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Microbiome-based solutions to address new and existing threats to food security, nutrition, health and agrifood systems' sustainability

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In addition to challenges like climate change and biodiversity loss, the sustainability and resilience of agrifood systems worldwide are currently challenged by new threats, such as the COVID-19 pandemic and the Ukraine war. Furthermore, the resilience and sustainability of our agrifood systems need to be enhanced in ways that simultaneously increase agricultural production, decrease post-harvest food losses and food waste, protect the climate, environment and health, and preserve biodiversity. The precarious situation of agrifood systems is also illustrated by the fact that overall, around 3 billion people worldwide still do not have regular access to a healthy diet. This results in various forms of malnutrition, as well as increasing number of people suffering from overweight and obesity, and diet-related, non-communicable diseases (NCDs) around the world. Findings from microbiome research have shown that the human gut microbiome plays a key role in nutrition and diet-related diseases and thus human health. Furthermore, the microbiome of soils, plants, and animals play an equally important role in environmental health and agricultural production. Upcoming, microbiome-based solutions hold great potential for more resilient, sustainable, and productive agrifood systems and open avenues toward preventive health management. Microbiome-based solutions will also be key to make better use of natural resources and increase the resilience of agrifood systems to future emerging and already-known crises. To realize the promises of microbiome science and innovation, there is a need to invest in enhancing the role of microbiomes in agrifood systems in a holistic One Health approach and to accelerate knowledge translation and implementation.

KEYWORDS

agrifood systems, ecosystem health, microbiome-based solutions, malnutrition, resilience

Introduction

Despite decades of global efforts, food insecurity and malnutrition have proven to be stubborn problems. The prevalence of food insecurity has continued to rise, jumping from 8.0 to 9.8% from 2019 to 2021. The estimated number of people affected in 2021 globally is in the range of 702–828 million (FAO, 2022). This represents an increase of about 150 million since the outbreak of the COVID-19 pandemic. COVID-19 has had major impact on food security, health, supply chains, commodity prices and economies.

As a result, acute food insecurity at crisis or worse levels (Integrated Phase Classification/Cadre Harmonisé Phase 3 or above) worsened dramatically in 2021, with globally 193 million people in 53 countries or territories being affected, and these figures are not yet including the anticipated impact of the Russian invasion of Ukraine (FAO, 2022). Conflicts are the main drivers of acute food insecurity, besides significant economic shocks, increasingly frequent and severe extreme climate events, and combinations of these such as the multi-faceted crisis which we are currently facing. Food insecurity is also aggravated due to substantial food loss or waste, which globally amounts to one third of the food produced in the world for human production (FAO, 2019).

Besides the immediate health and other impacts of the pandemic, COVID-19 infections often also manifest in severe long-term health problems, such as an increased risk of developing diabetes (Xie and Al-Aly, 2022). Moreover, the pandemic illustrates how nutrition is a key determinant of health, with diet-related non-communicable diseases (NCD) such as obesity and diabetes being associated with increased morbidity and mortality rates in COVID-19 patients. Malnutrition in all its forms is a major factor associated with higher risk and mortality for infectious diseases in general. With an estimated 10% of the world population undernourished, 40% overweight, 13% obese, and 3 billion people that did not have regular access to a healthy diet in 2020 (Ritchie, 2021), COVID-19 has increased the need to comprehensively tackle the simultaneous food insecurity, malnutrition and NCD crises.

BOX 1 Definitions of microbiomes and microbiome applications.

A microbiome is defined as a characteristic microbial community occupying a reasonable, well-defined habitat that has distinct physio-chemical properties. The microbiome not only refers to the micro-organisms involved but also encompasses their theater of activity, which results in the formation of specific ecological niches (Berg et al., 2020).

A microbiome application is knowledge-based and/or microbiome data-driven and has measurable, beneficial effects. Ideally, the mode of action is understood (Kostic et al.)[1].

Microbiome science, an emerging game-changer for agrifood system sustainability and resilience?

A radical transformation of agrifood systems is needed if we are to address both old and new challenges and achieve greater sustainability and resilience. Science, technology, and innovation have a key role to play in this endeavor. In particular, microbiome research is opening up new avenues to not only improve human nutrition and health, but also to address several of the productivity, economics, and environmental challenges that the agrifood systems face (Berg et al., 2020) (Box 1).

The human gut microbiome plays a key role in nutrition and diet-related diseases, and that the microbiomes of soils, plants, and animals play a comparable role in environmental and animal health, and agricultural production and productivity. Notably, new research results have also shown, that it is possible to enrich and improve microbiome both in composition and function. Thus, microbiome-based solutions offer diverse types of opportunities all along the food system for creating more sustainable and resilient food production systems and healthy diets (D'Hondt et al., 2021), including for:

1 Kostic, T., Arruda, P., Berg, G., Charles, T. C., Cotter, P., Kiran, G. S. et al. *Microbiome Applications: Need for Definition and Ensuing Recommendations*. (in revision).

- Diagnosis in the context of diseases or ecosystem functions from soils to humans and back; Identification of key features of and functions that support ecosystems/host health.
- Development of innovative products and processes supporting/improving microbiome functions.
- Improvement of agrifood production, processing, preservation, dietary and other practices that have direct positive impacts on the functioning of the microbiomes of humans, plants, animals, soils, water bodies, etc. with a view to preserve, restore and valorize these microbial communities ensuring a balance in favor of their beneficial services.
- Employ microbiomes for waste valorization and bioremediation of pollutants.

If implemented at scale, such microbiome-based solutions could help address the multi-pronged crises that we are currently facing by increasing the effectiveness of efforts to prevent and treat malnutrition and NCDs and provide realistic, more sustainable, and affordable bio-based alternatives to the use of various agrochemicals, such as inorganic fertilizers and pesticides, as well as veterinary drugs.

Because microbiomes are linked across ecosystems (soils, water bodies, plants, animals, and humans), the adoption of such microbiome-based practices all along the agrifood system has the potential to simultaneously generate impacts on human health, food security and nutrition, environmental health, livestock production and agrifood products and system performances. Altogether microbiome science has high potential to make agrifood production more sustainable, healthier, and more resilient against current and emerging crises.

Preventing and treating all forms of malnutrition, and NCDs

NCDs have taken on pandemic proportions with huge and growing socio-economic impacts. Many of these diseases are influenced in part by nutrition and the effect that diet has on the health and resilience of human microbiomes. The COVID-19 pandemic clearly demonstrates the impact of malnutrition also in the case of infectious diseases.

There is a rapidly growing body of evidence that the disruption of gut microbiome composition and functioning is an important factor in child mortality caused by susceptibility toward diarrhea, the development of malnutrition (i.e., undernutrition, obesity), and other NCDs. Diet is one of the major factors influencing the symbiotic relationship between a host and its microbiome, and the disruption of this relationship is increasingly widespread and linked to the westernization of diets across the world. Among other things, western diets are characterized by low fiber/high carbon content and the presence of xenobiotics such as some food additives in ultra-processed food, residues of pesticides, drugs, and other chemicals. These characteristics have been shown to have a negative impact on gut microbiome composition and may disturb its symbiotic functions.

Microbiome-informed predictive tools and early diagnosis will help to better design timely nutritional interventions for early disease risk detection, prevention, treatment, and for personalization. As an example, the gut microbiome of infants stabilizes only around the age of two to three years, and the impact of feeding practices in early months (breastfeeding vs. formula milk) and transition to first solid food have been shown to have a strong impact on the gut microbiome with possible association with development of NCDs later in life. In first years of life, acute malnutrition has been linked to microbiome immaturity and, in turn, microbiome immaturity has been proven to be causally involved in the developmental deficits of undernourished infants (Subramaniam et al., 2014). Also, low microbiome diversity and unhealthy dietary patterns have been associated with normal-weight children subsequently becoming overweight compared to those that maintained normal weight in a four-year follow-up (Rampelli et al., 2018). New therapeutic foods, as microbiota-directed complementary food (MDF) for infants specifically targeting bacterial taxa underrepresented in Moderate Acute Malnutrition (MAM) have shown very promising results in clinical trials and could in the future ensure more durable health support (Barratt et al., 2022; Kamil et al., 2022). MDF could be designed for other specific populations (i.e., pregnancy, childhood, adolescence, elderly), for reducing disease risk (i.e., overweight) and for specific medical purposes (i.e., diabetes).

Another potential avenue for dealing with various aspects of malnutrition and NCDs, but also infectious diseases, is through (dietary) interventions that target the microbiome composition, by either favoring the abundance of species with health beneficial effects or by supplying such species directly. There is increasing evidence of health benefits of biotics, although more knowledge is still needed to develop effective biotics for the general population/despite inter-individual microbiota variations as well as to meet regulatory standards for specific products and specific health benefits. To this end, it is interesting to note that some biotics are being tested in randomized control trials in the context of COVID-19 (Mirashrafi et al., 2021).

The whole diet composition also plays a major role in microbiome function, diversity, and stability and as such represents a powerful actionable tool accessible to everyone to promote health throughout life. Personalization of diet may further optimize the gut microbiome for better health. Understanding the unique interaction between diet and the gut microbiome in the genetic background of the host is expected to expand the options for preventive and personalized health management. Microbiome knowledge could reinforce the population-wide adoption of healthy dietary practices and help to formulate dietary recommendations and food-based dietary guidelines intended to nourish the holobiont (host and associated microbiome) with a larger impact on the health status of the overall population. Prevention of obesity and NCDs depends to a large extent on a long-term adherence to a healthy, microbiome-friendly diet. Highly important for gut microbiome functioning is the consumption of diverse plant-based foods that ensure high intakes of fibers and phytochemicals and reduction of ultra-processed food intake. Fermented foods, in addition to being an ancestral way of preserving food, particularly interesting in the context of resource poor environments, have been shown to have beneficial impacts on health through microbiome modulations, especially *via* anti-inflammatory metabolites, probiotic effects of the fermentative microorganisms and substrate break-down products with prebiotic effects (Leeuwendaal et al., 2022). Furthermore, probiotic, anti-inflammatory, gut-healthy feed reduces the need for antibiotic treatments in industrial meat and fish production, a practice which inherently carries a higher risk of antimicrobial resistance development and exposure of humans and the environment to drug residues.

A healthy, microbiome-friendly diet may have several implications all along the food system, including the need of healthy soils enabling resource-efficient production of healthy and nutritious food, and diverse crop species and varieties to facilitate diverse diets. Also, plant pathogens (including also mycotoxin producing fungi) need to be controlled without the use of chemical pesticides, such as by applying microbiome-based biocontrol agents and microbiome-based processing approaches may be used to ensure higher amounts of fibers and phytonutrients.

Sustainable ways of increasing agrifood production, productivity, and resilience

Crop production practices can have significant effects on the microbiome of soils and plants, with important knock-on effects in terms of crop productivity, crop health, as well as greenhouse gas fluxes, carbon storage, ecosystem health and climate. Intensive agricultural practices, such as heavy use of synthetic fertilizers and pesticides, as well as excessive irrigation and tillage amongst others, negatively impact the soil microbiome. Microbiome research is generating efficient microbiome-based solutions for plant protection, fertilization, stress alleviation and plant health, while promoting biodiversity and sustainability (Jurburg et al., 2022). This is even more important as synthetic energy-intensive agricultural inputs are becoming more expensive through the ongoing crises and regulation is underway to half the use of pesticides by 2030 (https://food.ec.europa.eu/plants/pesticides/sustainable-use-pesticides_en). The latter should favor the use of more sustainable solutions, including microbiome-based alternatives.

To date, our ability to preserve or manipulate the soil and crop microbial diversity for improved production is mostly focused on altering agricultural management practices, the addition of microbial products, or a combination of both strategies (Beed et al., 2011; Kendzior et al., 2022). Inoculants consisting mostly of individual strains are used for bioaugmentation and as biofertilizers to colonize the plant environment (e.g., rhizosphere or endosphere) (Beed et al., 2011; Uzoh and Babalola, 2018). Although limitations/hurdles remain (e.g., efficacy in various field conditions), which require knowledge advances (Compant et al., 2019), impressive success already exists, e.g., the application of N_2-fixing rhizobia as inoculants for soybean in Brazil saved ~US$ 10.2 billion in N fertilizers (Olmo et al., 2022). Also, a recent meta-study highlighted the potential of microbial inoculants as biofertilizer and to improve stress resilience (Li et al., 2022). Currently, strain combinations and tailored communities with improved performance are in development, but the regulatory burden associated with the registration of such products is a major barrier. To improve field success of microbial applications, different approaches have been proposed ranging from understanding the complexity and ecological behavior of microbial inoculants to the development of novel formulations and application technologies to improve shelf-life and persistence (Sessitsch et al., 2019). Currently, soil and plant microbiomes are investigated and new solutions, e.g., based on new strains or strain combinations, are developed to improve the efficacy of microbial applications in the field facing different environmental conditions. Adaptation of microbial solution may be also needed to face up-coming challenges such as the evolution and development of new pathogens.

To date, the application of microbial biocontrol agents has been most successful with the potential to replace several chemical pesticides. Other microbial products on the market or in development target partly devastating plant diseases for which no chemical pesticide is available. Less explored, but gaining importance, is the fact that soil- and/or plant-associated microorganisms can modulate the plant metabolism and microbial inoculation has shown to improve the nutritional quality of plants (Li et al., 2022). A myriad of different sustainable agricultural practices can positively modify the soil microbiome and increase microbial diversity on fruits and plants (Wassermann et al., 2019). For instance, reduced or no tillage enriches various microbial taxa including plant beneficial arbuscular mycorrhizal fungi, whereas tillage impacts diversity and functioning of soil microorganisms (Yang et al., 2021). Microbiome data can inform on sustainable farming practices, which modulate the indigenous microbiome to minimize fertilizer input, increase stress resilience and high nutritional quality. Furthermore, using the plant to modulate a microbiome and to integrate microbiome considerations in plant breeding has great potential (Hohmann et al., 2020).

By using such microbiome-based or -targeted alternatives to green revolution technologies such as conventional pesticides and synthetic fertilizers, both plant productivity (improving food security, nutrition, and health) and the environment stand to gain. However, to gain benefit, experts advise to better involve farmers and farmer associations as know-how sharing, experience and implementation results so far have been limited.

Microbiome research, methods and results have also provided the basis for valorizing agrifood side streams (Lange et al., 2021). Sustainable, resource-efficient, and affordable gut-healthy food and feed products can be generated by upgrading crop residues and agro-industrial side-streams through microbial and enzymatic processing of various biomasses. In this way, microbiome research also provides the basis for increased circularity of biological resources, leading to improved resource efficiency and thus to more responsible use of the global biological resources and contributes to climate change mitigation.

From microbiome science and innovation to policy and practice for improved food security

The potential of microbiome science as the basis for designing interventions for preventive and personalized nutrition and health management as well as for sustainable agrifood and environmental applications is beyond doubt. In particular, there is potential to make use of microbiomes to address the current threats to food security, nutrition, health and agrifood systems' sustainability and to rapidly translate existing knowledge to policy and practice. Rapid realization of microbiome potential will require that various issues be addressed (Figure 1), including:

- Closing of knowledge gaps through investment in trans- and interdisciplinary research and innovation, international research cooperation, and the application of new technologies (e.g., artificial intelligence/machine learning) across different microbiome fields.
- Putting in place adequate regulatory guidelines and frameworks for dealing with the unique nature, benefits and risks associated with microbiome applications in the nutrition, health and agrifood sectors and for accelerating knowledge translation and implementation.
- Robust studies that meet regulatory requirements to support eventual health claims for specific nutrition and health products.
- Robust studies that qualify and quantify both the benefits to be gained from and the risks associated with the use of products targeting agrifood production, productivity, and environmental goals in specific contexts.
- Create incentives for the development and uptake of microbiome-based solutions among various value chain actors and implement accompanying measures, such as communication, to facilitate consumer and producer acceptance.
- Inclusion of researchers and value chain actors (from farming to product and practice) in medium- and low-income countries in the co-development of new knowledge and innovations, and the establishment of co-learning processes targeted toward finding more effective and efficient solutions to address current and emerging challenges to agrifood systems in different contexts.
- Integrate microbiomes in a holistic One Health (FAO., 2021) concept in which microbiomes are considered an integral and essential part of healthy living organisms and ecosystems.

Conclusions

The COVID-19 pandemic and the effects of the Russian invasion of Ukraine on food security, nutrition, and agrifood systems, in addition to climate change and the unprecedented worldwide occurrence of drought, clearly illustrate the urgency with and the extent to which agrifood systems need to be transformed and made much more resilient globally. Even though microbiome science is still a relatively new area of research, it is already offering new potentially game-changing and multiple-win solutions for tackling malnutrition and diet-related NCDs through food and dietary approaches, while at the same time addressing various environmental and agrifood systems challenges, not the least improved robustness to climate change endured threats to food security. There are also wins in terms of sustainable economic development and green jobs, as microbiome science and innovation increasingly attract large private sector investments in new agrifood market opportunities, new products, and services, with job opportunities for young people and entrepreneurs, and alternative production practices that can help overcome the multiple challenges that the sector and society face. It may be counter-intuitive at a time where public resources are constrained, but now more than ever microbiome science is of utmost importance. While much still needs to be learned and discovered, innovative and implementable microbiome-based solutions are available. Decision makers should support and create the policy, regulatory, institutional and investment conditions to take these solutions to market without delay and at a scale, not only in high-income countries but also in medium and low-income countries where the need and opportunity may be highest.

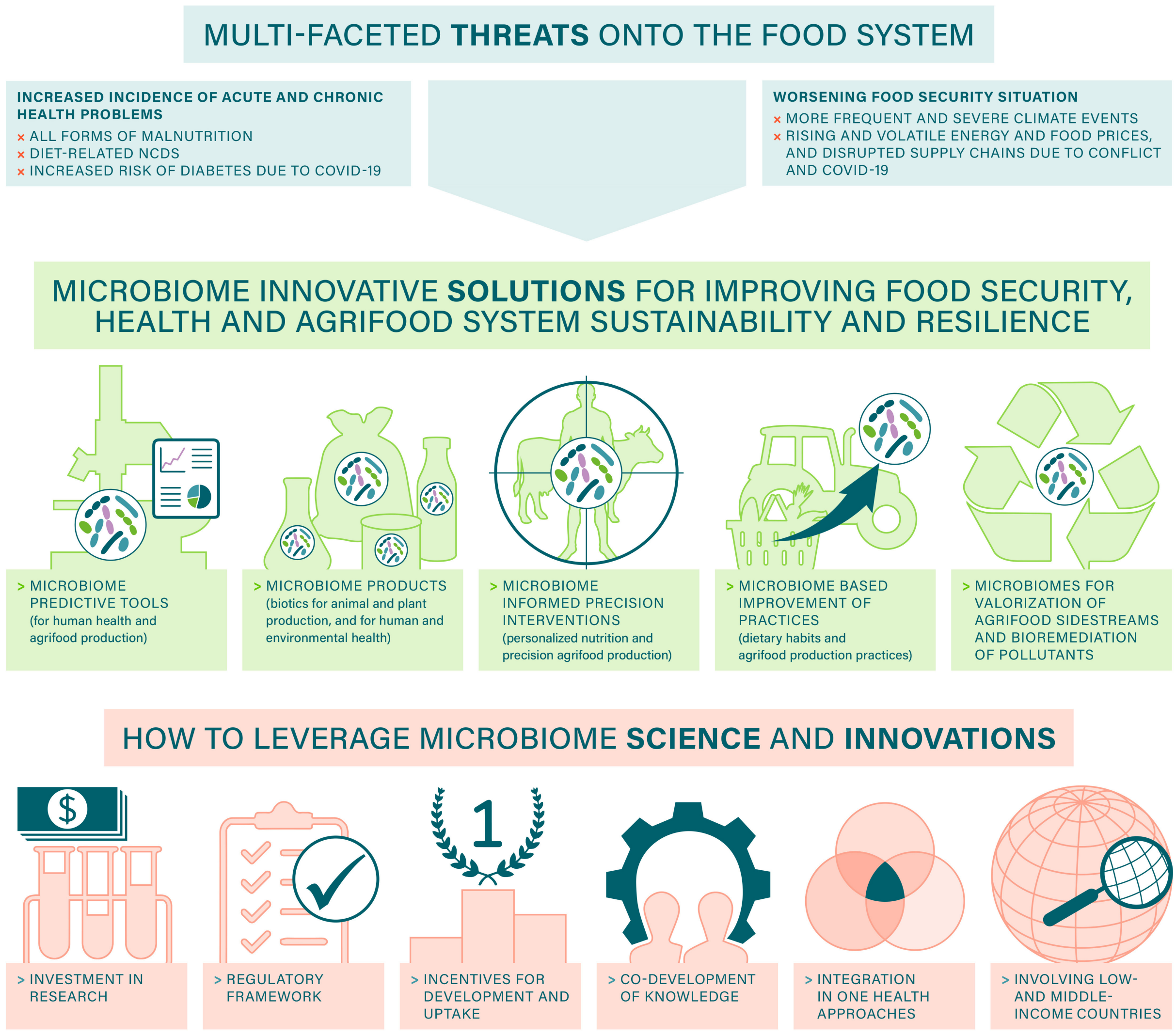

FIGURE 1
Food sytem threats, microbiome solutions and how to leverage microbiome science and innovation.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

All authors conceptualized the paper in frame of workshops. KC and AS drafted the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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