EMERGING FRONTIERS IN BIOLOGY AND HEALTH SCIENCES

Editor. Prof. Dr. Birkan TAPAN

DUVAR

EMERGING FRONTIERS IN BIOLOGY AND HEALTH SCIENCES

Editor

Prof. Dr. Birkan TAPAN*

* ORCID ID: 0000-0001-9425-7365

Emerging Frontiers in Biology and Health Sciences
Editor
Prof. Dr. Birkan TAPAN

General Director: Berkan Balpetek
Cover Design: Prof. Dr. Bülent GÜNDÜZ
Page Design: Duvar Design
Printing : August-2026
Publisher Certificate No: 49837
E-ISBN:978-625-8936-11-7

853 Sokak No:13 P.10 Kemeraltı-Konak/İzmir
Tel: 0 232 484 88 68
www.duvaryayinlari.com
duvarkitabevi@gmail.com

PREFACE

Biological sciences are undergoing an unprecedented transformation as advances in molecular biology, neuroscience, nutrition, microbiology, artificial intelligence, and public health continue to reshape our understanding of human health and disease. Increasingly, scientific discoveries reveal that biological systems do not function in isolation but are profoundly influenced by environmental, behavioral, and technological factors. This growing body of knowledge highlights the importance of interdisciplinary approaches in addressing contemporary health challenges and developing innovative strategies for disease prevention, diagnosis, and treatment.

This book brings together six complementary topics that collectively illustrate the evolving landscape of modern biological and health sciences. Beginning with the intricate relationship between melatonin, circadian rhythms, seasonal changes, and hair follicle biology, the volume explores how endogenous biological clocks regulate cellular functions and tissue homeostasis. It then broadens its perspective by examining the biopsychosocial foundations of public health, emphasizing the integration of biological, psychological, and social determinants in health management and patient safety.

Recognizing that health extends beyond the clinical setting, the book further investigates the biology of work, presenting current insights into the neurobiological and physiological mechanisms that influence organizational behavior, occupational performance, stress adaptation, and workplace well-being. This interdisciplinary perspective demonstrates how biological processes contribute to productivity, decision-making, and human interactions within increasingly complex work environments.

Nutrition remains one of the most powerful modifiable determinants of health. Accordingly, the volume reviews the current evidence regarding nutritional therapy in the management of insulin resistance, highlighting evidence-based dietary interventions and their clinical applications in combating one of the most significant metabolic disorders worldwide. Complementing this discussion, the book examines indoor microbiota dynamics and their influence on human health, underscoring the growing recognition that indoor environments represent complex microbial ecosystems capable of shaping immune function, respiratory health, and overall well-being.

Finally, the book looks toward the future by exploring the transition from traditional one-size-fits-all dietary recommendations to precision nutrition. Advances in artificial intelligence, microbiome research, multi-omics technologies, and personalized medicine are revolutionizing nutritional science, enabling dietary interventions tailored to individual biological characteristics and

health profiles. This emerging paradigm represents one of the most promising frontiers in preventive and personalized healthcare.

Although each chapter addresses a distinct scientific domain, together they reflect a common theme: the necessity of integrating biological mechanisms with environmental, technological, and behavioral perspectives to better understand human health. By combining foundational concepts with recent scientific advances, this volume aims to provide researchers, clinicians, healthcare professionals, educators, and graduate students with a comprehensive and up-to-date resource that encourages interdisciplinary thinking and inspires future research.

We hope that this book will serve not only as a valuable academic reference but also as a catalyst for new collaborations across disciplines. As biology continues to intersect with medicine, public health, environmental science, artificial intelligence, and organizational research, embracing these connections will be essential for addressing the complex health challenges of the twenty-first century.

Prof. Dr. Birkan TAPAN

TABLE OF CONTENTS

Chapter 1

The Effects of Melatonin, Circadian Rhythms, and Seasonal Changes on Hair Follicle Biology

Dilek GÜL[1], Bülent GÜNDÜZ[2]

The hair follicle is one of the rare continuously renewing organs in the mammalian body and possesses a complex hormonal regulatory mechanism. This article examines the modulatory roles of melatonin secreted from the pineal gland, as well as circadian rhythms and photoperiodic (seasonal) changes, on the hair cycle (anagen, catagen, telogen). In particular, it focuses on how melatonin, through its antioxidant properties and local receptors within the hair follicle, influences the growth phase.

The hair follicle is a highly dynamic and complex miniature organ capable of self-renewal within the human body. Its biology is governed not only by genetic inheritance but also by light cycles (photoperiod), hormonal fluctuations, and intrinsic molecular clocks. Hair growth is not a static process determined solely by genetic factors; rather, it is a dynamic system that continuously interacts with the organism's internal biological rhythms and environmental variables. In this context, hair follicles, like many other tissues in the body, are sensitive to timing mechanisms and, through these mechanisms, respond to both daily (circadian) and seasonal changes.

Hair growth occurs within a dynamic cycle consisting of the **anagen** (growth), **catagen** (regression), **telogen** (resting), and **exogen** (shedding) phases. Although this cycle is a biological process in which each hair follicle progresses independently, a partial synchronization in follicular behavior can emerge at certain periods. The anagen phase is the longest stage, during which the hair actively grows and can last for several years. This is followed by the catagen phase, a short transitional stage in which hair growth stops and the follicle begins to regress and shrink. The subsequent telogen phase represents the resting period of the hair; at the end of this stage (exogen), the hair shaft is shed and replaced by the growth of a new hair. Although the duration and onset of these cycles vary between individuals, it has been observed that environmental and physiological factors can drive a proportion of hair follicles into the same phase simultaneously. In particular, the tendency for a greater number of hairs to enter the telogen phase

[1] Kartal Medical Center, Kartal, İstanbul, Türkiye
[2] Department of Biology, Faculty of Science, Canakkale Onsekiz Mart University, Çanakkale, Turkey

during certain times of the year forms the basis of what is known as seasonal hair shedding. This synchronization can be influenced by several factors, including day length (photoperiod), temperature changes, hormonal fluctuations, and even nutritional status. Consequently, especially during the autumn months, an increase in the proportion of hairs in the telogen phase may lead to a noticeable rise in hair shedding. This condition is generally physiological and temporary, and normal balance is restored once the hair cycle returns to its regular pattern.

When seasonal cycles are examined, it is observed that hair shedding increases markedly during the autumn months, whereas the anagen (active growth) phase becomes more dominant in spring and summer. This pattern indicates that hair follicles do not function entirely independently; rather, they can exhibit partial synchronization in response to specific environmental cues. From an evolutionary perspective, this cyclical variation can be interpreted as part of the organism's adaptation to environmental conditions. In many mammalian species, seasonal coat changes (e.g., the development of a thicker fur in winter) are critical for survival. Although this mechanism has largely diminished in humans, traces of this evolutionary remnant can still be observed in what is described as "seasonal hair shedding." One of the most important environmental determinants in this process is **photoperiod** (day length). Changes in day length are transmitted via the retina to the hypothalamus, where neuroendocrine responses are initiated. In particular, alterations in the secretion of **melatonin** can indirectly influence the hair follicle cycle. During the summer months, longer daylight suppresses melatonin levels, while increased light exposure and the associated metabolic and hormonal activity may support the anagen phase of hair growth. In contrast, as days shorten in autumn, melatonin rhythms shift, and a larger proportion of hair follicles may enter the telogen (resting) phase. In addition to these physiological changes, the hormone **prolactin** has also been shown to play a regulatory role in the hair follicle cycle. Seasonal fluctuations in prolactin levels are important factors influencing coat cycles in mammals, and there is evidence suggesting that they may also modulate the human hair growth cycle. The presence of prolactin receptors within the hair follicle further supports the possibility of a direct effect. Statistical and clinical observations indicate that, in humans, the proportion of hairs in the telogen phase increases particularly in late summer and early autumn (July–October) (Randall & Ebling, 1991; Courtois et al., 1996). This increase can be explained by the synchronized transition of follicles into the resting phase following the prolonged anagen phase during summer. Similarly, more recent large-scale population analyses also support that hair shedding peaks in autumn. This phenomenon is often interpreted as a "reset" of the hair cycle following intense light exposure during the summer months.

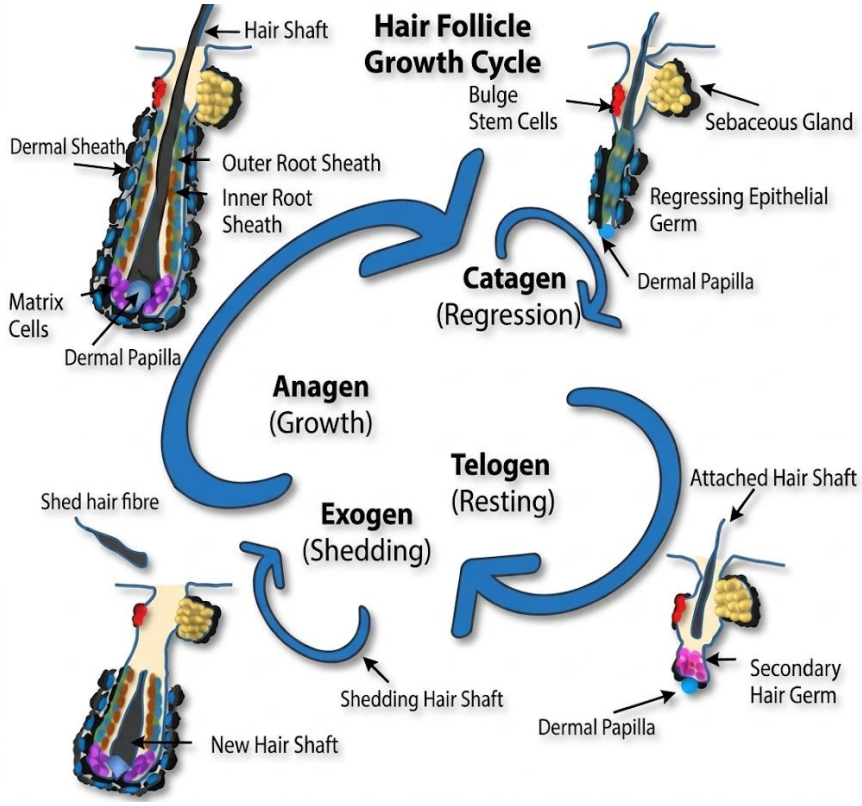

Figure 1: *Growth phase of the hair follicle (adapted and rearranged from Courtois et al. 1996).*

Current dermatological research also shows that the following factors may contribute to seasonal hair loss:

- UV exposure: Increased oxidative stress in the hair and scalp during summer months
- Vitamin D levels: Photoperiod-related changes
- Dietary habits: Seasonal dietary variations
- Stress and lifestyle changes

At the center of this mechanism lies the circadian system. In mammals, the Suprachiasmatic nucleus (SCN), located in the hypothalamus, functions as the central circadian clock and regulates intrinsic circadian physiological rhythms according to the external 24-hour light–dark cycle. This enables pronounced cyclical changes between high- and low-activity states.

The SCN synchronizes circadian physiological and behavioral rhythms—including sleep and wakefulness, body temperature, feeding, as well as

neuroendocrine and autonomic functions—to a 24-hour periodicity, thereby coordinating optimal internal temporal organization within the organism. The circadian regulatory effect of the SCN is largely influenced by light stimulation in domestic animals. Light not only regulates the SCN but also inhibits the synthesis of melatonin. The neural output signal generated by the SCN, in turn, initiates melatonin synthesis in the pineal gland during the night (Figure 2) (Hardeland et al., 2011). The pineal gland and the SCN of the hypothalamus interact through the sympathetic neurons of the superior cervical ganglion (SCG) to form the body's biological clock, with melatonin secreted by the pineal gland playing a central role in this process. Acting as the brain's central pacemaker, the SCN coordinates circadian physiological and behavioral rhythms, including deep sleep, wakefulness, body temperature, hunger, and neuroendocrine effects. The retinohypothalamic tract (RHT) regulates SCN oscillations and melatonin secretion by transmitting light signals from retinal inputs. The RHT consists of axons from light-sensitive retinal ganglion cells that express melanopsin in response to short-wavelength light.

During the light phase of the photoperiod, increased SCN activity reduces the sympathetic activation of the paraventricular nucleus (PVN) output to the pineal gland via the SCG. As a result, decreased norepinephrine release lowers the activity of N-acetyltransferase (NAT) in the pineal gland and reduces melatonin secretion. During the dark phase, however, the pineal gland secretes higher levels of melatonin; circulating melatonin acts through melatonin (MT1 and MT2) receptors to inhibit SCN activation (promoting sleep) and reset the circadian pacemaker (Figure 2).

One of the most important hormonal outputs of this system is melatonin produced and secreted by the pineal gland. Melatonin is primarily released during darkness and influences not only sleep regulation but also a wide range of processes, including cellular proliferation, reproduction, oxidative stress responses, and immune function (Reiter et al., 2014).

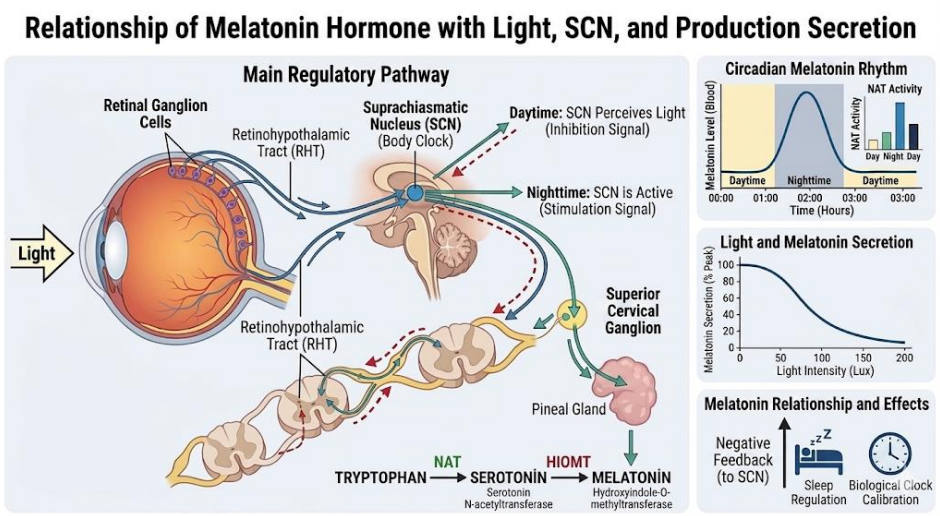

Figure-2 *The production of melatonin hormone from the pineal gland and its connection with light.*

Hair follicles have also been shown to possess their own local "peripheral clock" mechanisms. These clock genes regulate the cell cycle, DNA repair, and the expression of growth factors, thereby playing a role in the timing of hair growth phases. Clock genes such as *BMAL1, CLOCK, PER,* and *CRY* are expressed in hair follicle cells. These genes control the cellular signals that determine when the follicle will grow (Anagen), regress (Catagen), and rest (Telogen). Cell proliferation within the hair root does not occur randomly. In connection with the circadian rhythm, DNA synthesis and mitosis generally peak at certain times of the day—typically at night during periods of rest. This is an adaptation that supports tissue repair and growth. Melatonin can contribute to prolonging the anagen phase by exerting a regulatory effect on these local clock systems. In addition, thanks to its potent antioxidant properties, it protects the hair follicle against free radical damage. Hair follicles are exposed to high levels of oxidative stress during metabolic processes. As one of the strongest natural antioxidants, melatonin protects the follicle from free radicals and may help prevent premature hair loss. Melatonin may extend the anagen phase, which is the active growth stage of hair. This allows the hair to remain attached to the root for a longer period and to grow in a healthier manner. Research has also shown that hair follicles do not only obtain melatonin from the bloodstream, but are also capable of synthesizing it locally themselves (extrapineal synthesis). This demonstrates how sensitive the follicle is to environmental light changes (Fischer et al., 2008).

Environmental factors are also an important part of this process. Elements such as light exposure, sleep patterns, stress, nutrition, and lifestyle directly affect circadian rhythms. For example, irregular sleep, nighttime light exposure, or shift work can suppress melatonin production and negatively affect the hair growth cycle. Likewise, chronic stress may increase cortisol levels, forcing hair follicles into the telogen phase. Elevated cortisol can prematurely push the hair follicle into the catagen (regression) phase, potentially triggering Telogen Effluvium (sudden diffuse hair shedding). Seasonal variations in nutrient availability—such as reduced vitamin D synthesis during winter—can indirectly disrupt the follicular rhythm by affecting the energy supply and vitamin support required by the follicle.

Recent studies have demonstrated that the hair follicle is sensitive not only to hormonal signals, but also to immunological and neuroendocrine signals. This suggests that hair growth is actually regulated by a multilayered control system (Paus et al., 2015). The influence of seasonal changes on this system may therefore be interpreted as a strategy aimed at optimizing the organism's energy balance and environmental adaptation.

Melatonin Synthesis in the Skin and its Relationship to Hair Biology

Melatonin was long regarded solely as a hormone secreted by the pineal gland and responsible for regulating circadian rhythm. However, current studies have demonstrated that melatonin is also synthesized in peripheral tissues such as the skin and plays an active role in local biological processes. The skin contains a complex melatonergic system involving melatonin synthesis, metabolism, and receptor expression. This system has important functions such as reducing oxidative stress, regulating aging processes, and controlling the hair follicle cycle. Recent studies have revealed that melatonin is synthesized not only in the pineal gland but also in extrapineal tissues such as the skin. As an organ constantly exposed to environmental stress factors, the skin requires a strong local defense system. In this context, melatonin plays a significant role in maintaining skin homeostasis through both its antioxidant and regulatory effects (Kleszczyński & Fischer, 2012).

Studies conducted on Syrian hamsters have shown that melatonin synthesis in the skin occurs through the classical biochemical pathway that begins with tryptophan and proceeds via serotonin (Slominski et al., 2002). The principal enzymes involved in this process are tryptophan hydroxylase (TPH), aromatic L-amino acid decarboxylase (AADC), arylalkylamine N-acetyltransferase (AANAT), and hydroxyindole-O-methyltransferase (HIOMT/ASMT) (Slominski et al., 2002). These enzymes are expressed in keratinocytes,

melanocytes, fibroblasts, and hair follicle cells, demonstrating that the skin functions as an active center of melatonin production. Melatonin acts as a potent free radical scavenger that reduces oxidative stress and activates antioxidant enzyme systems, thereby protecting cells against UV-induced damage. It also reduces UV radiation–induced DNA damage and supports cellular repair mechanisms, contributing to the slowing of the photoaging process. In addition, melatonin may modulate melanin production by influencing melanocyte activity. The hair follicle is considered an independent neuroendocrine structure containing melatonin receptors (MT1 and MT2), and melatonin has been shown to prolong the anagen phase of the hair follicle cycle, delay the transition to the telogen phase, and increase cell proliferation. Melatonin delays skin aging by reducing oxidative stress, preserving mitochondrial function, and slowing collagen degradation. In addition, it helps maintain skin integrity by suppressing inflammation. Topical melatonin is currently used in hair loss treatments and anti-aging products, as local application provides the advantage of directly targeting the tissue. The skin also possesses its own biological clock mechanism, and the nighttime increase in melatonin levels supports cellular repair processes. Consequently, melatonin synthesis in the skin demonstrates that this molecule functions not only as a systemic hormone but also as a local regulator (Slominski et al., 2017). Melatonin plays an important role in processes such as hair growth, aging, and oxidative stress, and current evidence suggests that it has significant potential in dermatological treatments and cosmetic applications.

Hair health represents a “chrono-biological” balance. When our internal clock (sleep, nutrition) is synchronized with the external clock (seasons, day–night cycle), the hair follicle is able to express its genetic potential in the best possible way. Hair loss is not a problem that can be solved solely with shampoos or external treatments; rather, it is a holistic process that also involves the body’s biological clock, adaptation to seasonal changes, and melatonin balance.

References

Courtois M, Loussouarn G, Hourseau C, Grollier JF. Ageing and hair cycles. Br J Dermatol. 1995 Jan;132(1):86-93. doi: 10.1111/j.1365-2133.1995.tb08630.x. PMID: 7756156.

Fischer, T. W., Slominski, A., Tobin, D. J., & Paus, R. (2008). Melatonin and the hair follicle. *Journal of Pineal Research*, 44(1), 1–15.

Hardeland, R., Cardinali, D. P., Srinivasan, V., & Spence, D. W. (2011). Melatonin—a pleiotropic, orchestrating regulator molecule. *Progress in Neurobiology*, 93(3), 350–384.

Kleszczyński, K., & Fischer, T. W. (2012). Melatonin and human skin aging. *Dermato-Endocrinology*, 4(3), 245–252.

Paus, R., Hardman, J. A., & Bertolini, M. (2015). The hair follicle as a neuroendocrine organ. *Endocrine Reviews*, 36(4), 379–398.

Randall VA, Ebling FJ. Seasonal changes in human hair growth. Br J Dermatol. 1991 Feb;124(2):146-51. doi: 10.1111/j.1365-2133.1991.tb00423.x. PMID: 2003996.

Reiter, R. J., Tan, D. X., & Galano, A. (2014). Melatonin: exceeding expectations. *Physiology*, 29(5), 325–333.

Slominski, A.; Pisarchik, A.; Semak, I.; Sweatman, T.; Szczesniewski, A.; Wortsman, J. Serotoninergic system in hamster skin. J. Investig. Dermatol. 2002, 119, 934–942.

Slominski AT, Zmijewski MA, Semak I, Kim TK, Janjetovic Z, Slominski RM, Zmijewski JW. Melatonin, mitochondria, and the skin. Cell Mol Life Sci. 2017 Nov;74(21):3913-3925. doi: 10.1007/s00018-017-2617-7. Epub 2017 Aug 12. PMID: 28803347; PMCID: PMC5693733.

Chapter 2

Public Health and Biology: Biopsychosocial Perspectives in Health Management and Patient Safety

Birkan TAPAN[1]

1. Introduction: From the Biomedical Model to Biopsychosocial Health Management

Health services and their management were historically shaped by the biomedical model, which primarily explains disease through biological dysfunction. Although this approach remains indispensable for diagnosis and treatment, it is insufficient for understanding the complex burden of chronic disease, the effects of social inequalities, or the organizational conditions under which care is delivered. Engel's (1977) biopsychosocial model broadened this perspective by framing health as the product of interacting biological, psychological, and social processes. For healthcare managers, this framework also draws attention to the influence of staffing, workflow design, institutional culture, and access to care on clinical outcomes.

This chapter examines how selected biological mechanisms—especially cognitive limitations, stress physiology, and evolutionary mismatch—interact with healthcare management and patient safety. Clinical decisions are made by professionals whose attention, working memory, and emotional regulation are affected by fatigue, interruptions, time pressure, and chronic occupational stress. These constraints should therefore be treated as system-design considerations rather than solely as individual shortcomings (McEwen, 1998; Hall et al., 2016; Asgari et al., 2024).

The chapter also considers how health financing, accreditation, and digital decision-support systems may help organizations manage population-level risk and reduce preventable harm (World Health Organization, 2025). The central argument is not that biological explanations should replace psychological, social, or organizational analysis. Rather, biologically informed management can strengthen a genuinely biopsychosocial approach when it is combined with ethical governance, equitable financing, and human-centered care.

[1]Department of Health Management, Faculty of Health Sciences, Demiroglu Science University, Istanbul, Turkey

2. Neurobiology of Clinical Decision-Making and Cognitive Limitations

Healthcare delivery frequently requires rapid judgments under uncertainty. Executive functions associated with distributed prefrontal networks support working memory, inhibition, planning, and the flexible use of clinical information. Emotional salience and threat processing involve interconnected limbic and cortical networks, including the amygdala. These systems do not operate as two isolated or opposing centers; clinical reasoning emerges from their dynamic interaction with attention, memory, prior experience, and environmental demands (Arnsten, 2009).

Kahneman and Egan (2011) distinction between fast, intuitive processing and slower, deliberative processing provides a useful psychological framework for understanding clinical judgment. However, System 1 and System 2 should not be mapped directly onto the limbic system and prefrontal cortex. Both modes of processing depend on interacting neural networks. Under high workload or time pressure, clinicians may rely more heavily on familiar patterns and heuristics. Such strategies can be efficient, but they can also increase susceptibility to confirmation bias, premature closure, and other predictable errors.

Electronic health records, fragmented information, alerts, and frequent interruptions can add to clinicians' cognitive burden. When task demands exceed available working-memory resources, attention and decision accuracy may deteriorate (Sweller, 1988; Young et al., 2014). A recent narrative review found that aspects of electronic health record use are associated with cognitive load and burnout, although effects vary according to interface design, workflow, and organizational context (Asgari et al., 2024). Patient-safety interventions should therefore include usability testing, reduction of unnecessary alerts, protected handover processes, standardized communication, and adequate staffing rather than relying only on individual vigilance.

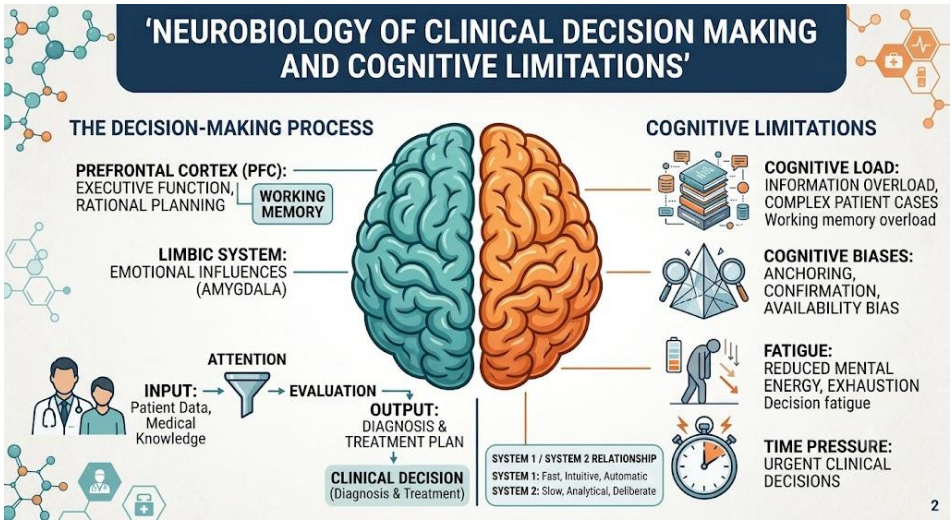

Figure 1. *Neurobiology of clinical decision-making and cognitive limitations. Executive control, emotional processing, attention, working memory, fatigue, and time pressure interact during clinical judgment; excessive demands may reduce decision quality and increase the risk of error.*

Source: *Prepared by the author based on the literature cited in this chapter.*

3. Chronic Stress, Allostatic Load, and Performance in Healthcare Professionals

The stress response is an adaptive process involving the autonomic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis. Short-term activation can mobilize energy and support action during acute demands. Problems arise when stressors are frequent, prolonged, or insufficiently followed by recovery. McEwen (1998) used the concept of allostatic load to describe the cumulative physiological burden associated with repeated adaptation. This burden reflects changes across multiple systems and should not be reduced to cortisol concentration alone.

Chronic occupational stress can affect sleep, mood, cardiovascular and metabolic regulation, attention, and executive functioning. Experimental and clinical evidence indicates that intense or persistent stress may alter prefrontal functioning and emotional regulation without implying that every stressed professional experiences irreversible neuronal damage (Arnsten, 2009; Guidi et al., 2020; Sapolsky and Berkrot, 2004). Individual responses also differ according to workload, control, social support, recovery opportunities, and personal circumstances.

For healthcare organizations, staff well-being is directly relevant to quality and safety. Burnout and poor well-being are associated with less favorable

patient-safety outcomes, although the direction and strength of these relationships vary across studies (Hall et al., 2016). Institutions should combine confidential psychological support with organizational interventions such as predictable scheduling, adequate rest, manageable workloads, team debriefing, supportive supervision, and a non-punitive reporting culture. These measures protect personnel while also improving the conditions for safe clinical performance.

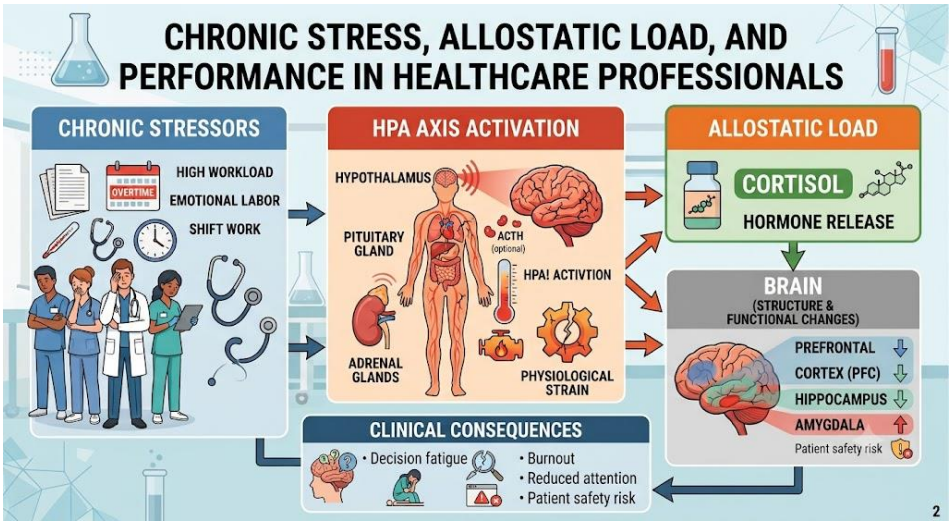

Figure 2. *Chronic stress, allostatic load, and clinical performance in healthcare professionals. Repeated occupational stress may contribute to cumulative physiological burden, fatigue, reduced attention, and impaired decision-making, with potential consequences for staff well-being and patient safety.*

Source: *Prepared by the author based on the literature cited in this chapter.*

4. Evolutionary Medicine and Public Health: Management of Metabolic Syndrome

Evolutionary medicine examines how traits that were advantageous in past environments may interact with contemporary conditions. Neel's (1962) thrifty-genotype hypothesis proposed that efficient energy storage could have offered an advantage during recurrent food scarcity, while becoming disadvantageous in environments of continuous caloric availability. The hypothesis has been influential but does not provide a complete or universally accepted explanation for obesity and diabetes. Genetic diversity, socioeconomic conditions, food systems, sleep, medication, stress, and physical activity all contribute to metabolic risk.

Modern environments often combine energy-dense foods, sedentary work, disrupted sleep, chronic stress, and limited opportunities for physical activity. This evolutionary mismatch perspective helps explain why individual behavior cannot be separated from the environments that shape choice (Lieberman, 2014). From a public-health perspective, effective prevention therefore requires more than advice to individuals. It also requires healthy food environments, opportunities for physical activity, early risk assessment, health literacy, and policies that reduce social and commercial determinants of metabolic disease.

Metabolic syndrome, obesity, and type 2 diabetes increase demand for long-term care and contribute to cardiovascular, renal, and other complications. In ageing populations, metabolic risk may coexist with sarcopenia and frailty, making nutrition assessment particularly important. Healthcare managers should integrate validated screening, dietetic services, physical-activity counseling, and continuity of care into chronic-disease pathways. In hospitals, timely nutrition assessment and evidence-based nutritional support can help reduce avoidable complications and support recovery, but protocols should be individualized and monitored by qualified professionals.

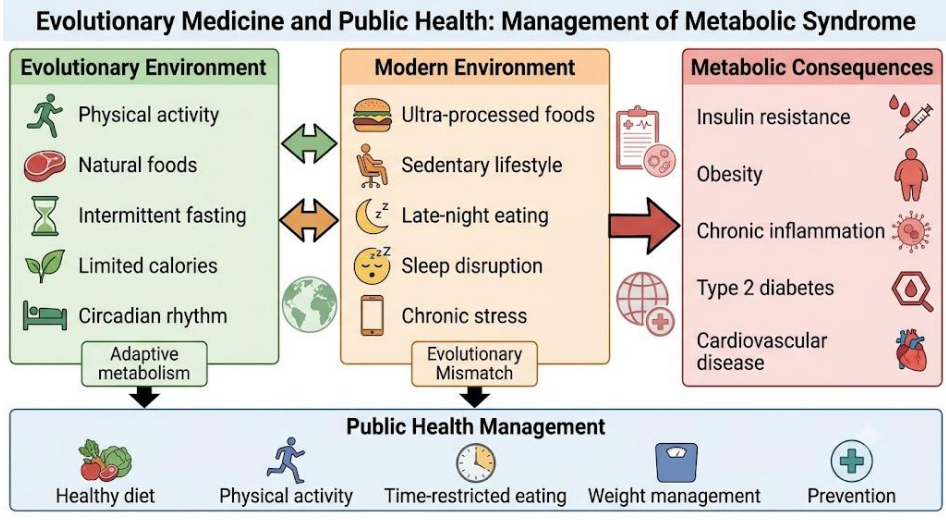

Figure 3. *Evolutionary medicine and public health: management of metabolic syndrome. The figure summarizes the interaction between ancestral adaptations, contemporary environments, metabolic consequences, and population-level prevention strategies.*

Source: *Prepared by the author based on the literature cited in this chapter.*

5. Health Financing and Biological Risk Management: Integrating Social and Complementary Insurance

Population ageing and the growing burden of chronic disease place sustained pressure on health-system financing. Risk pooling through General Health Insurance (GHI) can protect individuals from catastrophic expenditure and distribute financial risk across the population. Its sustainability, however, depends on revenue, benefit design, service prices, demographic change, prevention, provider incentives, and the efficiency and equity of service delivery. The World Health Organization's Fourteenth General Programme of Work emphasizes stronger primary care, financial protection, prevention, and resilient health systems as interconnected priorities (World Health Organization, 2025).

Complementary Health Insurance (CHI) may cover services, amenities, or cost-sharing elements outside the principal public package, depending on national regulation and policy design. Tapan (2008) discussed its potential contribution to the sustainability of Turkey's health-financing structure. Nevertheless, CHI should not be presented as a stand-alone biological or economic solution. Its effects depend on benefit design, affordability, regulation, coordination with public coverage, and the extent to which it avoids widening inequalities.

Insurance mechanisms may encourage preventive service use through evidence-based programs, but genetic screening, behavioral incentives, and risk-adjusted premiums require careful ethical and legal scrutiny. Uncritical use of biological or behavioral data may create discrimination, privacy risks, or barriers for people with pre-existing conditions. A responsible financing strategy should prioritize universal access, transparent benefit design, data protection, and evaluated prevention programs while maintaining solidarity in risk pooling.

6. A Systems Approach to Quality Accreditation and Patient Safety

Safe care cannot depend on flawless individual performance. Human attention and memory are limited, particularly during multitasking, fatigue, and interruptions. A systems approach therefore seeks to make correct actions easier, detect errors before they reach patients, and reduce reliance on memory. Standardization, checklists, medication reconciliation, structured handovers, and independent verification can function as barriers within a broader safety architecture.

Joint Commission International accreditation standards and the International Patient Safety Goals translate several of these principles into organizational

requirements (Joint Commission International, 2024). For example, the use of at least two patient identifiers reduces the risk of wrong-patient errors, while standardized labeling and verification processes strengthen medication safety. Accreditation does not eliminate risk by itself; its value depends on implementation, measurement, leadership commitment, and adaptation to the local clinical context.

A mature patient-safety culture encourages reporting, learning, and respectful communication. Punitive responses can suppress reporting and obscure system weaknesses, whereas a just-culture approach distinguishes human error, at-risk behavior, and reckless conduct. Safety-climate measurement tools can help organizations identify areas requiring improvement (Sexton et al., 2006). Healthcare managers should combine these data with incident reviews, staff feedback, patient experience, and outcome indicators to guide continuous improvement.

7. Digital Transformation in Healthcare Management: Artificial Intelligence and Decision-Support Systems

Digital health systems bring together clinical histories, laboratory results, imaging, medication data, and increasingly genomic or patient-generated information. Clinical decision-support systems can organize these data, identify patterns, and provide reminders or risk estimates. Artificial intelligence may support tasks such as image interpretation, deterioration prediction, and medication review, but its performance depends on data quality, population representativeness, validation, and the conditions in which it is used (Jiang et al., 2017; Topol, 2019).

AI should not be described as a zero-error technology. Algorithms can produce false positives, false negatives, biased outputs, or recommendations that fail when transferred to a new setting. Automation bias may also lead users to accept suggestions without sufficient scrutiny. Safe implementation therefore requires external and local validation, monitoring for performance drift, transparent responsibility, cybersecurity, privacy protection, and clear routes for clinicians to question or override recommendations.

Successful digital transformation is socio-technical rather than purely technological. Usability, training, professional trust, workflow compatibility, and patient communication influence whether a system improves or adds to cognitive workload. Managers should evaluate technology against defined clinical needs and measurable outcomes. Human oversight remains essential because clinicians must interpret recommendations in relation to the patient's values, preferences, comorbidities, and social circumstances. In this role, AI can

complement rather than replace professional judgment and therapeutic relationships.

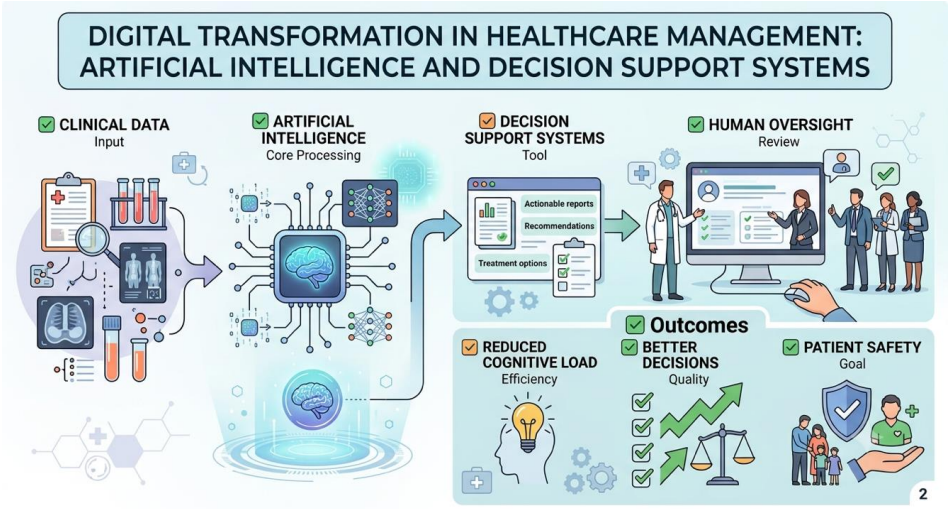

Figure 4. *Digital transformation in healthcare management: artificial intelligence and clinical decision-support systems. AI-enabled tools can integrate clinical data and support decisions, but safe use requires validation, human oversight, transparent governance, and continuous performance monitoring.*

Source: *Prepared by the author based on the literature cited in this chapter.*

8. Conclusion

Health outcomes emerge from interactions among biological processes, psychological experience, social conditions, and the organization of care. A biologically informed perspective can help healthcare managers understand cognitive limitations, occupational stress, and metabolic risk; however, biological explanations should not be used to obscure institutional responsibilities or social determinants of health.

Resilient healthcare systems are built by designing work around human capabilities, supporting staff recovery, strengthening prevention, maintaining equitable risk pooling, and applying accreditation standards as active quality-improvement tools. Digital decision support can contribute to this agenda when it is validated, governed transparently, and embedded in patient-centered workflows. Integrating neurobiology, evolutionary medicine, health financing, quality management, and responsible artificial intelligence thus offers a coherent framework for safer and more sustainable healthcare—provided that scientific uncertainty, ethics, and equity remain central to managerial decision-making.

References

Arnsten, A. F. T. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. Nature Reviews Neuroscience, 10(6), 410–422. https://doi.org/10.1038/nrn2648

Asgari, E., Kaur, J., Nuredini, G., Balloch, J., Taylor, A. M., Sebire, N., Robinson, R., Peters, C., Sridharan, S., & Pimenta, D. (2024). Impact of electronic health record use on cognitive load and burnout among clinicians: Narrative review. JMIR Medical Informatics, 12, e55499. https://doi.org/10.2196/55499

Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. Science, 196(4286), 129–136. https://doi.org/10.1126/science.847460

Guidi, J., Lucente, M., Sonino, N., & Fava, G. A. (2020). Allostatic load and its impact on health: A systematic review. Psychotherapy and Psychosomatics, 90(1), 11–27. https://doi.org/10.1159/000510696

Hall, L. H., Johnson, J., Watt, I., Tsipa, A., & O'Connor, D. B. (2016). Healthcare staff wellbeing, burnout, and patient safety: A systematic review. PLOS ONE, 11(7), e0159015. https://doi.org/10.1371/journal.pone.0159015

Jiang, F., Jiang, Y., Zhi, H., Dong, Y., Li, H., Ma, S., Wang, Y., Dong, Q., Shen, H., & Wang, Y. (2017). Artificial intelligence in healthcare: Past, present and future. Stroke and Vascular Neurology, 2(4), 230–243. https://doi.org/10.1136/svn-2017-000101

Joint Commission International. (2024). Joint Commission International accreditation standards for hospitals (8th ed.). Joint Commission Resources.

Kahneman, D., & Egan, P. (2011). *Thinking, fast and slow* (Vol. 1, No. 0, pp. 1-5). New York: Farrar, straus and Giroux.

Lieberman, D. E. (2014). *The story of the human body: evolution, health, and disease*. Vintage.

McEwen, B. S. (1998). Protective and damaging effects of stress mediators. New England Journal of Medicine, 338(3), 171–179. https://doi.org/10.1056/NEJM199801153380307

Neel, J. V. (1962). Diabetes mellitus: A 'thrifty' genotype rendered detrimental by 'progress'? American Journal of Human Genetics, 14(4), 353–362.

Sapolsky, R. M., & Berkrot, P. (2004). Why zebras don't get ulcers.

Sexton, J. B., Helmreich, R. L., Neilands, T. B., Rowan, K., Vella, K., Boyden, J., Roberts, P. R., & Thomas, E. J. (2006). The Safety Attitudes Questionnaire: Psychometric properties, benchmarking data, and emerging research. BMC Health Services Research, 6, 44. https://doi.org/10.1186/1472-6963-6-44

Sweller, J. (1988). Cognitive load during problem solving: Effects on learning. Cognitive Science, 12(2), 257–285. https://doi.org/10.1207/s15516709cog1202_4

Tapan, B. (2008). Genel sağlık sigortası'nın sürdürülebilirliği için tamamlayıcı sağlık sigortası'nın gerekliliği. Doktora Tezi, Kadir Has Üniversitesi- Sosyal Bilimler Enstitüsü, İstanbul.

Topol, E. J. (2019). High-performance medicine: The convergence of human and artificial intelligence. Nature Medicine, 25(1), 44–56. https://doi.org/10.1038/s41591-018-0300-7

World Health Organization. (2025). A global health strategy for 2025–2028: Advancing equity and resilience in a turbulent world—Fourteenth General Programme of Work. https://www.who.int/publications/i/item/9789240101012

Young, J. Q., Van Merriënboer, J., Durning, S., & Ten Cate, O. (2014). Cognitive load theory: Implications for medical education: AMEE Guide No. 86. Medical Teacher, 36(5), 371–384. https://doi.org/10.3109/0142159X.2014.889290

Chapter 3

The Biology of Working Life: The Neurobiological and Physiological Foundations of Organizational Behavior

Neşe ALGAN ÇAPRAZ[1], Emine İnci BALKAN[2], Birkan TAPAN[3]

Introduction

Human behavior plays a decisive role in organizational effectiveness. Accordingly, organizational behavior examines motivation, leadership, commitment, job satisfaction, burnout, cooperation, and performance (Robbins & Judge, 2017). Although the field has traditionally been shaped by psychology, sociology, and management, advances in neuroscience, psychophysiology, endocrinology, and behavioral biology have expanded interest in the biological foundations of behavior. This expansion does not imply that complex organizational phenomena can be reduced to brain regions or hormone levels. Rather, it supports a biopsychosocial view in which biological regulation interacts continuously with job demands, autonomy, social relationships, leadership, and institutional culture.

Modern working life creates biologically relevant exposures through high workload, performance pressure, digital connectivity, time scarcity, shift work, job insecurity, and rapidly changing work arrangements. When such demands are intense or prolonged, they may activate stress-regulatory systems, interfere with sleep and circadian timing, and constrain the cognitive resources needed for decision-making and emotional regulation. Poor work environments therefore affect more than employees' attitudes: they may influence physiological recovery, safety, absenteeism, turnover intentions, and service quality. The World Health Organization (2022) accordingly recommends that organizations address working conditions and psychosocial risks rather than relying exclusively on individual coping programs.

This chapter evaluates the neurobiological and physiological foundations of organizational behavior through six interconnected themes: stress and the hypothalamic-pituitary-adrenal (HPA) axis; allostatic load and burnout;

[1] Department of Business Administration, Faculty of Business and Management Information Systems, Demiroglu Science University, Istanbul, Turkey
[2] Department of Medical Laboratory Techniques, Vocational School of Health Services, Demiroglu Bilim University, Istanbul, Turkey
[3] Department of Health Management, Faculty of Health Sciences, Demiroglu Science University, Istanbul, Turkey

circadian rhythm and sleep; neuroleadership; psychophysiological measurement; and digital work. It then translates the evidence into implications for organizations and managers and critically examines methodological and ethical limitations. The central argument is that biological evidence is most useful when it clarifies mechanisms and informs humane work design, not when it is used to label, rank, or monitor employees without adequate safeguards.

Biological Foundations of Organizational Behavior

Behavior emerges from dynamic interactions among the central nervous system, endocrine signaling, autonomic regulation, immune activity, prior experience, and the social environment (Arnsten, 2009; McEwen & Akil, 2020). The prefrontal cortex supports executive functions such as planning, working memory, attention, inhibition, and flexible problem-solving. The amygdala and related limbic circuits contribute to the detection of threat and the allocation of attention to emotionally salient information. These systems do not operate as isolated modules; their activity changes with context, learning, sleep, metabolic state, and perceived control.

Under acute stress, catecholamines and glucocorticoids can temporarily mobilize energy and sharpen responses to immediate demands. When arousal becomes excessive, however, prefrontal functions may deteriorate while habitual or threat-focused responses become more dominant (Arnsten, 2009). At work, this shift may appear as narrowed attention, impulsive decisions, reduced creativity, interpersonal defensiveness, or difficulty considering long-term consequences. The same demand may also produce different responses across individuals because of differences in experience, health, chronotype, coping resources, and social support.

Biological explanations should therefore be probabilistic rather than deterministic. A cortisol value cannot by itself explain low commitment, and activity in a brain region cannot establish why a leader behaves in a particular way. Organizational outcomes arise through multiple levels of analysis. Biological measures are most informative when combined with validated psychological scales, work-design variables, behavioral indicators, and longitudinal observation.

Occupational Stress, the HPA Axis, and Allostatic Load

Occupational stress develops when work demands are perceived as exceeding the resources available to meet them. Karasek's Job Demand-Control Model proposes that high demands become especially harmful when employees have limited decision latitude (Karasek, 1979). Role ambiguity, effort-reward

imbalance, organizational injustice, job insecurity, inadequate staffing, and low social support may further intensify stress. These factors are organizational exposures, not merely individual weaknesses, and their effects are shaped by duration, predictability, controllability, and opportunities for recovery.

The HPA axis is a central component of the stress response. Stress-related neural signals stimulate the hypothalamus to release corticotropin-releasing hormone, which promotes pituitary secretion of adrenocorticotropic hormone. This signal triggers cortisol release from the adrenal cortex. In the short term, cortisol supports adaptation by mobilizing energy and modulating cardiovascular, immune, and cognitive functions. The activation pathway and its possible short- and long-term consequences are summarized in Figure 1.

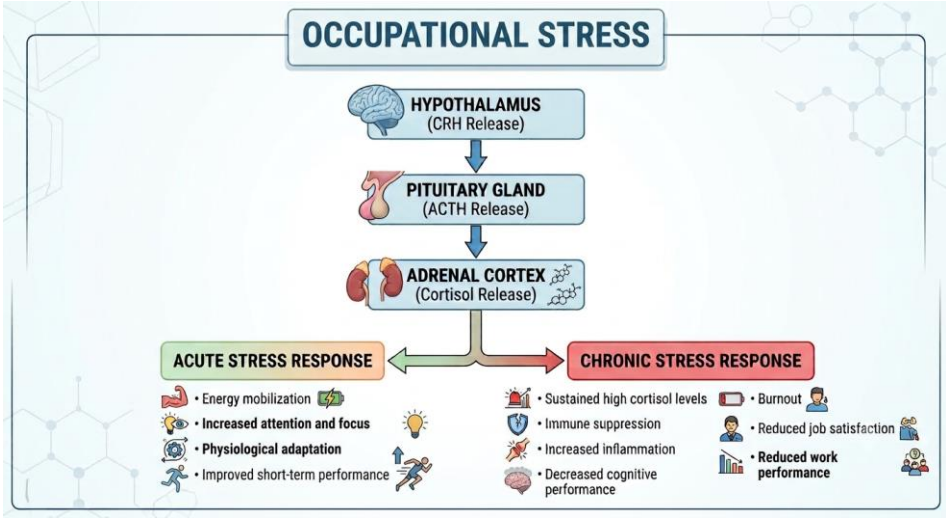

Figure 1. *Activation of the hypothalamic-pituitary-adrenal (HPA) axis in response to occupational stress and its potential effects on employee health and work performance.*

Source: *Created by the authors.*

Repeated activation without adequate recovery may contribute to allostatic load, the cumulative physiological burden associated with adapting to chronic or recurrent demands (McEwen, 1998; Juster et al., 2010). Dysregulation may involve not only persistently high cortisol but also a flattened diurnal slope, an altered awakening response, or reduced flexibility of the stress system. This distinction is important because a single cortisol sample cannot represent the full HPA pattern. Chronic stress may also interact with sympathetic activation, inflammation, blood pressure, metabolism, and sleep, increasing longer-term health risk (Ganster & Rosen, 2013; McEwen & Akil, 2020).

These mechanisms have organizational consequences. Impaired executive control can increase errors and reduce the quality of complex decisions; heightened threat sensitivity can undermine communication and cooperation; fatigue can increase presenteeism and reduce learning. A biologically informed organization therefore asks whether deadlines, staffing, role expectations, and recovery periods create repeated activation without sufficient control or restoration. The appropriate response is not simply to teach employees to tolerate excessive demands, but to redesign avoidable stressors while strengthening resources.

The Psychobiological Dimension of Burnout Syndrome

Burnout is characterized by exhaustion, increased mental distance or cynicism toward work, and reduced professional efficacy. It is associated with chronic workplace stress that has not been successfully managed and is best understood as an occupational phenomenon rather than a diagnosis established by a biomarker. High workload, low control, value conflict, insufficient reward, weak community, and perceived unfairness can each contribute to its development (Maslach & Leiter, 2016).

Biological studies have examined cortisol regulation, inflammatory markers, autonomic activity, immune function, sleep, and cellular aging in relation to burnout. Some studies report altered HPA-axis patterns, lower heart rate variability, or higher inflammatory activity, but findings are heterogeneous (Danhof-Pont et al., 2011). Differences in burnout definitions, sampling times, medication use, sleep, age, sex, comorbidity, and study design complicate comparisons. Consequently, no single biological marker can currently diagnose burnout or distinguish it reliably from depression, anxiety, sleep loss, or chronic occupational stress.

Sleep disturbance is both a potential contributor to and consequence of burnout. Insufficient or fragmented sleep impairs attention, working memory, emotional regulation, and error monitoring (Durmer & Dinges, 2005; Walker, 2009). This may initiate a reinforcing cycle: demands reduce recovery, poor recovery reduces performance, and reduced performance increases perceived pressure. Organizational practices that normalize after-hours availability or chronic understaffing can maintain this cycle even when individual wellness resources are offered.

A psychobiological interpretation is valuable when it prevents moralization. Exhaustion should not automatically be framed as a lack of resilience. At the same time, biological findings should not be used to medicalize every negative work experience. Assessment should combine employee reports, organizational

indicators, work-design analysis, and, only where justified, ethically collected physiological data.

Circadian Rhythm, Sleep, and Working Life

Circadian rhythms are approximately 24-hour patterns coordinated by the suprachiasmatic nucleus and synchronized primarily by light. They regulate sleep-wake timing, melatonin and cortisol rhythms, metabolism, body temperature, and cognitive performance. Sleep pressure and circadian phase interact, so performance depends not only on the number of hours slept but also on when sleep and work occur relative to internal biological time.

Night work exposes employees to light and activity when the biological system is prepared for sleep and requires sleep during a daytime period that is less favorable for sustained rest. The resulting circadian misalignment may reduce alertness, impair decision-making, alter metabolic regulation, and disturb cardiovascular rhythms. Evidence from new shift workers indicates that sleep and mental-health outcomes can worsen after the transition to shift schedules (Harris et al., 2024). Circadian misalignment has also been associated with unfavorable blood-pressure patterns (Shafer et al., 2024).

The organizational relevance is direct. Fatigue-related lapses can affect clinical errors, transportation safety, industrial incidents, and the quality of high-stakes decisions. Risk is shaped by shift timing, shift length, direction and speed of rotation, consecutive night shifts, commuting time, workload, and access to breaks. Individual chronotype matters, but it should not be used to transfer full responsibility to the employee.

Evidence-informed scheduling favors predictable rosters, adequate rest between duties, limits on extended and consecutive night shifts, forward rotation where practicable, and protected breaks. Strategic lighting and fatigue education may help, but they cannot compensate fully for unsafe staffing or excessive hours. Organizations should monitor fatigue-related near misses and absence patterns without penalizing workers for reporting them.

Neuroleadership and Brain-Based Approaches to Leadership

Neuroleadership seeks to connect findings from neuroscience with leadership, decision-making, emotion regulation, and social interaction. One influential conceptual account is the SCARF model, which proposes that status, certainty, autonomy, relatedness, and fairness shape social reward and threat responses (Rock, 2008). The model offers a useful vocabulary for understanding why opaque decisions, humiliating feedback, micromanagement, exclusion, and perceived injustice may generate defensive behavior; however, it

should be interpreted as an applied framework rather than as definitive neuroscientific evidence.

A biologically informed leader can reduce unnecessary threat by communicating predictably, explaining decisions, providing meaningful autonomy, inviting participation, and responding constructively to error reports. These practices can support psychological safety and preserve cognitive resources for learning and problem-solving. They are also consistent with established organizational theories of justice, support, and job design; neuroscience should enrich these theories rather than rebrand them.

The field nevertheless faces substantial criticism. Neuroimaging studies often use small samples and artificial tasks, while reverse inference may attribute a complex psychological state to activation in a particular region. Brain images can also create an unjustified impression of certainty. Lindebaum and Zundel (2013) caution against overstating what organizational neuroscience can explain. Leadership remains relational and contextual: power, culture, incentives, professional norms, and history cannot be inferred from neural activity alone.

Psychophysiological Measurements in Organizational Behavior Research

Psychophysiological methods can complement self-report measures by capturing processes that employees may not perceive or report accurately. Common indicators include salivary cortisol, heart rate and heart rate variability (HRV), electrodermal activity, electroencephalography (EEG), eye tracking, actigraphy, inflammatory markers, and, increasingly, functional near-infrared spectroscopy and wearable sensors. Each measure reflects a limited aspect of physiology and requires a clearly specified research question.

HRV is commonly used as an indicator of autonomic regulation, but it is influenced by respiration, posture, physical activity, age, fitness, medication, and measurement duration. Cortisol is sensitive to time of day, awakening, food, nicotine, medication, and acute events. EEG is vulnerable to movement and environmental artifacts. Consequently, measurement protocols, preprocessing decisions, and contextual variables must be reported transparently. Multimethod designs are preferable to treating one signal as a direct measure of stress, engagement, honesty, or performance (Kim et al., 2018).

Wearables create opportunities for repeated measurement in natural settings, allowing researchers to examine within-person change across shifts or high-demand periods. Yet workplace use creates a power asymmetry: an employee

may feel unable to refuse monitoring even when consent is formally requested. Data collected for wellness can later be repurposed for productivity scoring, discipline, insurance decisions, or selection. Responsible use requires purpose limitation, data minimization, meaningful consent, secure storage, restricted access, transparent algorithms, and a prohibition on adverse employment decisions based solely on physiological data.

Research designs should prioritize longitudinal and within-person approaches, establish preregistered hypotheses where possible, and combine biological measures with work characteristics and employee experience. Researchers must distinguish statistical association from individual diagnosis and should communicate uncertainty explicitly.

Digital Work, Technostress, and Remote-Work Biology

Digitalization has changed the temporal and attentional structure of work. Continuous notifications, multiple communication channels, video meetings, information overload, rapid software change, and expectations of permanent availability can increase cognitive switching and interfere with recovery. Technostress may therefore operate through familiar pathways: high demands, low control, uncertainty, social evaluation, and blurred boundaries between work and nonwork time (Dragano & Lunau, 2020).

Remote and hybrid work are not uniformly harmful or beneficial. Autonomy, reduced commuting, and greater flexibility can support well-being, whereas isolation, inadequate equipment, surveillance, work-home conflict, and after-hours connectivity can increase strain. Work-design research shows that effective remote work depends on autonomy, social support, manageable workload, and clear coordination (Wang et al., 2021). A systematic review of telework-related stress likewise identified psychological and physical strain associated with working from home, while emphasizing variation across working conditions (Gualano et al., 2023).

Biologically relevant consequences may include delayed sleep timing, prolonged sedentary behavior, visual fatigue, musculoskeletal strain, and insufficient detachment. Organizations should therefore evaluate digital workflows rather than merely count messages or screen time. Meeting-free periods, notification norms, realistic response expectations, ergonomic support, and a respected right to disconnect can reduce unnecessary activation while preserving flexibility.

Implications for Organizations and Managers

Biological evidence becomes practically meaningful when it informs primary prevention. The first priority is to modify harmful working conditions: excessive or conflicting demands, chronic understaffing, low control, unpredictable schedules, bullying, and unfair procedures. Individual interventions such as mindfulness, exercise, or sleep education may be helpful, but they should complement rather than substitute for organizational change. WHO guidance similarly prioritizes organizational interventions, manager training, worker participation, and support for people with mental-health conditions (World Health Organization, 2022).

Work design should provide employees with sufficient decision latitude, role clarity, resources, and opportunities for recovery. Managers can review workload peaks, redistribute tasks, protect uninterrupted focus time, and avoid unnecessary after-hours communication. Recovery should be treated as a performance condition rather than an absence of commitment. In high-risk sectors, staffing and scheduling decisions should explicitly consider fatigue and circadian timing.

Leadership practices should reduce avoidable social threat. Predictable communication, fair procedures, respectful feedback, and genuine participation can strengthen trust and psychological safety. Managers also need training to recognize distress, respond without stigma, and direct employees to appropriate support. Confidential support and reasonable work adjustments are especially important after illness, burnout-related absence, or major life events.

Measurement programs require governance before deployment. Organizations should state what is collected, why it is needed, how long it is retained, who can access it, and which decisions it may never be used to make. Participation in biometric monitoring should be genuinely voluntary and withdrawal should have no adverse consequence. Aggregate, de-identified information is generally more appropriate for improving work systems than individual dashboards used by supervisors.

Evaluation should include both health and organizational outcomes. Relevant indicators may include validated stress and burnout measures, sleep and recovery, turnover, absence, safety events, workload, perceived fairness, and service quality. Interventions should be tested over time and revised with employee participation. This approach prevents biological evidence from becoming a technological solution detached from the conditions that created the problem.

Future Perspectives and Critical Evaluation

Several methodological limitations constrain current conclusions. Much of the literature is cross-sectional, preventing confident causal inference. Selection effects are common because individuals who tolerate shift work or demanding occupations may remain while others leave. Small samples, multiple analytic choices, publication bias, and inconsistent definitions also reduce reproducibility. Biological measures vary across time and context, and group-level associations do not permit reliable prediction about a particular employee.

The ecological validity of laboratory studies is another concern. Controlled tasks can isolate mechanisms but cannot reproduce organizational power, interpersonal history, moral responsibility, or real consequences. Conversely, field studies provide realism but less experimental control. Progress requires longitudinal, multilevel research that combines within-person physiology, validated psychosocial measures, objective work characteristics, and organizational outcomes across diverse occupations and cultures.

Conceptually, the field must avoid neuroreductionism. Motivation, commitment, fairness, and leadership are not located in single brain regions or reducible to hormone concentrations. Biological accounts can clarify constraints and mechanisms, but social structures, meaning, identity, and power remain essential. The strongest explanations connect levels rather than replacing one level with another.

Ethically, increasingly sensitive sensors and artificial-intelligence systems may enable inferences about fatigue, emotion, health, or cognitive state. Such inferences may be inaccurate yet still influence employment decisions. Future governance must address consent under unequal power, data ownership, algorithmic bias, secondary use, cybersecurity, and workers' rights to explanation and contestation. Research and practice should follow the principle that physiological data are health-related personal data, not neutral productivity metrics.

Conclusion

The neurobiological and physiological foundations of organizational behavior provide a more complete understanding of working life. Occupational stress, burnout, sleep loss, circadian disruption, and digital overload are associated with interacting neural, endocrine, autonomic, immune, cognitive, and behavioral processes. These processes can affect decision quality, emotion regulation, cooperation, safety, absence, and sustained performance.

Biological knowledge should not be used to portray employees as programmable systems or to shift responsibility for harmful work onto

individuals. Its central contribution is to demonstrate that workload, control, fairness, scheduling, leadership, and recovery become embodied over time. Organizations therefore have a responsibility to design work that respects physiological limits and supports adaptation.

Future organizational research will benefit from interdisciplinary designs that integrate neuroscience, physiology, psychology, occupational health, ethics, and management. The most useful studies will be longitudinal, context-sensitive, transparent about uncertainty, and attentive to employee rights. In practice, biological measurement should remain proportionate and voluntary, while organizational interventions should take priority over surveillance.

Employees are psychological and social actors, but they are also biological systems whose performance and well-being are shaped by stress physiology, circadian timing, sleep, and recovery. Recognizing this reality can support healthier organizations, better decisions, stronger commitment, and sustainable performance—provided that biological evidence is used to improve working conditions rather than to control the people who work within them.

References

Arnsten, A. F. T. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. Nature Reviews Neuroscience, 10(6), 410–422. https://doi.org/10.1038/nrn2648

Danhof-Pont, M. B., van Veen, T., & Zitman, F. G. (2011). Biomarkers in burnout: A systematic review. Journal of Psychosomatic Research, 70(6), 505–524. https://doi.org/10.1016/j.jpsychores.2010.10.012

Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. Seminars in Neurology, 25(1), 117–129. https://doi.org/10.1055/s-2005-867080

Dragano, N., & Lunau, T. (2020). Technostress at work and mental health: Concepts and research results. Current Opinion in Psychiatry, 33(4), 407–413. https://doi.org/10.1097/YCO.0000000000000613

Ganster, D. C., & Rosen, C. C. (2013). Work stress and employee health: A multidisciplinary review. Journal of Management, 39(5), 1085–1122. https://doi.org/10.1177/0149206313475815

Gualano, M. R., Santoro, P. E., Borrelli, I., Rossi, M. F., Amantea, C., Daniele, A., & Moscato, U. (2023). TElewoRk-RelAted Stress (TERRA), psychological and physical strain of working from home during the COVID-19 pandemic: A systematic review. Workplace Health & Safety, 71(2), 58–67. https://doi.org/10.1177/21650799221119155

Harris, R., Kavaliotis, E., Drummond, S. P. A., & Wolkow, A. P. (2024). Sleep, mental health and physical health in new shift workers transitioning to shift work: Systematic review and meta-analysis. Sleep Medicine Reviews, 75, 101927. https://doi.org/10.1016/j.smrv.2024.101927

Juster, R.-P., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. Neuroscience & Biobehavioral Reviews, 35(1), 2–16. https://doi.org/10.1016/j.neubiorev.2009.10.002

Karasek, R. A. (1979). Job demands, job decision latitude, and mental strain: Implications for job redesign. Administrative Science Quarterly, 24(2), 285–308. https://doi.org/10.2307/2392498

Kim, H.-G., Cheon, E.-J., Bai, D.-S., Lee, Y. H., & Koo, B.-H. (2018). Stress and heart rate variability: A meta-analysis and review of the literature. Psychiatry Investigation, 15(3), 235–245. https://doi.org/10.30773/pi.2017.08.17

Lindebaum, D., & Zundel, M. (2013). Not quite a revolution: Scrutinizing organizational neuroscience in leadership studies. Human Relations, 66(6), 857–877. https://doi.org/10.1177/0018726713482151

Maslach, C., & Leiter, M. P. (2016). Understanding the burnout experience: Recent research and its implications for psychiatry. World Psychiatry, 15(2), 103–111. https://doi.org/10.1002/wps.20311

McEwen, B. S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. Annals of the New York Academy of Sciences, 840, 33–44. https://doi.org/10.1111/j.1749-6632.1998.tb09546.x

McEwen, B. S., & Akil, H. (2020). Revisiting the stress concept: Implications for affective disorders. Journal of Neuroscience, 40(1), 12–21. https://doi.org/10.1523/JNEUROSCI.0733-19.2019

Robbins, S. P., & Judge, T. A. (2017). Organizational Behavior 17th Global Edition. *Lego, Italy: Pearson*, 678-680.

Rock, D. (2008). SCARF: A brain-based model for collaborating with and influencing others. NeuroLeadership Journal, 1, 44–52.

Shafer, B. M., Kogan, S. A., & McHill, A. W. (2024). Pressure building against the clock: The impact of circadian misalignment on blood pressure. Current Hypertension Reports, 26(1), 31–42. https://doi.org/10.1007/s11906-023-01274-0

Walker, M. P. (2009). The role of sleep in cognition and emotion. Annals of the New York Academy of Sciences, 1156, 168–197. https://doi.org/10.1111/j.1749-6632.2009.04416.x

Wang, B., Liu, Y., Qian, J., & Parker, S. K. (2021). Achieving effective remote working during the COVID-19 pandemic: A work design perspective. Applied Psychology, 70(1), 16–59. https://doi.org/10.1111/apps.12290

World Health Organization. (2022). WHO guidelines on mental health at work. World Health Organization. https://www.who.int/publications/i/item/9789240053052

Chapter 4

Nutritional Therapy in the Management of Insulin Resistance: Current Evidence and Clinical Approaches

Serhat ÜZEL[1], Tuba KAYAN TAPAN[2], Emine İnci BALKAN[3]

Introduction

Insulin is a central regulator of postprandial energy metabolism. By promoting glucose uptake in skeletal muscle and adipose tissue, suppressing hepatic glucose production, and coordinating lipid and protein metabolism, it helps maintain metabolic homeostasis. Insulin resistance is characterized by an impaired biological response to insulin in target tissues despite normal or elevated circulating insulin concentrations. Compensatory hyperinsulinaemia may initially preserve near-normal glycaemia; with progression, however, β-cell capacity may become insufficient and dysglycaemia may emerge (Wilcox, 2005; Petersen & Shulman, 2018).

Insulin resistance is a major pathophysiological feature of type 2 diabetes, metabolic syndrome, cardiovascular risk and metabolic dysfunction-associated steatotic liver disease. Its development reflects interactions among genetic susceptibility, excess or ectopic adiposity, physical inactivity, dietary exposures, sleep and circadian disruption, medications, ageing and other clinical conditions. At the cellular level, ectopic lipid intermediates, inflammatory signalling, oxidative and endoplasmic-reticulum stress, mitochondrial adaptation and gut-derived signals may converge on insulin-signalling pathways (Samuel & Shulman, 2012; Hotamisligil, 2017; Petersen & Shulman, 2018; Tilg et al., 2020).

Lifestyle intervention remains central to risk reduction and metabolic management. Medical nutrition therapy can improve body weight, glycaemic measures and cardiovascular risk factors, but no single macronutrient distribution or named diet is optimal for every individual. Effective care therefore combines evidence-based principles with clinical status, cultural context, food access, preferences, treatment burden and the likelihood of long-term adherence (Evert et al., 2019; Muscogiuri et al., 2022; Caretto et al., 2026).

[1] Nutrition and Psychological Counseling Center, Istanbul, Türkiye
[2] Department of Nutrition and Dietetics, Faculty of Health Sciences, Demiroğlu Bilim University, Istanbul, Türkiye
[3] Department of Medical Laboratory Techniques, Vocational School of Health Services, Demiroğlu Bilim University, Istanbul, Türkiye

This narrative chapter integrates selected clinical guidelines, consensus statements, systematic reviews, meta-analyses and randomized trials. It treats insulin resistance as a multidimensional metabolic phenotype rather than an isolated laboratory value and discusses nutrition as one component of individualized, longitudinal care.

1. Pathophysiology of Insulin Resistance

Insulin binding activates the insulin receptor and insulin receptor substrate proteins, followed by phosphatidylinositol 3-kinase (PI3K) and Akt signalling. In skeletal muscle, this promotes translocation of glucose transporter type 4 (GLUT4) to the cell membrane; in the liver, it suppresses gluconeogenesis and supports glycogen synthesis; and in adipose tissue, it restrains lipolysis. Disruption at one or more points in this network produces tissue-specific and systemic metabolic consequences (Petersen & Shulman, 2018).

Persistent energy surplus can exceed the safe storage capacity of adipose tissue and promote lipid deposition in liver and skeletal muscle. Diacylglycerols and ceramides may activate kinases that interfere with insulin-receptor signalling. Adipose-tissue expansion may also alter adipokine secretion and recruit immune cells, contributing to chronic low-grade inflammation or "metaflammation." These mechanisms interact rather than operate in isolation (Samuel & Shulman, 2012; Hotamisligil, 2017).

Mitochondrial and oxidative stress can further modify substrate handling and signalling. In parallel, changes in microbial composition, microbial metabolites and intestinal-barrier function may influence host inflammation and metabolism. Human evidence supports an association between the gut microbiome and metabolic disease, although causal pathways and clinically actionable microbiome-based treatments remain incompletely defined (Tilg et al., 2020).

The principal interacting mechanisms that contribute to the development of insulin resistance are summarized in Figure 1.

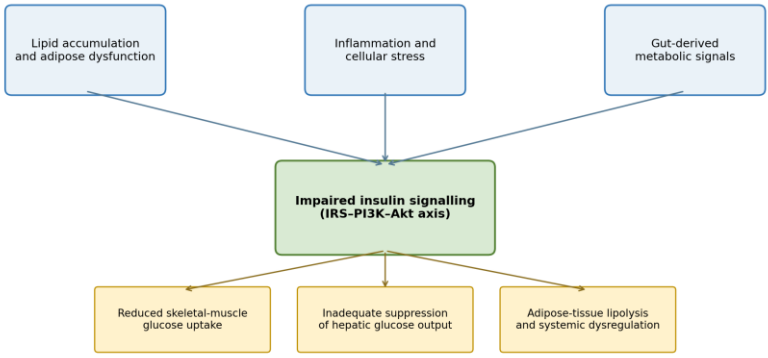

Figure 1. Interacting mechanisms contributing to insulin resistance.
Source: *Original schematic prepared for this chapter based on Samuel and Shulman (2012), Hotamisligil (2017), Petersen and Shulman (2018), and Tilg et al. (2020).*

2. Clinical and Biochemical Assessment

Insulin resistance is not established by a single universally accepted clinical test. The euglycaemic-hyperinsulinaemic clamp is widely regarded as a reference method for quantifying insulin sensitivity, but its complexity limits routine use. Surrogate indices such as the homeostatic model assessment of insulin resistance (HOMA-IR) are more practical in research and selected clinical settings. HOMA-IR is calculated from fasting glucose and insulin, but its interpretation is affected by population characteristics, insulin assays and analytical methods. Accordingly, a universal cut-off such as 2.5 should not be applied without population- and laboratory-specific validation (Wallace et al., 2004).

Fasting glucose, glycated haemoglobin and the oral glucose tolerance test assess glycaemic status and are used to identify prediabetes or diabetes; they do not directly measure insulin resistance. Fasting insulin may provide contextual information, but assay variability and the absence of standardized diagnostic thresholds limit its use as a stand-alone test. Clinical assessment should therefore integrate anthropometric measures, blood pressure, lipid profile, glycaemic measures, medication history, sleep, physical activity and signs of associated conditions. Central adiposity and acanthosis nigricans may increase clinical suspicion, but neither is diagnostic on its own (American Diabetes Association Professional Practice Committee, 2024a; Wallace et al., 2004).

Assessment is most useful when it changes management. The practical objective is to identify modifiable cardiometabolic risk, detect established

dysglycaemia or comorbidity, and define safe, measurable treatment priorities rather than to label a patient on the basis of one surrogate index.

3. Principles of Medical Nutrition Therapy

Medical nutrition therapy should begin with a collaborative assessment of dietary intake, weight history, eating pattern, food environment, cultural practices, readiness for change and relevant clinical data. When excess adiposity is present, a sustainable energy deficit is usually the principal driver of weight loss. A 5–10% reduction in body weight can produce clinically meaningful improvements in insulin sensitivity and multiple cardiometabolic risk markers, although responses vary and additional benefit may occur with greater weight loss when it is safe and sustainable (American Diabetes Association Professional Practice Committee, 2024b; Magkos et al., 2016).

Diet quality matters alongside energy balance. Emphasizing minimally processed foods, vegetables, fruit, legumes, whole grains, nuts and appropriate sources of unsaturated fat generally increases fibre and micronutrient density while reducing exposure to refined starches, added sugars and excess saturated fat. In a controlled inpatient trial, an ultra-processed diet increased energy intake and weight gain relative to an unprocessed diet despite diets being matched for presented calories and several nutrients, illustrating how food form can influence spontaneous intake (Hall et al., 2019).

Prescriptions should avoid unnecessary rigidity. The optimal plan is one that is nutritionally adequate, clinically appropriate, acceptable to the individual and feasible over time. Follow-up should address not only weight and laboratory values but also hunger, gastrointestinal tolerance, medication changes, psychological burden and the practical barriers that shape adherence.

A practical cycle for translating these principles into individualized assessment, goal setting, intervention and monitoring is presented in Figure 2.

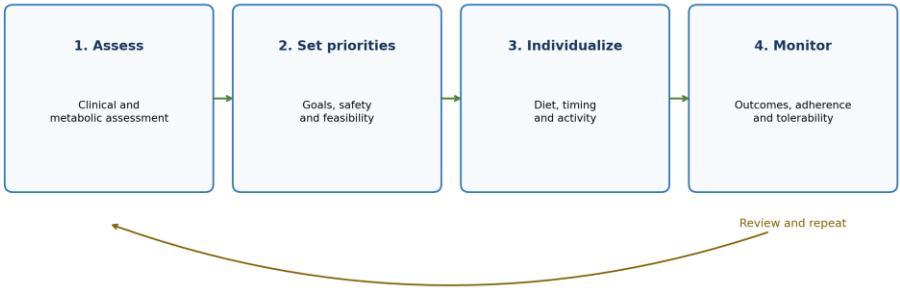

Figure 2. A practical cycle for individualized nutrition care in insulin resistance. ***Source:*** *Original schematic prepared for this chapter based on the American Diabetes Association Professional Practice Committee (2024b), Evert et al. (2019), and Muscogiuri et al. (2022).*

4. Dietary Patterns and Clinical Evidence

4.1 Mediterranean dietary pattern

The Mediterranean dietary pattern emphasizes vegetables, fruit, legumes, whole grains, nuts, olive oil and fish, with limited refined foods and processed meats. Its cardiometabolic effects likely reflect the combined influence of unsaturated fatty acids, fibre, polyphenols, lower energy density and displacement of less favourable foods. Randomized and synthesized evidence supports its use for cardiovascular risk reduction and improvement of several glycaemic outcomes, while the effect attributable to any single component remains difficult to isolate (Estruch et al., 2018; Schwingshackl et al., 2020).

4.2 Lower-carbohydrate approaches

Reducing carbohydrate intake can improve short-term glycaemic control and may reduce the need for glucose-lowering medication in some people with type 2 diabetes. However, "low carbohydrate" covers heterogeneous diets, and long-term differences between dietary patterns often diminish as adherence converges. Carbohydrate quality, replacement nutrients, medication adjustment and safety are therefore as important as the percentage of energy from carbohydrate. Very-low-carbohydrate approaches require clinical supervision in people using insulin, sulfonylureas, sodium–glucose cotransporter 2 inhibitors or other treatments that alter hypoglycaemia or ketoacidosis risk (Snorgaard et al., 2017; Evert et al., 2019).

4.3 Plant-forward dietary patterns

Healthful plant-forward patterns—rich in whole grains, legumes, vegetables, fruit, nuts and unsaturated oils—are associated with lower risk of type 2 diabetes.

The distinction between healthful and less healthful plant foods is essential: refined grains, sugar-sweetened beverages and highly processed plant products do not confer the same metabolic profile as fibre-rich whole foods (Satija et al., 2016). Adequate protein, vitamin B12, iron, calcium and other nutrients should be considered when animal foods are substantially restricted.

4.4 Intermittent fasting and time-restricted eating

Time-restricted eating limits daily energy intake to a defined window without necessarily prescribing specific calorie targets. Some benefits may arise from spontaneous energy reduction, while early time-restricted eating may also improve selected metabolic measures through circadian alignment independent of major weight loss. Trials have generally been short, protocols differ, and long-term adherence and clinical outcomes remain uncertain. Time-restricted eating should therefore be considered an optional structure rather than a universally superior diet (Sutton et al., 2018; Lowe et al., 2020).

5. Macronutrient Quality and Micronutrients

5.1 Carbohydrate and fibre

Carbohydrate recommendations should address both quantity and quality. Replacing refined grains and added sugars with legumes, intact or minimally processed whole grains, vegetables and whole fruit can moderate postprandial glycaemia and increase fibre intake. Glycaemic index and glycaemic load can be useful supplementary concepts, but meal composition, preparation, portion size and individual response also shape postprandial glucose excursions (Jenkins et al., 2002; Evert et al., 2019).

Dietary fibre may support satiety, bowel function, lipid metabolism and microbial production of short-chain fatty acids. Targets should be individualized and increased gradually when current intake is low, particularly in people with gastrointestinal symptoms.

5.2 Dietary fat

Fat quality is generally more clinically relevant than simply pursuing a low-fat diet. Replacing saturated fat with mono- and polyunsaturated fats can improve lipid risk profiles and may support glycaemic management. Olive oil, nuts, seeds and fish can be incorporated within an energy-appropriate pattern. Evidence does not justify describing omega-3 supplementation as an established treatment for insulin resistance; supplementation should be guided by the clinical indication rather than by insulin resistance alone (Evert et al., 2019; Schwingshackl et al., 2020).

5.3 Protein

Protein intake should be sufficient to support nutritional adequacy, satiety and preservation of lean mass during weight loss. Sources may include legumes, soy foods, dairy products, eggs, fish, poultry, nuts and seeds according to preference and clinical context. Blanket replacement of all animal protein is not required; the overall dietary pattern and the degree of processing are important. Renal disease, frailty and other conditions may require individualized targets.

5.4 Micronutrients and supplements

Magnesium and vitamin D participate in pathways relevant to glucose metabolism, but observational associations do not establish that routine supplementation reverses insulin resistance. Supplements should be used to correct documented deficiency, address a recognized risk state or meet another evidence-based indication. They should not replace dietary improvement, physical activity or appropriate medical care.

The principal nutritional strategies, their proposed pathways, clinical interpretation and overall evidence profile are summarized in Table 1.

Table 1. Evidence-informed nutritional strategies for insulin resistance

Strategy	Plausible/principal pathway	Clinical interpretation	Evidence summary
Sustainable energy deficit when indicated	Reduces excess and ectopic adiposity	Clinically meaningful weight loss can improve insulin sensitivity and risk markers	Consistent; magnitude varies
Mediterranean dietary pattern	Improves overall diet quality; replaces saturated fat/refined foods	Strong option for cardiometabolic risk management	Moderate to high for cardiometabolic outcomes
High-fibre, minimally processed foods	Lower energy density; improved satiety and microbial fermentation	Useful core principle across dietary patterns	Consistent for diet quality; direct IR effects vary
Lower-carbohydrate approach	Reduces postprandial glucose exposure; replacement nutrients matter	May improve short-term glycaemia; requires medication and safety review	Moderate short term; less certain long term
Time-restricted eating	Energy reduction and possible circadian alignment	Optional structure; not proven universally superior	Promising but heterogeneous and mostly short term

Source: *Synthesized from the American Diabetes Association Professional Practice Committee (2024b), Evert et al. (2019), and Muscogiuri et al. (2022).*

6. Meal Timing and Circadian Alignment

Glucose tolerance and insulin sensitivity show circadian variation, and metabolic responses to equivalent meals may differ by time of day. Observational and experimental findings suggest that habitual late eating and concentrating a large proportion of energy late in the day may be metabolically disadvantageous for some individuals. Nevertheless, meal timing interacts with sleep, chronotype, shift work, medication, total energy intake and meal composition, making universal clock-time prescriptions inappropriate (Garaulet & Gómez-Abellán, 2014; Jakubowicz et al., 2013).

When feasible, distributing intake earlier in the active period, avoiding large meals close to habitual sleep, and maintaining a reasonably consistent eating schedule may support metabolic management. For shift workers and people with irregular schedules, recommendations should be adapted to the sleep–wake cycle and occupational constraints rather than imposed as a rigid daytime schedule.

7. Physical Activity as an Adjunct to Nutritional Therapy

Muscle contraction stimulates glucose uptake through mechanisms that are partly independent of insulin signalling. A single bout of exercise can acutely increase glucose disposal, while repeated aerobic and resistance exercise can improve insulin action, mitochondrial capacity, body composition and cardiovascular fitness. Combining aerobic and resistance training is often practical because the modalities provide complementary benefits (Hawley & Lessard, 2008; Colberg et al., 2016).

Physical activity should be individualized to baseline fitness, mobility, complications, medication use and personal preference. Reducing sedentary time and increasing routine movement can complement structured exercise. Nutrition and activity plans should be coordinated, particularly when glucose-lowering medication creates a risk of hypoglycaemia.

8. Individualization, Monitoring and Clinical Implementation

The effectiveness of a nutrition intervention depends on more than its physiological rationale. Food security, cooking facilities, work schedule, family context, health literacy, cultural identity, eating-disorder risk and previous treatment experiences can materially alter feasibility and benefit. Shared decision-making helps convert broad evidence into a plan the individual can realistically follow.

Monitoring should use outcomes relevant to the clinical objective: weight and waist trajectory when appropriate; fasting and postprandial glycaemia or

HbA1c when dysglycaemia is present; lipid profile, blood pressure and liver-related measures when indicated; and patient-reported outcomes such as hunger, energy, gastrointestinal tolerance and treatment burden. A lack of response should prompt reassessment of adherence barriers, medication, sleep, comorbidity and the suitability of the intervention rather than automatic escalation of dietary restriction.

Precision-nutrition approaches based on genetics, metabolomics, continuous monitoring or microbiome profiles are scientifically promising, but their routine use requires validated effect sizes, demonstrated clinical utility and evidence that the information changes management. At present, these tools should complement—not replace—established clinical and contextual assessment.

9. Conclusion

Insulin resistance emerges from interacting disturbances in substrate handling, adipose-tissue function, inflammation, cellular stress and tissue-specific insulin signalling. Its management should therefore focus on overall cardiometabolic risk and sustainable behaviour change rather than on a single laboratory threshold or a single “best” diet.

The most defensible nutritional approach combines an appropriate energy intake with minimally processed, fibre-rich foods, favourable fat quality and an individualized dietary pattern that can be maintained. Mediterranean, lower-carbohydrate, plant-forward and time-restricted approaches may all be useful in selected contexts, but their effectiveness depends on diet quality, safety, adherence and clinical goals. Physical activity, sleep and medical management remain essential partners to nutrition therapy.

Future research may improve stratification through phenotypic, metabolic, genetic and microbiome information. Until such approaches demonstrate consistent clinical utility, individualized care should remain grounded in validated assessment, high-quality dietary evidence, shared decision-making and longitudinal monitoring.

References

American Diabetes Association Professional Practice Committee. (2024a). Diagnosis and classification of diabetes: Standards of Care in Diabetes—2024. *Diabetes Care, 47*(Suppl. 1), S20–S42. https://doi.org/10.2337/dc24-S002

American Diabetes Association Professional Practice Committee. (2024b). Obesity and weight management for the prevention and treatment of type 2 diabetes: Standards of Care in Diabetes—2024. *Diabetes Care, 47*(Suppl. 1), S145–S157. https://doi.org/10.2337/dc24-S008

Caretto, A., Zanardini, A., Frontino, G., & Pedone, E. (2026). Targeting insulin resistance through nutrition: Pathophysiological insights and dietary interventions. *Nutrients, 18*(7), 1119. https://doi.org/10.3390/nu18071119

Colberg, S. R., Sigal, R. J., Yardley, J. E., Riddell, M. C., Dunstan, D. W., Dempsey, P. C., Horton, E. S., Castorino, K., & Tate, D. F. (2016). Physical activity/exercise and diabetes: A position statement of the American Diabetes Association. *Diabetes Care, 39*(11), 2065–2079. https://doi.org/10.2337/dc16-1728

Estruch, R., Ros, E., Salas-Salvadó, J., Covas, M.-I., Corella, D., Arós, F., Gómez-Gracia, E., Ruiz-Gutiérrez, V., Fiol, M., Lapetra, J., Lamuela-Raventós, R. M., Serra-Majem, L., Pintó, X., Basora, J., Muñoz, M. A., Sorlí, J. V., Martínez, J. A., Fitó, M., Gea, A., … Martínez-González, M. A. (2018). Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. *New England Journal of Medicine, 378*(25), e34. https://doi.org/10.1056/NEJMoa1800389

Evert, A. B., Dennison, M., Gardner, C. D., Garvey, W. T., Lau, K. H. K., MacLeod, J., Mitri, J., Pereira, R. F., Rawlings, K., Robinson, S., Saslow, L., Uelmen, S., Urbanski, P. B., & Yancy, W. S. (2019). Nutrition therapy for adults with diabetes or prediabetes: A consensus report. *Diabetes Care, 42*(5), 731–754. https://doi.org/10.2337/dci19-0014

Garaulet, M., & Gómez-Abellán, P. (2014). Timing of food intake and obesity: A novel association. *Physiology & Behavior, 134*, 44–50. https://doi.org/10.1016/j.physbeh.2014.01.001

Hall, K. D., Ayuketah, A., Brychta, R., Cai, H., Cassimatis, T., Chen, K. Y., Chung, S. T., Costa, E., Courville, A., Darcey, V., Fletcher, L. A., Forde, C. G., Gharib, A. M., Guo, J., Howard, R., Joseph, P. V., McGehee, S., Ouwerkerk, R., Raisinger, K., … Zhou, M. (2019). Ultra-processed diets cause excess calorie intake and weight gain: An inpatient randomized controlled trial of ad libitum food intake. *Cell Metabolism, 30*(1), 67–77.e3. https://doi.org/10.1016/j.cmet.2019.05.008

Hawley, J. A., & Lessard, S. J. (2008). Exercise training-induced improvements in insulin action. *Acta Physiologica, 192*(1), 127–135. https://doi.org/10.1111/j.1748-1716.2007.01783.x

Hotamisligil, G. S. (2017). Inflammation, metaflammation and immunometabolic disorders. *Nature, 542*(7640), 177–185. https://doi.org/10.1038/nature21363

Jakubowicz, D., Barnea, M., Wainstein, J., & Froy, O. (2013). High caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. *Obesity, 21*(12), 2504–2512. https://doi.org/10.1002/oby.20460

Jenkins, D. J. A., Kendall, C. W. C., Augustin, L. S. A., Franceschi, S., Hamidi, M., Marchie, A., Jenkins, A. L., & Axelsen, M. (2002). Glycemic index: Overview of implications in health and disease. *The American Journal of Clinical Nutrition, 76*(1), 266S–273S. https://doi.org/10.1093/ajcn/76.1.266S

Lowe, D. A., Wu, N., Rohdin-Bibby, L., Moore, A. H., Kelly, N., Liu, Y. E., Philip, E., Vittinghoff, E., Heymsfield, S. B., Olgin, J. E., Shepherd, J. A., & Weiss, E. J. (2020). Effects of time-restricted eating on weight loss and other metabolic parameters in women and men with overweight and obesity: The TREAT randomized clinical trial. *JAMA Internal Medicine, 180*(11), 1491–1499. https://doi.org/10.1001/jamainternmed.2020.4153

Magkos, F., Fraterrigo, G., Yoshino, J., Luecking, C., Kirbach, K., Kelly, S. C., de las Fuentes, L., He, S., Okunade, A. L., Patterson, B. W., & Klein, S. (2016). Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. *Cell Metabolism, 23*(4), 591–601. https://doi.org/10.1016/j.cmet.2016.02.005

Muscogiuri, G., Barrea, L., Caprio, M., Ceriani, F., Chavez, A. O., El Ghoch, M., Frias-Toral, E., Mehta, R. J., Mendez, V., Paschou, S. A., Pazderska, A., Savastano, S., & Colao, A. (2022). Nutritional guidelines for the management of insulin resistance. *Critical Reviews in Food Science and Nutrition, 62*(25), 6947–6960. https://doi.org/10.1080/10408398.2021.1908223

Petersen, M. C., & Shulman, G. I. (2018). Mechanisms of insulin action and insulin resistance. *Physiological Reviews, 98*(4), 2133–2223. https://doi.org/10.1152/physrev.00063.2017

Samuel, V. T., & Shulman, G. I. (2012). Mechanisms for insulin resistance: Common threads and missing links. *Cell, 148*(5), 852–871. https://doi.org/10.1016/j.cell.2012.02.017

Satija, A., Bhupathiraju, S. N., Rimm, E. B., Spiegelman, D., Chiuve, S. E., Borgi, L., Willett, W. C., Manson, J. E., Sun, Q., & Hu, F. B. (2016). Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: Results from three prospective cohort studies. *PLOS Medicine, 13*(6), e1002039. https://doi.org/10.1371/journal.pmed.1002039

Schwingshackl, L., Morze, J., & Hoffmann, G. (2020). Mediterranean diet and health status: Active ingredients and pharmacological mechanisms. *British Journal of Pharmacology, 177*(6), 1241–1257. https://doi.org/10.1111/bph.14778

Snorgaard, O., Poulsen, G. M., Andersen, H. K., & Astrup, A. (2017). Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. *BMJ Open Diabetes Research & Care, 5*(1), e000354. https://doi.org/10.1136/bmjdrc-2016-000354

Sutton, E. F., Beyl, R., Early, K. S., Cefalu, W. T., Ravussin, E., & Peterson, C. M. (2018). Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. *Cell Metabolism, 27*(6), 1212–1221.e3. https://doi.org/10.1016/j.cmet.2018.04.010

Tilg, H., Zmora, N., Adolph, T. E., & Elinav, E. (2020). The intestinal microbiota fuelling metabolic inflammation. *Nature Reviews Immunology, 20*(1), 40–54. https://doi.org/10.1038/s41577-019-0198-4

Wallace, T. M., Levy, J. C., & Matthews, D. R. (2004). Use and abuse of HOMA modeling. *Diabetes Care, 27*(6), 1487–1495. https://doi.org/10.2337/diacare.27.6.1487

Wilcox, G. (2005). Insulin and insulin resistance. *Clinical Biochemist Reviews, 26*(2), 19–39.

Chapter 5

Indoor Microbiota Dynamics and Human Health

Hüseyin ÇAKAN[1]

INTRODUCTION

1. THE INVISIBLE NEIGHBORS IN OUR HOMES

Contrary to their evolutionary history, modern humans now spend approximately 90% of their time in enclosed spaces (Gilbert & Stephens, 2020). This lifestyle shift has led to the detachment of human biology from outdoor ecosystems, confining it within artificial spaces referred to as the "built environment". Although indoor areas may appear to be isolated and sterile sanctuaries from the outside, they are actually dynamic microscopic ecosystems where billions of microorganisms (bacteria, fungi, and viruses) coexist (Gilbert & Hartmann, 2024).

The indoor microbiota refers to the entirety of microbial communities living on all surfaces, in the air, and on objects within an enclosed area. Every surface we touch and every breath we take in our homes, offices, or public transportation vehicles brings us into continuous interaction with these invisible neighbors (Yong, E., 2018). While this exposure carries the risk of transmitting pathogenic microorganisms (Pessoa-Silva et al., 2004), it simultaneously facilitates a healthy immunological exchange between the environment and our body's own beneficial microbes, known as the commensal microbiome (Davis et al., 2012; Fujimura et al., 2014).

However, excessive sterilization and isolation processes in modern life disrupt the balance of this invisible ecosystem, exerting direct effects on human health. Our understanding of the ecological processes influencing indoor microbial movements remains limited; furthermore, the extent to which humans share microbes with indoor surfaces is only beginning to be understood (Meadow et al., 2014).

2. WHERE DO THESE MICROBES COME FROM?

The microbial structure of any indoor environment is not static; it is constantly updated based on its connection with the environment and its inhabitants. There are three primary sources that feed the diversity of microorganisms in enclosed spaces (Figure 1, 2) (Prison at al.,2015).

[1] Department of Biology, Faculty of Science, Canakkale Onsekiz Mart University, Çanakkale, Turkey

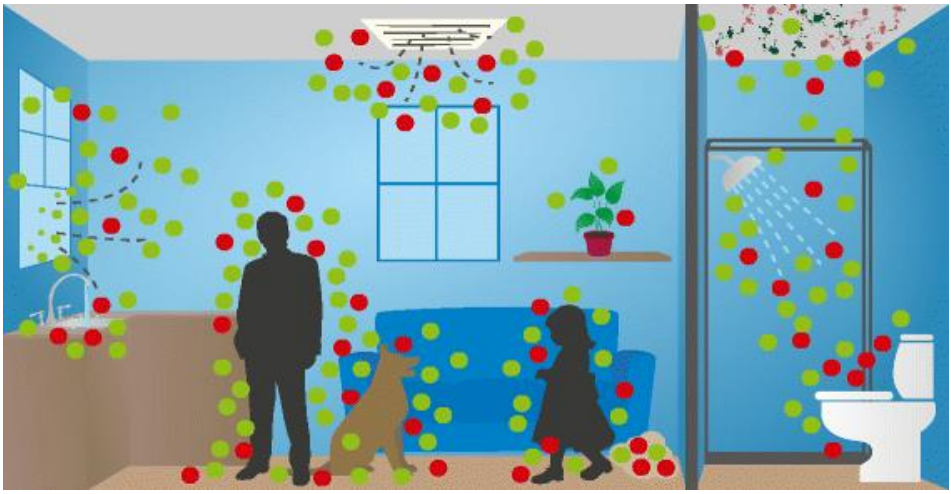

Fig. 1 *Sources of microbial bioaerosols in the built environment may include humans; pets; plants; plumbing systems; heating, ventilation, and air-conditioning systems; mold; resuspension of settled dust; and outdoor air. The green and red dots represent microorganisms that may be beneficial or detrimental to human health, respectively. Artwork by Tim Skiles*

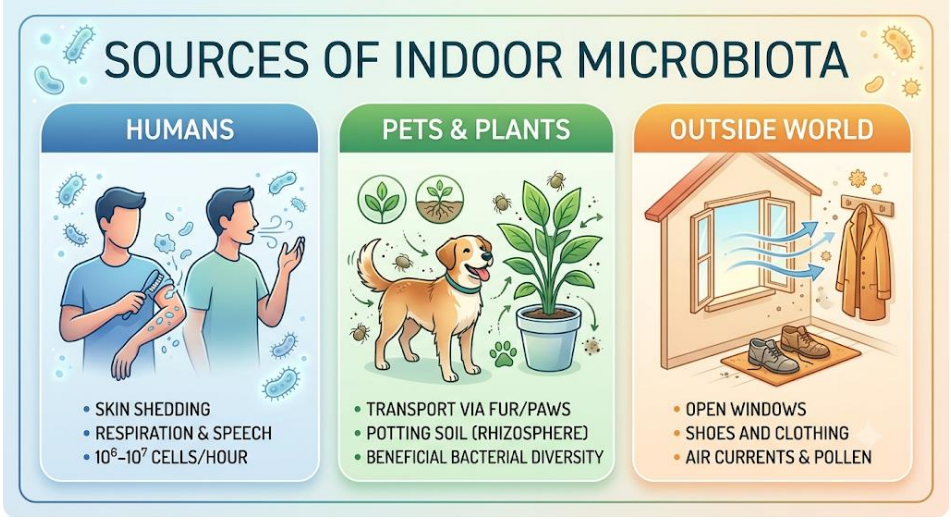

Fig.2 *Sources of indoor microbiota*

Human-Induced Dynamics

The largest and most active producers of indoor microbiota are the humans inhabiting that space. Humans shed approximately (10^6-10^7) microbial cells into their environment per hour. Micro-droplets released into the air during speech, invisible cells shedding from our skin during movement, and particles dispersed

from our clothing directly determine the microbial map of the room we occupy. The microbial community composition of any indoor surface is shaped by habitat-specific environmental constraints (e.g., surface material type) and dispersed sources, including humans, bio-aerosols, and other surfaces (Meadow et al., 2014).

Pets and Plants

Pets like cats and dogs, with whom we share our homes, tremendously increase indoor microbial biodiversity. Animals transport soil-derived beneficial bacteria from the outdoor environment into the house via their paws and fur. Research indicates that pet exposure enriches the microbial structure in house dust, contributing specifically to an increase in beneficial bacterial groups (such as *Lactobacillus*) that support respiratory defense mechanisms (Fujimura et al., 2014). Similarly, potted plants and the soil ecosystem around their roots (the rhizosphere) introduce natural and constructive microorganisms into the household air.

Connection with the Outside World

Open windows, doors, shoe soles, and clothing serve as bridges that carry the outdoor macro-ecosystem inside. Air currents, pollen, and soil particles entering through open windows prevent the indoor environment from becoming monotonous. In small buildings with low occupant density and stronger connections to outdoor air sources, outdoor-derived diversity stands as the most critical driver of indoor microbial community structure (Adams et al., 2013).

3. THE INVISIBLE BOND BETWEEN OUR BODIES AND OUR HOMES

Different regions of the human body (skin, mouth, intestines) possess their own distinct microbial communities (Costello et al., 2009; Grice et al., 2009). Our daily activities and contacts within the home cause these personal microbes to transfer onto indoor surfaces, and conversely, allow indoor microbes to adhere to our bodily barriers. Studies on the microbiological structure of multiple living spaces have demonstrated that the microbiological signature of a household can highly predict that household's microbiome and serves as a distinguishing feature among individuals within a home (Lax et al., 2014) (Figure 3).

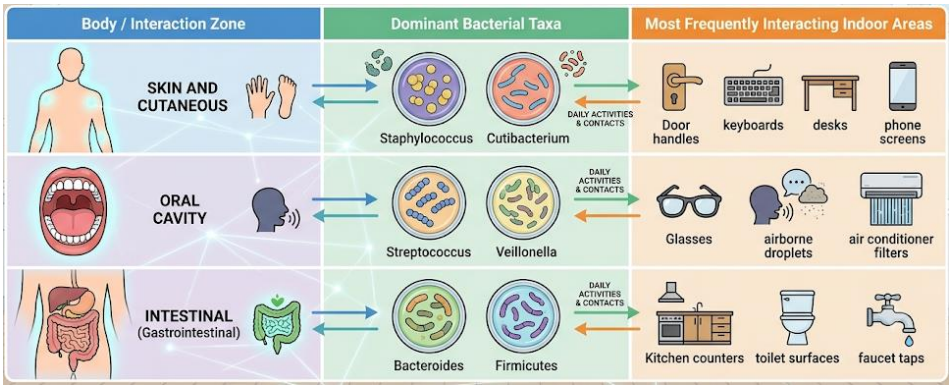

Fig. 3 *The Indoor Microbiome: Human-Surface Microbial Exchange*

Skin and Cutaneous Contact

Our hands and skin leave a literal microbial fingerprint by touching items throughout the day. The diversity of the skin microbiota is influenced by many factors such as gender, hand dominance, and washing habits (Fierer et al., 2008; Urku et al., 2026). The most common bacteria found on frequently touched kitchen and household surfaces directly match the bacterial taxa naturally occurring on human skin (Flores et al., 2013). Due to this shared surface contact, the skin microbiota of people living in the same house become similar over time.

Oral and Respiratory Tract

During routine actions such as speaking, coughing, and sneezing, microbes within the oral cavity adhere to saliva droplets and transform into bio-aerosols that can remain suspended in the air. Taxa that are core members of the oral flora accumulate heavily in the air of crowded, poorly ventilated rooms and inside air conditioner filters. This situation establishes a systemic homeostasis interaction (the oral-gut-environment axis) between the environment and human health through the inhalation of shared air (Park & Kim, 2024).

Kitchen and Restroom Dynamics

Kitchen and restroom surfaces represent areas where human-environment interaction is most acute. Studies in shared spaces reveal that microbes on restroom surfaces are not randomly distributed; rather, strong and distinct relationships exist between restroom surfaces and human intestinal and vaginal communities (Flores et al., 2011). The invisible cloud of water vapor generated upon flushing launches gut-derived bacteria into the air, and these microbes settle onto all vertical and horizontal surfaces in the restroom. In kitchen counters and

sinks, there is a complex distribution of microbial sources derived both from food (vegetables, raw meat) and transferred from human hands (Flores et al., 2013).

4. ENVIRONMENTAL FACTORS ALTERING INDOOR AIR AND HEALTH

There are three fundamental environmental factors that determine the balance of the invisible indoor ecosystem and render our homes either "healthy" or "sick" for us (Figure 4);

Fig. 4 *Indoor Environmental Factors*

The Danger of Moisture and Humidity

The humidity level of an enclosed environment is the most potent factor altering the direction of microbial life. An increase in indoor relative humidity (moisture) paves the way for the rapid proliferation of harmful microorganisms, particularly mold fungi. When this concentration—resulting from the presence of moisture along with the odors generated by certain other co-existing indoor microorganisms and pollutants—is inhaled, it triggers severe allergic reactions, asthmatic episodes, or similar chronic health problems (Keskin et al., 2005).

Cleaning Chemicals and Microbial Resistance

With evolving cleaning habits, excessive amounts of bleach, antibacterial detergents, and disinfectants are utilized in households. These chemical agents eradicate all microbes indiscriminately. However, while excessive sterilization eliminates beneficial commensal microbes within the home, it can also enhance

the survival and dissemination potential of pathogen strains that have developed resistance to disinfectants, such as Methicillin-Resistant *Staphylococcus aureus* (MRSA) (Davis et al., 2012).

Ventilation and Architectural Design

Architectural design has the potential to directly influence human health and well-being by altering the microbiology of the built environment (Kembel et al., 2014). In natural ventilation achieved by opening windows, rich outdoor soil and plant microbes enter to balance the indoor microbiome. Conversely, in modern smart buildings where windows cannot be opened and ventilation relies entirely on air conditioners and mechanical systems (HVAC), the connection with the outside world is severed. How design functions and ventilation types shape the indoor microbiome stands as the most critical determinant in the biogeography of buildings (Kembel et al., 2014).

5. DOES EXCESSIVE CLEANLINESS BRING DISEASE?

The Hygiene Hypothesis

The human immune system is a defense mechanism trained from birth by recognizing and fighting the microbes in its environment. The "Hygiene Hypothesis" posits that in the modern world, children growing up in ultra-sterile homes—approaching laboratory levels of purity—leaves the immune system untrained. A reduction in exposure to the microbial diversity found in house dust weakens respiratory immune defenses, thereby increasing susceptibility to allergens and viral infections (Fujimura et al., 2014). Finding no real microbial agents to combat in its surroundings, the immune system begins to perceive completely harmless substances, such as house dust, pollen, or pet dander, as major threats, triggering chronic health conditions like asthma.

Sick Building Syndrome

Structures that combine flawed architectural design, inadequate ventilation, and high humidity are defined in the literature as "Sick Buildings"(Gilbert & Hartmann, 2024). In research investigating the microbiological quality of a public building's indoor atmosphere alongside the perception of the work environment, it has been demonstrated that the ambient microbial load and poor indoor air parameters directly trigger symptoms of Sick Building Syndrome in employees (Keskin et al., 2005). Among individuals living or working in these buildings, chronic headaches, fatigue, burning eyes, and upper respiratory tract complaints become chronic, without a clearly defined medical cause.

6. HEALTHY HOMES OF THE FUTURE

Biophilic Design: Inviting Nature Into the Home

The architectural philosophy of the future does not view buildings merely as structures made of stone and concrete. Biophilic design, which aims to integrate nature into buildings, holds the key to a healthy indoor microbiota. Living plant walls (green walls) installed inside homes filter the air while releasing microorganisms that support human health into the environment. Architectural design features, including material choices and room connectivity, directly drive the biogeography of indoor bacterial communities (Kembel et al., 2014) (Figure 5) (Gilbert & Hartmann, 2024).

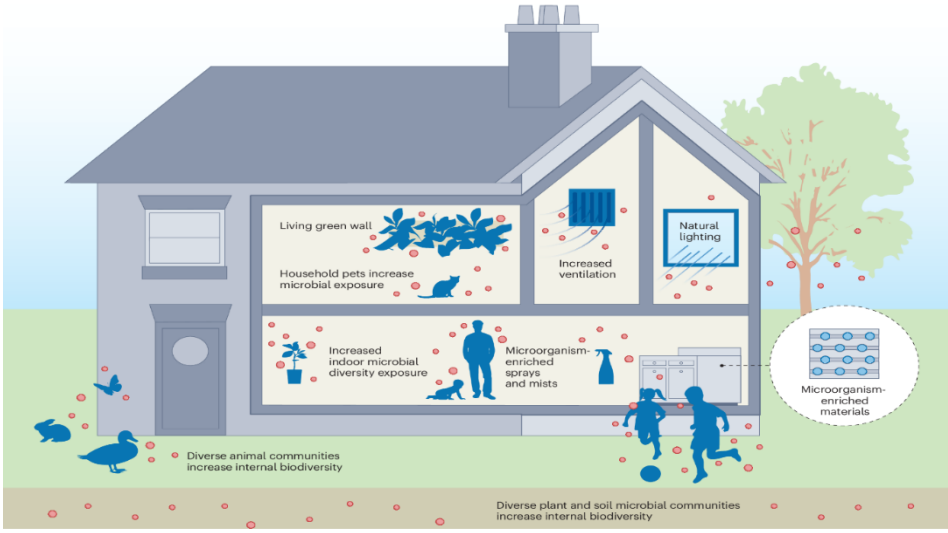

Fig.5 *The intersection of architecture and microbiology for a healthy built environment*

Probiotic Homes (Living Surfaces)

Instead of constantly scrubbing household surfaces with aggressive chemicals, the idea of inoculating these surfaces with beneficial bacteria that are harmless to human health is one of the most current topics in modern building biology. These beneficial bacteria form a protective biofilm layer on surfaces, preventing the proliferation of dangerous pathogens from the outside—such as MRSA or *Clostridioides difficile*—through a competitive exclusion mechanism. Consequently, a natural protective shield is established without the need for chemical poisoning (Ramos & Frantz, 2023; Strydom at al., 2020).

Daily Life Recommendations for a Healthy Home Microbiome

1. **Regular Natural Ventilation:** Open windows during the day to allow clean outdoor microbial diversity (soil and air bacteria) to enter the indoor space (Adams et al., 2013).
2. **Reduce Chemical Use:** Instead of excessive disinfectant and bleach utilization, opt for more natural cleaning methods that do not completely eradicate the microbial balance (Davis et al., 2012).
3. **Humidity Control:** Balance the humidity levels within the home to prevent mold, fungi, and associated allergic asthma conditions (Keskin et al., 2005).

Conclusion

Indoor microbiota dynamics constitute a complex ecosystem shaped by the interaction between human activities and environmental conditions. Understanding these dynamics contributes to designing healthier living and working spaces, reducing infection risks, and improving indoor air quality. Indoor microbiota is increasingly becoming a critical area of research, particularly for sustainable building design and public health initiatives.

Microbiota dynamics demonstrate that healthy living is not possible in a "zero-microbe" sterile room, but rather within a living home ecosystem where the "right and balanced microbes" coexist. In the future, public health and architectural policies should focus on strategies that optimize humidity and microclimate balance, possess controlled permeability with outdoor biodiversity, and support the development of beneficial microorganisms, rather than designing buildings as isolated, microbe-free cells. Elucidating the precise molecular mechanisms of this bidirectional flow between the built environment microbiome and the human microbiome will constitute the most vital step for future smart cities and preventive medicine applications.

As a result, rules governing indoor microbiota should focus not on ridding healthy human living environments of microorganisms, but on establishing a microbial equilibrium that is both human-friendly and immune-supporting.

7. REFERENCES

Adams, R. I., Miletto, M., Taylor, J. W., & Bruns, T. D. (2013). Dispersal in microbes: Fungi in indoor air are dominated by outdoor air and show dispersal limitation at short distances. *The ISME Journal*, 7(7), 1262–1273. doi: 10.1038/ismej.2013.28. Epub 2013 Feb 21.

Costello, E. K., Lauber, C. L., Hamady, M., Fierer, N., Gordon, J. I., & Knight, R. (2009). Bacterial community variation in human body habitats across space and time. *Science*, 326(5960), 1694–1697. doi: 10.1126/science.1177486. Epub 2009 Nov 5.

Davis, M. F., Iverson, S. A., Baron, P., Vasse, A., Silbergeld, E. K., Lautenbach, E., & et al. (2012). Household transmission of meticillin-resistant Staphylococcus aureus and other staphylococci. *The Lancet Infectious Diseases*, 12(9), 703–716. doi:10.1016/S1473-3099(12)70156-1.

Fierer, N., Hamady, M., Lauber, C. L., & Knight, R. (2008). The influence of sex, handedness, and washing on the diversity of hand surface bacteria. *Proceedings of the National Academy of Sciences*, 105(46), 17994–17999. doi: 10.1073/pnas.0807920105.

Flores, G. E., Bates, S. T., Knights, D., Lauber, C. L., Stombaugh, J., Knight, R., & Fierer, N. (2011). Microbial biogeography of public restroom surfaces. *PLoS ONE*, 6(11), e28132. doi: 10.1371/journal.pone.0028132

Flores, G. E., Bates, S. T., Caporaso, J. G., Lauber, C. L., Leff, J. W., Knight, R., & Fierer, N. (2013). Diversity, distribution and sources of bacteria in residential kitchens. *Environmental Microbiology*, 15(2), 588–596. doi: 10.1111/1462-2920.12036

Fujimura, K. E., Demoor, T., Rauch, M., Faruqi, A. A., Jang, S., Johnson, C. C., & et al. (2014). House dust exposure mediates gut microbiome Lactobacillus enrichment and airway immune defense against allergens and virus infection. *Proceedings of the National Academy of Sciences*, 111(2), 805–810. doi: 10.1073/pnas.1310750111

Gilbert, J. A., & Stephens, B. (2020). Microbiology of the built environment. *Nature Reviews Microbiology*, 18(7), 415–423. doi: 10.1038/s41579-018-0065-5.

Gilbert, J. A., & Hartmann, E. M. (2024). The indoor microbiome and human health. *Nature Reviews Microbiology*. Volume 22, pages 742–755 doi: 10.1038/s41579-024-01077-3

Grice, E. A., Kong, H. H., Conlan, S., Deming, C. B., Davis, J., Young, A. C., & et al. (2009). Topographical and temporal diversity of the human skin microbiome. *Science*, 324(5931), 1190–1192. doi. 10.1126/science.1171700

Kembel, S. W., Meadow, J. F., O'Connor, T. K., Mhuireach, G., Northcutt, D., Kline, J., & et al. (2014). Architectural design drives the biogeography of indoor bacterial communities. *PLoS ONE*, 9(1), e87093. doi: 10.1371/journal.pone.0087093. eCollection 2014.

Keskin, Y., Özyaral, O., Başkaya, R., Lüleci, N., Avci, S., & Acar, M. S. (2005). Bir kamu binası iç alan atmosferinin mikrobiyolojik kalitesi ve iş ortamı algısının hasta bina sendromu açısından sorgulanması. *Astım Allerji İmmünoloji*, 3(2), 56–67.

Lax, S., Smith, D. P., Hampton-Marcell, J., Owens, S. M., Handley, K. M., Scott, N. M. & et al. (2014). Longitudinal analysis of microbial interaction between humans and the indoor environment. Science (New York, N.Y.), 345(6200), 1048–1052. doi:10.1126/science.1254529

Meadow, J. F., Altrichter, A. E., Kembel, S. W., Moriyama, M., O'Connor, T. K., Womack, A. M., & et al. (2014). Bacterial communities on classroom surfaces vary with human contact. *Microbiome*, 2(1), 7. doi: 10.1186/2049-2618-2-7

Park, S. Y., & Kim, J. H. (2024). The oral-gut microbiome axis in environmental health and systemic homeostasis. *Trends in Microbiology*, 32(3), 245–258. doi: 10.1038/s41579-024-01075-5.

Pessoa-Silva, C. L., Dharan, S., Hugonnet, S., Touveneau, S., Posfay-Barbe, K., Pfister, R., & et al. (2004). Dynamics of bacterial hand contamination during routine neonatal care. *Infection Control & Hospital Epidemiology*, 25(3), 192–197. doi: 10.1086/502376.

Prussin, A. J., & Marr, L. C. (2015). Sources of airborne microorganisms in the built environment. *Microbiome*, *3*(1), Article 78. doi: 10.1186/s40168-015-0144-z

Ramos, A. M., & Frantz, A. L. (2023). Probiotic-based sanitation in the built environment—An alternative to chemical disinfectants. Clean Technologies, 5(2), 652-671. doi:10.3390/applmicrobiol3020038.

Strydom, M., Botha, A., & Ryerson, T. (2020). Disinfectant, soap or probiotic cleaning? Surface microbiome diversity and biofilm competitive exclusion. *Antibiotics*, *9*(11), 770. doi:10.3390/microorganisms8111726

Urku, R., Salman Yilmaz, S., & Çakan, H., (2026). Profiling microbiome signatures on mobile phones for forensic insights. Forensıc Scıence Internatıonal , vol.384. doi:10.1016/j.forsciint.2026.112915

Yong, E. (2018). Mikrobiyota. İçimizdeki mikroplar ve Yaşama büyüleyici bir bakış. Taş Ş.(çev.).İstanbul, 1.Baskı. Domingo Yayıncılık p.252-278.ISBN978 605 198 038 6

Chapter 6

From One-Size-Fits-All Diets to Precision Nutrition: The Transformation of Nutrition in the Age of Artificial Intelligence and the Microbiota

Tuba KAYAN TAPAN[1]

1. Introduction

For decades, nutrition science has relied on population-based dietary guidelines, estimated energy requirements, and average nutrient needs. These frameworks have delivered major public-health benefits and remain essential for preventing nutrient deficiencies and reducing diet-related disease. Nevertheless, people can show markedly different postprandial, metabolic, and behavioral responses to the same foods or dietary interventions. In PREDICT 1, substantial interindividual variation was observed in glucose, triglyceride, and insulin responses following standardized meals (Berry et al., 2020). Such findings expose the limits of assuming that a single recommendation will produce an equivalent response in everyone.

Precision nutrition seeks to refine—not replace—population guidance by using relevant individual information to improve the timing, intensity, and content of dietary advice. Depending on the clinical question, that information may include phenotype, medical history, food preferences, behavior, social context, genetics, metabolomics, gut microbiota, and data from wearable devices (Ordovas et al., 2018). The aim is not to produce a biologically perfect diet, but to select an intervention that is evidence-based, feasible, safe, culturally acceptable, and more likely to achieve a meaningful outcome for a particular person.

The field has accelerated through advances in high-throughput omics, continuous monitoring, and machine learning. Zeevi et al. (2015) demonstrated that postprandial glycemic responses to identical foods vary considerably and can be predicted by combining clinical, behavioral, and microbiome data. More recent trials have shown that personalized programs can improve selected dietary and cardiometabolic outcomes, although the magnitude, durability, and generalizability of benefit remain under investigation (Celis-Morales et al., 2017; Bermingham et al., 2024). This chapter critically examines the biological

[1] Department of Nutrition and Dietetics, Faculty of Health Sciences,
Demiroglu Bilim University, Istanbul, Turkey

foundations, technological tools, clinical promise, and unresolved limitations of precision nutrition.

2. Why Traditional Approaches Are Necessary but Incomplete

Energy balance remains a valid physiological principle: sustained changes in stored body energy reflect the relationship between intake, expenditure, and nutrient partitioning. The limitation lies not in the principle itself but in treating its components as fixed or behaviorally simple. Energy expenditure can adapt during weight loss, appetite signals may intensify, and adherence is shaped by food availability, sleep, stress, medication, culture, income, and the built environment. Persistent metabolic adaptation after substantial weight loss illustrates why long-term weight maintenance cannot be reduced to willpower or calorie counting alone (Fothergill et al., 2016).

Traditional guidelines describe patterns that are appropriate for most people and provide a foundation for public policy. Precision nutrition adds value when clinically relevant heterogeneity is likely to change the decision—for example, when glycemic responses, medication effects, food intolerances, disease stage, cultural preferences, or treatment adherence differ. Personalization without a sound population-level foundation may amplify noise, encourage unnecessary testing, and turn ordinary dietary variation into a medical problem.

Accordingly, the central question is not whether generic guidance or precision nutrition is superior in every setting. It is whether additional individual data improve decisions enough to justify their cost, burden, and potential risks. A useful precision approach must demonstrate analytical validity, clinical validity, clinical utility, and feasibility rather than merely generating a more detailed report.

3. The Concept and Levels of Precision Nutrition

Precision nutrition is a multidisciplinary approach that develops targeted dietary advice from individual or subgroup characteristics. It can operate at several levels. Basic personalization uses dietary intake, anthropometry, clinical history, preferences, and lifestyle. Intermediate approaches add biomarkers, continuous glucose monitoring, or detailed phenotyping. More experimental approaches incorporate genomics, metabolomics, microbiome profiles, and algorithmic prediction. Greater biological detail does not automatically produce greater clinical value; each additional layer should answer a defined question and lead to an actionable decision (Kirk et al., 2021). The principal information layers used in precision nutrition are summarized in Table 1.

Table 1. Information Layers in Precision Nutrition

Information layer	Examples	Potential contribution
Clinical and phenotypic	Diagnosis, medication, BMI, body composition, laboratory findings	Risk stratification and treatment targets
Behavioral and contextual	Dietary pattern, preferences, sleep, activity, culture, food access	Feasibility, adherence, and equity
Digital	CGM, wearables, food records, mobile applications	Repeated and real-time monitoring
Multi-omics	Genomics, epigenomics, metabolomics, proteomics, microbiome	Mechanistic insight and hypothesis generation
Analytical	Statistical models and machine learning	Pattern recognition and outcome prediction

The often-cited goal of delivering the right intervention to the right person at the right time should therefore include two further conditions: the recommendation must be supported by evidence and be realistically implementable. Precision should refer to better decisions, not simply to the quantity of data collected.

4. Gut Microbiota and Individual Metabolic Responses

The gastrointestinal tract contains a complex ecosystem of microorganisms whose genes and metabolites interact with the host. The microbiota contributes to fermentation of otherwise indigestible substrates, production of short-chain fatty acids, bile-acid metabolism, immune regulation, and maintenance of the intestinal barrier (Fan & Pedersen, 2021). Diet is an important determinant of microbiota composition and function, but responses are also shaped by age, medication—especially antibiotics—geography, lifestyle, and baseline community structure.

Microbial metabolites provide plausible links between diet and metabolic health. Short-chain fatty acids such as butyrate can support epithelial integrity and participate in immune and metabolic signaling; other microbial products may contribute to inflammation under particular conditions (Agus et al., 2021). These mechanisms are biologically compelling, but association should not be confused with causation. A taxonomic difference between groups does not by itself establish a diagnostic biomarker or a dietary treatment target.

Microbiome-informed prediction was an important component of the model developed by Zeevi et al. (2015). Nevertheless, microbiome profiles are dynamic, laboratory pipelines differ, and algorithms trained in one population may not transfer reliably to another. An international consensus statement concluded that evidence is currently insufficient to recommend routine microbiome testing broadly in clinical practice and emphasized the need for standardized methods, transparent interpretation, and clinically relevant validation (Porcari et al., 2025).

Direct-to-consumer microbiome reports should therefore be interpreted cautiously. A clinically responsible report would need validated collection and sequencing procedures, an appropriate reference population, reproducible results, and evidence that acting on the result improves outcomes. Until these conditions are met, microbiome testing is better regarded as a research or carefully defined specialist tool than as a stand-alone basis for routine dietary prescriptions.

5. Multi-Omics and a Systems-Biology Perspective

Multi-omics approaches combine different layers of biological information to characterize pathways rather than isolated markers. Their promise lies in identifying response patterns that are not apparent from a single measurement. Their challenge is dimensionality: datasets may contain many more variables than participants, creating risks of overfitting, false discovery, and unstable prediction. High-quality study design, prespecified analysis, replication, and external validation are therefore essential (Hasin et al., 2017).

5.1. Nutrigenetics and Nutrigenomics

Nutrigenetics examines how genetic variation influences responses to dietary exposure, whereas nutrigenomics considers how nutrients and dietary patterns affect gene expression and related pathways. Although variants such as those in FTO have been associated with obesity susceptibility, common metabolic outcomes are polygenic and strongly modified by environment and behavior. Single-variant advice is therefore rarely sufficient. Genetic information is most useful when the underlying gene–diet association is scientifically validated, leads to actionable dietary advice, and is interpreted alongside relevant clinical, phenotypic, dietary, and contextual information (Grimaldi et al., 2017).

Translation into practice requires a distinction between statistical association and actionable dietary guidance. A gene-diet interaction should be biologically plausible, replicated in independent samples, and supported by reliable measurement of both genotype and dietary exposure. The comparison should

also demonstrate that genotype-informed advice adds value beyond conventional assessment. Proposed evidence frameworks therefore recommend evaluating analytical validity, scientific validity, clinical utility, and ethical implications before incorporating a variant into dietary advice (Grimaldi et al., 2017). This is particularly important for direct-to-consumer tests, where risk estimates derived from one ancestry group may not transfer accurately to another and where small effects can be presented with unwarranted certainty.

5.2. Metabolomics and Metabolic Phenotyping

Metabolomics measures small molecules in biological samples and can provide a dynamic snapshot of processes related to glucose regulation, lipid metabolism, inflammation, oxidative stress, and dietary exposure. Compared with the genome, the metabolome is closer to current physiology but is also more sensitive to timing, recent food intake, medication, specimen handling, and analytical platform. Repeated or standardized measurements may therefore be required before a metabolic signature can guide treatment.

In cardiometabolic research, metabolomic profiles have identified recurring associations between branched-chain and aromatic amino acids, lipid species, and future type 2 diabetes risk; however, the predictive contribution of these markers varies across cohorts and analytical platforms (Guasch-Ferré et al., 2016). Their most defensible near-term role may be to refine metabolic phenotypes, generate mechanistic hypotheses, and monitor response in well-designed studies rather than to dictate a diet from a single blood sample. Clinical translation requires reference ranges, harmonized pre-analytical procedures, reproducible assays, prospective validation, and evidence that the resulting classification changes a treatment decision or improves an outcome.

5.3. The Exposome and Social Context

The exposome encompasses environmental influences accumulated across the life course, including sleep, psychological stress, physical activity, pollutants, medication, socioeconomic conditions, and the food environment. Incorporating these factors prevents precision nutrition from becoming biologically deterministic. A recommendation that ignores affordability, food access, cultural eating patterns, caregiving responsibilities, or health literacy may be biologically sophisticated yet clinically ineffective.

The exposome concept was proposed to complement genomic information with a systematic account of environmental exposures across the life course (Wild, 2005). In nutrition, this perspective broadens the unit of analysis from the individual to the conditions that shape dietary choice. Neighborhood food

availability, pricing, marketing, employment schedules, housing stability, and public policy can constrain what a person is realistically able to eat (Mozaffarian et al., 2018). These variables should not be treated merely as noise to be adjusted away. They may modify both biological response and the feasibility of an intervention, and they are essential for determining whether personalization reduces or reproduces health inequalities.

5.4. Integrating Multi-Omics Data for Actionable Decisions

The scientific value of multi-omics does not arise from stacking datasets, but from integrating them around a defined clinical question. Genomic data may indicate relatively stable susceptibility; transcriptomic, proteomic, and metabolomic measurements may reflect more dynamic pathway activity; microbiome and exposome data add ecological and contextual information. Integration methods can identify latent factors, networks, or subgroups that would remain hidden in separate analyses, but the resulting patterns are sensitive to batch effects, missing data, temporal mismatch, population structure, and model choice (Hasin et al., 2017). Samples collected at different physiological states cannot be assumed to represent a single coherent biological profile.

A clinically useful pipeline should therefore begin with an outcome and decision threshold, not with the availability of data. Feature selection and model development should be separated from independent validation; performance should be compared with a simpler model based on routinely available clinical variables; and the final output should be interpretable enough to support shared decision-making. Studies such as those by Zeevi et al. (2015) and Berry et al. (2020) illustrate how microbiome, dietary, clinical, and behavioral data can improve prediction of postprandial responses. They also underline the need to test transportability, because an integrated signature may capture local dietary patterns, laboratory procedures, or population characteristics rather than a universally applicable mechanism.

6. Artificial Intelligence as an Enabling Technology

Artificial intelligence can integrate heterogeneous data, detect patterns, classify foods from images, estimate intake, and predict selected metabolic responses. A 2025 scoping review identified rapid growth in AI-driven precision-nutrition research, especially in diabetes and cardiometabolic applications, but also highlighted limited attention to minority and cultural factors (Wu et al., 2025). The literature includes supervised learning, deep learning, natural-language processing, computer vision, and recommender

systems; however, development studies remain more common than rigorous evaluations of clinical impact. Major applications of artificial intelligence in precision nutrition, together with their potential benefits and limitations, are summarized in Table 2.

Table 2. Applications, Potential Benefits, and Limitations of Artificial Intelligence in Precision Nutrition

Application	Potential benefit	Main risk or limitation
CGM-supported prediction	Identification of glycemic patterns	Measurement burden and uncertain relevance in low-risk users
Food-image analysis	Faster dietary recording	Portion-size and mixed-dish errors
Mobile coaching and chatbots	Scalable reminders and behavioral support	Unsafe or context-insensitive advice
Risk prediction	Prioritization and treatment selection	Bias, overfitting, and poor transportability
Clinical decision support	Synthesis of complex information	Automation bias and unclear accountability

An accurate model is not automatically a useful clinical tool. Performance should be reported with appropriate discrimination and calibration measures, compared against existing practice, and tested in an independent population. Prospective evaluation should determine whether use of the system improves patient-important outcomes, adherence, workload, or equity. Models also require monitoring because changes in populations, sensors, food products, and clinical workflows can degrade performance over time.

Data governance is equally important. Dietary records, genomic information, microbiome profiles, and continuous sensor data can reveal sensitive health and behavioral information. Meaningful consent, data minimization, secure storage, transparent secondary use, conflict-of-interest disclosure, and routes to challenge automated recommendations are necessary components of responsible implementation (Panayotova, 2025; Wu et al., 2025).

7. From Scientific Promise to Clinical Utility

Precision nutrition has moved beyond proof-of-concept, but evidence is uneven across applications. Zeevi et al. (2015) and Berry et al. (2020) established substantial variability in postprandial responses. Food4Me showed that personalized advice can improve selected health-related behaviors (Celis-

Morales et al., 2017). In an 18-week randomized controlled trial, Bermingham et al. (2024) reported that a personalized dietary program improved several cardiometabolic outcomes compared with standard dietary advice. These studies support the concept, but they do not validate every commercial test, algorithm, or personalized diet.

Clinical utility requires more than statistical prediction. A useful intervention should improve outcomes that matter to patients, add benefit beyond accessible conventional care, avoid harm, and remain feasible over time. Long-term adherence, cost-effectiveness, implementation in routine services, and effects across diverse ethnic and socioeconomic populations remain important evidence gaps. The comparison group also matters: a complex personalized program may appear effective against minimal advice but offer less incremental benefit when compared with high-quality dietetic care. The key domains that should be evaluated before clinical implementation are summarized in Table 3.

Table 3. Evaluation Domains for the Clinical Implementation of Precision Nutrition

Evaluation domain	Key question before implementation
Analytical validity	Does the test or sensor measure the intended feature accurately and reproducibly?
Clinical validity	Is the measured feature reliably associated with the outcome in the target population?
Clinical utility	Does using the result improve decisions or patient-important outcomes?
Feasibility	Can patients and professionals use the intervention consistently in routine care?
Equity and ethics	Are benefits and burdens distributed fairly, with privacy and autonomy protected?

8. Will Artificial Intelligence Replace Dietitians?

AI can automate repetitive tasks, summarize large datasets, and support monitoring, but dietetic practice involves more than information processing. Dietitians assess nutritional status, identify clinical risk, interpret uncertain evidence, negotiate goals, adapt advice to culture and resources, and respond to changing medical and psychosocial needs. Empathy, therapeutic alliance, professional accountability, and safeguarding cannot be delegated to an algorithm without loss of essential clinical context. Current reviews therefore

position AI primarily as a support for dietary assessment, prediction, and decision-making rather than as an autonomous substitute for nutrition professionals (Panayotova, 2025; Wu et al., 2025).

The more plausible future is an AI-assisted hybrid model. In this model, technology performs bounded tasks under professional supervision, while the dietitian validates inputs, explains uncertainty, identifies contraindications, and integrates recommendations into person-centered care. Clear governance should define which decisions may be automated, which require review, how errors are reported, and who remains accountable. Digital competence and critical appraisal will therefore become increasingly important components of dietetic education. This human-supervision model is consistent with the World Health Organization's emphasis on protecting autonomy, promoting transparency, ensuring accountability, and maintaining human control over health-care decisions (World Health Organization, 2021).

9. A Responsible Implementation Pathway

The transition from research to practice should be staged. First, the clinical problem and target population must be specified. Second, the minimum data needed to answer that problem should be selected; collecting more information than necessary increases burden and privacy risk. Third, analytical and clinical validity should be established in the intended population. Fourth, the intervention should be compared prospectively with current best care. Finally, implementation should include monitoring for adverse effects, unequal performance, data drift, workload, and patient experience. These requirements align with established health-AI governance principles that call for transparency, responsibility, inclusiveness, responsiveness, and protection of human autonomy throughout the technology life cycle (World Health Organization, 2021).

Precision nutrition services should also preserve a meaningful non-digital alternative. Individuals who cannot afford wearables, do not have stable internet access, have limited digital literacy, or prefer not to share biological data should not receive inferior care. The success of precision nutrition should be judged not only by predictive accuracy, but by whether it improves health without widening existing nutritional and health inequalities.

10. Clinical Vignette: Applying Precision Nutrition Without Overmedicalization

Consider an adult with obesity and type 2 diabetes whose glycemic control remains above the individualized treatment target despite receiving standard

dietary education. The first step is not an omics panel or a commercial microbiome test. A dietitian would begin with a structured assessment of medication, meal timing, usual foods, portion patterns, hypoglycemia risk, sleep, physical activity, financial constraints, readiness for change, and the patient's priorities. Laboratory findings and anthropometry would be interpreted alongside the person's work schedule and culturally familiar meals. This establishes a clinically meaningful question: which modifiable pattern is most likely to improve glycemic control while remaining sustainable?

Population-based guidance would provide the foundation—for example, improving food quality, fiber intake, meal regularity, and the balance of carbohydrate-containing foods. Personalization would then refine the plan. If routine records suggest large and unpredictable postprandial excursions, a time-limited period of continuous glucose monitoring might be considered when the information is expected to change dietary or medical management. The patient and dietitian could compare responses to realistic meal alternatives rather than labeling individual foods as universally 'good' or 'bad.' Medication timing, sleep loss, and physical activity would be considered as possible explanations for variation.

More complex testing would be added only if it met a defined decision threshold. A direct-to-consumer microbiome test would not be used routinely because current evidence does not establish sufficient clinical utility for stand-alone dietary prescription (Porcari et al., 2025). Genetic or metabolomic testing would similarly require a validated indication and an actionable result. Progress would be evaluated using patient-important outcomes such as glycemic control, treatment burden, dietary adequacy, quality of life, and the ability to maintain the plan—not by algorithmic prediction alone.

This vignette illustrates a stepwise model of precision nutrition. Conventional clinical assessment and dietary guidance remain the base; low-burden individual data are used first; advanced technologies are introduced selectively; and every additional measurement must be justified by its capacity to improve a decision. The approach is therefore precise without becoming technologically excessive.

11. Precision Nutrition in the Context of Türkiye

Implementation in Türkiye should begin with national dietary guidance and local patterns of food preparation rather than importing algorithms developed primarily in other populations. Türkiye Beslenme Rehberi (TÜBER) 2022 provides the population-level foundation for healthy eating and can serve as the reference layer upon which clinically justified personalization is built (Republic

of Türkiye Ministry of Health, 2022). Algorithms and food-recognition systems should be evaluated with Turkish-language interfaces and datasets that adequately represent regional dishes, mixed meals, portion practices, socioeconomic diversity, age groups, and different levels of health literacy.

Cost and access are central considerations. Continuous glucose monitors, microbiome analyses, omics panels, and subscription-based applications may be unavailable or unaffordable for many individuals. Introducing these technologies without an assessment of incremental benefit could direct resources away from interventions with established value, including access to dietitians, diabetes education, healthy food environments, and long-term follow-up. Pilot programs should therefore compare technology-assisted care with high-quality conventional dietetic care and report cost-effectiveness, workload, adherence, and distribution of benefit across socioeconomic groups.

Data governance requires particular attention because precision nutrition can combine dietary behavior, medical history, sensor records, genetic information, and microbiome profiles. Under Türkiye's personal-data protection framework, health, genetic, and biometric data are treated as special-category personal data and require an appropriate legal basis together with strengthened technical and administrative safeguards (Kişisel Verileri Koruma Kurumu [KVKK], 2024). Consent materials should explain which data are collected, why they are needed, how long they will be retained, whether they will be transferred or reused, and how an individual can exercise applicable rights. Data minimization is especially important: a service should not collect genomic or continuous behavioral data merely because the technology permits it.

A responsible national pathway would combine multidisciplinary clinical governance, local validation, interoperable but secure digital systems, professional training, and meaningful patient involvement. Dietitians should participate in dataset design, outcome selection, algorithm evaluation, and the development of culturally appropriate recommendations. In this way, precision nutrition can complement Türkiye's public-health priorities while avoiding a two-tier model in which technologically intensive care is available only to those who can pay for it.

12. Conclusion

Nutrition science is moving from uniform recommendations toward a layered model in which population guidance is supplemented, when useful, by clinical, behavioral, digital, and biological information. Research on postprandial responses, the gut microbiota, multi-omics, and artificial intelligence has demonstrated genuine potential for more targeted nutritional

care (Ordovas et al., 2018; Berry et al., 2020). Randomized trials now provide early evidence of benefit for selected personalized programs (Celis-Morales et al., 2017; Bermingham et al., 2024).

At the same time, biological complexity should not be mistaken for clinical readiness. Microbiome tests, omics panels, and predictive algorithms vary in validity, transportability, cost, and usefulness. Safe implementation requires external validation, transparent governance, long-term outcome studies, and careful attention to privacy, social context, and equity. Precision nutrition is therefore best understood as an evidence-guided extension of high-quality dietetic practice—not as a replacement for public-health guidance or professional judgment.

References

Agus, A., Clément, K., & Sokol, H. (2021). Gut microbiota-derived metabolites as central regulators in metabolic disorders. Gut, 70(6), 1174–1182. https://doi.org/10.1136/gutjnl-2020-323071

Bermingham, K. M., Linenberg, I., Polidori, L., Asnicar, F., Arrè, A., Wolf, J., et al. (2024). Effects of a personalized nutrition program on cardiometabolic health: A randomized controlled trial. Nature Medicine, 30(7), 1888–1897. https://doi.org/10.1038/s41591-024-02951-6

Berry, S. E., Valdes, A. M., Drew, D. A., Asnicar, F., Mazidi, M., Wolf, J., et al. (2020). Human postprandial responses to food and potential for precision nutrition. Nature Medicine, 26(6), 964–973. https://doi.org/10.1038/s41591-020-0934-0

Celis-Morales, C., Livingstone, K. M., Marsaux, C. F. M., Macready, A. L., Fallaize, R., O'Donovan, C. B., et al. (2017). Effect of personalized nutrition on health-related behaviour change: Evidence from the Food4Me European randomized controlled trial. International Journal of Epidemiology, 46(2), 578–588. https://doi.org/10.1093/ije/dyw186

Fan, Y., & Pedersen, O. (2021). Gut microbiota in human metabolic health and disease. Nature Reviews Microbiology, 19(1), 55–71. https://doi.org/10.1038/s41579-020-0433-9

Fothergill, E., Guo, J., Howard, L., Kerns, J. C., Knuth, N. D., Brychta, R., et al. (2016). Persistent metabolic adaptation 6 years after 'The Biggest Loser' competition. Obesity, 24(8), 1612–1619. https://doi.org/10.1002/oby.21538

Grimaldi, K. A., van Ommen, B., Ordovas, J. M., et al. (2017). Proposed guidelines to evaluate scientific validity and evidence for genotype-based dietary advice. Genes & Nutrition, 12, 35. https://doi.org/10.1186/s12263-017-0584-0

Guasch-Ferré, M., Hruby, A., Toledo, E., Clish, C. B., Martínez-González, M. A., Salas-Salvadó, J., & Hu, F. B. (2016). Metabolomics in prediabetes and diabetes: A systematic review and meta-analysis. Diabetes Care, 39(5), 833–846. https://doi.org/10.2337/dc15-2251

Hasin, Y., Seldin, M., & Lusis, A. (2017). Multi-omics approaches to disease. Genome Biology, 18, 83. https://doi.org/10.1186/s13059-017-1215-1

Kirk, D., Catal, C., & Tekinerdogan, B. (2021). Precision nutrition: A systematic literature review. Computers in Biology and Medicine, 133, 104365. https://doi.org/10.1016/j.compbiomed.2021.104365

Kişisel Verileri Koruma Kurumu. (2024). Özel nitelikli kişisel verilerin işlenmesine ilişkin rehber [Guidance on the processing of special

categories of personal data]. https://www.kvkk.gov.tr/Icerik/8184/Ozel-Nitelikli-Kisisel-Verilerin-Islenmesine-Iliskin-Rehber

Mozaffarian, D., Angell, S. Y., Lang, T., & Rivera, J. A. (2018). Role of government policy in nutrition—barriers to and opportunities for healthier eating. BMJ, 361, k2426. https://doi.org/10.1136/bmj.k2426

Ordovas, J. M., Ferguson, L. R., Tai, E. S., & Mathers, J. C. (2018). Personalised nutrition and health. BMJ, 361, k2173. https://doi.org/10.1136/bmj.k2173

Panayotova, G. G. (2025). Artificial intelligence in nutrition and dietetics: A comprehensive review of current research. Healthcare, 13(20), 2579. https://doi.org/10.3390/healthcare13202579

Porcari, S., Mullish, B. H., Asnicar, F., et al. (2025). International consensus statement on microbiome testing in clinical practice. The Lancet Gastroenterology & Hepatology, 10(2), 154–167. https://doi.org/10.1016/S2468-1253(24)00311-X

Republic of Türkiye Ministry of Health. (2022). Türkiye Beslenme Rehberi (TÜBER) 2022 [Dietary guidelines for Türkiye]. General Directorate of Public Health. https://hsgm.saglik.gov.tr/media/attachments/2025/05/12/turkiye-beslenme-rehberi-2022.pdf

Wild, C. P. (2005). Complementing the genome with an ‘exposome’: The outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiology, Biomarkers & Prevention, 14(8), 1847–1850. https://doi.org/10.1158/1055-9965.EPI-05-0456

World Health Organization. (2021). Ethics and governance of artificial intelligence for health: WHO guidance. World Health Organization. https://www.who.int/publications/i/item/9789240029200

Wu, X., Oniani, D., Shao, Z., Arciero, P., Sivarajkumar, S., Hilsman, J., et al. (2025). A scoping review of artificial intelligence for precision nutrition. Advances in Nutrition, 16(4), 100398. https://doi.org/10.1016/j.advnut.2025.100398

Zeevi, D., Korem, T., Zmora, N., Israeli, D., Rothschild, D., Weinberger, A., et al. (2015). Personalized nutrition by prediction of glycemic responses. Cell, 163(5), 1079–1094. https://doi.org/10.1016/j.cell.2015.11.001