems an inevitable requirement. Here, however, we encounter the problem that “health” is notoriously difficult to define. First of all, health is often defined as the absence of disease or infirmity. This definition works to some extent because various diseases and infirmities are seen as more easily definable than health as such. Still, most concepts of health recognize that health entails more than the absence of disease and notably involves the capacity of the individual for self-realization, while public and social health concepts emphasise the interaction of the individuals with the social environment. Health is a relative state in which one is able to function well physically, mentally, socially, but it is also a dynamical process so that each person is located on a continuous spectrum ranging from wellness and optimal functioning to illness culminating in death. While biomedical concepts of health often emphasise biomarkers (e.g., when making diagnoses) more holistic understandings see health as closely linked with behaviour, lifestyle and the environment. A famous but also controversial effort to define health is the WHO definition of health, seeing health not merely as the absence of disease or infirmity, but as a state of complete physical, mental and social well-being. This definition has been severely criticised as well, however, because it seems almost unattainable. If taken literally, hardly anyone can be considered as healthy in such an optimal sense. In philosophy, the views on health developed by Canguilhem are influential. According to Canguilhem (1991) we must think of health in an interactive manner, in the sense that a healthy organism can address environmental challenges and adapts to new situations. This goes beyond what can be measured by physiology. Healthy individuals experience the world as an arena for learning and interaction rather than as an accumulation of threats from which to immunise themselves.

We have an intuitive understanding of what health is. We experience health or unhealth in our daily life, in practice. But how to define health scientifically? And can microbiome research shed

light on this? This question is addressed in WP4. The overall goal of this WP is "to outline a pathway towards defining the healthy microbiome." Scientists have grappled with the definition of a healthy microbiome by trying to identify a "core" set of microbial taxa in healthy individuals, differentially represented in disease states. However, vast variations in the relative abundances of different microorganisms across healthy individuals have revealed that such an approach is impractical. For that reason, WP4 intends to focus on the "healthy functional core" of the microbiome.[3] This is expected to open pathways towards translational applications in general practice and clinical settings for innovations ranging from preventive nutrition to microbiome-targeted therapies. During the workshop organised by WP4 in October 2022, the attendees recognised and discusses the difficulty of defining health. In the next chapter we explore how we can contribute to this debate from a philosophical perspective.

### Bullet points

- Websites informing the public about the possible applications of microbiome research for health tend to adopt a linear view on the translation of basic research to biomedical applications, thereby underestimating the complexity of the translation process from insight to product.
- Whereas there is a tendency to promise personalised information and advice, as a rule information provided by diagnostic tools for consumers contains general rather than personalised information on health and disease.
- We also encounter the tendency to by-pass the challenges involved in defining microbial health by adopting a compositional approach, while a functional and relational understanding of microbiome health seems more meaningful for self-management practices.

[3] WP4 internal progress report (M1-M12).

# Chapter 4. The concept of microbiome health

## A philosophical assessment

The study of the genomes of microbiomes—namely, microbiomics—is today central to the study of human health and disease (Inkpen, 2019). However, as we have seen in the previous Chapter, it has proven difficult to define what a *healthy microbiome* is and thus how we could promote healthy microbiomes (Karamalegos et al., 2020: 222). Before discussing the problem of determining what a healthy microbiome is, it is worth considering more precisely what the microbiome is and how it relates to health.

*Microbes* are microbial cells (or microscopic single-cellular entities) which live around and within the human body. Examples of these include bacteria, viruses and fungi. *Microbiata* is the ecological community of microbes inhabiting a given natural environment (e.g., the gut, the mouth, the skin, etc.)—with the gut microbiome being the largest and most dense of all of them. The combined genome of our microorganisms is known as the *microbiome* (Karamalegos, 2020: 221-2).

Although invisible to the naked eye, recent technological developments have engendered an explosion of new studies on the microbiome (particularly focusing on that of the gut) which has revealed the great complexity, density and diversity of the microbial communities that inhabit our bodies and surroundings. Recent estimations tell us that the microbes inhabiting the body are at least as many as our somatic cells, and that there are between 500-1000 different bacterial species among them (Karamalegos et al., 2020: 222; also see Sender et al., 2016). Each of these have a genome which contains thousands of genes, which means that it is not just our genes that affect our biology, but that there are billions and billions of microbial genes which do so too (ibid.; see Gilbert et al., 2018). In other words, "our biology is not only governed by our genes and our environment, but in fact by our genes, our environment *and* the genes and functions of our microorganisms" (Karamalegos et al., 2020: 222).

With the explosion of new research initiatives and studies in this field, it has become clear that the microbiome plays a vital role in the processes of human physiology, as explained in Chapter 1. Some of the most important functions performed by the microbiome include assistance with digestion, being responsible for the development of the immune system, and preventing colonization by pathogens (Inkpen, 2019: 3). As such, it is obvious that there is a strong connection

with questions of health, as there is with disease, generally speaking. Many of our physiological processes depend on our interactions with our microbiome (Karamalegos et al., 2020: 222). But what is in question when mentioning words such as "health"? Is it something applicable to the body of the organism as an individual, or rather to the ecosystem dynamically constituted by the complex interactions between the host organism and the billions of microbes both within and surrounding the individual in its environment?

It is in this sense that microbiome research has challenged the traditional concept of the individual. The dynamic and intricate interactions between the host and environmental microbes has given rise to the concept of the *holobiont*, which refers to the notion that "the human body is basically an ecosystem, containing multiple ecological niches and habitats in which a wide variety of cellular species collaborate and compete" (Cf. Chapter 1). As mentioned earlier, the notion of the *holobiont* entails that the body as ecosystem can be understood as a 'superorganism' rather than an individual, which involves a plethora of symbiotic multiple-species consortia. This raises the question of health in relation to the microbiome insofar as many aspects of our physiological processes depend on interactions with this complex ecosystem. It has been suggested that disturbances in the microbiome may directly contribute to "ill-health", as many studies associate dysbiosis—that is, "disturbances of the composition of the microbiome"—with various kinds of diseases ranging from intestinal disorders, metabolic syndrome, to mood disorders and neurodegenerative diseases (Karamalegos et al., 2020: 222).

Having established that there is a profound relationship between the microbiome and questions of health, researchers are confronted with the enigma of determining what a healthy microbiome is. Studies have shown that there is a great variation in the microbial composition among healthy individuals, which even seems to be the case among identical twins leading similar lifestyles (Turnbaugh et al., 2007). These findings suggest that healthy microbiomes, or the microbiomes of healthy individuals, take on various compositional forms, and that the question of a healthy microbiome is much more complicated than the composition of the microbiome. This has refuted an early definition which postulated that a healthy microbiome consists of an ideal core or set of microbial taxa that would be universally found among healthy subjects—where absence of these would entail dysbiosis and disease (Karamalegos et al., 2020: 231). This early suggestion of a definition for the healthy microbiome is thus concluded not to be a practical definition (Lloyd-Price et al., 2016). Karamalegos et al. argue that ultimately it is becoming clear that no such thing as a single healthy microbiome can currently be defined, and that there are great variations in microbial compositions not only between healthy individuals but also between populations.

They argue that a better way to think about a healthy microbiome may be sought by way of defining the *qualities* of healthy microbiomes (Karamalegos et al., 2020: 231-238). The authors describe these qualities as "the *diversity* of microbial species, *robustness*, and *resilience* to internal and external stresses"—which are factors protecting the host against "imbalances in the microbiome" which have been associated with several kinds of diseases (ibid.: 238). Rather than the identity of microbes, then, it is more likely that it is their metabolic functions that matters to defining microbiome health. Karamalegos et al. argue that (2020: 238):

> Gut microorganisms carry their own genomes and perform a set of biochemical and metabolic functions, and there are many examples of microbial species that perform functions with positive effects on host physiology. Each of these functions does not necessarily always need to come from the same microbial species, and possibly a healthy microbiome consists of a core of biochemical and metabolic functions, rather than specific microbial taxa or species. Only by dissecting the genes and biochemical functions of our microbiomes and pinning down the molecular mechanisms underlying the interactions between our bodies and microbial functions, will we be able to move from association to causation and to establish a molecular understanding of host-microbiome interactions.

Ultimately, they claim that while the current understanding of a healthy microbiome is quickly evolving, a real understanding of healthy microbiomes will be developed in the coming years.

This brings us to the concluding part of this brief discussion on microbiome health, which mentions a few different approaches to defining health in philosophy of medicine. The understanding of health which is believed to be arrived at in the coming years is then what is referred to in philosophy of medicine as a naturalist conception of health—that is, a view of health that is fully determined by objective-scientific criteria. However, this begs the question from the side of the constructivists (or normativists) who insist on the determining role of culture and human values in shaping our conception of health and disease (Murphy, 2019). The latter camp would likely argue that the purported understanding of health to be discovered in the coming years is value-laden and thus not an objective conception of health. Beyond the opposition of fact-based and evaluative based approaches to understanding health is the mixed or hybrid approach which aims to conceptualize health and disease without being completely naturalist or constructivist, and by rather striving for a more integrated and holistic approach. Ultimately, it seems that the problem of microbiome health is a problem which invites us to rethink what health is and what it means to be healthy beyond traditional frameworks (Inkpen, 2019: 3), including what kind of entities are relevant to health and healthiness, whatever it is that we may mean by these terms.

With the notion of the holobiont and the sense of host-microbiome ecology involved with the findings of microbiome research, these approaches in philosophy of medicine need to be critically rethought beyond their focus on the individual organism and its opposition to the natural environment. During the upcoming months, these issues will be discussed within the consortium, notably reflecting on findings and insights from WP4.

## Bullet points

- Microbiome research challenges traditional concepts of individuality
- Studies have shown that there is a great variation in the microbial composition among healthy individuals. These findings suggest that healthy microbiomes, or the microbiomes of healthy individuals, take on various compositional forms, and that the question of a healthy microbiome is much more complicated than determining the composition of an individual microbiome.
- Conceptions of microbiome health should acknowledge diversity as there are great variations in microbial compositions not only between healthy individuals but also between populations.
- Rather than mere composition, aspects such as functional resilience to internal and external challenges are important for our understanding of microbiome health. Microbiome research urges us to rethink our concept of health, emphasising relational and interactive dimensions.

# Chapter 5. Self-management and microbiome stewardship

## Introduction

Starting point of the IHMCSA project was the expectation that microbiome research may provide tools for assessing the condition of our microbiome, and for distinguishing between healthy (flourishing) and challenged or unhealthy microbiomes. This may give rise to opportunities for self-tracking and other practices of the self. In previous chapters, we already outlined some of the challenges entailed in this. The question emerges, for instance, how to distinguish realistic scenarios from overpromising, notably in view of the reputation of -omics fields for their tendency towards overpromising or "promisomics" as pointed out above (Chadwick & Zwart 2013). Will microbiome research indeed allow bio-citizens to become the managers of their own health, via self-monitoring and self-management devices, resulting in options for microbiome self-care? In the previous two chapters, we already addressed the issues involved in defining and distinguishing a healthy microbiome, a question that will be taken up further in dialogue with other partners, notably WP4. To the extent that microbiome research produces a range of medical decision support tools, validation and critical assessment of claims and promises ('expectation management') becomes an urgent task. In current practice, evidence for the reliability and effectivity of self-management tools is often fragile. This issue will also be addressed in D7.2.

**Commenté [jD1]:** This meets concerns mentioned in MS19. We could see with PRI if and how we could recommend a claim-validation process…

Assessment of self-management tools is obviously an important question for microbiome research as such and for our consortium in particular. What would be needed to develop robust self-management tools for health professionals, clinicians, and citizens? How to align lab developments with societal needs to foster translation into daily practice? Whereas most other WPs use the insight provided by microbiome research as their starting point, we will opt for a somewhat tilted perspective in the sense that we intend to adopt a societal perspective, staging a debate between science and society on microbiome management, resulting in developing a view on responsible microbiome research in D7.3 and D.7.4. This deliverable is an important step towards this goal. A note of caution seems called for (Parke et al. 2018). Yet, some points of attention for responsible microbiome management can nonetheless be outlined.

With the advent of self-tracking and the quantified self, increasingly large numbers of individuals are already using technological tools and wearable sensors to monitor, analyse and improve their daily activities, in order to enhance flourishing, health and wellness (Swann 2013; Gimbert and Lapointe 2015; Zwart 2018). Given the range of companies currently offering gadgets to self-track your microbiome, this market is likely to grow in size. Via smart self-tracking gadgets, the microbiome becomes a window into the metabolism of the body. How to address the promises and pitfalls of microbiome self-tracking? The traditional situation is one in which various types of experts either promote or problematise, either commercialise or criticize the uptake of 'microbiome speak' by citizens. How to integrate robust microbiome insights into decision and advice processes of general practitioners, clinicians, dieticians and other professionals? The focus will often be on regulation and control of ethical issues surrounding self-management tools.

Self-management entails a number of steps. Initially, self-management is a more or less intuitive practice, taking place in the lifeworld, assisted by low-tech contrivances. Subsequently, more evidence-based options become available, but this creates a diremption between technoscientific insights and life world experiences, between quantifiable indicators and more intuitive practices. Currently, we seem about to supersede this divide between technoscientific knowledge (the laboratory world) and experiential knowledge (lifeworld knowledge). All the world is becoming a living laboratory. We are all research subjects, potentially at least, conducting multiple personal (N=1) experiments, with the help of a plethora of electronic gadgets. Rather than seeing the extrapolation from laboratory world to lifeworld as a linear, top-down process, with experts in charge, we should now see it as a dialectical, interactive endeavour. Our bodies and life worlds become field labs or test beds for interactive, participatory trials (giving rise to the quest for new methodologies, e.g., citizens science, crowdsourcing, social labs).

Initially, practices of the self were based on practical experience. Subsequently, laboratories were created for the production of reliable, evidence-based knowledge, resulting in a tension between lifeworld experience (opinion) and laboratory findings (validated knowledge). In the current situation, although laboratories remain prolific producers of more or less reliable knowledge claims, it is important to find out how these results work out in practice, in the messy, complex, socio-cultural environment outside laboratories. All citizens may become citizen scientists, or participatory research subjects, in principle at least, and this offers opportunities for developing a more interactive and comprehensive view, taking experiences from individuals on board. Bio-citizens are becoming research subjects in their own experimental (technology-based) practices of the self, sharing results and experiences with multiple others. This offers opportunities for participatory

research, seeing citizens as life-world experts, using public intelligence as a decisive source of information. Anecdotal insights from single individuals (N=me) may provide insights about the dynamics of the microbiome in a societal context, as a "complementary" approach to top-down lab inquiries (Gimbert and Lapointe 2015). The next section describes an exploratory effort to organise such a process.

## Our microbial selves

On the 19th and 20th of September 2022, Work Package 7 held an online workshop for mutual reflection on expectations for microbiome self-management tools. We will describe the rationale for the workshop, as well as the methodology employed, and the results obtained from the activities performed during the event. By using s semi-structure focus group methodology, we brought together stakeholders from different academic disciplines to discuss their views on health, the microbiome and the role of microbiome self-management in cultivating health. We provide a preliminary contextualisation of the results in light of the existing literature and reflect on limitations and further opportunities for research on the topic, resulting in D7.3.

As indicated earlier, microbiome research entails the promise to open up new avenues for promoting health, as well as treating and preventing illnesses. The microbiome has been shown to contribute to essential biological processes in the human body (Han et al 2021) and its important role in maintaining homeostasis within many systems in the human body has shifted biomedical research towards a systemic perspective on biological processes (Bapteste et al 2021). While the implication of the microbiome in such processes opens up potential for new applications in health care, scientific evidence for microbiome-based treatments and diagnostic procedures are still scarce and microbiome researchers caution against the hype that such applications have generated (Marcon et al 2021).

Despite this lack of sufficient evidence, many tools for mapping and managing the microbiome have entered healthcare practice. For example, health providers have begun offering microbiotic mapping, where the species composing our gut microbiome are identified (Gimbert & Lapointe, 2015). Based on such mapping, strategies to promote the growth of certain microbial species and starve others are recommended, where microbial species are classified as 'good' or 'bad' according to the effect they have on human health (Arias-Sánchez et al, 2019). Similarly, fecal transplants and probiotic supplements are used to alter one's microbiomes in search for health. Ultimately, these diagnostic

**Commenté [jD2]:** Fecal microbiota transfer is highly regulated, used in only one clinical infection, and not open for the general public (unless by Do-it-yourself videos!!)

and treatment technologies aim to offer a way to control and "use" microbes to achieve a healthy body.

On the other hand, managing the microbiome through lifestyle or self-care practices such as adopting a healthy diet or consuming fermented food has been a staple in many cultures. Unlike practices that have been developed after the advent of microbiome research, these traditional practices do not aim to manage the microbiome composition but rather increase microbiome health in a more holistic manner, seeing microbes as yet another part of our body rather than foreign organisms that can be used for human gain (Redvers et al 2020).

Underlying such modern and traditional practices is the way that humans understand the microbes that live within us. Whether we understand them as foreign organisms that inhabit our clearly delimited human bodies or another important component of the complex systems that make up our bodies, these understandings shape the way that we deal with our microbiome. Therefore, to understand what is expected of the emerging microbiome self-management tools and microbiome research in general, it is necessary to explore how people conceptualize their human selves in relation to the microbiome, and how they cultivate a relationship with the microbes that inhabit their bodies.

## Mutual learning workshop

In our online, two half days, co-creative event we attempted to bring together people from different backgrounds to reflect on how we relate to the microbes that live within our bodies, how that relationship affects the way we view our own selves as humans and how it affects the way we view our health and well-being. For this mutual learning event we invited participants that represent various perspectives (citizens, health care providers, academic scholars, policy experts, and others). Our workshop centred on experiential knowledge rather than scientific knowledge. This focus on experience meant that we invited participants to come together not only in the role of experts in their subject matter or area of practice but also to bring their perspectives that originate from the other roles in their lives and from the relationships that they have with the people and world around them.

The workshop was held on the 19$^{th}$ and 20$^{th}$ of September, through the Zoom platform for videoconference. We used MIRO as an interactive visual environment to facilitate discussion. We used a semi-structured focus group format (Longhurst 2016), which meant that a set of questions was prepared ahead of time to spark conversation between the participants. Nonetheless, we allowed for participants to ask each other questions, and the main facilitator also asked follow-up questions when

concepts needed to be clarified or when ideas that contributed to the main discussion could be further developed by the participants. However, unlike in a traditional focus group, the organisers and facilitators did not take a distanced and neutral position. Rather, we used the oblique perspective approach (Zwart 2017) where we were not only observers to the discussion but rather actively contributed to the mutual learning process. Table 1 shows the questions that were asked during the workshops.

*Table 1 - Questions asked during the workshop*

| Day | Section of the workshop | Questions |
|---|---|---|
| First day | Understanding health | What does it mean to be healthy for you? |
| | | Is health a state, a (set of) practice(s) or something in between? |
| | | What actions and practices do you associate with health? |
| | Health and the microbiome | What does a healthy microbiome look like to you? |
| | | How does a healthy microbiome relate to your own health? |
| | Self-monitoring and the microbiome | How do you think people who engage in microbiome self-monitoring practices see the microbes that inhabit their bodies? |
| | | What do you think people who engage in microbiome self-monitoring practices are hoping to achieve, if anything? |
| Second day | Cultivating a relationship with the microbiome | What kind of health practices do you engage on a day to day? How do you think they relate to your microbiome, if at all? |
| | | What practices do you engage with to avoid contact with microbes that might seem harmful? |
| | Connecting with others through the microbiome | How do you see the practices outlined in the previous activity influencing the interaction between your microbiome and the microbiomes of your environment and other beings around you? |
| | Engaging with knowledge | Do you engage in any of the practices mentioned in a conscious effort to relate to your/other's microbiome? |
| | | What kinds of knowledge do you engage with when cultivating such relationship? |

When discussing what health meant for them, some participants emphasised the importance of physical, mental and social wellbeing. Others mentioned that health meant being free from pain and other health complaints, not being impaired by challenges. In general, the comments provided by participants followed two main trends: health as absence of something negative (such as pain or suffering) or presence of a positive state (physical or mental wellbeing). Nonetheless, most participants mentioned the dynamic and subjective character of health, where being able to interact with and care for others, as well as respond to one's environment in a meaningful way, are important aspects. Living a good life is possible even in a moment in which someone could be considered unhealthy, such as in cases of chronic illness, and that capacity of living a good life should be considered when defining health. Finally, participants mentioned that thinking about health also means coming to terms with the fact that everyone must face not being healthy at some point in their lives.

When questioned about the practices they associate with health, participants mentioned that prevention makes up a large percentage of those practices. Maintaining a plant-based and healthy diet was mentioned by most participants. Sports and physical activity were also mentioned, not only as a way to maintain health but also as a diagnostic tool to understand when there is a shift from health to illness in one's body. Mindfulness practices were also associated with health by the participants, who mentioned how important it is for them to pay attention to their environments and have a good relationship with other beings, human or otherwise. Mindfulness, as well as the other practices above, were mentioned to foster resilience and play a crucial role in protecting against stress, be it physical or mental.

## Health and the microbiome

When asked about how they pictured a healthy microbiome, many participants highlighted microbial diversity as a characteristic to strive for in the microbiome. Mutual care was mentioned as a strategy to foster that diversity, where even though microbes lack the intention of taking care of their hosts, they still provide us with functions that are crucial to maintaining a healthy body when we ensure that they have an environment where diverse communities of microbes can thrive.

Some participants also discussed the idea of pathogenic bacteria and how that is a category that is often seen as absolute, meaning that pathogens are always considered harmful regardless of context. On the other hand, other participants mentioned that while these bacteria that can be considered

pathogenic have virulence factors that can enable them to cause disease, their pathogenic potential is more related to the environment in which they are inserted, where they can be maintained subdominant and harmless and where diversity plays a key role in preventing infection.

Participants were asked about how they saw the connection between a healthy microbiome and a healthy body and mind. It was mentioned by many participants that the definition of a healthy microbiome cannot be dissociated from a healthy host and that these definitions relate to the healthy interactions between both microbiome and host. While the microbiome and the human body put boundaries on each other, those boundaries are malleable, meaning that our microbiome is interwoven into who we are. Humans are ecosystems, symbioses. This conceptualisation of the human being as a complex and relational organism prompts us to consider health beyond the medical model. Within the context of discussing how a healthy microbiome relates to a healthy human body and mind, participants were asked how people engaged in microbiome self-management practices. It was mentioned that users of microbiome self-management tools see microbes as a part of them, a different type of self but still somewhat separate from their own human self. While managing the microbes that compose our microbiome can be seen as instrumentalising these microbes in pursuit of health, a holistic approach can also be taken to them, where caring for those bacteria and fostering diversity can yield a healthier body and microbiome. However, as it was mentioned by one participant, the very existence and use of these self-management technologies can push people towards viewing bacteria as either good or bad, without considering the context that makes bacteria beneficial or harmful to a specific human being at a certain time and place.

Bacteria, according to the participants, can be seen as complimentary, where beneficial and harmful bacteria regulate each other depending on context. On the other hand, adopting and promoting such systemic view on microbes can be difficult, especially while we are in a pandemic and have been told that we need to protect ourselves from pathogens. During the pandemic, public health messaging was important but in general, when communicating about microbes, participants emphasised that preventive communication should be done to initiate a dialogue about friendly and supportive microbes. Nonetheless, as one participant cautioned, communicating about the benefits of microbes and the importance of caring for them should not rely on exaggerating their role on promoting health and such communication should align with the existing data. This communication should focus not only on the general public but also on clinicians and other health professionals, who can help people in making decisions about their health and microbiome in a way that makes sense for their specific context.

## Cultivating a care relationship with our microbiome

In the final section of the workshop, participants were asked about the health practices in which they engage to pursue, achieve and maintain their health. Many participants mentioned contact with nature and paying attention to their environment as a way to manage mental and physical stress. Diet was also mentioned by most participants as a way to stay healthy, and particularly as a way to cultivate a relationship with their microbiome. While these practices were mentioned as tools for maintaining health and cultivating a relationship with the microbiome, it was also mentioned that people must compromise sometimes and make decisions that may be harmful to their microbiome, such as taking antibiotics or ingesting alcohol. Balancing these decisions with care for your microbiome was highlighted as a source of tension for some participants and taking protective measures when engaging in these behaviours that might not be microbiome-friendly was suggested as a way to relieve such tension.

Following, participants were prompted to discuss the practices in which they engage to avoid contact with harmful bacteria. Most participants emphasised the need to meet microbes throughout life, and particularly in childhood. For them, avoiding contact with potentially harmful bacteria is not a goal to strive for. Instead, they spoke about taking protective measures that prevent infection if contact happens. They also discussed their discomfort with the focus on decontamination, especially during the pandemic period, since abusing decontaminants can potentially have negative consequences for immunity and contribute to antimicrobial resistance.

When discussing how the practices in which participants engaged to care for their microbiome and avoid infection from harmful microbes influence the way in which they interact with their environment, participants explained how their perception of themselves as symbiotic beings contributed to their understanding of their connection to their environment and other living beings. Participants mentioned that the pandemic has made us fear the potential diseases that others might spread and suggested that we strive to balance that with understanding that contact with other people's microbes is natural since all beings are part of a larger microbial environment.

One participant raised the concern that because we are always exchanging microbes with other beings, any changes that we might make to our microbiome, whether intentionally or unintentionally, have consequences for other people and those consequences are inflicted without their consent. Because of that entanglement between the choices that we make relating to our microbiome and the consequences for the microbiome of others, there are important ethical issues that need to be

considered when people engage in self-management practices, which intentionally modify the microbiome composition.

## Engaging with knowledge

Finally, participants were asked with which kind of knowledge they engaged when making decisions about the practices in which they chose to engage to care for their microbiome. They mentioned that scientific literature comprises much of the body of knowledge with which they engage when choosing how to care for their microbiome and when recommending microbiome-friendly products and practices to family and friends. They engage not only with primary (pre-clinical and clinical) literature but also with evidence-based recommendations from medical societies for example. Participants also mentioned that experience plays a role in the decisions they make regarding their microbiome. They highlighted the importance of using clinical observations as source of information, as well as their own experiences and the experiences of people around them. Moreover, they mentioned that they engage with traditional knowledge when caring for their microbiome, for example by using herbs that traditional Chinese medicine proposes to be microbiome friendly.

## Discussion and conclusion

Human microbiome research sheds light on the complexity and importance of the microbial communities that live within our bodies. Through investigating how microbes interact with our bodily systems, microbiome research has had significant epistemological and ontological ramifications for thinking about what constitutes the human self (Rees et al 2018). By understanding how our microbiome interacts with the other cells in our bodies, we move away from the immunitarian biomedical model, where microbial 'others' need to be eradicated by our immune systems to prevent illnesses (Ironstone 2019). Instead, we are prompted to consider our bodies not as autonomous living units but as an ecosystem, always situated, in flux and in relation. Thus, the boundaries between self and non-self are blurred.

In the discussion facilitated during the workshop, participants highlighted the connection between the dynamic character of health and the ever-shifting nature of the microbiome. The human body is part of a larger microbial system that encompasses all other beings, human or otherwise, as well as the environment they live in and these microbes within our bodies are always in contact and

in exchange with other microbes (Suárez & Stencel, 2020). Since the microbiome is a part of a complex system, as the participants stated, the diversity in these microbial communities is crucial for cultivating resilience and thus maintaining health of the microbiome and by extension of the human body.

Practices of care towards the microbiome were mentioned as a larger strategy for self-care, which indicates that participants understand their microbiome as part of them, and their human selves as microbial, as an ecosystem in itself. Many of the practices which participants mentioned during the workshop emphasized individual responsibility in caring for the microbiome, where compromise had to be made in choosing to engage in certain practices that are not microbiome-friendly. Individualization of responsibility regarding healthcare, and similarly in the management of the microbiome, has been shown to be a growing trend in discourse about health (Maroney, 2020). On the other hand, collective responsibility was briefly mentioned when caring for the microbiome, given that microbiomes across bodies are in constant exchange and any choices we make to alter our microbiome might have consequences for the beings around us.

Overall, this discussion provides a preliminary conceptual framework on self-management of the microbiome through which we can further develop through mutual learning. By engaging in the discussion described above, we were able to co-reflect on the boundaries of the human self and the microbes that live in and on our bodies, understanding how these boundaries shape the practices in which we engage to relate to such microbes, such as self-management practices.

## Further reflections

The workshop required participation of actors with varied backgrounds to ensure we got a holistic perspective on the topic. We sent invitations to academics from different disciplines (philosophy, biology), dietitians, clinical practitioners, traditional medicine practitioners, journalists, visual artists, and designers. Unfortunately, we had a low number of acceptances to our invitations and an even lower number of attendees in our workshop. Nonetheless, we were able to have a productive discussion between participants.

In the future, we recommended that further events are organised to reach a wider public. Most participants in our workshop were academics, which meant that a significant part of our discussion comprised of speaking of current research in microbiome sciences or adjacent fields. In order to understand how other types of knowledge are produced and used when fostering relationships with our microbiome, it would be valuable to reach out to people outside of academia who engage with

practices of care towards their microbiome, either in their professional or personal lives. Healthcare professionals, artists, microbiome influencers, people in the food industry could be some of the groups that are involved in future workshops, with the aim to obtain a more comprehensive understanding of how people relate to their microbiome and how they engage with the microbiome through care or self-management practices.

Based on the result of the workshop in combination with the results from our literature review, we are conducting a series of interviews on microbiome awareness and lifestyle. Participants described health as a fluid concept and their relationship with their microbiome as a mutual and dynamic partnership, while practices were informed by a range of knowledge forms. This will provide input for D7.3 on responsible microbiome research.

### Bullet points

- Health is a fluid concept, including the practices that we engage in in pursuit of health
- The relationship with our microbiome is a mutual and dynamic one
- Resilience and diversity were key characteristics which participants seek to cultivate through care practices for their microbiome
- Practices were informed through a range of different knowledges, such as scientific evidence, traditional knowledge and lifeworld experience
- Participants also emphasized the importance of embracing the fluidity of the microbiome, not engaging in excessive decontamination practices but rather cultivating resilience

# Chapter 6. Implications for governance and policy

Starting point of the IHMCSA project was the expectation that microbiome research may provide tools for assessing the condition of our microbiome, and for distinguishing between healthy (flourishing) and challenged or unhealthy microbiomes. This may give rise to opportunities for self-management and other practices of the self. In previous chapters, we addressed a number of challenges encountered, including the difficulties of providing a definition for a healthy microbiome as well as the multiple knowledge forms involved in practices of the self. Various microbiome tools for self-management have entered the health and wellness market claiming to support consumers in taking responsibility for their microbiome. How to distinguish hype from hope? This raises numerous issues such as validation, standardisation, and regulation. The development of policies and regulations for self-management tools is the objective of D7.2 (M36). This deliverable will offer recommendations for policies needed to ensure appropriate regulation of self-management tools. PRI is currently benchmarking the self-management tools available on the European/US market to analyse their regulatory status regarding the new In Vitro Diagnostics regulation and General Data Protection Regulation. This will serve as input for the workshop with policy makers on regulation and governance of self-management tools led by PRI (MS21). The question in this chapter his what advice we may offer on the basis of the work described in D7.1?

First of all, in view of the newness of the issues involved, we propose a mutual learning process, involving multiple stakeholders and perspectives, rather than a top-down approach based on extrapolation of existing policies and regulations. Microbiome governance should recognise the specificity of the challenges involved.

Secondly, policies and regulation need to be evidence-based and microbiome research can contribute to this, e.g., by providing tools for a critical assessment and validation of diagnostic tools in terms of reliability and credibility. From a normative perspective, empowerment requires information about evidence and validation for product claims.

Thirdly, we notice as an overall observation that, whereas microbiome diagnostic tools often claim to contribute to personalisation by providing assessment and advice tailored to individual customers, in practice the information and advice generated by tools tends to by generic rather than personalised.

Finally, a critical assessment should build on our understanding of the microbiome also on a more fundamental level. So far, most or the tests or kits provided by companies directly to consumers focus on microbiome composition. They propose an analysis of the microbiome composition based on the examination of a microbiome specimen collected at-home. Often, compositional information will be linked to risks to develop certain diseases according to the microbiome composition analysis. As indicated in previous chapters, this is a questionable starting point. When it comes to understanding microbiome health, we should opt for a functional and relational, rather than a compositional approach.

As indicated, these issues will be addressed in more detail in D7.2. PRI has organised an expert workshop to discuss self-management tools available on the market and proposing an analysis of the faecal microbiome composition. Six different microbiome testing kits offered by six different companies were discussed resulting in recommendations or actions to increase quality of the microbiome self-management tools and to avoid overpromising messages to the consumer.

## Bullet points

- The development of a governance strategy of microbiome self-management tools that is anticipatory, inclusive, responsible, and reflective requires a mutual learning approach involving multiple stakeholders, perspectives and sources of knowledge and experience.
- Microbiome research can provide critical assessments of diagnostic tools to foster reliability and credibility of product claims.
- Whereas microbiome diagnostic tools often claim to contribute to personalisation, providing tailored advice to individual customers, in practice the information and advice generated by tools tends to by generic rather than personalised.
- Most self-management tools provide compositional microbiome information. Yet, self-management can profit from a deepening of our understanding of health that opts for a functional and relational rather than a composition approach.

**Commenté [jD3]:** I couldn't agree more. I see a future for symbiosis monitoring where the prescription could include both microbiome parameters and host parameters (the usual biology parameters for todays' medicine).

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