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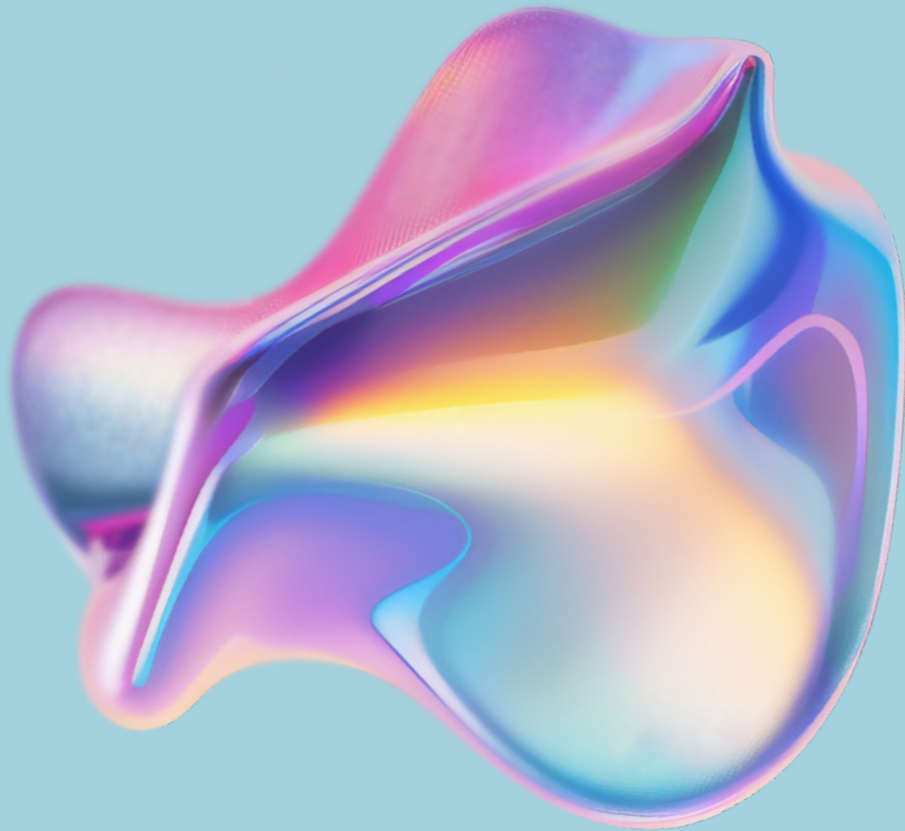
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THE ESSENCE

of HEALTH *and* HUMANITY





PREVENTION *beats* INTERVENTION

Oral health is a neglected area of global health and has traditionally registered low on the radar of national policy makers. Dentists have also taken little interest in advocacy to promote good oral health, preferring to treat rather than prevent oral diseases. And, because poor oral health affects morbidity more than mortality, governments have viewed oral conditions as less important than other, more life-threatening diseases.

Yet, globally, the burden of major oral diseases and conditions is high. Dental caries is one of the most common chronic diseases worldwide. 90% of people have had dental problems or toothache caused by caries, and in low-to-middle income countries most caries remains untreated. Severe periodontitis affects 5–15% of most populations. Oral cancer is the eighth most common cancer worldwide and the most common in men in southeast Asia.

But training more dentists and building dental clinics (the western curative model of care), is costly and unrealistic in most low-income and middle-income countries. Prevention of oral disease is therefore key, largely possible, and should be a routine part of other health professionals’ work.

The daily use of fluoride is the most cost-effective, evidence-based approach to reduce dental decay. Water or salt fluoridation are possible population-wide approaches, but their implementation depends on the development and infrastructure of the country as well as political will and community acceptance. Promoting the daily use of effective fluoride toothpaste is a more realistic strategy but its cost prohibits its widespread use in many low-in-

come and middle-income countries. Governments can remove taxes on fluoride toothpaste, which in some countries represent up to 50% of the product’s price, and they can work with manufacturers to produce lower cost toothpaste.

Policies that address the risk factors for oral diseases, such as intake of sugars, and tobacco use, can also be implemented, especially because these moves will help reduce chronic diseases. Oral diseases and chronic diseases, such as cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes share many common risk factors.

Promoting good oral health could also help countries to achieve child-related development goals. Caries can negatively affect a child’s ability to eat, sleep, and do schoolwork. Preliminary studies have suggested that dental caries, and related pain and sepsis might contribute to undernutrition and low weight and height in children in developing countries. In developed countries, studies show that when dental caries are treated, children start to put on weight and thrive. Oral pain is also one of the most common reasons for school absenteeism.

Preventing oral disease is important and achievable. Evidence-based, simple, and cost-effective preventive approaches exist, but they need to be rigorously promoted and implemented. Professionally, health workers, including physicians, nurses, pediatricians, and pharmacists can all deliver prevention messages about the use of fluoride and the risk factors for oral disease. Political, commitment is needed to integrate oral disease prevention into programs to prevent chronic diseases and into public-health systems.

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Marcel J. Scacchi
 Executive Director of AVOLA

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The Spirit of Bern

Author — Marcel J. Scacchi

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Prof. em. Dr. Daniel Buser (far left), Chairman of the Board of Trustees of the Spirit of Bern, was pleased that a varied, top-class program was put together again this year. More than 60 speakers took a stand on various topics, led by the Minister of Health, Elisabeth Baume-Schneider.

Premium increase of 146 % in 15 years

Many Swiss hospitals are doing so badly financially, that they can no longer stand on their own feet. At the same time, premiums for policyholders have been rising incessantly since 1996. While the “average premium” was still around CHF 1,539 per year in 1996, it had risen to CHF 3,788 by 2021, an increase of 146 percent.

It seems that there is no decline in premium growth in sight, as healthcare costs will continue to rise in the future. This is caused by the further increase of costs in medical progress and the associated expansion of the catalogue of benefits in basic insurance. New medical treatments such as immunotherapy and gene therapies in oncology, the use of high-resolution imaging techniques are costly. But they allow not only better treatment of existing patients, but also the treatment of more patients. This part of the cost growth certainly has broad legitimacy.

What solution strategies are available?

There is potential for savings in unnecessary services such as laboratory tests for asymptomatic patients or elective procedures, which are carried out excessively in Switzerland. However, this requires solving the structural incentive problems in the Swiss healthcare system.

The “Spirit of Bern”, that’s where health professionals, politicians and entrepreneurs meet – a potential role-model for AVOLA.

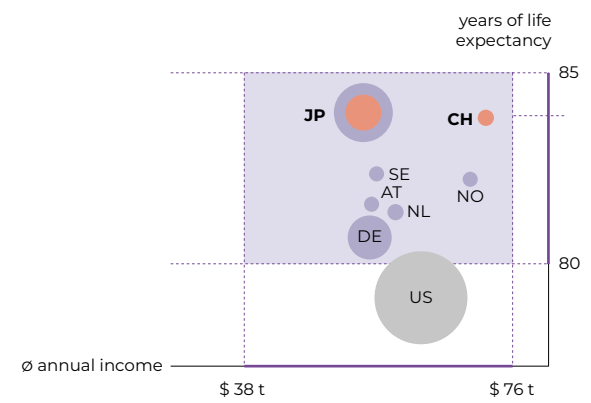
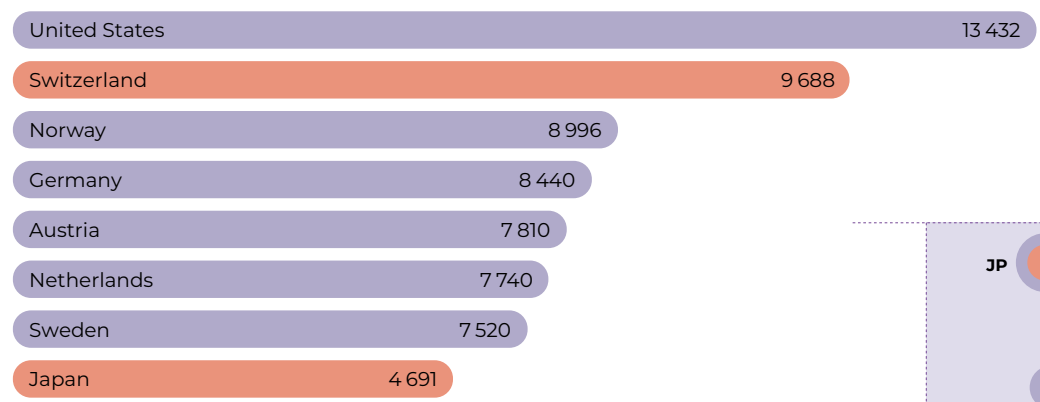
In summary, it can be stated that there are already many concepts (electronic patient record, digitization of administration/processes, etc.) and measures around, that have already been implemented (Care@Home, use of generic drugs, integrated care concepts such as Réseau de l’Arc, etc.), but they must be coordinated much better in order to avoid resource losses, leading to cost

savings more quickly. With its federal structure, staff shortages and a general high-cost pressure, Switzerland will be extremely challenged in the future.

¹ average of all premiums actually paid across all insurance models and deductibles

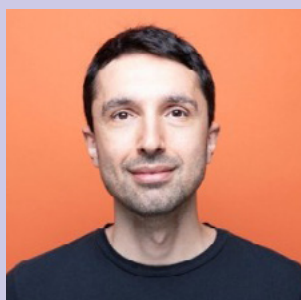
FIGURE 1

Health Spending 2023 p/y/\$



Source: EU National Health Expenditure (2023); Eidg. Amt f. Statistik (2024); Gapminder (2024)

Food for Thought: How Nutrition Shapes Mental Health



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The connection between nutrition and mental health is gaining recognition, with evidence showing that traditional diets rich in whole, minimally processed foods and emerging approaches like ketogenic metabolic therapy (KMT) may offer protective and therapeutic benefits for mood disorders, anxiety, and depression. By balancing nutrients that support brain function, reducing inflammation, and improving gut health, these dietary strategies hold promise for advancing mental well-being.

In the realm of psychiatry, we find ourselves at a crucial juncture. The predominant paradigm, heavily reliant on pharmacotherapy, has yielded but modest advancements in tackling the pervasive challenges of mental health worldwide [1]. Acknowledging the intricate web of factors that shape mental health, a growing body of persuasive evidence underscores the pivotal role of nutrition in the emergence and course of mental disorders. Begdache et al. underscored the intricate interplay between mental well-being and healthy lifestyle practices – a self-reinforcing loop where poor habits erode mental health, which in turn weakens the resolve to adopt healthier choices [2]. Beyond diet as a whole, deficiencies or imbalances in key micronutrients can subtly yet profoundly shape mood and mental health [3]. This recognition beckons a fundamental shift: psychiatry must regard diet with the same gravity that cardiology, endocrinology, and gastroenterology have long afforded it [4]. This realization compels us to widen the lens of psychiatric practice, acknowledging nutrition not as a peripheral concern but as a fundamental pillar of mental health – one that demands thoughtful integration alongside traditional interventions [5]. Emerging evidence points to poor nutrition as a silent accomplice in the onset and course of mental disorders –

undermining both treatment and recovery [6]. The International Society for Nutritional Psychiatry Research calls for embedding nutritional medicine into mainstream psychiatry – urging research, education, policy, and advocacy to drive this essential shift [7]. Yet, this integration faces hurdles, as both mental health and nutrition are intricate, multifaceted domains – resisting simple solutions [8]. The research community is increasingly focused on food as a variable influencing mood and mental health [9]. Given the brain's reliance on nutrition for its structure and energy metabolism, diet should logically be central to mental health. Yet, despite this, there is a notable lack of research, particularly of high quality, on the role of diet in mental health. The field of nutritional psychiatry has long been overlooked, with many studies in this area suffering from poor design [10]. Mental health disorders are multifaceted and typically lack a singular cause or treatment that ensures lasting relief. This review advocates for integrating nutritional strategies into comprehensive psychiatric treatment, alongside established interventions like psychopharmacology (when necessary), psychotherapies, occupational therapy, social work interventions, exercise, etc.

Microbiome-Gut-Brain-Axis

The microbiome-gut-brain axis (MGBA) represents the dynamic, bidirectional dialogue between the gut – including its vast microbial ecosystem – and the brain, intertwining emotional and cognitive processes with intestinal function. Trillions of symbiotic bacteria reside in the gut, exerting a profound influence on brain regulation and behavior [11]. The exact mechanisms of gut-brain interplay remain under exploration, yet key players include the vagus nerve, endocrine and immune pathways, and the gut's role in metabolizing neurotransmitters and bioactive compounds (reviewed in [12]). The human colon harbors a dense and diverse microbial community, reaching $\sim 10^{11}$ microorganisms per gram of content, predominantly anaerobic bacteria. Beyond bacteria, this ecosystem includes archaea, yeasts, and other eukaryotes, forming a complex network within the gut. Collectively, the gut microbiome, comprising ~ 100 trillion microorganisms, carries a genetic repertoire nearly 150 times larger than the human genome. [13]. The gut microbiota harbors enzymes and metabolic pathways absent in the host, enabling the breakdown of complex molecules like dietary fibers and other indigestible compounds. Within the colon, microbes synthesize and release vital vitamins, including K, biotin, pantothenic acid, and select B vitamins. Diet and nutritional supplements, such as probiotics and prebiotics, can modulate the gut microbiome, influencing its composition and function [14,15]. Evidence suggests that consistent use of probiotic supplements can alleviate depressive symptoms [16,17]. Additionally, consuming fermented foods appears to have a positive impact on mood [18]. The term psychobiotics has been coined to describe prebiotics, probiotics, and postbiotics (metabolites produced by the microbiome) that, when consumed, promote mental health through their interactions with the gut's commensal bacteria [19]. A recent review outlined five mechanisms through which the microbiota may impact brain health: 1) modulation of the hypothalamic-pituitary-adrenal axis, 2) alteration of inflammation and gut permeability, 3) vagus nerve stimulation

affecting gut function, 4) production of neurotransmitters and hormonal changes, and 5) modification of myelination and gene expression in the pre-frontal cortex [20].

The Simultaneous Rise of Metabolic and Mental Health Disorders

Over one-third of the global population is estimated to be overweight or obese, with a body mass index (BMI) of 25–29.9 defining overweight and 30 or higher marking obesity. This rising prevalence, steadily increasing over recent decades, highlights the pressing need to address obesity as a significant public health challenge [21]. Mental health disorders, affecting roughly 25% of the population, carry a significant global burden. Obesity, in turn, is increasingly recognized as a key factor that intensifies the risk and severity of these conditions [22]. Indeed, two out of five individuals with overweight or obesity are diagnosed with a psychiatric disorder, most commonly mood disorders, anxiety disorders, psychotic spectrum disorders (PSD), or eating disorders [23]. The temporal relationship between obesity and psychiatric disorders, including major depressive disorder (MDD), anxiety disorders, and PSD, remains debated. This complexity is further heightened by the many proposed biological, psychosocial, and economic connections between these conditions. Beyond the reciprocal psychosocial impacts of obesity on mental well-being and the influence of impaired mental health on lifestyle, biological mechanisms like inflammation and cellular stress, as well as the iatrogenic effects of psychopharmacological treatments – often accompanied by adverse metabolic outcomes – demand close scrutiny [24–27]. What is often termed the Standard American or Western Diet is rapidly spreading worldwide. This diet is characterized by high levels of refined carbohydrates, especially sugar, a high glycemic load, ultra-processed foods, and a significant proportion of unhealthy fats from refined seed oils rather than natural, unprocessed fats [28]. The Western diet is increasingly linked to a range of health risks, including obesity, metabolic dysfunction, mental health disorders, and disruption of the gut microbiota [29].

The Good, the Bad, and the Ugly
Ultra-processed foods are industrially produced items made from compounds extracted, derived, or synthesized from food or food substrates [30]. These products generally contain five or more ingredients, including artificial additives like preservatives, colorants, texturizing agents, and flavor enhancers – substances seldom found in home-cooked meals. Ultra-processed foods are often inexpensive, convenient, shelf-stable, easy to consume, and highly palatable [31]. In early 2021, a systematic review and meta-analysis revealed that ultra-processed foods accounted for 17% to 56% of total daily energy intake, with an average of 37%, across 28 countries [32]. Emerging evidence increasingly connects higher

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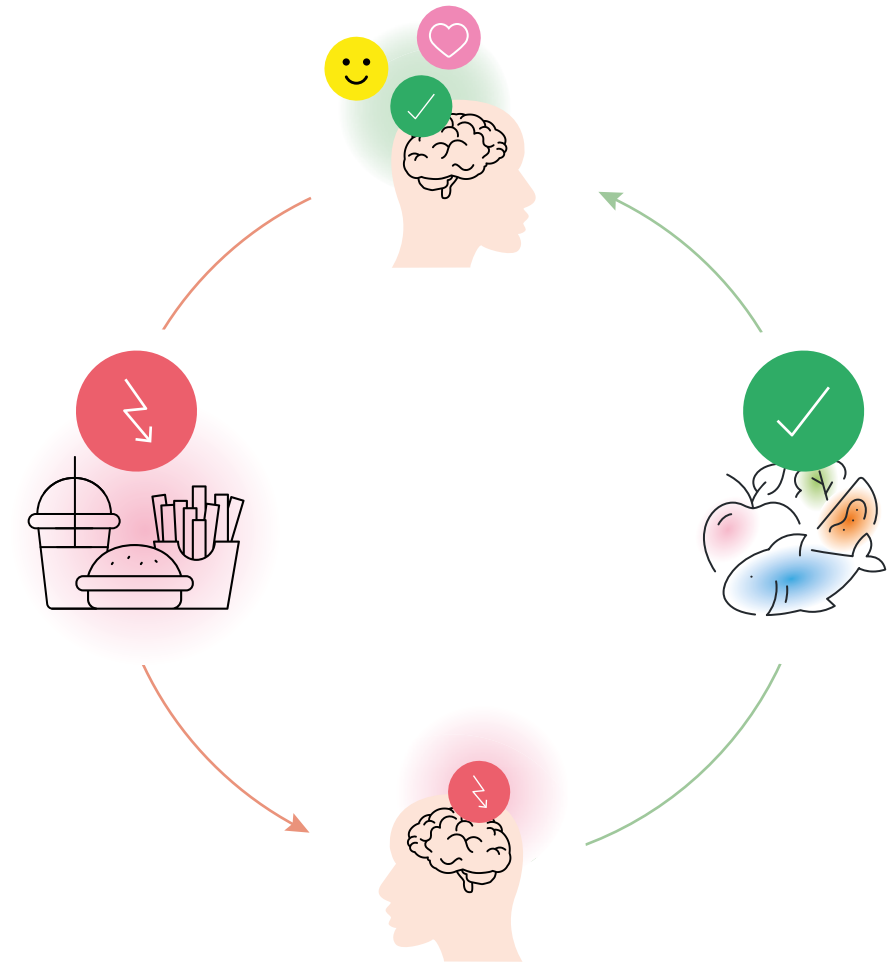
consumption of ultra-processed foods with greater risks of cardiovascular disease-related mortality, type 2 diabetes, and adverse mental health outcomes [33]. Pesticides are widely used in agriculture, gardening, households, and veterinary practices globally, with this trend expected to continue [34]. In the general population, pesticide exposure primarily occurs through consuming food and drinking water contaminated with pesticide residues [35]. Several studies suggest a strong association between pesticide use and negative mental health outcomes, including anxiety, depression, and suicidal behavior

[36–41]. Consumption of conventionally grown fruits and vegetables leads to higher pesticide exposure, potentially carrying long-term health risks. Emerging evidence indicates that certain pesticides may disrupt the gut microbiota, influencing the gut-brain axis [42,43]. A similar concern pertains to microplastics in human food chains [44]. However, the impacts of microplastics on mental health remain largely unknown at present. Modern diets are typically high in refined seed oils. Growing evidence suggests that highly processed oils are pro-inflammatory, increasing oxidative stress in the body. This contributes to damage across multiple organ systems and disrupts metabolism [45]. In contrast, virgin oils have been shown to exert beneficial effects on the gut microbiota, which in turn influence both the nervous system and overall health, while also helping to regulate inflammatory and metabolic changes [46].

Healthful Diets – Current Evidence

Many authors regard mental health disorders as “diseases of modernity” [47]. This perspective highlights the notion that a departure from traditional lifestyles is driving the increasing prevalence of mental health disorders [9,48]. This theory aligns with the evolutionary mismatch hypothesis, which posits that the rising incidence of mental disorders, such as depression, stems from a stark contrast between the environments humans have evolved to thrive in and the modern environment [49]. Food is a key factor shaping modern environments, distinctly differing from pre-modern conditions [50]. Evidence suggests that traditional diets are more favorable to health [51]. Several population studies have established a link between adherence to traditional dietary practices and a reduced risk of anxiety and depression [52–57]. For historical reasons, much of nutritional research has disproportionately focused on the so-called Mediterranean diet. However, this may also apply to traditional diets as a whole, both within and outside the Western world [58]. A substantial body of evidence indicates that the Mediterranean diet offers protection against depressive symptoms and major depression [59,60]. This finding is supported by both population surveys and

randomized controlled trials [61–67]. The health benefits of the Mediterranean diet may be attributed to its high content of antioxidants, fibers, monounsaturated and omega-3 fatty acids, phytosterols, and probiotic microorganisms [68,69]. The Mediterranean diet is also rich in lacto-fermented foods, such as pickles and dairy products like yogurt and cheese, which are fermented by lactic acid bacteria [70]. The traditional Japanese diet is abundant in fermented foods, including probiotic-rich items like black rice vinegar, soy sauce, miso, natto, and tempeh. These foods are made using time-honored methods that rely on a mix of microorganisms such as lactic acid bacteria, acetic acid bacteria, sake yeast, koji molds, and natto bacteria [71]. Adherence to traditional Japanese dietary customs has been linked to lower rates of depressive symptoms [72,73].



Graphical summary: Risky eating behaviors, often linked to a Western diet, are characterized by refined carbohydrates, sugars, high glycemic load, ultra-processed foods, and pro-inflammatory ingredients – while lacking essential nutrients. These factors contribute to mental health disorders. In contrast, traditional diets like the Mediterranean or Japanese diets, rich in whole foods and nutrients, support brain and mental health. Well-formulated ketogenic diets, high in healthy fats and essential nutrients, foster recovery from mental illness through ketosis.

Source: Baumgartner, Imfeld & Persson et al., J Periodontol (2009)

Metabolic Psychiatry and Ketogenic Metabolic Therapy

The ketogenic diet significantly reduces carbohydrate intake, typically allowing only 20–50 grams of net carbs per day, which makes up about 5% of daily caloric intake. In contrast, fat intake is increased to 75–80% of calories. By limiting carbohydrates and promoting

lipolysis, the diet stimulates the production of ketone bodies, which can be measured through reliable, self-administered tests. This makes the ketogenic diet unique in offering a clear biomarker to assess both physiological target achievement and adherence [74]. These ketone bodies provide an alternative fuel source for the brain, reducing its dependence on glucose [75]. Furthermore, ketone bodies have a range of

therapeutic effects, including improving metabolic function (such as lipid profile and insulin stability), inhibiting the mTOR signaling pathway, enhancing mitochondrial function and energy production, reducing oxidative stress and inflammation, and rebalancing the inhibitory-excitatory balance in the brain [76–79]. Therefore, we suggest reserving the term “ketogenic diet” for an interesting but still inadequately scientifically validated approach to illness prevention and wellness in healthy individuals. In contrast, its therapeutic use in serious disorders, based on pathophysiological reasoning, should be referred to as “ketogenic metabolic therapy” (KMT). Ketosis has a long history in human biology, with mild ketosis commonly observed in both mothers and infants during the third trimester of pregnancy and at birth [80]. Prolonged fasting and ketosis were the norm during human evolution, particularly in the Paleolithic era, when social structures were centered around small groups of hunter-gatherers [81,82]. The use of ketogenic diets for therapeutic purposes in modern medicine dates back to the 1920s [83]. A century ago, the ketogenic diet was a standard treatment for diabetes, extending the lives of children with type 1 diabetes and managing type 2 diabetes in adults. However, the discovery of insulin in the 1920s allowed people with diabetes to control hyperglycemia, even on high-carbohydrate diets [81]. Today, the ketogenic diet is an established, effective non-pharmacologic treatment for drug-resistant epilepsy in both children and adults, earning its place in modern epilepsy treatment guidelines [84]. Randomized controlled trials have shown that short-term ketogenic interventions consistently reduce body weight and visceral adipose tissue, improve metabolic health markers (including increased HDL cholesterol, lowered triglycerides, HbA1c, and diastolic blood pressure), all while preserving muscle mass [79]. However, research on the ketogenic diet’s efficacy in psychiatric illness is still in its early stages. In a study of 28 treatment-resistant patients with MDD, bipolar disorder, and schizophrenia, KMT led to a significant reduction in psychiatric symptoms for

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all patients. Clinical remission was achieved by 43%, and 64% were discharged with reduced psychiatric medication. Metabolic health improved, and nearly all patients, except one, experienced significant weight loss [85]. In a 4-month single-arm pilot trial involving 23 patients with bipolar disorder and schizophrenia, KMT reversed metabolic syndrome. Patients with schizophrenia showed an average improvement of 32% on the Brief Psychiatric Rating Scale. Additionally, 69% of participants with bipolar disorder had a greater than one-point improvement on the Clinical Global Impression score. Overall,

Abstract

The growing prevalence of both metabolic and mental health disorders has led to increasing interest in the relationship between nutrition and mental well-being. Evidence suggests that traditional diets, which prioritize minimally processed whole foods and avoid highly industrially processed oils and refined sugars, may play a crucial role in preventing and treating mental health conditions. These diets promote a balance of nutrients that support brain function and reduce inflammation, offering a potential protective effect against mood disorders, anxiety, and depression. Ketogenic metabolic therapy (KMT), which has demonstrated significant success in treating drug-resistant epilepsy, is gaining attention for its potential in psychiatric applications. Preliminary studies suggest that KMT may offer therapeutic benefits in mental health conditions such as depression, bipolar disorder, and schizophrenia. The diet works by altering metabolism to promote ketone body production, which provides an alternative energy source for the brain and may have neuroprotective effects. Additionally, KMT has been shown to improve metabolic health, reduce oxidative stress, and stabilize insulin levels, providing dual benefits for both brain and body health. Moreover, the gut microbiome plays an essential role in regulating brain function and behavior, with emerging evidence highlighting its impact on psychiatric disorders. While initial studies indicate that well-formulated ketogenic diets may modulate the gut microbiome in beneficial ways, further high-resolution human trials are necessary to fully understand these effects, particularly in the context of mental health. Thus, both traditional diets and the emerging KMT offer promising approaches to preventing and treating mental health disorders.

the trial suggests dual metabolic and psychiatric benefits from KMT [86]. In another pilot trial lasting 6 to 8 weeks, KMT in bipolar disorder, involving 27 participants, demonstrated the feasibility and safety of this approach in a psychiatric population [87]. Before the recent surge of trials on KMT in mental illness, a series of studies in the pediatric domain showed its potential to alleviate core symptoms and improve key features of autism spectrum disorder [88–91]. Despite limitations such as small sample sizes and the lack of control groups, existing studies have shown the feasibility, tolerability, and significant improvements in psychiatric symptoms associated with ketogenic metabolic therapy in various severe, chronic, and refractory mental disorders. Preliminary evidence indicates that ketogenic nutrition may alter the gut microbiome. Well-designed human trials suggest potential neuroprotective modulation through ketogenic diets. In a randomized crossover trial involving subjects with mild cognitive impairment, a Mediterranean-style ketogenic diet increased the beneficial genus *Akkermansia muciniphila*, reduced fecal lactate and acetate, and raised propionate and butyrate compared to the American Heart Association diet [92]. Preliminary animal research suggests that this bacterium may have antidepressant effects [93]. In a weight-loss trial, a very low-calorie ketogenic diet (VLCKD) increased gut microbiota diversity compared to a standard low-calorie diet (LCD) [94]. In an RCT with obese individuals, calorie restriction (CR), intermittent fasting (IF), and ketogenic diet significantly increased microbiota diversity compared to a habitual ad libitum diet. Only the ketogenic diet group showed an increase in the beneficial *Faecalibacterium prausnitzii* [95]. Secondary analysis of this trial suggested that lipopolysaccharide (LPS)-induced inflammatory processes may mediate the favorable impact of gut microbiota modulation on mitochondrial function. Changes with ketogenic nutrition depend on the specific formulation and control condition. In a recent RCT comparing therapeutic carbohydrate restriction (<8% of daily calories) with a moderate-sugar and

a low-sugar diet adhering to public health guidelines, no differences were observed between groups after 12 weeks in taxonomic composition, circulating short-chain fatty acids, or lipopolysaccharide-binding protein (a proxy for intestinal barrier integrity) [96]. Further high-resolution studies on microbiota changes in controlled human trials are essential to fully understand the impact of ketogenic regimes on the human gut microbiota, especially within the psychiatric context, where such research remains scarce.

Conclusions
Nutritional neurometabolic factors are increasingly recognized in psychiatry. The concurrent rise in metabolic and mental health disorders has sparked exploration into their shared mechanisms. Traditional diets, focused on whole, minimally processed foods, show strong potential for preventing and treating mental illness. Complementarily, ketogenic metabolic therapy offers a promising treatment for certain psychiatric patients (Figure 1).

References

- 1 Baxter AJ, Patton G, Scott KM, et al. Global Epidemiology of Mental Disorders: What Are We Missing? *PLoS One*. 2013;8:e65514. doi: 10.1371/journal.pone.0065514
- 2 Begdache L, Chaar M, Sabounchi N, et al. Assessment of dietary factors, dietary practices and exercise on mental distress in young adults versus matured adults: A cross-sectional study. *Nutr Neurosci*. 2019;22:488–98. doi: 10.1080/1028415X.2017.1411875
- 3 Popper CW. Single-Micronutrient and Broad-Spectrum Micronutrient Approaches for Treating Mood Disorders in Youth and Adults. *Child Adolesc Psychiatr Clin N Am*. 2014;23:591–672. doi: 10.1016/j.chc.2014.04.001
- 4 Firth J, Solmi M, Wootton RE, et al. A meta-review of “lifestyle psychiatry”: the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. *World Psychiatry*. 2020;19:360–80. doi: 10.1002/wps.20773
- 5 Sarris J, Logan AC, Akbaraly TN, et al. Nutritional medicine as mainstream in psychiatry. *Lancet Psychiatry*. 2015;2:271–4. doi: 10.1016/S2215-0366(14)00051-0
- 6 Kris-Etherton PM, Petersen KS, Hibbeln JR, et al. Nutrition and behavioral health disorders: depression and anxiety. *Nutr Rev*. 2021;79:247–60. doi: 10.1093/nutrit/nuaa025
- 7 Sarris J, Logan AC, Akbaraly TN, et al. International Society for Nutritional Psychiatry Research consensus position statement: nutritional medicine in modern psychiatry. *World Psychiatry*. 2015;14:370–1. doi: 10.1002/wps.20223
- 8 Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: Diet, sleep and exercise. *J Affect Disord*. 2013;148:12–27. doi: 10.1016/j.jad.2013.01.014
- 9 Sanchez-Villegas A, Martínez-González MA. Diet, a new target to prevent depression? *BMC Med*. 2013;11:3. doi: 10.1186/1741-7015-11-3
- 10 Selhub EM, Logan AC, Bested AC. Fermented foods, microbiota, and mental health: ancient practice meets nutritional psychiatry. *J Physiol Anthropol*. 2014;33:2. doi: 10.1186/1880-6805-33-2
- 11 Valdes AM, Walter J, Segal E, et al. Role of the gut microbiota in nutrition and health. *BMJ*. 2018;361:k2179. doi: 10.1136/bmj.k2179
- 12 Cryan JF, O’Riordan KJ, Cowan CSM, et al. The Microbiota-Gut-Brain Axis. *Physiol Rev*. 2019;99:1877–2013. doi: 10.1152/physrev.00018.2018
- 13 Qin J, Li R, Raes J, et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*. 2010;464:59–65. doi: 10.1038/nature08821
- 14 Firth J, Gangwisch JE, Borsini A, et al. Food and mood: how do diet and nutrition affect mental wellbeing? *BMJ*. 2020;m2382. doi: 10.1136/bmj.m2382
- 15 Liwinski T, Elinav E. Harnessing the microbiota for therapeutic purposes. *American Journal of Transplantation*. 2020;20:1482–8. doi: 10.1111/ajt.15753

16 Schaub A-C, Schneider E, Vazquez-Castellanos JF, et al. Clinical, gut microbial and neural effects of a probiotic add-on therapy in depressed patients: a randomized controlled trial. *Transl Psychiatry*. 2022;12:227. doi: 10.1038/s41398-022-01977-z

17 Ng QX, Peters C, Ho CYX, et al. A meta-analysis of the use of probiotics to alleviate depressive symptoms. *J Affect Disord*. 2018;228:13–9. doi: 10.1016/j.jad.2017.11.063

18 Aslam H, Green J, Jacka FN, et al. Fermented foods, the gut and mental health: a mechanistic overview with implications for depression and anxiety. *Nutr Neurosci*. 2020;23:659–71. doi: 10.1080/1028415X.2018.1544332

19 Sarkar A, Lehto SM, Harty S, et al. Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals. *Trends Neurosci*. 2016;39:763–81. doi: 10.1016/j.tins.2016.09.002

20 Sproten R, Nohr D, Guseva D. Nutritional strategies modulating the gut microbiome as a preventative and therapeutic approach in normal and pathological age-related cognitive decline: a systematic review of preclinical and clinical findings. *Nutr Neurosci*. 2024;27:1042–57. doi: 10.1080/1028415X.2023.2296727

21 World Health Organization (WHO). Obesity and overweight. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.

22 Kessler RC, Chiu WT, Demler O, et al. Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:617. doi: 10.1001/archpsyc.62.6.617

23 Lin H-Y, Huang C-K, Tai C-M, et al. Psychiatric disorders of patients seeking obesity treatment. *BMC Psychiatry*. 2013;13:1. doi: 10.1186/1471-244X-13-1

24 Milaneschi Y, Lamers F, Bot M, et al. Leptin Dysregulation Is Specifically Associated With Major Depression With Atypical Features: Evidence for a Mechanism Connecting Obesity and Depression. *Biol Psychiatry*. 2017;81:807–14. doi: 10.1016/j.biopsych.2015.10.023

25 Marx W, Lane M, Hockey M, et al. Diet and depression: exploring the biological mechanisms of action. *Mol Psychiatry*. 2021;26:134–50. doi: 10.1038/s41380-020-00925-x

26 Serretti A, Mandelli L. Antidepressants and Body Weight. *J Clin Psychiatry*. 2010;71:1259–72. doi: 10.4088/JCP.09r05346blu

27 Musil R, Obermeier M, Russ P, et al. Weight gain and antipsychotics: a drug safety review. *Expert Opin Drug Saf*. 2015;14:73–96. doi: 10.1517/14740338.2015.974549

28 Clemente-Suárez VJ, Beltrán-Velasco AI, Redondo-Flórez L, et al. Global Impacts of Western Diet and Its Effects on Metabolism and Health: A Narrative Review. *Nutrients*. 2023;15:2749. doi: 10.3390/nu15122749

29 Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: what they are and how to identify them. *Public Health Nutr*. 2019;22:936–41. doi: 10.1017/S1368980018003762

30 Monteiro CA, Cannon G, Moubarac J-C, et al. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health Nutr*. 2018;21:5–17. doi: 10.1017/S1368980017000234

31 Lane MM, Davis JA, Beattie S, et al. Ultraprocessed food and chronic noncommunicable diseases: A systematic review and meta-analysis of 43 observational studies. *Obesity Reviews*. 2021;22. doi: 10.1111/obr.13146

32 Lane MM, Gamage E, Du S, et al. Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. *BMJ*. 2024;e077310. doi: 10.1136/bmj-2023-077310

33 Tudi M, Daniel Ruan H, Wang L, et al. Agriculture Development, Pesticide Application and Its Impact on the Environment. *Int J Environ Res Public Health*. 2021;18:1112. doi: 10.3390/ijerph18031112

34 FAO/WHO. Pesticide residues in food: Maximum residue limits/extraneous maximum residue limits. Rome 2010.

35 Zanchi MM, Marins K, Zamoner A. Could pesticide exposure be implicated in the high incidence rates of depression, anxiety and suicide in farmers? A systematic review. *Environ Pollut*. 2023;331:121888. doi: 10.1016/j.envpol.2023.121888

36 Koh S-B, Kim TH, Min S, et al. Exposure to pesticide as a risk factor for depression: A population-based longitudinal study in Korea. *Neurotoxicology*. 2017;62:181–5. doi: 10.1016/j.neuro.2017.07.005

37 Beseler CL, Stallones L. A cohort study of pesticide poisoning and depression in Colorado farm residents. *Ann Epidemiol*. 2008;18:768–74. doi: 10.1016/j.annepidem.2008.05.004

38 Beseler CL, Stallones L, Hoppin JA, et al. Depression and pesticide exposures among private pesticide applicators enrolled in the Agricultural Health Study. *Environ Health Perspect*. 2008;116:1713–9. doi: 10.1289/ehp.11091

39 Khan N, Kennedy A, Cotton J, et al. A Pest to Mental Health? Exploring the Link between Exposure to Agrichemicals in Farmers and Mental Health. *Int J Environ Res Public Health*. 2019;16. doi: 10.3390/ijerph16081327

40 Wu H, Li K, Wang Y, et al. Suicide and suicidality in people exposed to pesticides: A systematic review and meta-analysis. *Environmental Pollution*. 2023;327:121542. doi: 10.1016/j.envpol.2023.121542

41 Sharma T, Sirpu Natesh N, Pothuraju R, et al. Gut microbiota: a non-target victim of pesticide-induced toxicity. *Gut Microbes*. 2023;15. doi: 10.1080/19490976.2023.2187578

42 Matsuzaki R, Gunnigle E, Geissen V, et al. Pesticide exposure and the microbiota-gut-brain axis. *ISME J*. 2023;17:1153–66. doi: 10.1038/s41396-023-01450-9

43 Mamun A AI, Prasetya TAE, Dewi IR, et al. Microplastics in human food chains: Food becoming a threat to health safety. *Science of The Total Environment*. 2023;858:159834. doi: 10.1016/j.scitotenv.2022.159834

44 Shanahan C. Dark Calories: How Vegetable Oils Destroy Our Health and How We Can Get It Back. UK: Hachette 2024.

45 Hashempour-Baltork F, Farshi P, Alizadeh AM, et al. Nutritional Aspects of Vegetable Oils: Refined or Unrefined? *European Journal of Lipid Science and Technology*. 2022;124. doi: 10.1002/ejlt.202100149

46 Hidaka BH. Depression as a disease of modernity: Explanations for increasing prevalence. *J Affect Disord*. 2012;140:205–14. doi: 10.1016/j.jad.2011.12.036

47 Logan AC, Selhub EM. Vis Medicatrix naturae: does nature 'minister to the mind'? *Biopsychosoc Med*. 2012;6:11. doi: 10.1186/1751-0759-6-11

48 Li NP, van Vugt M, Colarelli SM. The Evolutionary Mismatch Hypothesis: Implications for Psychological Science. *Curr Dir Psychol Sci*. 2018;27:38–44. doi: 10.1177/0963721417731378

49 Chang Y, Durante KM. Why consumers have everything but happiness: An evolutionary mismatch perspective. *Curr Opin Psychol*. 2022;46:101347. doi: 10.1016/j.copsyc.2022.101347

50 Morris KC, Puoane T. Why traditional diets are more relevant than ever today. *South African Journal of Clinical Nutrition*. 2024;37:197–9. doi: 10.1080/16070658.2024.2400441

51 Jacka FN, Mykletun A, Berk M, et al. The Association Between Habitual Diet Quality and the Common Mental Disorders in Community-Dwelling Adults. *Psychosom Med*. 2011;73:483–90. doi: 10.1097/PSY.0b013e318222831a

52 Jacka FN, Pasco JA, Mykletun A, et al. Association of Western and Traditional Diets With Depression and Anxiety in Women. *American Journal of Psychiatry*. 2010;167:305–11. doi: 10.1176/appi.ajp.2009.09060881

53 Sánchez-Villegas A, Delgado-Rodríguez M, Alonso A, et al. Association of the Mediterranean Dietary Pattern With the Incidence of Depression. *Arch Gen Psychiatry*. 2009;66:1090. doi: 10.1001/archgenpsychiatry.2009.129

54 Akbaraly TN, Brunner EJ, Ferrie JE, et al. Dietary pattern and depressive symptoms in middle age. *British Journal of Psychiatry*. 2009;195:408–13. doi: 10.1192/bjp.bp.108.058925

55 Skarupski KA, Tangney CC, Li H, et al. Mediterranean diet and depressive symptoms among older adults over time. *J Nutr Health Aging*. 2013;17:441–5. doi: 10.1007/s12603-012-0437-x

56 Rienks J, Dobson AJ, Mishra GD. Mediterranean dietary pattern and prevalence and incidence of depressive symptoms in mid-aged women: results from a large community-based prospective study. *Eur J Clin Nutr*. 2013;67:75–82. doi: 10.1038/ejcn.2012.193

57 Burt K. A historical analysis of the Mediterranean Diet's rise to prominence through the lens of Critical Race Theory. *Critical Dietetics*. 2021;5:41–52. doi: 10.32920/cd.v5i2.1329

58 Sánchez-Villegas A, Henríquez P, Bes-Rastrollo M, et al. Mediterranean diet and depression. *Public Health Nutr*. 2006;9:1104–9. doi: 10.1017/S1368980007668578

59 Lang UE, Beglinger C, Schweinfurth N, et al. Nutritional Aspects of Depression. *Cellular Physiology and Biochemistry*. 2015;37:1029–43. doi: 10.1159/000430229

60 Yin W, Löf M, Chen R, et al. Mediterranean diet and depression: a population-based cohort study. *International Journal of Behavioral Nutrition and Physical Activity*. 2021;18:153. doi: 10.1186/s12966-021-01227-3

61 Sánchez-Villegas A, Martínez-González MA, Estruch R, et al. Mediterranean dietary pattern and depression: the PREDIMED randomized trial. *BMC Med*. 2013;11:208. doi: 10.1186/1741-7015-11-208

62 Bayes J, Schloss J, Sibbritt D. A randomised controlled trial assessing the effect of a Mediterranean diet on the symptoms of depression in young men (the 'AMMEND' study): a study protocol. *British Journal of Nutrition*. 2021;126:730–7. doi: 10.1017/S0007114520004699

63 Sánchez-Villegas A, Cabrera-Suárez B, Molero P, et al. Preventing the recurrence of depression with a Mediterranean diet supplemented with extra-virgin olive oil. The PREDI-DEP trial: study protocol. *BMC Psychiatry*. 2019;19:63. doi: 10.1186/s12888-019-2036-4

64 Parletta N, Zarnowiecki D, Cho J, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). *Nutr Neurosci*. 2019;22:474–87. doi: 10.1080/1028415X.2017.1411320

65 Opie RS, O'Neil A, Jacka FN, et al. A modified Mediterranean dietary intervention for adults with major depression: Dietary protocol and feasibility data from the SMILES trial. *Nutr Neurosci*. 2018;21:487–501. doi: 10.1080/1028415X.2017.1312841

66 Wade AT, Davis CR, Dyer KA, et al. A Mediterranean diet supplemented with dairy foods improves mood and processing speed in an Australian sample: results from the MedDairy randomized controlled trial. *Nutr Neurosci*. 2020;23:646–58. doi: 10.1080/1028415X.2018.1543148

67 Morris L, Bhatnagar D. The Mediterranean diet. *Curr Opin Lipidol*. 2016;27:89–91. doi: 10.1097/MOL.0000000000000266

68 Davis C, Bryan J, Hodgson J, et al. Definition of the Mediterranean Diet; a Literature Review. *Nutrients*. 2015;7:9139–53. doi: 10.3390/nu7115459

69 Naureen Z, Bonetti G, Medori MC, et al. Foods of the Mediterranean diet: lacto-fermented food, the food pyramid and food combinations. *J Prev Med Hyg*. 2022;63:E28–35. doi: 10.15167/2421-4248/jp-mh2022.63.2S3.2744

70 Murooka Y, Yamshita M. Traditional healthful fermented products of Japan. *J Ind Microbiol Biotechnol*. 2008;35:791–8. doi: 10.1007/s10295-008-0362-5

71 Nanri A, Mizoue T, Poudel-Tandukar K, et al. Dietary patterns and suicide in Japanese adults: The Japan Public Health Center-based Prospective Study. *British Journal of Psychiatry*. 2013;203:422–7. doi: 10.1192/bjp.bp.112.114793

72 Suzuki T, Miyaki K, Tsutsumi A, et al. Japanese dietary pattern consistently relates to low depressive symptoms, and it is modified by job strain and worksite supports. *J Affect Disord*. 2013;150:490–8. doi: 10.1016/j.jad.2013.04.044

73 Kraeuter A-K, Guest PC, Sarnyai Z. Protocol for the Use of the Ketogenic Diet in Preclinical and Clinical Practice. 2020:83–98.

74 Jensen NJ, Wodschow HZ, Nilsson M, et al. Effects of Ketone Bodies on Brain Metabolism and Function in Neurodegenerative Diseases. *Int J Mol Sci*. 2020;21:8767. doi: 10.3390/ijms21228767

75 Ludwig DS, Willett WC, Volek JS, et al. Dietary fat: From foe to friend? *Science* (1979). 2018;362:764–70. doi: 10.1126/science.aau2096

76 Phillips MC. Metabolic Strategies in Healthcare: A New Era. *Aging Dis*. 2022;13:655–72. doi: 10.14336/AD.2021.1018

77 Shamshtein D, Liwinski T. Ketogenic Therapy for Major Depressive Disorder: A Review of Neurobiological Evidence. *Recent Progress in Nutrition*. 2022;2:1–1. doi: 10.21926/rpn.2201003

78 Patikorn C, Saidoung P, Pham T, et al. Effects of ketogenic diet on health outcomes: an umbrella review of meta-analyses of randomized clinical trials. *BMC Med*. 2023;21:196. doi: 10.1186/s12916-023-02874-y

79 Cunnane SC, Crawford MA. Survival of the fattest: fat babies were the key to evolution of the large human brain. *Comp Biochem Physiol A Mol Integr Physiol*. 2003;136:17–26. doi: 10.1016/S1095-6433(03)00048-5

80 Ludwig DS. The Ketogenic Diet: Evidence for Optimism but High-Quality Research Needed. *J Nutr*. 2020;150:1354–9. doi: 10.1093/jn/nxz308

81 Watanabe M, Tozzi R, Risi R, et al. Beneficial effects of the ketogenic diet on nonalcoholic fatty liver disease: A comprehensive review of the literature. *Obesity Reviews*. 2020;21. doi: 10.1111/obr.13024

82 Paoli A, Bosco G, Camporesi EM, et al. Ketosis, ketogenic diet and food intake control: a complex relationship. *Front Psychol*. 2015;6:27. doi: 10.3389/fpsyg.2015.00027

83 van der Louw E, van den Hurk D, Neal E, et al. Ketogenic diet guidelines for infants with refractory epilepsy. *European Journal of Paediatric Neurology*. 2016;20:798–809. doi: 10.1016/j.ejpn.2016.07.009

84 Danan A, Westman EC, Saslow LR, et al. The Ketogenic Diet for Refractory Mental Illness: A Retrospective Analysis of 31 Inpatients. *Front Psychiatry*. 2022;13. doi: 10.3389/fpsyt.2022.951376

85 Sethi S, Wakeham D, Ketter T, et al. Ketogenic Diet Intervention on Metabolic and Psychiatric Health in Bipolar and Schizophrenia: A Pilot Trial. *Psychiatry Res*. 2024;335:115866. doi: 10.1016/j.psychres.2024.115866

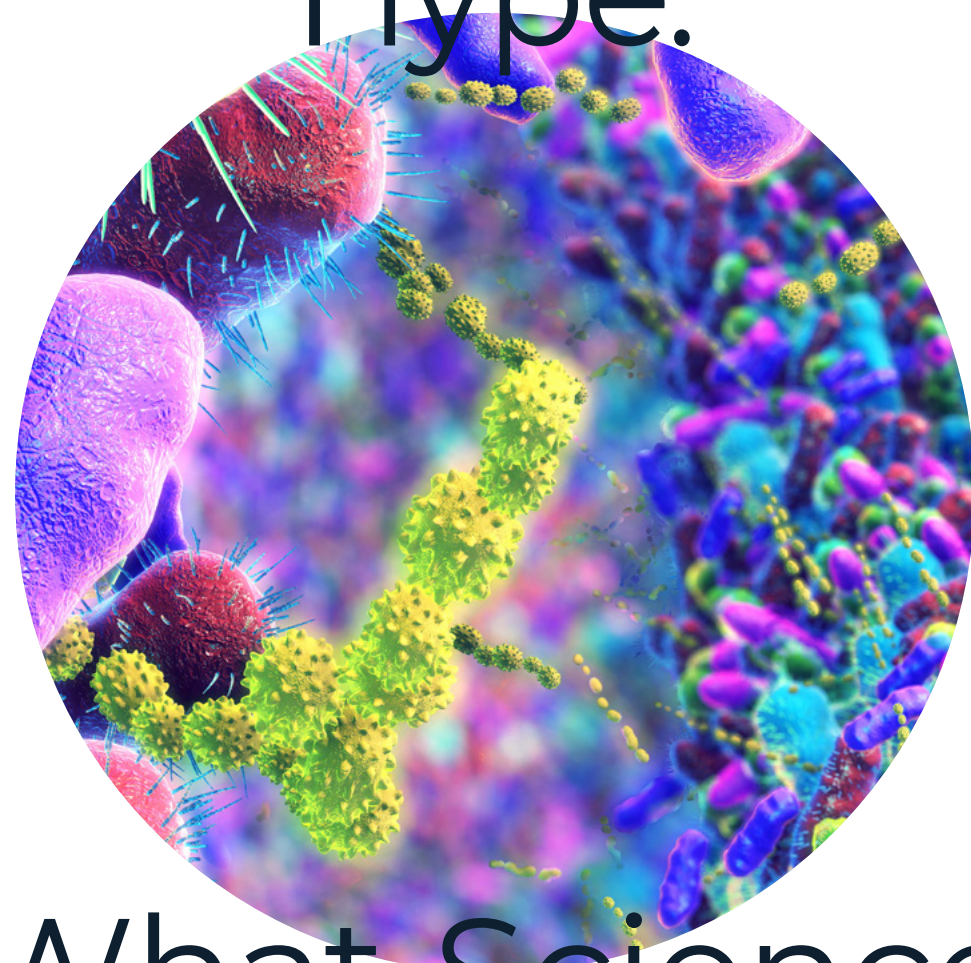
86 Needham N, Campbell IH, Grossi H, et al. Pilot study of a ketogenic diet in bipolar disorder. *BJPsych Open*. 2023;9:e176. doi: 10.1192/bjo.2023.568

87 Mu C, Corley MJ, Lee RWY, et al. Metabolic Framework for the Improvement of Autism Spectrum Disorders by a Modified Ketogenic Diet: A Pilot Study. *J Proteome Res*. 2020;19:382–90. doi: 10.1021/acs.jproteome.9b00581

88 Lee RWY, Corley MJ, Pang A, et al. A modified ketogenic gluten-free diet with MCT improves behavior in children with autism spectrum disorder. *Physiol Behav*. 2018;188:205–11. doi: 10.1016/j.physbeh.2018.02.006

89 El-Rashidy O, El-Baz F, El-Gendy Y, et al. Ketogenic diet versus gluten free casein free diet in autistic children: a case-control study. *Metab Brain Dis*. 2017;32:1935–41. doi: 10.1007/s11011-017-0088-z

Beyond the Hype:



What Science Really Says About Your Gut Bacteria



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The gut microbiome has become a scientific and public fascination, with new studies and health claims emerging daily. While diet is often cited as the key factor shaping gut bacteria, research suggests a far more complex picture. With over 200 variables influencing an individual's microbiome and only a fraction of its variability explained, the idea of a universally “healthy” gut remains elusive. Popular microbiome tests and interventions may not tell the whole story – especially when stool samples only offer a partial snapshot of the vast intestinal ecosystem. This article explores the intricate relationship between diet, microbiome diversity, and health, challenging common assumptions and highlighting the unanswered questions in this rapidly evolving field.

Recent years have generated an enormous interest in the gut microbiome in both the academic arena but also in the public domain. Dozens of new scientific papers appear on a daily basis, and the media are eager to immediately bring new findings to the public. This has caused a growing demand for products and services – with many companies offering microbiome profiling from a self-collected stool sample, usually coupled to advice on “how to shape the microbiome”, or by offering prebiotics, probiotics or symbiotics. And it is generally believed and often stated that nutrition is the most important factor in defining and altering the gut microbiome. However, numerous studies have now identified around 200 variables that contribute to an individual's microbiome, and which, in total, can currently explain around 15–20% of the variance found in a population. That leaves most of the variability in the human gut microbiome so far unexplained (1). This also calls for caution in using the term dysbiosis, which suggests an altered or

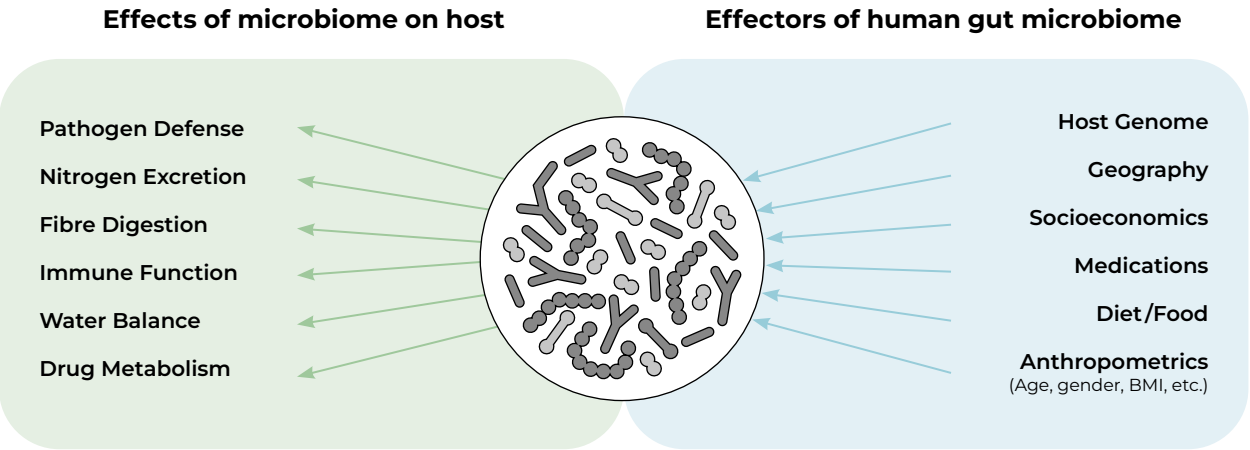
“unhealthy” state of the microbiome. What characterises a “healthy” microbiome is essentially not known and subject to scientific discussion (2); although most experts seem to agree that a high species diversity is the expression of a healthy microbiome (3). A high diversity is often found in populations that live in rural environments, and their microbiome often matches that of prehistoric humans, but they also quite often carry nematodes in their gut (4,5), and these seem to drive bacterial diversity and are thus a major confounder in the diversity debate. What should always be kept in mind is that the microbiome as determined in a stool sample does not truly represent the ecosystem found in the large intestine which hosts the majority of bacteria (6) and, moreover, almost all studies found have relative abundance of bacteria as outcome. But this does not match with the true number of bacteria (7) and, when bacterial numbers rather than relative abun-

dance are taken as outcome measure, some of the associations of gut microbiome profiles with diseases (from diabetes to Alzheimer dementia and many others) are less strong or even vanish (8). What also needs to be considered is that stool volume and frequency, stool water content and stool appearance (colour and consistency) are critical determinants of bacterial density and diversity in a faecal sample (9,10). Those parameters are also quite different in people living in rural, low-income as compared to high-income countries (11) and that may as well define the differences in bacterial diversity. However, these large differences in microbiomes are often interpreted as a consequence of “unhealthy diets” consumed in high income countries that then promote non-communicable diseases. Exposure of the host to a large spectrum of bacteria and their products constantly challenges the host immune system, of which a large part is found in the intestine, with a high density of immune cells in the lamina propria (see Fig. 1).

FIGURE 1

The Gut Microbiome – Facts and Figures

Colonic volume:	~ 100–250 ml
Microbiome mass:	~ 100–150 g
Bacterial density:	~ 10 ⁴ /g in small intestine ~ 10 ⁷ /g in colon
Number of species:	3,000 different identified individuals harbor ~ 200–400 species



The diversity of the microbiome is thus a critical factor in immune system conditioning and its ability to generate immune tolerance towards millions of harmless microorganisms in the lumen, and to summon rapid responses to fight pathogenic bacteria. Although the intestinal lining is covered with a mucus layer that is comprised of a sticky inner and almost sterile part adjacent to the epithelium and a fluffy outer layer in which bacteria can be found at low density, the underlying immune system receives a multitude of signals from the lumen to adapt accordingly.

Diets and gut microbiome – energetics effects

The gut microbiome is estimated to represent 50-100 g of bacterial mass (12), with the highest density of bacteria in colon. Around 15g of bacteria are excreted in faeces per day and need to be replaced (13). That requires 100 to 200 kcal* per day for bacterial growth and maintenance of this biomass. During extended fasting/starvation, the microbiome changes substantially (14). In the absence of food intake, bacteria live

on nutrients that enter the gut from secretions and from the glycoproteins of the gastrointestinal mucus and shaded mucosal cells. Diet has a direct effect on the microbiome and delivers “food” for the bacteria – mainly in the form of otherwise non-digestible and usable dietary fibres from cell walls or storage carbohydrates such as inulin and other sugars in plant-based diets. These are substrates for bacterial metabolism and deliver a variety of short-chain organic acids, of which the short-chain fatty

acids (SCFA) – mainly acetate, butyrate and propionate – are the dominant types. They are partially absorbed and provide the host with 1.5 to 2.0 kcal/g. Butyrate is mainly used by the colonic tissue as an energy substrate, while propionate and acetate are mainly utilised in the liver.

It is interesting to observe that very few of the thousands of scientific papers on the human gut microbiome have examined how much energy is excreted with the stool. With the idea that the gut microbiome contributes to overweight and obesity, the amount of calories excreted from the amount of energy ingested through food and drink becomes an issue. Careful analysis of energy excretion with a dye technique revealed that around 8% of the calories ingested are found in the stool (15,16). In order to calculate how many calories are made available to the host from the utilisation of undigested food components in the colon, the amount of calories that pass from the small into the large intestine needs to be known. This is of course not easy to determine and

Around
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can only be estimated from studies in patients with an ileostomy, which allows the collection of gut contents that would normally pass into the colon. These studies show that an estimated 300 kcal per day are released to the microorganisms in the colon, of which around 200 kcal are then found in faeces, leaving around 100 to 150 kcal that can be obtained by the host from microbial metabolism. It is hard to imagine that differences in this small amount between individuals has a major influence on the development of the host’s body weight. Moreover, various trials, in which faeces from lean or obese individuals were transplanted into the intestines of lean or obese volunteers to investigate the effects on body weight, did not observe any significant effects on body weight management. A recent thorough re-analysis of all rodent studies that originally suggested that the microbiome was a significant contributor to obesity in mice and rats also con-

cluded that the influence of the microbiome, if at all, is very small (17).

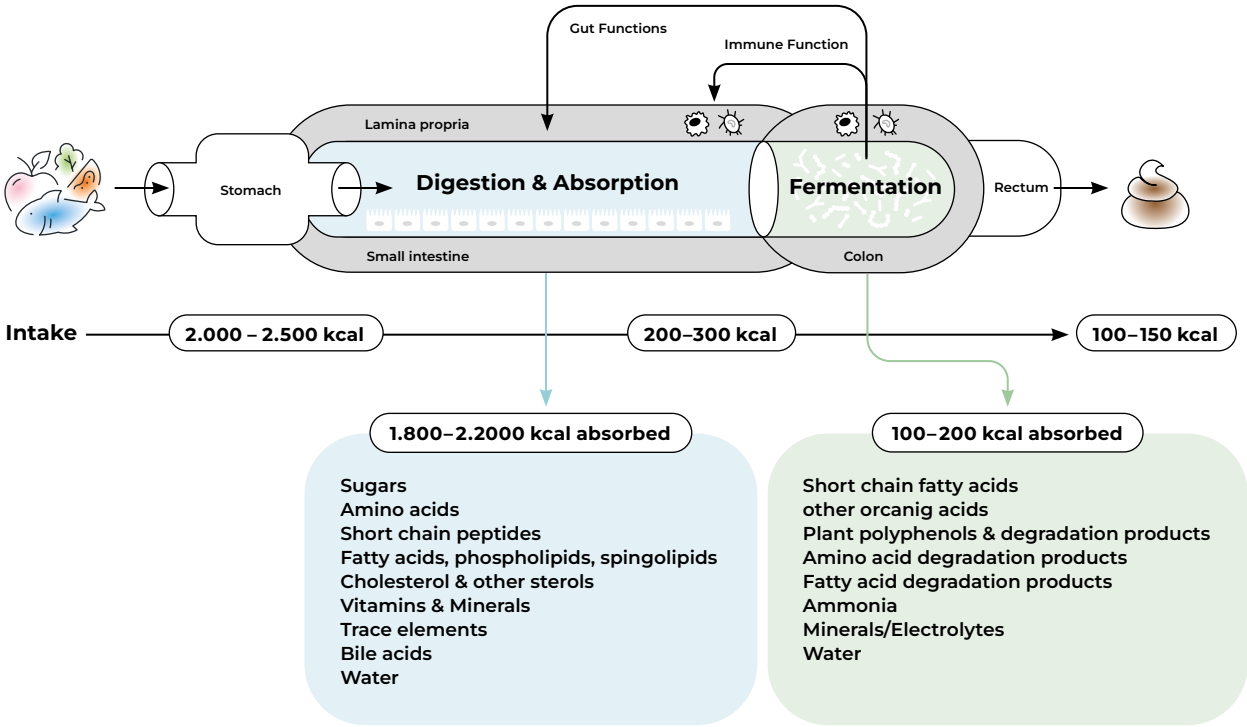
Diets and microbiome – qualitative aspects

With reference to the diversity of the gut microbiome as a surrogate for a “healthy microbiome”, very recent studies have compared the diversity in faecal samples from vegans, vegetarians and omnivores. A study of > 21,000 individuals from 5 international cohorts found only minor differences in bacterial richness, with significant differences in only two cohorts, where richness was greater in omnivores than in vegans (18). From a similar study but with only around 30 individuals in each arm, the authors conclude: “compared to the general inter-individual differences, habitual diet appears to have a limited effect on the composition of the microbiota at the species level” (19). An early study in which volunteers ate a vegan diet for 5 days, and after a five-day washout

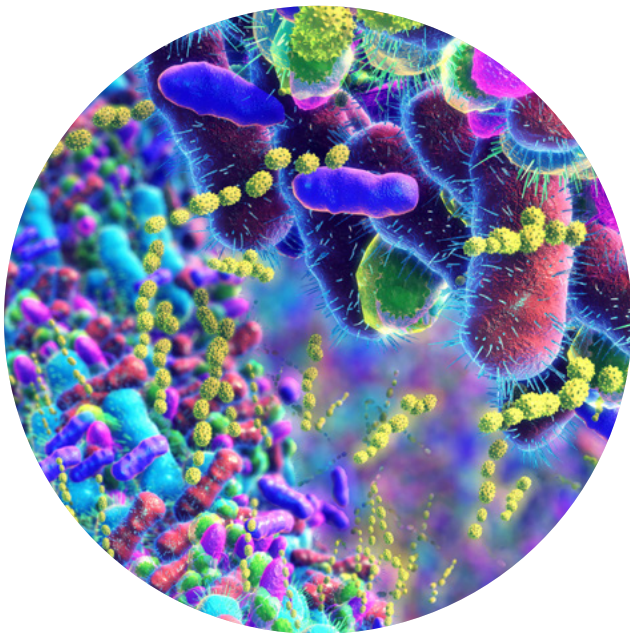
period ate only animal products (20), also found only minor differences in the measurement of bacterial diversity, despite major differences in nutrient and fibre intake. When a Mediterranean diet with 54 g of fibre was tested on healthy volunteers compared to a Western-style diet with only 5g of fibre per day, the differences in bacterial diversity were also minor, and the authors stated: “taxonomic profiles of microbial communities in faecal samples were similar, suggesting little influence of the diet on the core members of the gut microbiota” (21). Intervention studies with fermentable fibres consistently found a selective increase in Bifidobacteria species and SCFA, while microbial diversity remained unaltered against a background of high inter-individual variability (22,23). Gut bacteria and their diverse biochemical capacities can produce a huge spectrum of metabolites that, when absorbed, can affect host metabolism.

FIGURE 2

Digestion, Absorption and Fermentation



Many of the hundreds of plant constituents that we consume with fruits and vegetables enter the colon and are transformed into hundreds of different chemicals (24). They partially appear in the blood and are later excreted via urine. The spectrum of these compounds can vary greatly from person to person, and their biological activities are correspondingly quite different. Products of bacterial transformation of ingested diet components are often modified further in the human metabolism and some of those products are considered to contribute to the development of chronic diseases, examples are TMAO (trimethylamine oxide) or PAG (phenylacetylglutamine), which are both considered to participate in the development of cardiovascular diseases (25). But the repertoire of compounds produced by the gut microbiome that influence human health for “better or for worse” is still emerging. All in all, research in recent years has produced a wealth of information about the gut microbiome. This development has been driven primarily by low-cost, high-throughput sequencing, data processing and interpretation techniques. The presence of microbes in the human large intestine and their ability to produce the beneficial SCFA has been known for decades, but modern life sciences essentially ignored their role in health and disease. This has changed drastically – new findings about the microbiome appear in the public domain every day, suggesting even to non-experts that it is of the utmost importance for health and disease, and that changes in the composition of the microbiome in turn have a major impact. It is obvious that our diet has an influence on the microbiome and the associated health impacts. However, thorough studies suggest that the effects are minimal, at least in terms of microbiome diversity, which is considered an indicator of a healthy microbiome. The biological activities of the bacteria are diverse and the substances they produce are extremely varied. Their functions are not yet fully understood. The greatest challenge facing any approach to intervention – whether through diet, medication or dietary supplements – is the enormous and largely unexplained variability in the microbial spectrum between individuals.



Glossary

Microbiome and Microbiota

Microbiota describes the living microorganisms found in a defined environment. Microbiome refers to the collection of genomes from all the microorganisms in the environment, which includes not only the community of the microorganisms, but also the microbial structural elements, metabolites, and the environmental conditions (taken from Hou, K., Wu, ZX., Chen, XY. et al. Microbiota in health and diseases. Sig Transduct Target Ther 7, 135 (2022). <https://doi.org/10.1038/s41392-022-00974-4>).

Probiotics

Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host according to the definition of the International Association of Probiotics and Prebiotics 2016.

Prebiotics

A substrate that is selectively utilized by host microorganisms conferring a health benefit according to the definition of the International Association of Probiotics and Prebiotics 2016.

Symbiotics

A combination of probiotics and prebiotics.

References

- Gacesa R, Kurilshikov A, Vich Vila A, Sinha T, Klaassen MAY, Bolte LA, Andreu-Sánchez S, Chen L, Collij V, Hu S, Dekens JAM, Lenters VC, Björk JR, Swarte JC, Swertz MA, Jansen BH, Gelderloos-Arends J, Jankipersadsing S, Hofker M, Vermeulen RCH, Sanna S, Harmsen HJM, Wijmenga C, Fu J, Zhernakova A, Weersma RK. Environmental factors shaping the gut microbiome in a Dutch population. *Nature*. 2022 Apr;604(7907):732-739. doi: 10.1038/s41586-022-04567-7. Epub 2022 Apr 13. PMID: 35418674.
- Shanahan F, Ghosh TS, O'Toole PW. The Healthy Microbiome-What Is the Definition of a Healthy Gut Microbiome? *Gastroenterology*. 2021 Jan;160(2):483-494. doi: 10.1053/j.gastro.2020.09.057. Epub 2020 Nov 27. PMID: 33253682. Language, numeracy and logic in microbiome science.
- Shanahan F, Hill C. Language, numeracy and logic in microbiome science. *Nat Rev Gastroenterol Hepatol*. 2019 Jul;16(7):387-388. doi: 10.1038/s41575-019-0163-5. Erratum in: *Nat Rev Gastroenterol Hepatol*. 2019 Jul;16(7):448. doi: 10.1038/s41575-019-0170-6. PMID: 31168062.
- Rubel MA, Abbas A, Taylor LJ, Connell A, Tanes C, Bittinger K, Ndze VN, Fonsah JY, Ngwang E, Essiane A, Fokunang C, Njamnshi AK, Bushman FD, Tishkoff SA. Lifestyle and the presence of helminths is associated with gut microbiome composition in Cameroonians. *Genome Biol*. 2020 May 25;21(1):122. doi: 10.1186/s13059-020-02020-4. PMID: 32450885; PMCID: PMC7249393.
- Wibowo MC, Yang Z, Borry M, Hübner A, Huang KD, Tierney BT, Zimmerman S, Barajas-Olmos F, Contreras-Cubas C, García-Ortiz H, Martínez-Hernández A, Luber JM, Kirstahler P, Blohm T, Smiley FE, Arnold R, Ballal SA, Pamp SJ, Russ J, Maixner F, Rota-Stabelli O, Segata N, Reinhard K, Orozco L, Warinner C, Snow M, LeBlanc S, Kostic AD. Reconstruction of ancient microbial genomes from the human gut. *Nature*. 2021 Jun;594(7862):234-239. doi: 10.1038/s41586-021-03532-0. Epub 2021 May 12. PMID: 33981035; PMCID: PMC8189908.
- Vaga S, Lee S, Ji B, Andreasson A, Talley NJ, Agréus L, Bidkhorji G, Kovatcheva-Datchary P, Park J, Lee D, Proctor G, Ehrlich SD, Nielsen J, Engstrand L, Shoaie S. Compositional and functional differences of the mucosal microbiota along the intestine of healthy individuals. *Sci Rep*. 2020 Sep 11;10(1):14977. doi: 10.1038/s41598-020-71939-2. PMID: 32917913; PMCID: PMC7486370.
- Vandeputte D, Kathagen G, D'hoë K, Vieira-Silva S, Valles-Colomer M, Sabino J, Wang J, Tito RY, De Commer L, Darzi Y, Vermeire S, Falony G, Raes J. Quantitative microbiome profiling links gut community variation to microbial load. *Nature*. 2017 Nov 23;551(7681):507-511. doi: 10.1038/nature24460. Epub 2017 Nov 15. PMID: 29143816.
- Nishijima S, Stankevicius E, Aasmets O, Schmidt TSB, Nagata N, Keller MI, Ferretti P, Juel HB, Fullam A, Robbani SM, Schudoma C, Hansen JK, Holm LA, Israelsen M, Schierwagen R, Torp N, Telzerow A, Hercog R, Kandels S, Hazenbrink DHM, Arumugam M, Bendtsen F, Brøns C, Fonvig CE, Holm JC, Nielsen T, Pedersen JS, Thiele MS, Trebicka J, Org E, Krag A, Hansen T, Kuhn M, Bork P; GALAXY and MicrobLiver Consortia. Fecal microbial load is a major determinant of gut microbiome variation and a confounder for disease associations. *Cell*. 2025 Jan 9;188(1):222-236.e15. doi: 10.1016/j.cell.2024.10.022. Epub 2024 Nov 13. PMID: 39541968
- Zhernakova A, Kurilshikov A, Bonder MJ, Tigchelaar EF, Schirmer M, Vatanen T, Mujagic Z, Vila AV, Falony G, Vieira-Silva S, Wang J, Imhann F, Brandsma E, Jankipersadsing SA, Joossens M, Cenit MC, Deelen P, Swertz MA; LifeLines cohort study; Weersma RK, Feskens EJ, Neeta MG, Gevers D, Jonkers D, Franke L, Aulchenko YS, Huttenhower C, Raes J, Hofker MH, Xavier RJ, Wijmenga C, Fu J. Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity. *Science*. 2016 Apr 29;352(6285):565-9. doi: 10.1126/science.aad3369.
- Vandeputte D, Falony G, Vieira-Silva S, Tito RY, Joossens M, Raes J. Stool consistency is strongly associated with gut microbiota richness and composition, enterotypes and bacterial growth rates. *Gut*. 2016 Jan;65(1):57-62. doi: 10.1136/gutjnl-2015-309618. Epub 2015 Jun 11. PMID: 26069274; PMCID: PMC4717365.
- Rose C, Parker A, Jefferson B, Cartmell E. The Characterization of Feces and Urine: A Review of the Literature to Inform Advanced Treatment Technology. *Crit Rev Environ Sci Technol*. 2015 Sep 2;45(17):1827-1879. doi: 10.1080/10643389.2014.1000761. PMID: 26246784; PMCID: PMC4500995.
- Ma Z, Zuo T, Frey N, Rangrez AY. A systematic framework for understanding the microbiome in human health and disease: from basic principles to clinical translation. *Signal Transduct Target Ther*. 2024 Sep 23;9(1):237. doi: 10.1038/s41392-024-01946-6. PMID: 39307902; PMCID: PMC11418828.
- Stephen AM, Wiggins HS, Cummings JH. Effect of changing transit time on colonic microbial metabolism in man. *Gut*. 1987 May;28(5):601-9. doi: 10.1136/gut.28.5.601. PMID: 3596341; PMCID: PMC1432874.
- Wu F, Guo Y, Wang Y, Sui X, Wang H, Zhang H, Xin B, Yang C, Zhang C, Jiang S, Qu L, Feng Q, Dai Z, Shi C, Li Y. Effects of Long-Term Fasting on Gut Microbiota, Serum Metabolome, and Their Association in Male Adults. *Nutrients*. 2024 Dec 26;17(1):35. doi: 10.3390/nu17010035. PMID: 39796469; PMCID: PMC11722564.
- Bao R, Guo Y, Hu Y, Ning G, Pan S, Wang W. Standardized assessment of energy excretion in healthy adults: a novel methodology. *Am J Clin Nutr*. 2024 Dec 18;S0002-9165(24)01470-9. doi: 10.1016/j.ajcnut.2024.12.016. Epub ahead of print. PMID: 39701422.
- Boekhorst J, Venlet N, Procházková N, Hansen ML, Lieberoth CB, Bahl MI, Lauritzen L, Pedersen O, Licht TR, Kleerebezem M, Roager HM. Stool energy density is positively correlated to intestinal transit time and related to microbial enterotypes. *Microbiome*. 2022 Dec 12;10(1):223. doi: 10.1186/s40168-022-01418-5. PMID: 36510309; PMCID: PMC9743556.
- Dalby MJ. Questioning the foundations of the gut microbiota and obesity. *Philos Trans R Soc Lond B Biol Sci*. 2023 Oct 23;378(1888):20220221. doi: 10.1098/rstb.2022.0221. Epub 2023 Sep 4. PMID: 37661739; PMCID: PMC10475866.
- Fackelmann G, Manghi P, Carlino N, Heidrich V, Piccinno G, Ricci L, Piperni E, Arré A, Bakker E, Creedon AC, Francis L, Capdevila Pujol J, Davies R, Wolf J, Birmingham KM, Berry SE, Spector TD, Asnicar F, Segata N. Gut microbiome signatures of vegan, vegetarian and omnivore diets and associated health outcomes across 21,561 individuals. *Nat Microbiol*. 2025 Jan;10(1):41-52. doi: 10.1038/s41564-024-01870-z. Epub 2025 Jan 6. PMID: 39762435; PMCID: PMC11726441.
- Huang KD, Müller M, Sivapornnukul P, Bielecka AA, Amend L, Tawk C, Lesker TR, Hahn A, Strowig T. Dietary selective effects manifest in the human gut microbiota from species composition to strain genetic makeup. *Cell Rep*. 2024 Dec 24;43(12):115067. doi: 10.1016/j.celrep.2024.115067. Epub 2024 Dec 13. Erratum in: *Cell Rep*. 2025 Jan 17;44(1):115252. doi: 10.1016/j.celrep.2025.115252. PMID: 39673707.
- David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, Ling AV, Devlin AS, Varma Y, Fischbach MA, Biddinger SB, Dutton RJ, Turnbaugh PJ. Diet rapidly and reproducibly alters the human gut microbiome. *Nature*. 2014 Jan 23;505(7484):559-63. doi: 10.1038/nature12820. Epub 2013 Dec 11. PMID: 24336217; PMCID: PMC3957428.
- Barber C, Mego M, Sabater C, Vallejo F, Bendezu RA, Masihiy M, Guarnier F, Espín JC, Margolles A, Azpiroz F. Differential Effects of Western and Mediterranean-Type Diets on Gut Microbiota: A Metagenomics and Metabolomics Approach. *Nutrients*. 2021 Jul 30;13(8):2638. doi: 10.3390/nu13082638. PMID: 34444797; PMCID: PMC8400818.
- Birkeland E, Gharagozlian S, Birkeland KI, Valeur J, Måge I, Rud I, Aas AM. Prebiotic effect of inulin-type fructans on faecal microbiota and short-chain fatty acids in type 2 diabetes: a randomised controlled trial. *Eur J Nutr*. 2020 Oct;59(7):3325-3338. doi: 10.1007/s00394-020-02282-5. Epub 2020 May 21. Erratum in: *Eur J Nutr*. 2020 Oct;59(7):3339-3340. doi: 10.1007/s00394-020-02314-0. PMID: 32440730; PMCID: PMC7501097.
- Canfora EE, van der Beek CM, Hermes GDA, Goossens GH, Jocken JWE, Holst JJ, van Eijk HM, Venema K, Smidt H, Zoetendal EG, Dejong CHC, Lenaerts K, Blaak EE. Supplementation of Diet With Galacto-oligosaccharides Increases Bifidobacteria, but Not Insulin Sensitivity, in Obese Prediabetic Individuals. *Gastroenterology*. 2017 Jul;153(1):87-97. e3. doi: 10.1053/j.gastro.2017.03.051. Epub 2017 Apr 8. PMID: 28396144.
- Culp EJ, Nelson NT, Verdegaal AA, Goodman AL. Microbial transformation of dietary xenobiotics shapes gut microbiome composition. *Cell*. 2024 Oct 31;187(22):6327-6345.e20. doi: 10.1016/j.cell.2024.08.038. Epub 2024 Sep 24. PMID: 39321800; PMCID: PMC11531382.
- Zhang L, Yin Y, Jin S. Gut microbial metabolites: The bridge connecting diet and atherosclerosis, and next-generation targets for dietary interventions. *Microbiol Res*. 2025 Mar;292:128037. doi: 10.1016/j.micres.2024.128037. Epub 2024 Dec 26. PMID: 39752807.



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Oral Health and Planetary Health: The Interconnection Between Nutrition, Environment, and Oral Health



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The Planetary Health concept highlights the critical connections between human health, ecosystems, and the environment. By addressing the root causes of health challenges – such as climate change, biodiversity loss, and pollution – it offers a transformative framework for safeguarding both population health and the planet's future.

The Planetary Health concept stems from evolving approaches to public and environmental health. It integrates the close connections between human health, the environment, and ecosystems, emphasizing how disruptions to natural systems impact human health – such as climate change, biodiversity loss, and pollution. Historically, global health efforts focused on combating infectious diseases and improving worldwide healthcare. Over time, this perspective expanded to include the One Health approach, which connects human health, animal health, and ecosystems (OHHLEP, 2022).

In the 2010s, as the impacts of climate change, pollution, and biodiversity loss increasingly affected human health, the concept of Planetary Health emerged. Formulated in 2015 by The Lancet Commission on Planetary Health (Whitmee, 2015), this framework goes beyond One Health by incorporating a systemic approach: human health directly depends on the condition of ecosystems and natural resources. This integration calls for cross-sectoral policies to safeguard both population health and planetary health (Gonzalez-Holguera, 2022).

The erosion of natural ecosystems and the rise of chronic diseases demand an integrated approach, with oral health recognized as a vital indicator of global well-being. Although often treated separately, oral health plays a crucial role due to its links with diet, product usage, and environmental change (Fisher, 2024). Oral health is a key marker of overall health, directly influenced by lifestyle changes and food systems. However, its environmental impact – especially concerning resource consumption and waste – is often overlooked (Martin, 2024).

The Role of Oral Health in Planetary Health

Oral health is a cornerstone of global health, with significant implications for Planetary Health. Research increasingly links the oral microbiome, nutrition, and systemic diseases (Bourgeois, 2022). Oral diseases, including periodontal disease, are associated with higher risks of systemic conditions such as cardiovascular disease, diabetes, and other chronic inflammatory disorders (Sanz, 2022; Genco, 2020).

These conditions share common roots in dietary habits, industrial practices, and consumption patterns that directly impact the environment. Diets high in sugars and ultra-processed foods exacerbate oral health problems, underscoring the need for sustainable dietary practices that benefit both individual health and the planet (Cascaes, 2022). Sustainable agricultural practices promoting diverse, environmentally friendly crops play a crucial role. A shift towards plant-based, biodiverse, and organic diets, such as those featuring ancient grains and legumes, benefits both oral health and environmental sustainability (Inchingolo, 2024). These diets support a balanced oral microbiome, reduce meat consumption, and decrease greenhouse gas emissions. In addition to the health benefits, these practices offer substantial environmental advantages, particularly in terms of reducing ecological footprints (Dixon, 2023).

The Oral Microbiome and its Systemic Implications

The oral microbiome, as an extension of the gut microbiome, plays a critical role in oral health and the management of systemic diseases (Rajasekaran, 2024). Diets rich in antioxidants, such as fruits and vegetables, along with essential nutrients like omega-3s, polyphenols, polyunsaturated fatty acids, and probiotics, promote a more diverse and resilient oral microbiome. This can help reduce the risk of periodontal disease and cavities (Santonocito, 2022; Pytko-Polończyk, 2021). For example, green tea consumption has been shown to decrease the growth of *Porphyromonas gingivalis* by 30% (Paczkowska-Walendowska, 2025). Environmental factors such as air pollution and climate change can also disrupt the balance of the oral microbiome. Pollutants like ultrafine particles (PMo.1) have been shown to affect oral microbiota, promoting inflammation, particularly in children (Gupta, 2022). Climate change may also create conditions favorable for the proliferation of pathogenic bacteria in the mouth. Areas experiencing global warming could see a 15% increase in periodontal disease risk due to the optimal conditions for certain oral bacteria (Lin, 2021).

The Importance of Sustainable Diets for Oral and Systemic Health

Adopting sustainable diets that emphasize organic, plant-based, and antioxidant-rich foods, while also managing environmental factors, can prevent oral microbiome disruption and reduce the risk of systemic diseases (Martinon, 2021). A plant-based diet promoting a balanced oral microbiome can reduce the risk of bacterial migration to other organs, exacerbating systemic inflammation, especially in cardiovascular diseases. Diets such as vegetarian, vegan, and Mediterranean offer beneficial approaches to improving oral health, partially due to the absence of saturated fats and animal products.

Oral health is a cornerstone of global health, with significant implications for Planetary Health.

These diets, rich in fruits, vegetables, legumes, nuts, and seeds, reduce gingival inflammation by neutralizing the free radicals responsible for oxidation and inflammation (Augimeri, 2024). Furthermore, they have a positive environmental impact by lowering meat consumption and promoting sustainable food choices, thus contributing to global planetary health. Incorporating foods from dietary biodiversity, particularly those high in fiber, cruciferous vegetables, and colorful fruits, has also been shown to reduce cancer risk (Mentella, 2019). Their antioxidant and anti-inflammatory properties help protect against cancers by inhibiting cell proliferation and promoting the elimination of cancer cells.

Challenges and Considerations

Despite the benefits, some studies suggest that vegetarian diets may increase the risk of dental erosion (Smits, 2020). Comparative studies have also shown that plant-based products may not be as effective as dairy products in maintaining healthy teeth (Shkempi, 2023). In terms of environmental benefits, the rise of edible insects as a sustainable protein alternative has gained attention. According to EU Food Regulation (EU) 2015/2283, insects are now recognized as a potential food source. Incorporating alternative proteins and omega-3 fatty acids from such sources can support oral tissue regeneration and reduce gingival inflammation (Mazur, 2025).

Conclusion

Integrating oral health into the broader concept of Planetary Health represents a critical shift in how we approach public and environmental health. The discussions and findings presented in this paper underscore the interconnectedness of human health, food systems, professional practices, and public health policies. It is becoming clear that oral health issues must not be treated in isolation from environmental and societal challenges. Understanding the oral microbiome and its links to systemic diseases opens the door to new prevention strategies based on sustainable nutrition and reduced consumption of ultra-processed foods. Ultimately, oral health must be incorporated into a global, sustainable framework, where prevention, education, and scientific innovation converge to create a healthier future for both individuals and the planet.

References

One Health High-Level Expert Panel (OHHLEP); Adisasmito WB, Almu-hairi S, Behravesh CB, Bilivogui P, Bukachi SA, Casas N, Cediel Becerra N, Charron DF, Chaudhary A, Ciacci Zanella JR, Cunningham AA, Dar O, Debnath N, Dungu B, Farag E, Gao GF, Hayman DTS, Khaitisa M, Koopmans MPG, Machalaba C, Mackenzie JS, Markotter W, Mettenleiter TC, Morand S, Smolenskiy V, Zhou L. One Health: A new definition for a sustainable and healthy future. *PLoS Pathog.* 2022 Jun 23;18(6):e1010537. doi: 10.1371/journal.ppat.1010537. PMID: 35737670; PMCID: PMC9223325.

Whitmee S, Haines A, Beyrer C, Boltz F, Capon AG, de Souza Dias BF, Ezeh A, Frumkin H, Gong P, Head P, Horton R, Mace GM, Marten R, Myers SS, Nishtar S, Osofsky SA, Pattanayak SK, Pongsiri MJ, Romanelli C, Soucat A, Vega J, Yach D. Safeguarding human health in the Anthropocene epoch: report of The Rockefeller Foundation-Lancet Commission on planetary health. *Lancet.* 2015 Nov 14;386(10007):1973-2028. doi: 10.1016/S0140-6736(15)60901-1. Epub 2015 Jul 15. Erratum in: *Lancet.* 2015 Nov 14;386(10007):1944. doi: 10.1016/S0140-6736(15)61180-1. PMID: 26188744.

Gonzalez-Holguera J, Gaille M, Del Rio Carral M, Steinberger J, Marti J, Bühler N, Kaufmann A, Chiapperino L, Vicedo-Cabrera AM, Schwarz J, Depoux A, Panese F, Chèvre N, Senn N. Translating Planetary Health Principles Into Sustainable Primary Care Services. *Front Public Health.* 2022 Jul 13;10:931212. doi: 10.3389/fpubh.2022.931212. Erratum in: *Front Public Health.* 2022 Nov 08;10:1075712. doi: 10.3389/fpubh.2022.1075712. PMID: 35937241; PMCID: PMC9355637.

Fisher J, Splieth C, Matanhire-Zihanzu C, Glick M. Advancing the concept of global oral health to strengthen actions for planetary health and One Health. *Int J Equity Health.* 2024 Apr 15;23(1):71. doi: 10.1186/s12939-024-02176-6. PMID: 38622718; PMCID: PMC11017574.

Martin N, Hunter A, Constantine Z, Mulligan S. The environmental consequences of oral healthcare provision by the dental team. *J Dent.* 2024 Mar;142:104842. doi: 10.1016/j.jdent.2024.104842. Epub 2024 Jan 17. PMID: 38237717.

Bourgeois D, Gonçalves LS, Lima-Junior JDC, Carrouel F. Editorial: The Oral Microbiome Is a Key Factor in Oral and Systemic Health. *Front Microbiol.* 2022 Feb 14;13:855668. doi: 10.3389/fmicb.2022.855668. PMID: 35237254; PMCID: PMC8883028.

Sanz M, Del Castillo AM, Jepsen S, Gonzalez-Juanatey JR, D'Aiuto F, Bouchard P, Chapple I, Dietrich T, Gotsman I, Graziani F, Herrera D, Loos B, Madianos P, Michel JB, Perel P, Pieske B, Shapira L, Shechter M, Tonetti M, Vlachopoulos C, Wimmer G. Periodontitis and Cardiovascular Diseases. Consensus Report. *Glob Heart.* 2020 Feb 3;15(1):1. doi: 10.5334/gh.400. PMID: 32489774; PMCID: PMC7218770.

Genco RJ, Graziani F, Hasturk H. Effects of periodontal disease on glycemic control, complications, and incidence of diabetes mellitus. *Periodontol 2000.* 2020 Jun;83(1):59-65. doi: 10.1111/prd.12271. PMID: 32385875.

Cascaes AM, Silva NRJD, Fernandez MDS, Bomfim RA, Vaz JDS. Ultra-processed food consumption and dental caries in children and adolescents: a systematic review and meta-analysis. *Br J Nutr.* 2022 Jul 27;110. doi: 10.1017/S0007114522002409. Epub ahead of print. PMID: 35894293. Martinon P, Fraticelli L, Giboreau A, Dussart C, Bourgeois D, Carrouel F. Nutrition as a Key Modifiable Factor for Periodontitis and Main Chronic Diseases. *J Clin Med.* 2021 Jan 7;10(2):197. doi: 10.3390/jcm10020197. PMID: 33430519; PMCID: PMC7827391.

Inchingolo F, Dipalma G, Guglielmo M, Palumbo I, Campanelli M, Inchingolo AD, de Ruvo E, Palermo A, Di Venere D, Inchingolo AM. Correlation between vegetarian diet and oral health: a systematic review. *Eur Rev Med Pharmacol Sci.* 2024 Mar;28(6):2127-2143. doi: 10.26355/eur-rev_202403_35716. PMID: 38567575.

Dixon KA, Michelsen MK, Carpenter CL. Modern Diets and the Health of Our Planet: An Investigation into the Environmental Impacts of Food Choices. *Nutrients.* 2023 Jan 30;15(3):692. doi: 10.3390/nu15030692. PMID: 36771398; PMCID: PMC9919910.

Rajasekaran JJ, Krishnamurthy HK, Bosco J, Jayaraman V, Krishna K, Wang T, Bei K. Oral Microbiome: A Review of Its Impact on Oral and Systemic Health. *Microorganisms.* 2024 Aug 29;12(9):1797. doi: 10.3390/microorganisms12091797. PMID: 39338471; PMCID: PMC11434369.

Santonocito S, Giudice A, Polizzi A, Troiano G, Merlo EM, Sclafani R, Grosso G, Isola G. A Cross-Talk between Diet and the Oral Microbiome: Balance of Nutrition on Inflammation and Immune System's Response during Periodontitis. *Nutrients.* 2022 Jun 11;14(12):2426. doi: 10.3390/nu14122426. PMID: 35745156; PMCID: PMC9227938.

Pytko-Polończyk J, Stawarz-Janeczek M, Kryczyk-Poprawa A, Muszyńska B. Antioxidant-Rich Natural Raw Materials in the Prevention and Treatment of Selected Oral Cavity and Periodontal Diseases. *Antioxidants (Basel).* 2021 Nov 21;10(11):1848. doi: 10.3390/antiox10111848. PMID: 34829719; PMCID: PMC8614929.

Paczkowska-Walendowska, M.; Grzegorzewski, J.; Kwiatek, J.; Leśna, M.; Cielecka-Piontek, J. Green Tea: A Novel Perspective on the Traditional Plant's Potential in Managing Periodontal Diseases. *Pharmaceuticals* 2025, 18, 409. <https://doi.org/10.3390/ph18030409>

Gupta N, Yadav VK, Gacem A, Al-Dossari M, Yadav KK, Abd El-Gawaad NS, Ben Khedher N, Choudhary N, Kumar P, Cavalu S. Deleterious Effect of Air Pollution on Human Microbial Community and Bacterial Flora: A Short Review. *Int J Environ Res Public Health.* 2022 Nov 22;19(23):15494. doi: 10.3390/ijerph192315494. PMID: 36497569; PMCID: PMC9738139.

Lin, H.-J., Tsai, S. C.-S., Lin, F. C.-F., Hsu, Y.-C., Chen, S.-W., Chou, R.-H., Lin, C.-L., Hsu, C. Y., & Chang, K.-H. (2021). Prolonged Exposure to Air Pollution Increases Periodontal Disease Risk: A Nationwide, Population-Based, Cohort Study. *Atmosphere*, 12(12), 1668. <https://doi.org/10.3390/atmos12121668>. Augimeri G, Caparello G, Caputo I, Reda R, Testarelli L, Bonofiglio D. Mediterranean diet: a potential player in the link between oral microbiome and oral diseases. *J Oral Microbiol.* 2024 Mar 19;16(1):2329474. doi: 10.1080/20002297.2024.2329474. PMID: 38510981; PMCID: PMC10953787.

Mentella MC, Scaldaferrri F, Ricci C, Gasbarrini A, Miggiano GAD. Cancer and Mediterranean Diet: A Review. *Nutrients.* 2019 Sep 2;11(9):2059. doi: 10.3390/nu11092059. PMID: 31480794; PMCID: PMC6770822.

Smits KPJ, Listl S, Jevdjevic M. Vegetarian diet and its possible influence on dental health: A systematic literature review. *Community Dent Oral Epidemiol.* 2020 Feb;48(1):7-13. doi: 10.1111/cdoe.12498. Epub 2019 Oct 1. PMID: 31571246; PMCID: PMC6972589.

Shkempi B, Huppertz T. Impact of Dairy Products and Plant-Based Alternatives on Dental Health: Food Matrix Effects. *Nutrients.* 2023 Mar 18;15(6):1469. doi: 10.3390/nu15061469. PMID: 36986199; PMCID: PMC10056336.

Vauterin A, Steiner B, Sillman J, Kahiluoto H. The potential of insect protein to reduce food-based carbon footprints in Europe: The case of broiler meat production.

J. Clean. Prod., 320 (2021), 10.1016/j.jclepro.2021.128799.

Mazur M, Jedliński M, Duś-Ilnicka I, Ndoka Aj, Carrouel F, Ottolenghi L, Bourgeois D. Proteins from insects: A sustainable alternative for oral health within the one health concept and the planetary health diet. *Human Nutrition & Metabolism*, Volume 39, 2025, 200299, ISSN 2666-1497, <https://doi.org/10.1016/j.hnm.2025.200299>.

The Silent Crisis: Why Oral Health Deserves a Seat at the Global Health Table



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Oral health has long been neglected in global health discussions, despite its profound impact on billions of lives worldwide. With inequalities stark and preventable diseases rampant, the time has come to shift from neglect to action, integrating oral health into universal health coverage and making it a cornerstone of global health equity. Our author describes in his article the neglect of global oral health and delivers symptoms, root causes and possible solutions.



Prof. Dr. Dr. Habib Benzan

Despite decades of growing scientific evidence and continued advocacy, oral health remains one of the most neglected areas of global health. With more than 3.6 billion people affected, oral diseases are the most prevalent non-communicable diseases (NCDs) worldwide.¹ They are also largely preventable, yet oftentimes left untreated, let alone systematically addressed. There is no other NCD with comparable numbers of untreated cases.

The global divide is stark: while affluent populations enjoy access to the full range of high-cost, high-tech dental care – often cosmetic and elective – billions of people around the world lack even the most basic oral health services. In many countries, oral health is excluded from Universal Health Coverage (UHC) schemes, marginalized in health planning, and financed largely through private out-of-pocket payments, creating major barriers to access.

This paradox – a massive disease burden, high overall spending, and limited population-level access – continues

to plague health systems across high-, middle-, and low-income countries alike. The result is a reality of oral healthcare that serves the few, while neglecting the many.

This persistent neglect is not due to a lack of evidence or technical solutions. It reflects the consequences of fragmented systems, misguided policy priorities, and a global health architecture that has long tolerated, if not normalized, profound disparities in oral health.

A global disease burden – massive, preventable, and unjust

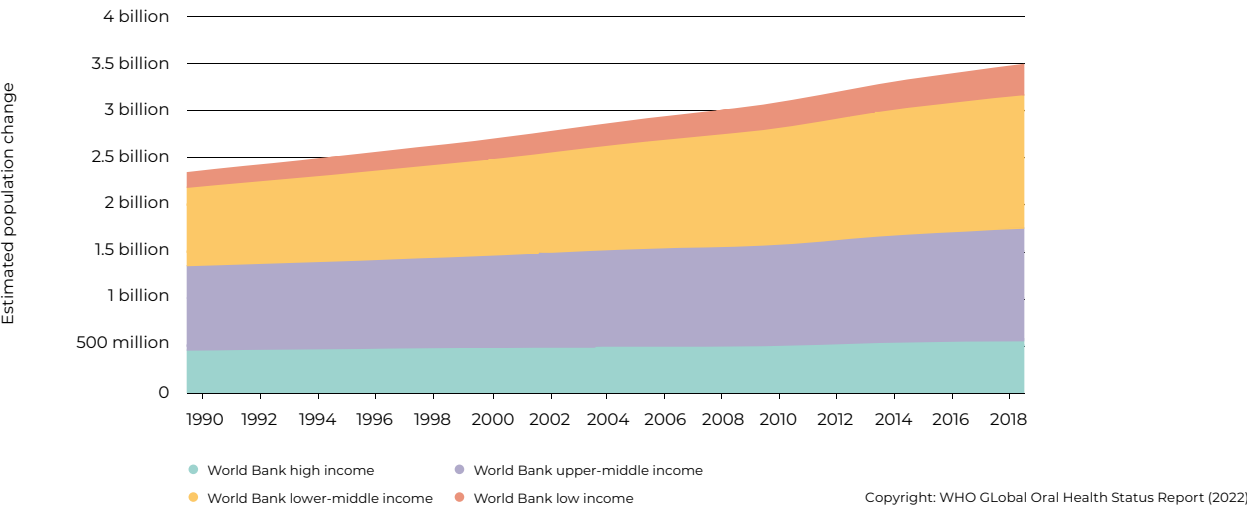
Oral diseases, including untreated dental caries, severe periodontal disease, tooth loss, oral cancers, rank among the most common conditions in the world. According to the WHO Global Oral Health Status Report 2022 and using estimates from 2019, more than 3.5 billion people live with untreated oral diseases. Dental caries of permanent

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teeth alone affects 2.5 billion individuals, while an estimated 1 billion suffer from severe periodontal disease.^{2,3} Since then, updated estimates for 2021 increased the number of cases of oral disease to almost 3.7 billion.¹ Children are not spared. In many countries, tooth decay is the leading cause of chronic illness among children, leading to pain, missed school days, and long-term consequences for growth and development. Among adults, oral diseases reduce employability, quality of life, and self-esteem. Among older persons, tooth loss and poor oral function affect nutrition, speech, and mental health – especially in settings where rehabilitative care is unaffordable or unavailable. The burden is highest in low- and middle-income countries (LMICs), where access to prevention and care is limited. But even in high-income settings, the distribution of oral diseases mirrors broader patterns of inequality: poverty, social exclusion, and limited access to care compound the effects of poor oral health. The global divide plays out not only in availability of services, but in lived experiences of pain, stigma, and neglect.⁴

FIGURE 1

Estimated case numbers of the major oral diseases combined between 1990 and 2019 per WB country income group (excluding lip/oral cavity cancer)



Oral diseases are the most prevalent noncommunicable diseases (NCDs) worldwide.

What’s more, the burden is intergenerational. Parents with poor oral health often pass on risk factors, habits, and vulnerabilities to their children, creating a vicious cycle of disease and disadvantage. Oral diseases may not rank high on mortality charts, but they cause extensive pain, suffering, stigma, and disability; and they interact with other chronic diseases and general health in complex, harmful ways.^{5,6}

A cost spiral: High spending, low equity, poor outcomes

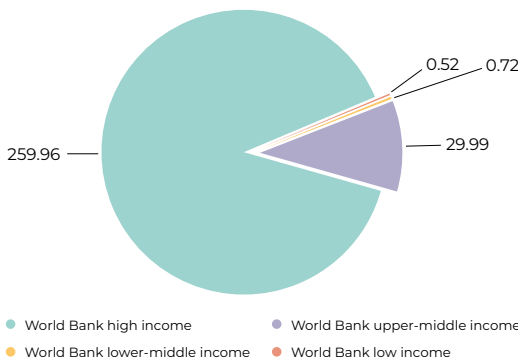
One of the most sobering features of global oral health is not only how much we fail to treat, but also how much

we spend, and how little impact that spending has. Estimates suggest that close to USD 390 billion are spent globally every year on oral health care, making it one of the most expensive disease categories. However, this figure is deceptive: the vast majority of this expenditure occurs in high-income countries and goes toward restorative or high-tech dental services – fillings, crowns, implants, and cosmetic procedures.⁷

Prevention, on the other hand, receives a tiny fraction of resources. Community-based programs like school toothbrushing or sugar reduction policies are

FIGURE 2

Per capita direct dental expenditure in US\$ per WB country income group (2019)



Copyright: WHO GLObal Oral Health Status Report (2022)

underfunded or absent in most health systems. Worse still, oral health is predominantly financed through out-of-pocket (OOP) spending – more than any other area of healthcare. Across countries and income levels, oral health consistently ranks as the health sector with the highest share of private expenditure.⁸⁻¹⁰ This global divide in oral healthcare financing is especially harmful. In LMICs, even a simple tooth extraction may be unaffordable for many households. In high-income countries, those without dental insurance often face the choice between foregoing dental care or financial hardship. Meanwhile, those who are able and willing to pay have access to advanced treatments, often disconnected from actual health needs. This model violates the very principles of UHC and health equity. At the same time, it appears that the burden of oral diseases has not markedly changed over the last 35 years. As Bernabé et al. state in the most recent publication of the global oral disease burden estimates: “The results show that insufficient action over the past three decades has led to little change in population oral health; without fu-

Oral health has waited too long in the shadows of global health.

ture sizeable and impactful action, this trend is likely to continue.”¹

Structural causes of neglect: Why oral health stays marginal

The roots of this neglect run deep. Among the many reasons that contribute to the current state of global oral health, a few stand out as particularly impactful. First, there is a historical and institutional divide. Dentistry evolved as a separate profession, with its own training, infrastructure, and financing mechanisms, often outside the public

health system. Integration in primary health care is limited. In most countries, dental care is almost exclusively provided through private providers and is considered an “optional” service rather than a core component of healthcare.¹¹

Second, commercial determinants, especially the global sugar industry, continue to shape risk environments that promote oral diseases. Sugar consumption is a primary cause of dental caries, yet regulation is weak and often undermined or even resisted by powerful interests of the food and beverage industries and their allies who apply strategies similar to the tobacco industry to change the public discourse.¹² Public policies to reduce sugar intake, such as taxes, advertising restrictions, or front-of-pack labelling, as well as measures to reduce the negative health impacts of ultra-processed foods, remain politically contested and take time to gain traction.¹³⁻¹⁵

Third, political invisibility and lack of leadership have kept oral health off the global health agenda for decades. There has been no major donor investment, no vertical initiative, and no strong integration with NCD strategies. Oral health has lacked the institutional champions and advocacy networks that have helped drive progress in areas like HIV, maternal health, or immunization.¹⁶⁻¹⁸

Fourth, and perhaps most insidious, is the cultural perception that oral health is a personal matter, a question of hygiene, behaviour, and individual responsibility. This perception fosters the notion that public investments to control oral diseases are not justified and reinforces a private market approach that exacerbates inequality.

The turning point: From neglect to global commitment

Yet, for the first time in decades, global oral health may be at a turning point. One of the watershed moments came in 2019, when *The Lancet* published its groundbreaking Series on Oral Health, for the first time placing oral diseases on the agenda of one of the most influential medical journals.¹⁹ The Series provided a stark critique of the global state of oral health, describing it as a “global public health failure” and exposing how

deeply inequities, commercial determinants, and systemic neglect shape outcomes across countries. It called for a paradigm shift: from treatment to prevention, from fragmentation to integration, and from commercial exploitation to public accountability. The *Lancet* Series served as a wake-up call and laid the intellectual and policy foundations for renewed engagement from global health leaders, including the World Health Organization (WHO). Acknowledging the absence of oral health in global health discourses, the World Health Assembly in 2021 adopted a landmark resolution on oral health, the first in over 15 years.^{20,21} This was followed by the development of the WHO Global Oral Health Strategy (2022), a bold document that recognizes oral health as integral to overall health and essential to achieving UHC. The Strategy outlines a vision for embedding oral health within national health systems, emphasizing prevention, primary care integration, and addressing commercial determinants. Building on this, the Global Oral Health Action Plan (2023–2030) was endorsed by WHO Member States.²² It provides concrete targets and milestones for action at national and global levels, including universal access to oral health services by 2030, integration of oral health in UHC benefit packages, and reduction of the burden of oral diseases. For the first time in the history of global oral health, there is now a global monitoring framework

and a defined path forward for tangible improvements. This new momentum was reaffirmed at the first-ever WHO Global Oral Health Meeting in Bangkok in December 2024, where delegations from more than 100 countries gathered to discuss implementation progress of the Global Oral Health Action Plan. A key outcome was the *Bangkok Declaration: Towards Universal Health Coverage for Oral Health by 2030*, which emphasizes the core principle that “there is no health without oral health.”²³ The Declaration calls on countries to translate commitments into national plans, to invest in prevention and service integration, and to hold themselves accountable for progress. The adoption of the Bangkok Declaration was a moment of unprecedented consensus. But turning this consensus into real impact will require sustained political attention, cross-sectoral collaboration, and courageous leadership at all levels, from global actors to national ministries to frontline health workers and empowered communities.

Solutions that work: From evidence to action

What must change? First, oral health must be integrated into primary health care systems. This means that preventive, diagnostic, and essential oral healthcare services are available where people live and work, especially in community clinics, schools and workplaces, and underserved areas.

Second, we need robust public health approaches. Policies to control and reduce risks, like sugar taxes or tobacco control policies, combined with measures to improve access to fluorides, preventive interventions and health promotion campaigns must become standard features of national NCD strategies. Oral health must be visibly included and adequately addressed in health budgets, national plans, and accountability frameworks. Third, workforce reform is essential. Task-shifting models, training of non-dental health professionals in basic oral health, and expansion of mid-level oral health providers can increase access and coverage in resource-constrained settings. Fourth, financing must be restructured. Oral health services should be part of essential benefit packages in UHC systems and available without financial hardship. Relying on out-of-pocket payment is incompatible with equity and sustainability, particularly in LMICs. Finally, we must build advocacy coalitions – across sectors, professions, and communities – to make oral health a political priority and ensure that the global divide in oral health does not deepen further.

A call to action: From recognition to reform

Oral health has waited too long in the shadows of global health. The burden is vast, the inequalities are stark, and the economic costs are significant. We can no longer afford to treat the mouth as separate from the body – or dental care as separate from health care. The momentum is here: *The Lancet* Series lit the fuse, WHO has taken unprecedented steps, and countries have declared their intention to act. But declarations alone will not relieve pain, close gaps, or stop decay. Reform requires bold policy change, adequate financing, meaningful accountability, and the moral clarity to treat oral health as a right, not a privilege. Oral health is not cosmetic. It is not optional. It is not the concern of the privileged few. It is a matter of justice, a test of our commitment to UHC, and a measure of whether our health systems truly serve people. There is no health without oral health.

Yet this call to action comes at a precarious time. The global health landscape is under increasing strain. A climate of insecurity, austerity, and shifting political priorities is sweeping across donor and domestic budgets alike. Development assistance is being reduced, multilateral institutions face tightening fiscal space, and national health systems are being forced to make difficult decisions about what services to prioritize, or sacrifice. In this climate, oral health is at risk of once again being sidelined, deemed too costly, too specialized, or not “essential enough.” The danger is that hard-won progress made in recent years could unravel just as implementation begins, especially in countries already facing severe health system constraints. That makes it even more important to keep the momentum alive, and the voice for oral health loud and unified. Professional associations, advocates, policymakers, and the public must all play a role in ensuring that oral health remains visible, funded, and protected from the rollback of essential services. A crucial moment is on the horizon: the 4th United Nations High-Level Meeting on Noncommunicable Diseases in September 2025.²⁴ This summit of heads of state and ministers from all 194 member states of the United Nations will review global progress on NCDs and UHC and define the path toward 2030 and beyond. It is an opportunity to reinforce oral health as a core component of NCD prevention and control and to solidify its place within future global health commitments.²⁵ By that time, the aspirations of the WHO Global Oral Health Action Plan to provide essential oral health services for all must no longer be aspirations alone. There must be tangible progress in national policy, funded priorities, and measurable realities. This is the moment to turn commitments into action, declarations into delivery of care, and promises into protection for all. We know what needs to be done. Now we must do it, with urgency, equity, and resolve. Because the mouth is not separate from the body. And people cannot wait any longer.

References

1. Bernabé E, Marcenes W, Abdulkader RS, Abreu LG, Afzal S, Alhailaiaq FN et al. Trends in the global, regional, and national burden of oral conditions from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet*. 2025;405(10482):897-910.
2. World Health Organization (WHO). Global Oral Health Status Report - Towards Universal Health Coverage for Oral Health 2030. Available at: <https://www.who.int/team/noncommunicable-diseases/global-status-report-on-oral-health-2022>. Geneva: WHO; 2022
3. Benzian H, Watt R, Makino Y, Stauf N, Varenne B. WHO calls to end the global crisis of oral health. *The Lancet*. 2022;400(10367):1909-1910.
4. Kearns C, Taylor G, Oberoi S, Mertz E. Dominant power and the concept of caste: Implications for dentistry and oral health inequality. *Community Dent Health*. 2022;39(2):137-142.
5. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur M, Listl S, Celeste RK, Guarnizo-Herreño C, Kearns C, Benzian H, Allison P, Watt RG. Oral diseases: a global public health challenge. *Lancet*. 2019;394:249-260.
6. Seitz MW, Listl S, Bartols A, Schubert I, Blaschke K, Haux C, Van Der Zande MM. Current knowledge on correlations between highly prevalent dental conditions and chronic diseases: An umbrella review. *Prev Chronic Dis*. 2019;16:E132.
7. Jevdjovic M, Listl S. Global, regional, and country-level economic impacts of oral conditions in 2019. *Journal of Dental Research*. 2025;104(1):17-21.
8. Benzian H, Schwendicke F. Economic considerations in oral health: Bridging gaps, broadening horizons. *J Dent Res*. 2024;103(12):1165-1166.
9. Bernabé E, Masood M, Vujicic M. The impact of out-of-pocket payments for dental care on household finances in low and middle income countries. *BMC Public Health*. 2017;17(1):109.
10. Winkelmann J, Gómez Rossi J, van Ginneken E. Oral health care in Europe: Financing, access and provision. *Health Systems in Transition*. Copenhagen: European Observatory on Health Systems and Policies, WHO; 2022
11. Watt RG, Daly B, Allison P, Macpherson LMD, Venturelli R, Listl S, Weyant RJ, Mathur M, Guarnizo-Herreño C, Celeste RK, Peres MA, Kearns C, Benzian H. Ending the neglect of global oral health – time for radical action. *Lancet*. 2019;394:261-272.
12. Kearns CE, Watt RG. Transnational corporations and oral health: examples from the sugar industry. *Community Dent Health*. 2019;36(2):157-162.
13. Global report on the use of sugar-sweetened beverage taxes 2023. Available from: <https://www.who.int/publications/i/item/9789240084995>. Geneva: World Health Organization (WHO);
14. Abbas H, Guarnizo-Herreño CC, El Tantawi M, Tsakos G, Peres MA. Challenges and way forward for implementation of sugar taxation in the Middle East and North Africa (MENA). *Community Dent Oral Epidemiol*. 2024;52(4):375-380.
15. Benzian H, Naidoo S, Wen Ng S. Beyond sugar-sweetened beverages: Tackling oral health risks of ultraprocessed foods. *J Am Dent Ass*. 2025;156(3):257-260.
16. Benzian H, Hobdell M, Holmgren C, Yee R, Monse B, Barnard JT, van Palenstein Helderman W. Political priority of global oral health: an analysis of reasons for international neglect. *Int Dent J*. 2011;61(3):124-130.
17. McAuliffe U, Whelton H, Harding M, Burke S. 'Toothless'-the absence of political priority for oral health: a case study of Ireland 1994-2021. *BMC Oral Health*. 2022;22(1):95.
18. Janakiram C, Sanjeevan V, BR R, Joseph J, Stauf N, Benzian H. Political priority of oral health in India: analysis of the reasons for neglect. *Journal of Public Health Dent*. 2018;78(2):144-153.
19. Oral health at a tipping point (Editorial). *The Lancet*. 2019;394:188.
20. World Health Organization (WHO). Oral Health. World Health Assembly Resolution WHA74/A74.R5 (31 May 2021) Available from: https://apps.who.int/gb/ebwha/pdf_files/WHA74/A74_R5-en.pdf.
21. Benzian H, Beltrán-Aguilar E. The return of oral health to global health is significant for public health everywhere. *Journal of Public Health Dentistry*. 2021;81(2):87-89.
22. World Health Organization (WHO). Global strategy and action plan on oral health 2023-2030. Available from: <https://www.who.int/publications/i/item/9789240090538>.
23. Bangkok Declaration – No Health without Oral Health. Towards Universal Health Coverage for oral health by 2030. Adopted 29 November 2024. Available from: <https://cdn.who.int/media/docs/default-source/ncds/mnd/oral-health/bangkok-declaration-oral-health.pdf>.
24. Alleyne G, Coll-Seck AM, Frieden TR, Tufton C. Fourth time a charm? How to make the UN High-Level Meeting on Noncommunicable Diseases effective. *JAMA*. 2025 (online first 10 Feb 2025)
25. Winkelmann J, Listl S, van Ginneken E, Vassallo P, Benzian H. Universal health coverage cannot be universal without oral health. *Lancet Public Health*. 2023;8(1):e8-e10.

“We commit to ensuring essential oral health services are accessible, affordable and acceptable for all, without financial hardship.”

A key statement of the Bangkok Declaration on Oral Health.



Swiss Healthcare System: Role Model or Latecomer?



Dr. rer. pol. Heinz Locher

Health Economist with extensive experience as a management consultant in the healthcare sector in Switzerland and abroad.

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The Swiss healthcare system is one of the “best” in the world, but is it also the most efficient? A look beyond national borders shows that other countries are implementing strategies in areas such as digitalisation, hospital planning and the regulation of medical products – in some cases more successfully. An international comparison provides valuable input for the further development of Swiss health policy.

Danish-style hospital planning, digitalisation modelled in Estonia, a new health insurance system based on the Singaporean model, and, lastly, ‘smart’ regulation of medical products like in Canada – and many of the challenges facing the Swiss healthcare system would be overcome. At least that’s what we get to read regularly, not only in specialist publications but also increasingly in the daily media. Indeed, other places do things differently, and it can be useful to take a look beyond the established state of affairs. A stocktake of domestic health policy and its effects based on a comparison with other countries provides valuable information for Switzerland. However, it is important to be mindful of the principle that leadership is not achieved through orientation towards the average. The international perspective can be incorporated at various levels and from different angles.

Switzerland’s health foreign policy
Amid the hectic debate on health policy, it is often overlooked that Switzerland has a comprehensive, coherent health foreign policy. The Federal Council has defined six areas of action, which combine protecting Swiss interests with a commitment to international solidarity.

The six action areas of Swiss health foreign policy 2019 – 2024/2028

- 1. Health security and humanitarian crises
- 2. Access to medicine
- 3. Sustainable healthcare and digitalisation
- 4. Determinants of health
- 5. Global health governance
- 6. Addiction policy

Source: Federal Council decree of 20 November 2023

Switzerland is a long-standing and reliable international partner that honours its commitments.

Overall system level
After years of sitting on the sidelines, Switzerland now regularly participates in comparative studies and analyses of healthcare systems with a key focus on access to services, the scope and quality of services and the financial burden on the economy and individuals. Happily, the days are gone when the phrase ‘Switzerland – not available’ frequently showed up in comparative tables and footnotes.

Although the assessment of Swiss health policy is generally positive, some challenges remain that have been better addressed elsewhere.

Regulatory instrument level
The examples mentioned relate to the level of regulatory instruments. When adopting foreign regulations, it is important to bear in mind that healthcare systems are closely intertwined with a country’s system of government and political culture. Examples include:

- The role of constituent states (cantons, federal states)
- The fundamental policy choice between a health insurance system and a national health service
- The scope left to private, profit-orientated players

However, an intermediate level of ‘generic’ questions allows different approaches of individual countries to be compared with each other:

- How can we ensure that ‘genuine’ emergencies are dealt with by the emergency services promptly and that ‘non-genuine’ emergencies do not unnecessarily burden the emergency infrastructure?
- Creating new job profiles (Advanced Nurse Practitioner)
- New tariff systems

Today, it is fair to say that the old adage – that the charm of Swiss policymaking lies in independently following the mistakes of foreign countries with a ten-year delay – no longer holds true.

Sources

OECD (2023), Health at a Glance, OECD Indicators, OECD Publishing, Paris

Federal Council decree of 20 November 2023, Swiss Health Foreign Policy 2019-2024/2028

Federal Office of Public Health: www.bag.admin.ch (various departments)

Ensuring good healthcare

Summary of the presentation by Anne Lévy, Director of the Federal Office of Public Health (FOPH), at the Health Insurance Days 2024 in Interlaken.

The main goal of Switzerland’s healthcare policy is to maintain the high quality of the healthcare system while containing costs – a complex challenge involving many stakeholders, from hospitals and insurers to doctors and patient organizations. Despite cost-saving measures such as lower drug prices, reduced lab fees, and the promotion of generics, healthcare costs continue to rise due to an aging population, medical advances, and high service utilization. Patients are often the weakest link in the system, even though their well-being should be central. The Federal Office of Public Health (FOPH) aims to balance the interests of all parties for the benefit of patients and premium payers. To ensure appropriate care – neither too much nor too little – the FOPH has launched initiatives to address over-, under-, and misprovision of care. Regional differences in treatment rates highlight the need for better coordination and use of resources, including expanding the roles of pharmacists and other healthcare providers. Innovation is encouraged through pilot projects and new insurance models, supported by a legal framework for experimentation. Upcoming referendums address concerns about rising costs and healthcare financing, with the government proposing counterproposals focused on incentives and shared responsibility between federal and cantonal authorities. A major reform is the unified financing of outpatient and inpatient care (EFAS), designed to eliminate financial disincentives and promote cost-effective, patient-friendly treatments. Further priorities include fair pricing and rapid access to innovative medicines, as well as ensuring the supply of essential drugs. Prevention remains crucial: many chronic diseases could be avoided through healthy lifestyles, vaccinations, and screenings. Digitalization is another key focus, aiming for interoperable data systems and streamlined processes. New digital tools, such as the health insurance dashboard and the electronic patient record, are intended to improve transparency, efficiency, and patient empowerment. Overall, the Swiss healthcare system faces the challenge of maintaining excellence amid demographic, technological, and financial pressures. Success will depend on compromise, innovation, and keeping the needs of patients at the center of reform.

Achievements and challenges of the Swiss healthcare system

Area	Switzerland’s position	Best practice / notes
Avoidable mortality	Very good outcome (top group)	
Life expectancy at birth	83.9 (top group)	Japan 84.5
Healthcare expenditure in % GDP	11.3% – high share	Luxembourg, Turkey
Per capita healthcare expenditure	Very high	Romania, Turkey
Out-of-pocket share	High share	Czechia, Luxembourg
Prevention share	Ranks last	Slovenia, Estonia
Unmet needs in oral healthcare policy	Ranks 16th, not funded by social insurance	Germany, Netherlands, Austria




Own representation based on OECD (2023)

Healthcare systems compared




Author — Angel Gonzalo

A comparison of the Swiss healthcare system with those of Japan and Denmark shows significant differences in structure, expenditure and quality. The following analysis focuses on expenditure, quality and economic aspects.

1. Healthcare system structure

-  **Switzerland**
- **System type:** Tends liberal and privately dominated
 - **Funding:** Compulsory health insurance (Health Insurance Act HIA), but with private insurance and high co-payments (deductible, excess)
 - **Provision:** Comprehensive, but dependent on the scope of insurance cover
 - **Providers:** Mainly private and competitive
-  **Japan**
- **System type:** Social insurance with state regulation
 - **Funding:** Compulsory insurance through employers or local authorities; citizens pay income-based contributions
 - **Provision:** Very broad, virtually no co-payments
 - **Providers:** Mainly private but strongly regulated
-  **Denmark**
- **System type:** Tax-funded and state-organised healthcare
 - **Funding:** Through taxation, no direct health insurance premiums
 - **Provision:** Comprehensive, free at point of use
 - **Providers:** Combination of public- and private-sector providers


2. Healthcare system expenditure

-  **Switzerland**
- **Total expenditure:** Around 12 to 13% of GDP (one of the highest shares worldwide)
 - **Per capita expenditure:** Above average (approx. USD 9,500 per year)
 - **Main drivers:** High medicine prices, administration costs due to competition, and co-payments
-  **Japan**
- **Total expenditure:** Approx. 10% of GDP (moderate in a global comparison)
 - **Per capita expenditure:** Approx. USD 4,500
 - **Main drivers:** Aging population, but low medicine prices and rigorous price regulation
-  **Denmark**
- **Total expenditure:** Approx. 10 to 11% of GDP
 - **Per capita expenditure:** Approx. USD 5,000 to 6,000
 - **Main drivers:** Focusing on prevention and digitalisation reduces costs, but high tax burden


3. Quality and access

-  **Switzerland**
- **Quality:** Very high medical standards and wide availability of specialists
 - **Access:** Good, but highly income-dependent due to high co-payments
 - **Challenges:** System is fragmented, inefficiencies
-  **Japan**
- **Quality:** High standards, particularly in primary care
 - **Access:** Universal and income-independent, relatively short waiting times
 - **Challenges:** Overuse of healthcare services, aging society
-  **Denmark**
- **Quality:** Focus on prevention and coordinated patient access
 - **Access:** Free at point of use, but with longer waiting times for non-urgent cases
 - **Challenges:** Strain caused by centralisation and limited capacities

5. What Switzerland could learn

-  **From Japan**
1. **Regulating medicine prices:** Japan sets strict price caps to control costs.
 2. **Cost-benefit assessments:** Japan conducts regular treatment assessments to avoid unnecessary expenditure.
 3. **Promoting prevention:** A strong focus on prevention could help to reduce costs in the long run.
-  **From Denmark**
1. **Funding through taxation:** A model of progressive tax funding could reduce social inequality with regard to the insurance premium burden.
 2. **Digitalisation:** Efficient IT systems to coordinate patients could ease the fragmentation of the Swiss system.
 3. **Prevention and integrated care:** Denmark's focus on prevention and coordinated health-care could improve efficiency.

4. Economic aspects

-  **Switzerland**
- Premium-based funding is a burden on households, particularly on low-income ones.
 - High medicine prices and strong market forces lead to exploding costs.
 - Administration costs (competition between insurers) are a problem.
-  **Japan**
- Income-based contributions ensure social equality.
 - Price regulations for medicines keep costs under control.
 - The aging population represents a growing burden.
-  **Denmark**
- Funding through taxation ensures social equality.
 - Prevention and digitalisation reduce costs in the long term.
 - High tax burden might become unpopular in the long term.

Switzerland has a high-quality but expensive healthcare system. From Japan it could learn from price regulation and a more strictly regulated insurance system, from Denmark from prevention programmes and digitalisation. Both models could contribute to lowering high costs and at the same time improve access while alleviating social inequalities.

The Digital Pill: How Technology is Transforming Healthcare

Interview — Angel Gonzalo Photos — Noor Staring

Healthcare is at a turning point: digitalization offers enormous opportunities to increase efficiency, promote preventive measures and democratize access to medical services. New technologies and data analysis not only improve the quality of medical services, but also establish a new way of thinking about health and illness. Digitalization is on the verge of revolutionizing healthcare and opening up new possibilities, from prevention to treatment. Dr. Fleisch, a professor at ETH Zurich and the University of St. Gallen, explains in an exclusive interview for The Essence how digital technologies will increase efficiency, reduce costs and transform the healthcare system in the long term.

Dr. Fleisch, you are a professor at ETH Zurich and also at the University of St. Gallen. Your area of expertise is information technology. How is it that you are writing a book about digitalization in healthcare and reflecting on the future of our healthcare system?

The so-called “Internet of Things”, in which the computer becomes omnipresent and at the same time disappears into everyday things, was the original

field of research that my team and I started over 20 years ago. The fields of application for this technological vision have literally exploded, and we have focused on a few areas of application: retail, manufacturing and healthcare. Here, together with colleagues from the medical faculty, we are building new applications and investigating how new technologies are changing healthcare.

Thanks in part to medical advances, we have doubled our life expectancy in the last 100 years. So we are living longer, but are we paying more and more for the treatment of illnesses?

Yes, it's incredible what medicine has achieved in this period of time. We are living longer, but more and more often we are also ill for longer – chronically ill. We have soon realized that digitalization in healthcare is particularly important, also and especially because of chronic illnesses. These are the big issue in medicine in the future and also the big cost drivers.

Non-communicable chronic diseases – cancer, diabetes, cardiovascular and respiratory diseases, as well as mental illnesses – are the big challenge. Will it remain that way for future generations?

As we age, we become more susceptible to chronic illnesses. It is somewhat of a paradox that our healthcare system is on the verge of collapsing in terms of costs precisely because it is so effective. Our healthcare system was established about 100 years ago, and at that time acute illnesses were the most common cause of death. Today, chronic illnesses are. Our healthcare system was not built for this. However, there is a promising aspect: from twin studies, we now know that about 70 to 80% of

Prof. Dr. Elgar Fleisch

Elgar Fleisch is Professor of Information and Technology Management at ETH Zurich and the University of St. Gallen (HSG). His currently largest laboratory, the Center for Digital Health Interventions, investigates how digital technologies are changing our healthcare system. It combines the disciplines medicine, informatics & economics.

Elgar Fleisch and team have published their findings in over 600 papers, including the book *The Digital Pill*. He is co-founder of several spin-off and start-up companies and member of various supervisory boards as well as academic steering committees.

Elgar Fleisch did his doctorate in Vienna, in the field of artificial intelligence, and his habilitation in St. Gallen on the topic of network companies. He spent his sabbaticals at MIT and Dartmouth College.



chronic diseases can be prevented. So it is not primarily the luck of the genes that keeps us healthier, but the behavior of each individual. Through my behavior, I can decisively influence the risk factors and thus prevent chronic diseases. That is the big opportunity.

You raise an important point: precaution and prevention are given a low priority in our healthcare system. Less than 3 percent of healthcare costs are spent on prevention. What are the reasons for this?

That's a very important question. Well, the most apt answer is: "There is no glory in prevention". I don't know of any sensible doctor, researcher, insurance or pharmaceutical manager who says that prevention is nonsense. Even if the long-term effect of preventive interventions is much more difficult to prove, I hear from my esteemed medical colleagues that prevention is less a medical issue than a business case issue. The fact is that the incentives are set for repair and not for prevention. Whether or not prevention is widely adopted is ultimately a question of the business model. Hospitals need to fill their beds, and doctors' offices need to pay back the loans for their expensive equipment. And today they only get reimbursed for repairs, not for prevention. Even if you are the best and most idealistic doctor in the world, the incentive system will eventually catch up with you. To put it figuratively: a patient who is healthy does not generate any income for you. Only a visible illness is the ticket to today's healthcare system.

In Singapore, the Health Promotion Board was founded over 20 years ago with the aim of enabling people to take control of their own health. How does that work exactly? Is this model also applicable in Switzerland?

Yes, absolutely. There are several initiatives in this direction worldwide. They start by creating the necessary awareness that health is important and can be influenced. We learn a lot of things at school, but we actually learn just as little about "health literacy" as we do about "financial literacy". What do I need to do to feel good physically

“Our healthcare system is a disease system, because only visible disease is the entry ticket into today's healthcare system.”

and mentally? This includes nutrition, exercise, sleep, stress, how to deal with addictive substances and basic knowledge about health. A person who knows more about health stays healthier. Health literacy has a decisive influence on our health.

In your book “The Digital Pill”, you, as co-author, describe five levers that show how digitalization can be a central key to the healthcare world of tomorrow. The first lever you describe is the promotion of behavioral change through digitalization. How does that work exactly?

Everyone knows how difficult it is to break old habits. In my view, bringing about and anchoring behavioral change is the biggest challenge in prevention. The power of small nudges is emphasized everywhere, but their effect is often very limited. Changes are easier to bring about when it is not a major burden for the patient and when they can clearly see or even feel the necessity for it. The further in the future the positive effect lies and the greater the effort involved in the changeover, the more difficult it becomes. Digital technologies can help here in a big way. They extend the doctor or therapist from the few minutes in the practice to 24/7 care around the clock. If they are

well designed, they are fun, motivating and informative. They are the personal trainer for everyone. They can be very effective, especially in combination with the doctor, and at the same time extremely cost-effective.

The digitalization of healthcare is about technology, apps, algorithms, data and sensors. Does this mean we are moving away from a humane medicine?

No, if we do it right, the opposite will happen. Technology supports and extends the doctor, it does not replace him or her. And it supports the patient. Technology helps us to be much closer to the individual and to involve the doctor when support is really needed.

In the area of prevention, it works a bit like with a car. There, dozens of parameters such as oil temperature and tire pressure are constantly measured without saying. If a parameter leaves its normal range, an orange or red light comes on. With digitalization, this can be more and more the case with people. Our digital helpers are constantly measuring our blood pressure, blood sugar levels and heartbeat in the background and report before the disease becomes visible. We cannot feel blood pressure and triglyceride levels ourselves, and the same applies in healthcare: what I cannot measure, I cannot manage.

Are we Europeans generally less open-minded about new technologies?

Unfortunately, it is a European perspective to emphasize the risks. Digitalization fuels many fears in us. The Chinese are more open in this regard, as are North Americans. Let me explain: in our part of the world, the first question is always about regulation and security. Innovation then takes place elsewhere, not here in Switzerland or in Europe. We may have the most comprehensive data protection laws, but we have hardly any digital business. We are beginning to regulate AI before we understand it. I have the uncomfortable feeling that our biggest export is the raised index finger. And yet innovation is becoming faster and faster, more agile. We have to have a certain basic trust in the legality and solidity of innovative

people and companies that produce new things. Innovative companies are where you can try out new things, and that is often no longer the case here.

In many countries, health systems are controlled by the way they are financed. This is often primarily about business with a wide range of vested interests. Can digitalization help to untangle this?

I am convinced it can. But we have to remember that information technology acts as an amplifier. If I digitize a poorly organized system without changing it, without an overarching concept, then it will become much worse. So, let's say I have a hospital and I require all departments and doctors to manually enter all medical data into a computer. That's not a good idea.

Has the Covid-19 pandemic helped us in terms of digitalization?

Yes, massively. Necessity has become a virtue. Good telemedical services have been developed quickly. In Sweden, 45% of appointments with general practitioners are handled by telemedicine. This relieves the pressure on the healthcare system there enormously. In terms of digitalization, Scandinavian countries have developed faster than the rest of Europe. We can learn from that.

“There is no glory in prevention.”

Does digitalization also increase efficiency? Where do you see inefficiency and where can costs be saved without a loss of quality?

Many cost drivers are due to inefficiencies, that is, to "waste" in the system. Digitalization helps here to create transparency and avoid redundancies by giving every treating physician easy access to all previous examination results and health data concerning his or her patient. Digitally supported triage systems can also help to relieve the pressure on expensive and notoriously

overburdened hospital emergency rooms. From a medical point of view, up to 55% of emergency room visits are unnecessary or avoidable.

You mention that digitalization is democratizing medicine. Can you explain that?

Medical services that can be provided digitally are many times cheaper and are not tied to time or location. They are accessible and affordable for almost everyone. They are also easy to measure and thus transparent and comparable. And they enable every citizen, whether sick or healthy, to

easily access their health data and secure health knowledge. This strengthens a patient's autonomy and changes the relationship between patients and doctors.

Can digitalization significantly improve the quality of medical services? Is it already doing so?

In a lecture at the University of Zurich on the occasion of a medical congress, I asked the question to a full lecture hall: Do you think that digital therapies in 2030 will be better than the poorer half of conventional therapies? The doctors voted anonymously via an



app. Even I was surprised by the result: the vast majority voted yes. The reason is simple: medical knowledge is exploding. It expands with every new scientific publication. A single researcher can hardly keep up in his or her field, and a practicing physician has no chance at all. A good AI, whether in the field of diagnosis or intervention, will soon be consistently better than the average doctor. In some areas, such as imaging techniques, this is already the case.

Thanks to digitalization, medical knowledge can be created from data, which basically benefits everyone. However, the handling of health data as a public good is the subject of heated and controversial discussion. How do you assess this development?

Medicine is an empirical science. Its core, clinical studies, are conducted to collect and analyze data in order to test hypotheses and make evidence-based decisions. Not only data from clinical studies helps, but increasingly also health data that patients themselves generate and collect digitally. From a medical point of view, this is an infinite treasure trove that is becoming

massively more important with digitalization. Countries in which this data is not available due to ideological data protection will be at a disadvantage in medical research in the medium term. The latest developments will then take place elsewhere. Unfortunately, I speak from experience here.

When you see what people post on Facebook and Instagram, you get the impression that it's not the general public that has a problem with data protection, but just a small, loud and, above all, healthy elite. Anyone who is ill and looking for help is very willing to share their data – anonymized and secure, of course – for research purposes. In my view, donating data is the new blood donation.

“Donating data is the new blood donation.”



You are talking here about so-called “citizen scientists”. These could provide a sound knowledge base. What does that mean and how great is the real potential?

Every single person can contribute to medical progress by collecting their health data and making it available to research in anonymized form. Firstly, my data helps me for prevention purposes and in the event of illness. Secondly, they contribute a tiny bit to my children and grandchildren being able to benefit from better medicine. Some people are already going a step further in specially organized programs by participating in voluntary studies, for example on the effects of different eating habits. They are then called citizen scientists.

Do you advocate making health data widely available for medical research?

Yes, definitely. If the data is anonymized and secure, then the vast majority have no problem with it, but see it as a contribution to the future health of society. Therefore, I am a big fan of the opt-out variant, in which citizens who do not want to donate data must actively decide against donating data and are otherwise included by default. Incidentally, this is one of the few small nudges with a big impact.

According to the WHO, integrated health systems should play an important role in the future. This will increase efficiency and the quality of services because coordination will improve. How do you assess this development?

Today, the reality is often that patients run from one doctor to another, from one specialist to another, examinations are carried out multiple times, redundancies arise and different data sets are created. The individual players are not coordinated with each other and certainly not integrated. Integrated would mean that the patient is truly the focus, and all parties have an interest in the patient recovering as quickly as possible. This would mean that at least a good portion of the compensation would be based on results. The medical service providers would be judged by the success of the healing process and

not by the input, i.e. the examinations carried out and medications prescribed. This requires that they all pursue the same goal, are incentivized in parallel and work together. Everyone accesses the same data and works together for the good of the patient. A good example of this is an integrated type I diabetes clinic in the Netherlands that has just been analyzed in the renowned New England Journal of Medicine Catalyst.

You say that prevention today fails mainly because of the lack of a business model. Are there any examples that point to a possible way forward?

I am particularly fascinated by models that take a personalized and evidence-based approach. The first company we noticed that does this is called **insidetracker.com** and is based in Cambridge near Boston, USA. I can upload my blood count as a PDF and an AI will use it to derive personalized nutrition recommendations. Each of these recommendations is backed up with the scientific publications on the clinical studies. A few months later, I can upload my new values and see if anything has changed for the better or worse. The logic of measuring and managing is implemented. **Function Health**, also based in the US, offers a similar service, as does the company **Aware** in Germany and **Care.me** in Switzerland. These are used by people who want to age healthily and cannot find the appropriate support in the traditional healthcare system.

Are these new players in the healthcare sector in competition with traditional medicine?

No, I don't see it that way. Rather, they complement it; each has its own focus and is optimally aligned with its core task in terms of costs. Healthy customers who, as part of prevention, are diagnosed with conditions such as prediabetes, switch to the traditional healthcare system and then come back again. This can already be seen today at Care.me, for example.

What role does technology play in prevention?

Prevention must be accessible to everyone and as straightforward and cost-effective as possible. Digital tech-

Centre for Digital Health Interventions

The Center for Digital Health Interventions (www.c4dhi.org) is a joint initiative of ETH Zurich, the University of Zurich and the University of St. Gallen (HSG). For over 10 years, interdisciplinary teams from computer science, medicine and social sciences have been working there on evidence-based and cost-effective personalized digital therapies for the treatment and prevention of chronic diseases. They develop and evaluate digital biomarkers, digital and hybrid interventions, and new business models. The center is financed by projects of the Swiss National Science Foundation (SNSF), the US NIH, the Singapore NRF, the Swiss Health Promotion Foundation and companies such as CSS. It publishes its results in leading scientific journals, in books, teaching materials and in the form of open source software. Elgar Fleisch is co-founder and co-chair of the center.

nologies play a key role here because their marginal costs are almost negligible. An evidence-based, personalized, patient-centered, always up-to-date, easily accessible and affordable prevention service is hardly conceivable without massive digitalization. That is why we at the Center for Digital Health Interventions at ETH Zurich, UZH and HSG are working with partners in North America and Singapore on digital biomarkers, digital health interventions and the corresponding platforms.

In your book “The Digital Pill”, you ask the rhetorical question “Why isn’t health a compulsory school subject?” Yes, why not?

We all went to school and didn't really learn anything about how to maintain and promote our health, except maybe a few physical exercises (laughs). Perhaps the time has come for us to integrate health as a comprehensive topic into a school subject. Basically, it's about an essential life topic, such as social studies or financial literacy. It could be based on the four pillars of health prevention in an appealing way: exercise, nutrition, sleep and stress management. In such a subject, you would not primarily learn for school, but for life.

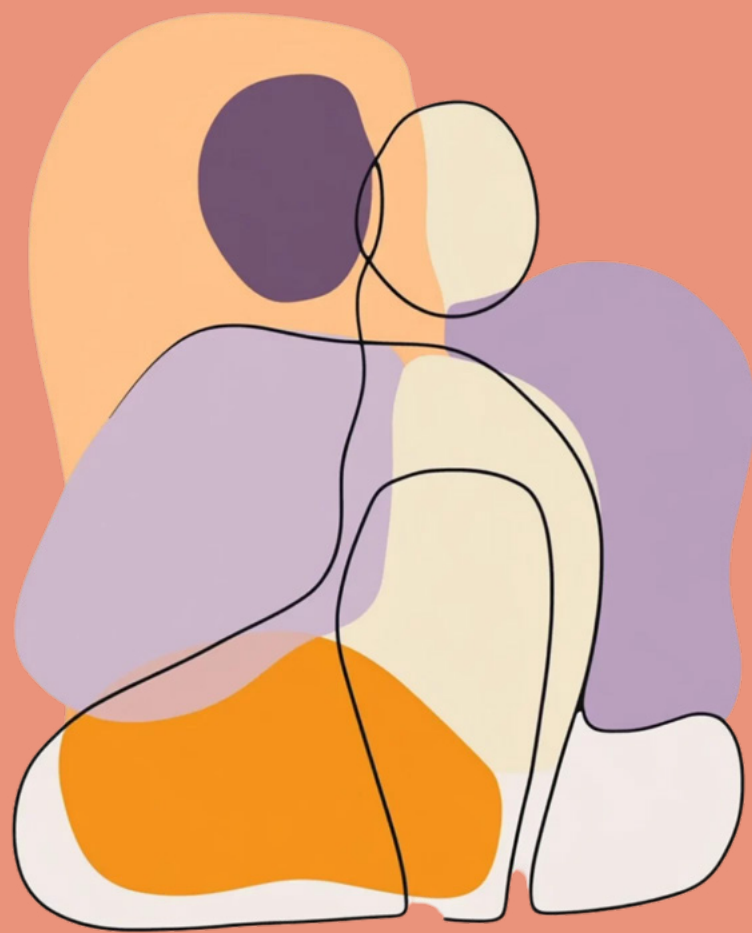
“The Digital Pill”, the book



Our healthcare system is under great pressure to change: groundbreaking medical advances are allowing us to live longer, but our increasingly unhealthy lifestyles

mean that we suffer from chronic illnesses more and more often. This is driving up healthcare costs and undermining our successful system. Accelerating digitization in healthcare is one way to counter rising costs while providing better care for the sick. “The Digital Pill – A Journey into the Future of Our Healthcare System” (Campus Verlag) provides a global overview of today's healthcare system, its considerable successes and the challenges posed by medical progress and an aging population, and shows how digitalization can help solve these problems. Using the example of five chronic illnesses, this publication shows what digital innovations can already achieve today and takes us on an exciting journey into the digital future of our healthcare system.

An Introduction to Mind Body Medicine



Claudia M. Witt, MD, MBA

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Mind Body Medicine is a modern, integrative health concept that bridges the connection between body and mind, promoting self-care as both a preventive and therapeutic concept. By combining research data and experience from health professionals from different fields (complementary medicine, psychology, nutrition, and sports science), Mind Body Medicine empowers individuals to manage symptoms and build resilience. Managing stress and its impact on mind and body is an important aspect of Mind Body Medicine.

The modern scientific exploration of Mind Body Medicine gained momentum in the 20th century, particularly through the work of Herbert Benson. A cardiologist at Harvard Medical School, Benson is best known for recognizing the Relaxation Response – a physiological state counteracting the stress-induced fight-or-flight response. Building upon this foundation, Gustav Dobos and Anna Paul advanced Mind Body Medicine in Germany by including more evidence-based complementary therapies. In Switzerland, we introduced Mind Body Medicine in 2014 and strongly linked it with health psychology as shown by the combined postgraduate training for health professionals at the University of Zurich [1].

In 2024, we decided to foster a Whole Person Health approach and expand upon the principles of Mind Body Medicine by looking beyond individual symptoms to the broader interplay of biological, behavioral, social, and environmental factors. As defined by the National Institutes of Health in the USA, Whole Person Health is an approach that considers the individual as an interconnected system rather than a collection of separate organs or symptoms [2].

Instead of solely treating illness, Whole Person Health focuses on empowering individuals and communities to take an active role in their well-being through self-care, lifestyle, and behavioral interventions [2]. The “Temple of Health” visualizes this concept and shows how different levels can be used to promote self-care and self-efficacy and reduce symptoms through multimodal therapies. A key aspect of the Mind Body Medicine concept is its personalized approach, tailoring interventions to individual needs in both individual and group settings. The Temple of Health (Figure 1) visualizes the relevant el-

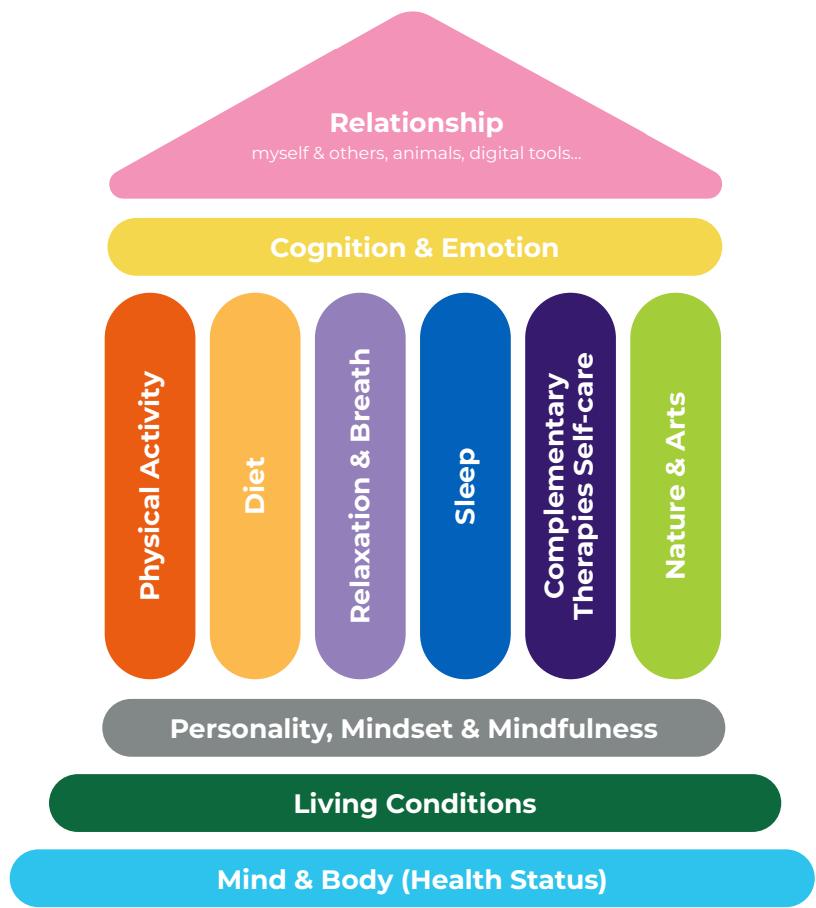
ements of the Whole Person Health-Mind Body Medicine concept. The foundation of the temple illustrates essential aspects that should be considered in Mind Body Medicine recommendations, such as physical and mental health status, living circumstances, personality, and mindset. Mindfulness is seen as a foundational element that can be nurtured through specific interventions or combined with other approaches. The six pillars serve as resources that can be strengthened through targeted interventions. They include physical activity, nutrition, relaxation and breathing, sleep, complementary self-care

**Whole Person Health
considers the individual as
an interconnected system rather
than a collection of separate
organs or symptoms.**

therapies, and nature and the arts. Five of the pillars have long been fundamental to Mind Body Medicine, while the sixth was only recently introduced. Increasing scientific evidence showed that contact with nature positively impacts health and well-being. Additionally, the arts – including music, painting, dance, and museum visits – have been shown to further reduce symptoms and enhance overall well-being. The Mind Body Medicine approaches displayed in the ceiling support emotional regulation and cognitive processes. The temple’s various levels also shape the relationships with ourselves, others, and digital tools as displayed in the roof of the temple.

FIGURE 1

The Temple of Health



Whole Person Health Mind Body Medicine © 2024 by Witt, C.M. et al. is licensed under CC BY-ND 4.0.

The Science behind Mind Body Medicine: Evidence and Application Mind Body Medicine interventions are evidence informed and based on the three pillars of Evidence Based Medicine: clinical research, experience of the health professionals, values and needs of the patients/persons. The interventions applied in Mind Body Medicine have shown positive effects across multiple health domains. Within the concept, they are usually adapted to the respective treatment aim (e.g. stress management, fatigue in cancer patients). For example, Mind Body interventions have shown to be in managing distress in patients with chronic pain or cancer. Therefore, interventions such as yoga,

qigong, mindfulness, acupressure and others are recommended in clinical practice guidelines for supportive cancer care [3] or treatment of chronic low back pain [4]. Practices like yoga, tai chi/qigong, Pilates, mindfulness, and breathwork can be cost-effective approaches to managing anxiety [5]. Other studies taking a more preventive approach have found that medical students and healthcare professionals can also benefit from Mind Body Medicine courses. Participants in these courses developed higher levels of self-compassion [6].

The Digital Age: Challenges and Opportunities

At its core, Mind Body Medicine is about connection – between mind and body, but also within an increasingly digital world. While artificial intelligence (AI) and digitalization can be misconstrued as disruptions that blur this connection, research suggests they can also serve as bridges, strengthening self-awareness and well-being when used intentionally. The key is learning to navigate this evolving landscape: identifying stressors, recognizing opportunities, and leveraging technology to enhance, rather than diminish, mind-body integration. To understand Mind Body Medicine is to understand the power of connection – in all its forms.

The rise of AI in the workplace brings both challenges and opportunities for Mind Body Medicine. While AI itself doesn’t directly cause burnout, it creates conditions that can heighten stress, such as role ambiguity, increased job expectations, and job security concerns [7]. Many employees experience the classic burnout triad: emotional exhaustion, depersonalization, and a diminished sense of accomplishment [7]. How individuals perceive these technological shifts plays a crucial role – those with confidence in their ability to adapt report lower stress levels, while uncertainty about mastering AI-related skills can intensify anxiety [8].

At the same time, AI is expanding the potential of Mind Body Medicine, offering personalized approaches to stress management and well-being. Wearable devices, biofeedback systems, and re-

laxation apps for patients with certain diseases and symptoms [9] now provide real-time insights and interventions that were once accessible only through specialized practitioners [10]. In the workplace, AI-supported well-being programs have the potential to individualize preventive and therapeutic support, while virtual counseling platforms make professional guidance more accessible [11]. However, for these digital Mind Body Medicine tools to be truly effective, they must address key concerns, including algorithmic bias, privacy issues, and the need for human-centered design. AI should complement, not replace, traditional practices, ensuring technology enhances rather than diminishes the holistic nature of healing [10] [11]. The future of Mind Body Medicine in the digital age lies in striking this balance – leveraging AI’s capabilities while preserving the deeply personal and integrative essence of the Mind Body Medicine practices.

Mind Body Medicine in Switzerland and Beyond

Globally, Mind Body Medicine adoption varies widely, from implementation of single interventions (e.g. yoga) to application of a more conceptional approach. Despite growing evidence supporting Mind Body Medicine’s role in patient care, widespread implementation remains inconsistent due to the heterogeneity of offers and gaps in awareness, education, and integration into healthcare systems. Dispelling misconceptions will be key to shifting health care toward a more holistic, preventative model – one that empowers individuals to take an active role in their health. As Mind Body Medicine gains recognition, its future lies in its conceptional and personalized approaches that tailor interventions to individual needs, optimize treatment frequency, and seamlessly integrate into mainstream healthcare [12]. In Switzerland, the Mind Body Medicine Association for Health Professionals (www.sfmbm.org) and the structured postgraduate university training improve the quality of Mind Body Medicine Services. Digital tools can support better integration into daily life, thus expanding

Mind Body Medicine is about connection – between mind and body, but also within an increasingly digital world.

FIGURE 2



accessibility. Many individuals seek to take an active role in their health, whether during intensive medical treatment, after completing therapy, or as part of general health maintenance and prevention. In such situations, self-care measures can offer valuable support. We provide access to a range of these methods, including relaxation techniques, mindfulness practices, and a specific range of exercises that can be performed in nature (Figure 2).

References

1. March 2025; Available from: <https://www.psychologie.uzh.ch/de/bereiche/sob/ang-soz/CAS.html>.
2. Health, N.C.f.C.a.I. Whole Person Health: What It Is and Why It's Important. 2021 [cited 2025 Feb 27 2025]; Available from: <https://www.nccih.nih.gov/health/whole-person-health-what-it-is-and-why-its-important>.
3. Onkologie, L. Guideline Complementary Medicine in the Treatment of Oncological Patients. 10 March 2025; Available from: <https://www.leitlinienprogramm-onkologie.de/leitlinien/komplementaermedizin>.
4. Qaseem, A., et al., Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*, 2017. 166(7): p. 514-530.
5. Lin, X., et al., The effects of mind body exercise on anxiety: A systematic review and meta-analysis of randomized controlled trials. *Mental Health and Physical Activity*, 2024. 26: p. 100587.
6. Brinkhaus B, S.B., Witt CM, Ortiz M, Herrmann M, Adam D, Vogelsänger P., Reducing stress, strengthening resilience and self-care in medical students through Mind-Body Medicine (MBM). *GMS J Med Educ.*, 2025. 42.
7. Kim, B.-J. and J. Lee, The mental health implications of artificial intelligence adoption: the crucial role of self-efficacy. *Humanities and Social Sciences Communications*, 2024. 11(1): p. 1561.
8. Pereira, V., et al., A systematic literature review on the impact of artificial intelligence on workplace outcomes: A multi-process perspective. *Human Resource Management Review*, 2023. 33(1): p. 100857.
9. Schläpfer, S., et al., Engagement With a Relaxation and Mindfulness Mobile App Among People With Cancer: Exploratory Analysis of Use Data and Self-Reports From a Randomized Controlled Trial. *JMIR Cancer*, 2024. 10: p. e52386.
10. Lekadir, K., et al., FUTURE-AI: international consensus guideline for trustworthy and deployable artificial intelligence in healthcare. *BMJ*, 2025. 388: p. e081554.
11. García-Madurga, M.-Á., et al., The Role of Artificial Intelligence in Improving Workplace Well-Being: A Systematic Review. *Businesses*, 2024. 4(3): p. 389-410.
12. Dossett, M.L., G.L. Fricchione, and H. Benson, A New Era for Mind-Body Medicine. *N Engl J Med*, 2020. 382(15): p. 1390-1391.

Accelerators of Vital Processes



Author — Angel Gonzalo

Our body needs enzymes to function properly. We need them for all metabolic processes. Without enzymes, we would not be able to live. They also play a crucial role in our oral health. This is why Swiss Dental Company CURADEN has been investing for years in basic research into enzymatic applications.

Dr Michel-Angelo Sciotti is an innovation researcher and project manager for Life Sciences at the University of Applied Sciences Northwestern Switzerland in Muttens. A molecular biologist, he has extensive experience in the application of enzymes. He has been working on the use of enzymes in toothpastes for CURADEN since 2013. The backstory is that CURADEN's owner Ueli Breitschmid initiated a meeting with Sciotti and on the spur of the moment exclaimed: "Enzymes are a great thing!" And indeed they are: our genes are essentially a 'construction manual' for enzymes and other proteins. "To put it simply," says Sciotti, who took Breitschmid's opening gambit with good humour, "genes are basically the code text, and enzymes are able to read this code, interpret it and process it further." Looked at like this, enzymes form the basis of life. "Of course that's great..." Sciotti jokes. Enzymes are a main category of proteins that are regarded as 'little chemists' because they control the chemical processes in our cells. Composed of amino acids, they are highly complex molecules that act as biocatalysts. This means that they have the ability to accelerate the reaction rate of biochemical processes. There are around 5,000 reactions that can be accelerated by enzymes. Each enzyme is responsible for one function.

Enzymes enable metabolism

Molecular biologists such as Sciotti know that it is primarily enzymes that enable cells and thus organisms to function and make life possible in the first place. They are required for all chemical reactions that take place in the human body. These include, for example, the regeneration of cells or

tissue and the removal of waste products and toxins, as well as supporting the immune system. Enzymes are the driving force in our body and are therefore responsible for all the functions of every single organ in our body.

Enzymes make it possible to metabolize and use energy from food. They help the body to digest food and absorb nutrients from proteins, carbohydrates, fats and plant fibres. But we also need them to see, hear, smell, taste, breathe and move.

Receptors are molecules on the cell surface that respond to a chemical signal from outside the cell and trigger mechanisms that generally lead to the function of certain genes that influence cell function. Interestingly, almost all receptors are also enzymes or exert their effect through the activation of an enzyme. Simply put: enzymes really get our organism going!

Enzymes in saliva

Like other bodily fluids, saliva is hardly a tasteful conversation topic. But this secretion deserves our appreciation, not only because it lubricates our mouths and enables us to swallow food. Salivary glands are found in many animal species and have evolved in animals over millions of years for all sorts of purposes. Snakes use them to produce venom, fly larvae use them to produce silk and mosquitoes use them to inject chemicals to prevent blood from clotting as they suck our blood. Some birds even use their saliva as 'glue' to build their nests. For humans, saliva and the enzymes and other substances it contains are vital in a different way. Our taste buds need a liquid medium so that the molecules we perceive as flavours can reach them. This is what allows us to distinguish between different flavours in our food. Saliva has evolved for precisely this function. Saliva is also responsible for initial 'digestion' in the mouth: It contains enzymes that break down food, including amylase, which converts starch into sugar. Its work continues on the food residue between the teeth. A little attention is all it takes to notice its effect: the more we chew a piece of bread, the sweeter it tastes. This is why babies love to suck on a piece of bread.

Calcium and fluoride not only in toothpaste

If dentists are so keen to insist that we eat less sugar, it is because among the 700 types of bacteria in the mouth, there are some that feed on these sweet substances and produce acids that attack our tooth enamel and cause tooth decay. Fortunately, saliva constantly washes away bacteria and restores the neutral pH of the mouth. Most drinks are a little acidic, including orange and apple juice – and even milk. They taste sweet because they contain sugar. Cola drinks typically have a pH of 2.5. By way of explanation, the lower the value on a scale of 0 to 14, the higher the acidity, with pure water being the benchmark for a neutral pH of 7. Saliva is not only the first barrier against bacteria, but also contains calcium, phosphate and fluoride. These elements adhere to tooth enamel and repair it. Proteins stored in saliva coat the enamel and protect it from acids. Bacterial colonies, for their part, form 'protective shields' after eating. If calcium is then added with the saliva, tartar forms.

Toothpaste containing enzymes

This makes saliva a special 'juice' with a variety of functions for dental and oral health: it cleans, protects and regenerates the teeth. How important it is often doesn't become clear until it is

It is primarily enzymes that enable cells and thus organisms to function and make life possible in the first place.

lacking. This is because a reduced saliva flow, as well as an altered composition, significantly increases the risk of tooth decay, tooth erosion and periodontitis. An enzymatic toothpaste intensifies the protective functions of saliva, uses and activates the natural defence systems and activates new ones inspired by other biological systems. CURADEN's 'Be you' toothpaste, for example, mimics the enzymatic antibacterial protection of, among others, honey. And these defence systems are urgently needed. When combating tooth decay, the aim is to reduce the population of certain bacteria and the protective plaque they form (e.g. *Streptococcus mutans*), but without eradicating them completely. *Streptococcus mutans* is a typical 'pioneer' of oral flora: it stimulates the colonization of other bacteria and – if our oral hygiene is out of balance – it may cause the acidification that is responsible for caries formation. But basically, these bacteria are our 'table guests' and cannot simply be regarded as bad guys, especially as they prevent opportunistic infections caused by other germs and are important for a healthy, rich oral flora. But only as long as proper oral hygiene is practised. Opportunistic pathogens, i.e. fungi and bacteria that are not part of our oral flora, are often responsible for inflammation and clinical conditions. The approach adopted by innovation researcher and molecular biologist Michel-Angelo Sciotti: "We add enzymes to the toothpaste, i.e. we strengthen a naturally existing system by adding enzymes obtained from the black mould *Aspergillus Niger*." The better the enzymatic reaction works, the better it supports the natural system of our oral flora. And this is precisely at the core of Sciotti's research work for CURADEN, which has already been successfully applied in toothpastes such as 'Be you'. "The principal aim of our next development in enzyme application," Sciotti says, "is to find specific enzymes in the databases that can break down or render harmless unfavourable and/or harmful substances such as plaque, caries or periodontal disease-promoting components – or, on the contrary, to produce positively acting substances that reduce the bacterial population and plaque formation."

Tidbits of Science

Fish casings for flawless skin?



How fish casings could play a role in future skincare products

There are some pretty weird ingredients in cosmetics and skincare products. One example is snail mucin, which is used for its moisturizing and antioxidant properties. But researchers reporting in the journal *ACS Omega* may have found something even stranger to smear on your face: molecules made by fish gut bacteria. In cultured cells, the compounds showed skin-lightening and wrinkle-preventing properties, making them potential ingredients for your future skincare routine.

Even though fish intestines seem to be the absolute last place to look for cosmetic active ingredients, the idea is not completely far-fetched. Many important drugs have been found in bizarre places – the antibiotic properties of penicillin were famously discovered after a failed experiment went moldy. More recently, the brain cancer drug marizomib has been extracted from microbes found in marine sediments on the seabed. Two potentially untapped sources of new compounds could be the gut microbes of red sea bream and black-headed sea bream, fish found in

the western Pacific. Although these microbes were first identified in 1992 and 2016, respectively, there have been no studies on the compounds they make. Hyo-Jong Lee and Chung Sub Kim therefore wanted to find out whether these bacteria produce any metabolites that could have cosmetic benefits. The team identified 22 molecules formed by the gut bacteria of red sea bream and black-headed sea bream. They then investigated the ability of each compound to inhibit the enzymes tyrosinase and collagenase in lab-grown mouse cells. (Tyrosinase is involved in melanin production, which causes hyperpigmentation in aging skin. Collagenase breaks down the structural protein collagen and thus causes wrinkles). Three molecules from the red sea bream bacterium inhibited both enzymes best without damaging the cells, making them promising anti-wrinkle and skin-lightening agents for future cosmetic products.

¹ **Red sea bream**, Order Eupercaria, Family Sparidae
Marine fish with regularly ossified skeleton. Body oblong, quite deep, with small head, of superior profile quite convex and short nose. Large eyes. Medium mouth; the front teeth of both jaws are curved and pointed. Silver gray, pinkish or reddish color and a black spot on the lateral line.

Stardust in the bathroom

EMPA³ researchers and biotech start-up develop nanoceramics against skin diseases

Widespread skin diseases such as psoriasis or neurodermatitis are difficult to treat. Together with an industrial partner, EMPA researchers have found an innovative solution: nanoceramic stars create tiny skin wounds and allow nucleic acid molecules to reach their site of action.

When materials scientists look at the stars, they may be able to see the future – at least when it comes to stars made of nanoceramics. EMPA researchers in Dübendorf and Thun are developing innovative treatment methods for widespread skin diseases together with their industrial partner ALDENA Therapeutics. The team relies on nanoceramic stars that “go through the skin”.

Channeling therapies into the skin

Modern active ingredients would not penetrate deep enough into the affected skin layers if they were applied to conventional ointments or lotions. However, if the skin could be made permeable in the short term, the large therapeutically effective molecules could be channeled to their destination. For



example, siRNA molecules, short for “small interfering RNA”, are used for new therapies. These molecules can contribute to the regulation of protein production through targeted interactions with the body’s own messenger RNA (mRNA). This can interfere with disease processes and block damaging processes. Drugs with this principle of action already exist for some metabolic disorders and hereditary diseases. Michael Stuer and Patrick Hoffmann (EMPA) therefore used nanoceramics made from alumina particles to create a three-dimensional, sharp-edged shape. After sintering, three-armed stars with a diameter of around 0.8 millimeters were formed, which can be used to temporarily open the skin barrier for the siRNA molecules. “The 3D stars with tapered arms cause micro-wounds in the skin that quickly close on their own,” explains Michael Stuer. However, there is enough time for the active ingredient molecules to penetrate the skin.

Prick-free medication

But EMPA and its industrial partner ALDENA Therapeutics want to go even further: In a next step, Stuer wants to change the recipe so that the nanoceramic stars become biodegradable or decay into (star) dust after application. In the future, the current ceramic material could be bound to a biopolymer or replaced by a bioglass. This would significantly expand the area of application. “Patients could then simply wash off the therapy stars after application,” says Stuer.

And finally, the area of application is not limited to skin diseases. For example, up to 30 percent of all children and young adults suffer from a phobia of injections. Administering a remedy by injection to those affected triggers great anxiety and even fainting. In everyday medical practice, this is a challenge for everyone involved. The nanoceramic stars could also be a good solution to supply these people with the necessary drugs or vaccines easily and without skin pricks, according to the EMPA researcher.

³ Swiss Federal Laboratories for Materials Science and Technology

Ig Nobel Prize goes to Takanori Takebe for his study on “breathing with the butt”

Go ahead, make jokes – but seriously, this research could one day save lives.

On the one hand, Takanori Takebe (MD, PhD), would prefer to be remembered for his numerous groundbreaking contributions to organoid medicine. On the other hand, the expert from Cincinnati Children’s and Tokyo Medical and Dental University may never be forgotten for his work showing that people can “breathe” through their butts. Takebe’s unusual finding about an alternative way to oxygenate the bloodstream made headlines when a successful animal model study was published

tom dweller gets into water that contains too little oxygen. In this case, the fish supplements water respiration through its gills by sucking surface air directly into its intestines.

What if people could do something similar? Well, it seems quite possible.

“There are numerous health conditions, including shortness of breath in newborns, that can threaten life because the ability of the lungs to deliver oxygen to the bloodstream is disrupted. These include injuries or inflammation of the airways, pneumonia that fills the lungs with fluid, and so on. During the COVID pandemic, many patients suffered from



on the cover of the journal “Med” in June 2021. Now he has received the ultimate biting scientific award: an Ig Nobel Prize².

Takebe is from Japan and has held academic positions in Tokyo and the United States. At Cincinnati Children’s, Takebe is director of commercial innovation at the Center for Stem Cell and Organoid Research and Medicine (CuS-TOM). In Japan, he is a professor at the Tokyo Medical and Dental University Research Institute.

A few years ago, he was also concerned about a strange, eel-like fish called loach. Sometimes this freshwater bot-

the global shortage of ventilators and limited access to ECMO,” says Takebe. “Enteral ventilation could be an important alternative for oxygen supply. Our initial studies show that our ventilation system is able to support patients with severe respiratory failure.”

The concept of butt-breathing involves the administration of a liquid (perfluorocarbon) that can be loaded with much more oxygen than water normally contains. Administered through a rectal tube, the lower intestine can absorb oxygen from the fluid and direct it directly into the bloodstream – similar to an enema. Takebe and colleagues have shown that this method has helped rodents and pigs survive oxygen-deficient conditions that would otherwise have been fatal. More research is needed to evaluate and fine-tune the delivery system, especially for sick people in different situations.

¹ The **Ig Nobel Prize** (ig = ignoble) is a satirical award to honor achievements that *first make people laugh and then make them think*. The prize is awarded by the Cambridge-based journal *Annals of Improbable Research*.

Fighting pests with biodiversity instead of insecticides

Genotype mixing can increase yields of wheat and rice and reduce pesticide usage

Pesticides are not always needed: In an extensive field study, researchers at the University of Zurich have shown that biodiversity within a plant species can be used for pest control. This is because species with different genotypes work together to ward off the attacks of herbivorous insects. Plants interact with the individuals they surround – just like humans. If, for example, people in the environment are susceptible to infections, one’s own risk of infection increases. However, if they are resistant, it decreases. The same applies to plants: when different genetic types of the same species are planted together, certain combinations are more resistant to pests and diseases. This positive effect on biodiversity is called associative resistance.

Food security and biodiversity protection

One of the challenges of modern societies is to reconcile food security with environmental protection and biodiversity. Pests and diseases threaten harvests, which is why chemical pesticides are used in agriculture. However, pesticides can reduce the diversity of insect species. “This is where associative resistance as a cultivation method to secure food production and at the same time preserve biodiversity could help,” says Kentaro Shimizu, Director

of the Institute of Evolutionary Biology and Environmental Sciences at the University of Zurich (UZH). But which combinations of plants with different genotypes – the individual genetic endowments – should be planted in mixed stands to ward off pests and diseases? For example, if you want to select two out of a total of 199 genotypes, there are 19,701 possible combinations. With the help of a physical model, UZH researchers have now developed a new method to predict possible interactions between individuals at the genetic level.

Extensive fieldwork on the Irchel campus

The researchers conducted large-scale experiments on the Irchel campus of UZH and in Japan over a period of two years. The genome sequences for the 199 genotypes of the plant *Arabidopsis thaliana* collected worldwide were already available. The researchers randomly mixed more than 30 individuals of each of the 199 genotypes and planted a total of 6,400 individuals. This immense data set, which was collected on the Irchel campus thanks to the university’s research garden, was the key to this study,” says UZH Professor Shimizu. Until now, there have been no analytical methods to investigate the interactions at the level of the genome – the entire

genetic information – between neighboring plant individuals. Dr. Sato’s team therefore developed a new computer method: a genome-wide association study called “Neighbor GWAS”. This is based on a model of physics used to analyze interactions between magnets. The team used it to analyze how pest infestation is influenced by the combination of juxtaposed individuals with different genotypes. At the same time, the researchers took into account the results of the field trials.

Pest reduction of up to 25 percent

The analysis showed that numerous genes are involved in interactions with surrounding individuals. Using machine learning, the plant scientists were able to use the model to predict the damage of herbivores and identify advantageous combinations of genotype pairs that have associated resistance. Over the course of two years, another large-scale field trial was carried out and around 2,000 plant individuals were planted in pairs with those genotypes for which three levels of associative resistance were predicted. The results from the field trial showed that – compared to planting a single genotype – the mixture of two genotypes reduced damage caused by herbivores by 24.8 percent and 22.7 percent, respectively, at the highest and second-highest levels of associative resistance, respectively.

Future developments

“This study is a milestone in research into the interactions between plant individuals. It shows how important biodiversity is: Firstly, the genetic diversity of crops itself can reduce pest infestation. Secondly, fewer pesticides in agriculture contribute to preserving biodiversity, including insects,” Kentaro Shimizu summarizes. Meta-studies show that wheat and rice, for example, achieve between 4 and 16 percent higher yields when genotypes are randomly mixed. According to Shimizu, thanks to the genome information available for these crop species, the new method could optimize the selection of genotype mixtures by predicting associated resistance, thus increasing the yields of these agriculturally important plant species even further, while reducing pesticide use.



Cause of the “yo-yo effect” deciphered

Fat cells have a “memory” that is based on epigenetics.

Fat cells store memories of obesity in their cell nucleus. These memories remain even after a weight loss program, making it more likely for someone to put the weight back on. Researchers at ETH Zurich demonstrated this in mice and found evidence that similar mechanisms are also present in humans.

Anyone who has ever tried to get rid of a few extra kilos knows the frustration: the weight drops initially, only to be back within a matter of weeks – the yo-yo effect has struck. Researchers at ETH Zurich have now been able to show that this is all down to epigenetics. Epigenetics is the part of genetics that’s based not on the sequence of genetic building blocks but on small yet characteristic chemical markers on these building blocks. The sequence of building blocks has evolved over a long period of time; we all inherit them from our parents. Epigenetic markers, on the other hand, are more dynamic: environmental factors, our eating habits and the condition of our body – such as obesity – can change them over the

course of our lifetime. But they can remain stable for many years, sometimes decades, and during this time, they play a key role in determining which genes are active in our cells and which are not. “Epigenetics tells a cell what kind of cell it is and what it should do,” says Laura Hinte, a doctoral student in the group led by Ferdinand von Meyenn, Professor of Nutrition and Metabolic Epigenetics.

An epigenetic memory of obesity

The researchers looked for the molecular causes of the yo-yo effect in mice. They analyzed fat cells from overweight mice and those that had shed their excess weight through dieting. Their investigations revealed that obesity leads to characteristic epigenetic changes in the nucleus of fat cells. What’s special about these changes is that they remain even after a diet. “The fat cells remember the overweight state and can return to this state more easily,” von Meyenn says. The scientists were able to show that mice with these epigenetic markers regained weight more quickly when they again had access to a high-fat diet. “That means we’ve found a molecular basis for the yo-yo effect.”

“Because of this memory effect it is so important to avoid being overweight in the first place”

Ferdinand von Meyenn

They also found evidence for this mechanism in humans. The ETH Zurich researchers analyzed fat tissue biopsies from formerly overweight people who had undergone stomach reduction or gastric bypass surgery. The tissue samples came from various studies carried out at Karolinska Instituted in Stockholm and at Hospitals in Leipzig, Dresden and Karlsruhe. In these samples, the researchers analyzed gene expression rather than epigenetic markers. However, the results are consistent with those of the mice.

Prevention is the key

Something the researchers haven’t investigated is how long fat cells can remember obesity. “Fat cells are long-lived cells. On average, they live for ten years before our body replaces them with new cells,” Hinte says.

It’s not currently possible to change the relevant epigenetic marks in the cell nucleus with drugs and thus erase the epigenetic memory. “Maybe that’s something we’ll be able to do in the future,” Hinte says. “But for the time being, we have to live with this memory effect.” Von Meyenn adds: “It’s precisely because of this memory effect that it’s so important to avoid being overweight in the first place. Because that’s the simplest way to combat the yo-yo phenomenon.” The researchers are directing this message primarily at children and young people and their parents.

With their work, the ETH researchers have shown for the first time that fat cells possess an epigenetic memory of obesity. However, they don’t assume that fat cells are the only cells with such a memory. “Other body cells might also play a part in the yo-yo effect,” von Meyenn says. It’s quite conceivable that cells in the brain, blood vessels or other organs also remember obesity and contribute to the effect. Whether this is actually the case is what the researchers want to find out next.



A new era of allergy treatment

Scientists reveal the early molecular key to curing life-threatening allergies

In a groundbreaking clinical trial just published in Nature Communications, researchers have uncovered the early immune mechanisms behind the extraordinary success of insect venom immunotherapy. In the study, early molecular and cellular changes were detected as early as 8 hours immediately after the first administration of immunotherapy, changes that will pave the way for healing immune tolerance. Overall, it provides new insights that could revolutionize allergy management and improve outcomes for millions of people suffering from chronic immune disorders.

Allergic diseases are increasing rapidly worldwide and are becoming the most common chronic diseases mediated by the immune system, largely due to modern lifestyle factors and environmental influences. While allergen-specific immunotherapy (AIT) is the only available treatment that can potentially cure certain allergies, its effectiveness varies widely across different forms of allergies. Insect venom allergies – such as those caused by bee or wasp stings – are the exception, for which AIT offers clinical cure rates of over 90–95%.

By examining how the immune system develops long-term tolerance to insect venom, the clinical research study identified key molecular and cellular switches that occur in the early stages of treatment, giving hope for improvement in AIT in other allergic conditions where AIT is less successful, and contributing to the overall efforts to combat the worldwide allergy epidemic.

“This work is a breakthrough for allergy science,” explained the study’s first author, Prof. Sebastian Bode. “We have uncovered early immune responses, in-

cluding the regulation of IL-6 – a molecule normally associated with inflammation – that could play a completely unexpected crucial role in restoring immune tolerance. These findings could drive the development of more effective treatments for other allergies.”

The study included over 200 blood samples from patients recruited, treated and analyzed in depth at CHL by a team of allergy specialists. This is the most comprehensive and thorough data analysis ever performed on patients with insect bite allergy. This allergy affects around 2.6% to 4% of the population in Europe and globally, i.e. around 13 to 20 million people in the EU and the UK, who are at risk of an insect bite being fatal if they are not treated with an insecticide AIT.

In addition to its scientific contributions, the study also has practical implications. It shows the importance of considering circadian rhythms when planning clinical trials, as immune responses fluctuate throughout the day. The results have also led to the creation of an interactive immune data platform that is directly linked to the publication, allowing researchers worldwide to explore the results of the study and use them as a basis for further research.

“This is translational research at its finest,” added Professor Jan Guter-muth from the Department of Dermatology at Vrije Universiteit Brussel. “Our work bridges clinical practice and cutting-edge science by using insect venom immunotherapy as a clinical model to unlock the secrets of immune tolerance. The potential to change the treatment of allergies is immense.”

“The findings are expected to have far-reaching implications, not only for improving allergy treatments, but also for understanding immune tolerance in other chronic diseases. By deciphering the ‘molecular magic’ of insect venom immunotherapy, researchers are one step closer to tackling the global allergy epidemic and advancing personalized medicine,” concluded Professor Markus Ollert, lead author of the paper and director of the LIH Department of Infection and Immunity.



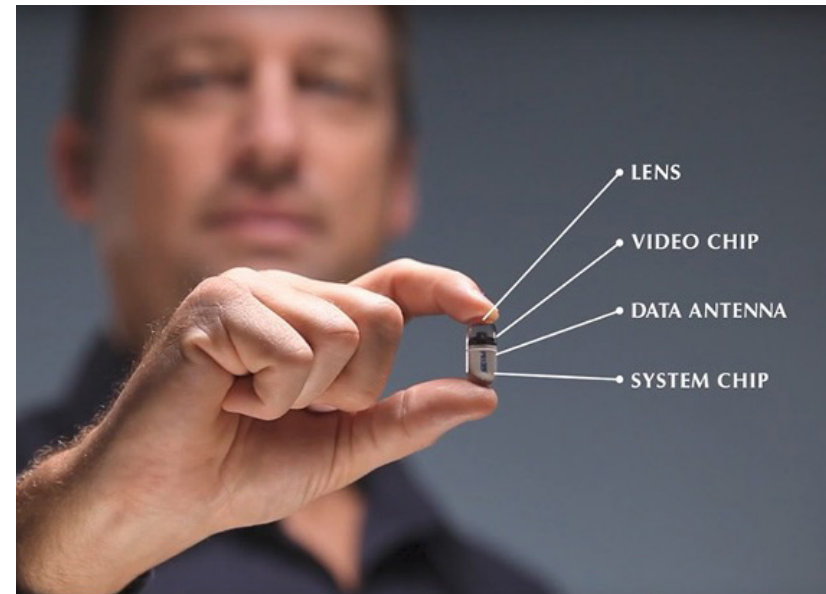
How the latest sensors analyze body fluids

A new generation of wearable sensors will fundamentally change medicine.

The next generation of wearables will also be able to measure biochemical data from body fluids. Continuous, minimally invasive and non-invasive measurement of certain biomarkers is possible in almost every phase of life, regardless of location. ETH Zurich researchers have shown what particular points need to be taken into account to ensure that such devices can be used successfully in the future.

Using a smartwatch to measure pulse, and a smartphone app to monitor blood pressure: wearable sensors already track some of the body’s vital functions fairly reliably, and some of these devices can already be used in clinical diagnostics. However, diagnoses based on biochemical data still require samples of body fluids such as blood and urine, which have to be sent to the lab for analysis. Collecting these can be painful and complicated as well as time-consuming and often costly.

But the next generation of wearable sensors is set to provide biochemical analyses as well. In the future, such sensors will gather valuable insights into their wearer’s state of health by analyzing body fluids such as sweat, breath, saliva, tears and urine. Although many of these advances are not yet ready for the market, they are certainly feasible. This is what led Dr. Noé Brasier, Early-Career Fellow at the Collegium Helveticum, and ETH Professor Jörg Goldhahn to join forces with leading researchers in the field of wearable sensors and conduct a comprehensive review. Their overview was recently published in the journal Nature.



From infants to senior citizens

The advantages of wearable sensors are obvious: they allow continuous monitoring of health variables without patients having to visit a doctor’s surgery or pharmacy. “For elderly people who suffer from heat stress, it would make life a lot easier if a wearable device could remind them in good time to drink enough, or if a sensor could sound an alarm when their electrolytes reach a critical level,” says Brasier, himself a physician and the paper’s lead author.

Moreover, such sensors are either non- or only minimally invasive. Brasier provides an example: “Attempts to take blood from babies and infants, not to mention to insert a catheter, aren’t always successful. This can lead to significant delays and is often distressing for the young patients and their parents. It would be much easier and more convenient to have a sensor on the baby’s skin or in their nappy perform the laboratory and/or urine analysis.” Equally, face masks that were additionally capable of detecting viruses such as SARS-CoV-2 without the need for an unpleasant nasal swab would have been welcome during the last pandemic.

A lot is possible – but does it make sense?

The researchers’ creativity is impressive, as is the sheer variety of conceivable devices – ranging from a dummy that measures whether infants are

dehydrated, to tattoos that indicate blood sugar levels and contact lenses that provide data from the wearer’s tears. “When we discussed the possibilities with engineers, physicians and colleagues from other disciplines a year ago, we realized that we needed to think about what kinds of sensor make sense and what points ought to be given particular weight when developing such devices,” says Goldhahn, the paper’s senior author.

The key consideration is self-evident: the wearables must be something that patients want to wear. “That’s why we recommend always developing the sensors together with the people who will need them later,” Brasier says. But the medical benefits of such devices also need to be critically assessed. Not everything measured offers a clinical benefit. “It’s not about measuring any old variable. It’s a question of what that reading means in the relevant context and what the clinical consequences are,” he says.

For example, CRP is a marker for inflammation in the body and is measured in milligrams per liter. In healthy adults, the CRP level is normally physiologically below 5 mg/l. “If a patient has a blood-CRP level of 150 mg/l, this only tells us so much. What’s decisive for a clinical assessment is whether the value on the previous day was normal, or whether it was 300 mg/l. Then we can

say whether the person’s health has deteriorated or improved.”

Display the readings well

Then there are the technical hurdles: How long can a sensor keep measuring? How can it be stored and cleaned? How much electricity does it consume, and from what source? And most importantly, how good and reliable is the data it provides? “Careful validation of the measurement data will be key to whether a given device becomes established or not,” Goldhahn says, “because nobody is going to rely on uncertain readings.”

In a further step, the signals from the wearables must be processed, interpreted and displayed in a way that makes sense to users – be they the patients themselves or healthcare professionals. In the future, that will increasingly be a job for artificial intelligence, which in turn will further accelerate the development of wearables.

Fascinated by sweat

It was sweat that led the lead author Brasier to become acquainted with wearables. While many people turn up their noses at the thought of this body fluid, Brasier can’t speak of it highly enough: “Different situations will always cause us to sweat differently and on different parts of the body. But that’s not the only reason why our sweat contains an incredible amount of information.” Using this information is a simple and straightforward way to draw conclusions about someone’s state of health. “The surface of the skin is my clear favorite, but the choice of sensor naturally depends on the medical application. In the case of pneumonia, for instance, it’s probably better to analyze the patient’s breath,” Brasier says. However, having prepared the new overview, he is well aware that there is a lot of research and development work still left to do – not least when it comes to clinical concepts. Only then will the new wearables ultimately be granted official approval and provide a benefit for everyone involved, especially patients.

The secret of barn dust

Findings open up new avenues for the treatment of sick children.



For small children, it acts like a protective elixir against asthma and other allergies from birth: the dust from the traditional cowshed. What exactly conveys this effect is of great interest to researchers. However, deciphering it in terms of allergy prevention is a lengthy process, but it has now taken another step forward: Researchers at the Dr. von Hauner Children's Hospital of the LMU Hospital have analyzed how cells of the immune system react to barn dust and thus contribute to the "protective farm effect". The results were recently published in the journal "Allergy". The hygiene hypothesis is now established in science. Tenor: The child's immune system should be "trained", especially in the preschool years, through regular contact with certain "good" microorganisms. The immune system must learn not to react excessively and not to attack harmless substances or to attack the body's own structures.

Dust from the cowshed has a preventive effect

Researchers at the Dr. von Hauner Children's Hospital of the LMU Hospital Munich have shown that the frequent and continuous contact of young children with the farm environment, especially with the dust from the cowshed,

has a preventive effect. Children growing up there, for example, get significantly less asthma than those who live in the city. Based on these findings from epidemiological studies, scientists are researching the basics of this phenomenon in their laboratories worldwide. What changes in the immune system through stimulation with barn dust? On the one hand, they want to know which specific substances or microorganisms trigger the protective effect. On the other hand, they are interested in what exactly changes in the immune system so that it does not attack the body's own or harmless structures, and a healthy balance of the immune system is established. In this sense, a team led by Prof. Dr. Bianca Schaub has now taken a big step forward. In a cell culture approach in the laboratory, they stimulated various immune cells of the blood with stable dust.

Study shows that barn dust affects the immune system of children already suffering from asthma

"We were able to show that in children with manifest asthma, certain cells of the innate immune system are reduced

after stimulation with farm dust," says study first author Claudia Beerweiler, "whereas subgroups of cells of the acquired immune system are increased, including B cells and certain T helper cell populations. In addition, certain molecules associated with inflammation, cell toxicity, antigen presentation, and special T helper cells are reduced. Cell toxicity is the ability of certain substances or microorganisms to damage or destroy cells. Antigen presentation is a central process in a defense reaction in which structures of microorganisms are made recognizable to certain immune cells.

Anti-inflammatory effect already proven in earlier studies

"We now know that the innate immune system plays a much greater role in the development of allergies, and also in their prevention, than we thought for decades," says Bianca Schaub. Previous work has already shown that protection by farm dust is mediated by an anti-inflammatory effect. In a recently published study with the participation of LMU researcher Prof. Dr. Erika von Mutius, it turned out that dusts from the cowshed contain transport proteins, so-called lipocalins. They modulate the function of the human immune system. Two of these substances are found in significantly increased levels in barn dust.

Findings open up new avenues for the treatment of sick children

So, one building block follows the other to reveal the secret of the barn dust. The researchers have a clear goal: to identify the beneficial substances and administer them to all those children who do not live on a farm – in which form is currently being explored. The target group of children that could be treated in this way also needs examining in detail. "The fact that stimulation with barn dust can modulate the immune reactions in the laboratory even in asthmatics with disease," says Bianca Schaub, "may also open up new avenues for the therapy of already symptomatic children."

How much energy does a quantum computer consume?

If you were to use a quantum computer to solve any simple problem right now, it would consume much more energy than a conventional computer, but quantum computers are not going to be used for that type of situation.

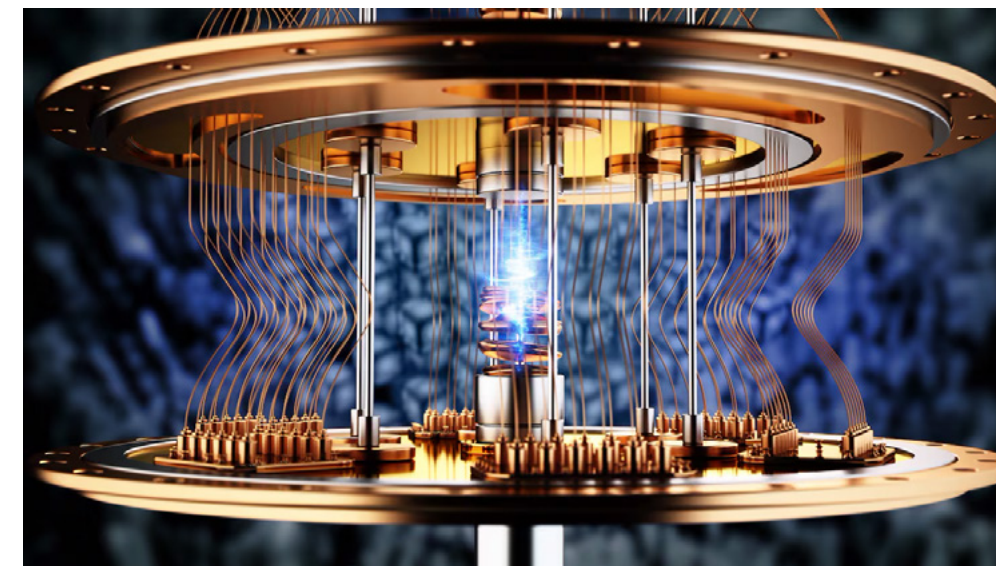
This question is difficult to answer because the technology is still under development. To give you an idea: Currently, only small quantum computers with many errors exist. We do not yet have a fault-tolerant quantum computer, i.e., a computer that performs operations that we can trust 100% and with which we can efficiently solve relevant problems. Errors occur because quantum physics is very sensitive. Quantum states consist of a superposition of states (e.g., several different positions) and lose this superposition as soon as they interact with the environment, causing the information they contain to be lost. For this reason, the quantum systems we can control are small and must be kept at a very low temperature. The greatest energy consumption of quantum computers currently comes from cooling these systems to temperatures close to absolute zero (approx. -273 °C) and from the control systems used to stabilize the quantum states. However, performing the quantum operations themselves requires almost as much energy as a conventional computer.

Even under these conditions, quantum states remain unstable, so we need what is known as error correction. This error correction is achieved by adding additional qubits, which are the quantum mechanical equivalent of conventional arithmetic operations, so that some of these qubits are used to correct those intended for the calculation. Once we have overcome this technological hurdle, we will be able to solve problems that a classical computer cannot solve, so it will no longer make sense to compare the energy consumption of one with that of the other. Regardless of how much energy it consumes, the quantum computer will be much more efficient in

that it can solve problems that are impossible for a classical computer. If you now ask a quantum computer to solve a simple problem, it will consume much more than a conventional computer, but quantum computers will not be used for such problems. That would be like trying to light your living room with a spotlight from a football stadium.

Quantum computers are not yet efficient, but they will be in the future.

To illustrate: a laptop has a power output of around 60 watts. And the power output is proportional to the energy consumption. 60 watts is the typical power output of a light bulb. For quantum computers, it would be around 20 kilowatts, or 20,000 watts. This means that



if I want to solve a problem and need an hour to do so, a laptop consumes 60 watt hours of energy, while a quantum computer would consume 20,000 watt hours. Furthermore, tests have shown that quantum computers take much longer to solve a simple problem than traditional computers because they have not yet been optimized. They are not yet efficient, but they will be in the future. Another interesting point is that with a classic computer, computing power increases linearly with the number of processors, i.e., if you use twice as many processors, you have twice as much computing power. With a quantum computer, however, performance increases exponentially: with five qubits, you can process 25 states, but with ten qubits, you can already process 210. The difference is enormous.

We can say in advance that the energy consumption of quantum computers will no longer be a limitation once we have optimized quantum computers, i.e., fault-tolerant computers with more efficient cooling and control systems.

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