Current Studies for Sustainable Health

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Preface

Sustainable health has become an essential organizing principle for contemporary health research, policy, and practice, as societies confront escalating chronic disease burdens, demographic transitions, environmental degradation, and widening social inequities. The concept extends well beyond the prevention or treatment of illness; it encompasses the capacity of individuals, communities, and health systems to maintain well-being across the life course while safeguarding social, economic, and environmental resources for future generations. Current Studies for Sustainable Health brings together a diverse body of scholarship that reflects this expanded understanding, offering an integrated and multidisciplinary perspective on how sustainable health can be conceptualized, operationalized, and advanced.

The chapters in this volume collectively position health as a dynamic and interconnected process shaped by biological regulation, environmental exposures, social participation, professional practice, and institutional structures. Several contributions foreground biological sustainability by examining how early-life programming, circadian organization, microbiota host interactions, and reproductive capacity influence long-term health trajectories. The discussion of the microbiota gut brain axis in mood disorders illustrates how nutrition, lifestyle, and ecological considerations intersect with neuropsychiatric health, providing potentially low-risk and sustainable adjuncts to conventional therapies. Similarly, the examination of fetal origins of adult disease highlights the intrauterine period as a critical window in which environmental toxicants and maternal health exert lasting effects across generations, underscoring the importance of preventive and holistic approaches.

Temporal biology and circadian rhythms further enrich this biological framework by demonstrating that alignment with endogenous timing systems is central to physiological resilience, rehabilitation outcomes, and chronic pain modulation. Chronotherapy, exercise timing, sleep hygiene, and light exposure emerge as evidence-informed, resource-efficient strategies that integrate clinical effectiveness with sustainability principles. Complementing these perspectives, the chapter on fertility preservation situates reproductive autonomy within sustainable health, emphasizing how medical, technological, and ethical advances support long-term psychological well-being, social continuity, and equitable human development.

Prevention and early intervention are recurring themes throughout the volume. The synthesis of contemporary evidence on skin cancer illustrates how molecular pathophysiology, genetic susceptibility, and environmental exposure converge in a largely preventable disease burden. By emphasizing primary prevention, photoprotection, and early detection, this contribution reinforces the role of public health strategies in reducing long-term healthcare demands and associated resource use. In parallel, maternal health and pregnancy-focused exercise interventions, such as Pilates-based breathing and pelvic floor training, demonstrate how low-cost, accessible practices can support healthy pregnancies, facilitate recovery, and contribute to sustainable outcomes for both mother and child.

Equally central to this book is the recognition that sustainable health cannot be achieved without addressing social justice, participation, and equity. Chapters focusing on homelessness, caregiving for children with special needs, and community-based rehabilitation frame health as inseparable from meaningful occupation, social inclusion, and human rights. These contributions highlight how occupational deprivation, caregiver burden, and structural vulnerability undermine long-term well-being, and they demonstrate the value of rights-based, community-oriented, and interdisciplinary models in restoring participation and resilience. From this perspective, sustainability is not only environmental or economic, but also ethical and social.

Health professionals are presented as key agents in advancing sustainable health systems. The evolving roles of physiotherapists, occupational therapists, and rehabilitation professionals illustrate a shift from narrowly defined clinical practice toward broader engagement in public health, education, policy development, and intersectoral collaboration. Rehabilitation services, particularly community-based and home-centered models, are shown to enhance long-term survival, quality of life, and social participation while supporting system-level efficiency. Within the Turkish context, these discussions are grounded in demographic realities, institutional challenges, and policy priorities, offering context-sensitive insights with broader international relevance.

At the systems and policy level, the volume critically examines the environmental footprint of healthcare and the necessity of embedding sustainability into infrastructure, service delivery, and professional education. Eco-friendly facility design, resource efficiency, and sustainability-focused curricula are identified as prerequisites for resilient health systems. Traditional and complementary medicine is addressed as an evolving domain that requires regulatory oversight, scientific evaluation, and evidence-based integration to ensure safety, effectiveness, and coherence with sustainable health goals.

Taken together, Current Studies for Sustainable Health offers a comprehensive and forward-looking synthesis that bridges molecular science, clinical practice, social theory, and policy analysis. By integrating diverse disciplinary perspectives and situating health within its broader ecological and societal context, the book aims to inform researchers, clinicians, educators, and policymakers seeking to design health systems that are preventive, inclusive, ethically grounded, and sustainable over the long term.

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In This Book

Chapter 1

Major depressive disorder (MDD) and anxiety are prevalent psychiatric conditions often resistant to conventional pharmacological and psychotherapeutic interventions. Recent advances highlight the gut microbiota as a central regulator of mental health through the microbiota–gut–brain axis, influencing immune, endocrine, and neural pathways. Dysbiosis is associated with systemic inflammation, neurotransmitter imbalance, and hypothalamic-pituitary-adrenal (HPA) axis dysfunction, all contributing to mood symptoms. This chapter explores microbiota-targeted interventions-psychobiotics, prebiotics, omega-3 fatty acids, polyphenols, and sustainable diets such as the Mediterranean diet-as adjuncts or alternatives to antidepressants. Evidence from clinical and preclinical studies suggests these strategies improve depressive and anxiety symptoms, enhance microbial diversity, and offer fewer side effects. Future directions include multi-omics profiling, microbiome-informed precision psychiatry, and novel approaches such as designer probiotics and postbiotics, integrating sustainability with mental health care.

Chapter 2

Physiotherapists are assuming an progressively significant role in the pursuit of the Sustainable Development Goals (SDGs), transcending their traditional role as individual health service providers to become pivotal agents in community health promotion and the mitigation of health inequalities. Within the SDG framework, physiotherapists have a multifaceted role that extends beyond the mere improvement of patients' functional capacity. They participate in public health programmes, education and awareness campaigns, community-based interventions, and contribute to policy development processes. The active involvement of these professionals in national and international collaborations has been demonstrated to enhance the sustainability of healthcare services by fostering knowledge and resource sharing, and contributing to the reduction of carbon footprints. Consequently, physiotherapists serve as a critical bridge in the implementation of the SDGs and directly facilitate the achievement of the sustainable development vision by improving health and well-being at both individual and societal levels.

Chapter 3

Homelessness is a complex public health and social justice issue that extends far beyond the lack of shelter and profoundly affects individuals' physical health, mental well-being, safety, and social participation. This chapter examines homelessness within the framework of community health principles and occupational justice, emphasizing that participation in meaningful daily activities -including self-care, education, work, and leisure- is a fundamental human right. The chapter outlines definitions and classifications of homelessness, explores its national and international context, and details its wide-ranging impacts on health. Drawing on global and local best-practice models, including Housing First, street medicine, and services developed by municipalities and civil society in Türkiye, the chapter highlights how sustainable, rights-based, and interdisciplinary approaches are essential in addressing homelessness.

From an occupational therapy perspective, homelessness creates profound occupational deprivation, imbalance, alienation, and marginalization. Occupational therapists play a key role in restoring participation by supporting basic needs, strengthening daily living skills, enhancing mental well-being, promoting community belonging, and advocating for accessible environments and housing. The chapter offers multilevel (individual, community, national) intervention strategies grounded in occupational therapy principles, and concludes with sustainable policy recommendations aimed at improving quality of life, fostering social inclusion, and advancing occupational justice for individuals experiencing homelessness.

Chapter 4

This chapter examines sustainable health within the context of parents caring for children with special needs, emphasizing that protecting the long-term physical, psychological, and social well-being of caregivers is essential for both family functioning and the quality of care provided. Sustainable health is understood not only as addressing existing health problems but also as maintaining well-being through supportive environments, community resources, and equitable health policies. The chapter highlights the significant challenges faced by caregivers -including high caregiving demands, stress, disrupted family dynamics, and social isolation- and discusses how these challenges affect their health and daily functioning. Within this framework, occupational therapy plays a critical role by offering holistic, family-centered, and resilience-focused interventions that strengthen caregivers' daily living skills, promote participation in meaningful activities, facilitate "me time," and support psychological empowerment. Through co-occupation, ergonomic strategies, and education-based interventions, occupational therapists help caregivers manage stress, enhance self-efficacy, and sustain their caregiving roles more healthily. Drawing on international frameworks such as the WHO's sustainable health goals and Türkiye's 2030 Barrier-Free Vision, the chapter emphasizes the importance of community-based services, social support systems, and interdisciplinary collaboration in promoting sustainable caregiver health. Ultimately, the chapter argues that evidence-based occupational therapy interventions, integrated with national and community-level policies, can significantly enhance caregivers' quality of life, support long-term health, and contribute to more resilient and inclusive societies.

Chapter 5

Sustainability refers to the coordinated efforts and actions taken to conserve the Earth's finite natural resources, ensuring they remain available for future generations. The dominant post-World War II model of consumption-driven growth led to significant ecological problems. As the negative effects of this approach became a serious threat to the well-being of subsequent generations, the concept of sustainability became critically important. In fact, the continued prosperity of development efforts depends on achieving sustainability. Therefore, sustainability must be understood as a multifaceted issue, encompassing environmental, economic, social, and health-related concerns.

The healthcare sector is a vital area for sustainability initiatives because it heavily consumes energy, water, chemicals, and single-use items. Integrating environmentally sound practices into this field is essential for protecting both the environment and public health. This integration is complex, however, as it must be accomplished without diminishing the quality or effectiveness of healthcare services. Both healthcare organizations and their personnel bear significant responsibility in this pursuit. A key strategy for improving the sustainability performance of healthcare facilities is to design and build them as eco-friendly, energy-efficient structures based on resource conservation principles. Moreover, healthcare workers' involvement and understanding of sustainability can be developed through focused professional training and institutional education programs. A notable deficiency in the current literature is the lack of dedicated sustainability courses and practical modules in the core curricula of medical and nursing schools. In conclusion, sustainability is a comprehensive concept requiring an integrated assessment of its environmental, economic, and social components. Consequently, embedding sustainability into the structures of the healthcare sector and its educational groundwork is crucial for current and future success. Progress in this domain has the potential to substantially contribute to global sustainability targets.

Chapter 6

Multilevel thresholding is a fundamental image segmentation technique widely used in medical image processing and computer vision applications. Although Otsu's variance-based method provides effective segmentation results, its computational cost increases exponentially with the number of threshold levels, making it unsuitable for high-dimensional and real-time medical imaging tasks. To overcome this limitation, metaheuristic optimization algorithms have been extensively employed due to their ability to efficiently search complex solution spaces. However, many conventional metaheuristics suffer from premature convergence, slow convergence speed, and insufficient balance between exploration and exploitation, particularly at higher threshold levels.

In this study, the Red Fox Optimization (RFO) algorithm and an enhanced version, termed Modified Red Fox Optimization (MRFO), are investigated for multilevel image thresholding applications. Inspired by the adaptive hunting behavior of red foxes, RFO offers an effective balance between global exploration and local exploitation. To further improve its performance, MRFO incorporates several strategic enhancements, including chaotic map integration, an adaptive control factor, a modified position update mechanism, and an adaptive mutation operator. These improvements are designed to enhance population diversity, accelerate convergence, and prevent entrapment in local optima.

The proposed MRFO algorithm is evaluated on Brain MRI, Retina, Cells3D, and Mitosis image datasets for multilevel thresholding problems involving 2 to 5 threshold levels. Its performance is compared with Particle Swarm Optimization (PSO), Genetic Algorithm (GA), Ant Colony Optimization (ACO), and Grey Wolf Optimization (GWO). Experimental results demonstrate that MRFO consistently achieves superior segmentation performance in terms of PSNR and SSIM while exhibiting faster computational efficiency and more stable convergence behavior than the compared algorithms. The findings confirm the effectiveness of MRFO as a robust and efficient optimization framework for complex medical image segmentation tasks.

Chapter 7

In this chapter, we present an up-to-date synthesis of the pathophysiology and epidemiology of skin cancer, with emphasis on both melanoma and non-melanoma entities. We review contemporary data on global incidence, geographic distribution, demographic risk profiles, and the potential contribution of diagnostic intensity and overdiagnosis to rising case numbers. We then examine UV radiation–induced DNA damage and the involvement of major oncogenic and tumor suppressor pathways (TP53, RAS/MAPK, PI3K/AKT/mTOR, CDKN2A), as well as germline susceptibility (including MC1R variants and genodermatoses) and the cutaneous microbiome. Finally, we underscore that primary prevention, early detection, and evidence-based photoprotection remain critical to reducing the global burden of skin cancer.

Chapter 8

This chapter synthesizes the foundational role of circadian rhythms (CRs) as ubiquitous endogenous biological timing systems that are primarily responsible for synchronizing organisms to the 24-hour environmental cycle. Their detailed architecture involves a hierarchical organization in which the central pacemaker, the suprachiasmatic nucleus (SCN), governs tissue-specific peripheral clocks through coordination by the molecular machinery of the transcriptional–translational feedback loop (TTFL). Circadian rhythms are critically important in rehabilitation sciences, as they regulate essential physiological processes such as physical performance, muscle strength, and the rhythmic secretion of key hormones, including growth hormone and cortisol.

Importantly, sustained circadian misalignment, referred to as chronodisruption, is strongly associated with the pathophysiology of chronic musculoskeletal pain and the development of heightened central sensitization. This dysregulation often manifests clinically as abnormal vascular rhythms, such as non-dipper blood pressure patterns. Chronotherapy offers a strategic framework to correct this temporal dissonance through the timed application of potent environmental synchronizers, or Zeitgebers. These include structured exercise timing (chronexercise), controlled light exposure, and rigorous sleep hygiene practices. This review highlights the scientific imperative for physiotherapists to integrate principles of circadian biology into clinical practice to optimize patient recovery trajectories and maximize physiological responsiveness.

Chapter 9

The global rise in the incidence of chronic diseases during the late twentieth century has underscored that disease etiology extends beyond genetic predispositions and adult lifestyle factors. Within this framework, the Fetal Origins of Adult Diseases (FOAD) hypothesis highlights a strong association between low birth weight and the subsequent development of various chronic conditions, identifying the intrauterine period as a critical biological window that programs long-term health outcomes. This hypothesis aligns with the holistic approach historically emphasized in numerous traditional medical systems, which posit that maternal health before and during pregnancy is decisive for the well-being of future generations. These traditions advocate for the physical, emotional, and spiritual equilibrium of the mother, as well as her preparation for the birthing process. The FOAD hypothesis is grounded in the concept of "developmental plasticity," whereby the fetus adapts to in utero environmental cues through metabolic reprogramming as a survival strategy. Nevertheless, the escalating environmental toxicity associated with modern lifestyles adversely affects these adaptive processes. Contemporary research demonstrates that the placenta is permeable to a wide range of synthetic toxicants, exposing the fetus to chemical burdens even before birth. The detection of hundreds of chemicals in umbilical cord blood indicates that fetal development occurs under substantially greater environmental stress than previously recognized. This heightened toxic exposure can cause permanent disruptions in organogenesis and contributes to the pathogenesis of congenital anomalies and later-life conditions, including hormonal disorders, infertility, diabetes, and cancer. Consequently, the environmental toxic burden associated with modern living constitutes a significant threat to both maternal and fetal health, with long-term implications for subsequent generations. Mitigating this risk and promoting sustainable health necessitates the reduction of environmental toxicants and the enhancement of endogenous detoxification pathways, ideally through a comprehensive, holistic health approach.

Chapter 10

Contemporary health systems must be designed not only to provide accessible and equitable care but also to ensure long-term economic viability and social responsiveness. In this context, rehabilitation services in their physical, psychosocial, and vocational dimensions—constitute a vital pillar of sustainable health systems. This chapter aims to examine the long-term contributions of rehabilitation services to public health and to explore the key principles of sustainability within the context of the Turkish healthcare system.

The chapter synthesizes evidence, demonstrating that rehabilitation's impact extends beyond acute recovery. International data from stroke, cardiac, and geriatric rehabilitation studies reveal that sustained rehabilitation practices significantly enhance long-term survival, reduce hospital readmission rates, and markedly improve quality of life. Specifically, Community-Based Rehabilitation (CBR) and home-based care models ensure systemic sustainability by strengthening not only functional independence but also social participation and community adaptation.

Türkiye’s rapid demographic shifts (an aging population and growing chronic disease burden) increase the demand for rehabilitation, necessitating that services are financially viable, institutionally integrated, and socially inclusive.The Turkish literature underscores the importance of preventive rehabilitation in chronic disease management and vocational rehabilitation for persons with disabilities, while simultaneously pointing to structural challenges such as the lack of long-term care insurance and regional infrastructural inequities.

Key principles for establishing sustainable rehabilitation systems are emphasized: accessibility, system integration, resource efficiency, community engagement, and data-driven monitoring. Drawing on international examples (e.g., rural models in New Zealand, cultural adaptation strategies), the chapter recommends expanding tele-rehabilitation, strengthening the family physician network, and enhancing multidisciplinary capacity within the Turkish context.

In conclusion, rehabilitation must be transformed from a marginal service into a core function of the health system. Policy priorities such as addressing the lack of longitudinal cohort studies, standardizing outcome measures like the ICF, and establishing long-term care insurance mechanisms are critical for building a resilient and equitable rehabilitation ecosystem for the future. This chapter reinforces the thesis that sustainable rehabilitation is an investment that not only preserves individual function but also strengthens public health resilience and social cohesion.

Chapter 11

Traditional and Complementary Medicine (TCM) encompasses a wide array of culturally rooted practices used throughout history to prevent, diagnose, and treat physical and mental illnesses. Although definitions vary globally, institutions such as the World Health Organization (WHO), the U.S. National Center for Complementary and Integrative Health (NCCIH), and the European Federation for Complementary and Alternative Medicine (EFCAM) have contributed to a conceptual framework distinguishing traditional, complementary, alternative, and integrative approaches. In Turkey, regulatory progress has been significant, culminating in the 2014 Traditional and Complementary Medicine Practices Regulation, which standardized training requirements, practitioner qualifications, and authorized medical centers. This regulatory framework formally recognizes 15 therapeutic modalities, including phytotherapy, larval therapy, prolotherapy, music therapy, osteopathy, mesotherapy, chiropractic, homeopathy, ozone therapy, reflexology, cupping therapy, hirudotherapy, apitherapy, hypnotherapy, and acupuncture.

Each modality carries distinct historical foundations and therapeutic mechanisms. Phytotherapy employs standardized medicinal plants; larval therapy utilizes Lucilia sericata larvae for selective debridement; prolotherapy promotes connective tissue repair via controlled inflammation; and music therapy provides psychological and physiological benefits traced back to ancient civilizations. Manual approaches such as osteopathy and chiropractic focus on restoring structural and functional balance. Other modalities such as mesotherapy, homeopathy, ozone therapy, cupping, and apitherapy offer diverse applications ranging from immunomodulation to localized therapeutic stimulation.

Public interest in TCM has grown globally and in Turkey due to increased life expectancy, chronic disease prevalence, dissatisfaction with conventional treatment limitations, and widespread informal information sources. Despite high usage rates particularly among older adults, cancer patients, and families—professional guidance remains limited. This gap highlights the need for clinicians to engage in evidence-based discussions, ensuring safe integration of traditional practices with conventional medical care. Overall, TCM represents an evolving healthcare dimension that necessitates informed regulation, scientific evaluation, and interdisciplinary collaboration to support sustainable health systems.

Chapter 12

Pregnancy is a critical period in a woman's life when her bio-psychosocial balance shifts, her roles within the family and workplace change, and the parent-child bond between mother and baby is established. During pregnancy, changes occur in physiological and physical characteristics. Pilates exercises can be performed during each trimester of pregnancy. The most important of these exercises are breathing-focused exercises and pelvic floor exercises. Pilates exercises can be performed during each trimester, but there are points to consider. Pilates exercises should be performed during pregnancy. A comfortable pregnancy is important for the delivery and postpartum period.

Chapter 13

Unlike the classical nutritional model, which focuses solely on the chemical components of food, the quantum nutrition approach addresses the material, energy, and information dimensions of life within a holistic framework. Based on the assumption that the human body functions as an electromagnetic system, the vibrational frequencies of foods, their biophoton content, and their ability to regulate energy flow at the cellular level form the basis of this approach. Fresh, natural, and sun-grown foods are believed to carry high frequencies, while processed and refined foods weaken cellular communication, leading to energy blockages.

Quantum nutrition defines the sustainability of health through three dimensions: the physical matter dimension, the energy frequency dimension, and the biophoton-mediated information dimension. Optimizing mitochondrial energy production, reducing electromagnetic environmental loads, mineral balance, and regular water consumption are important components of this process. Alkaline and natural spring waters, in particular, are said to strengthen the energy landscape and support cellular communication.

Nutritional timing is critical for aligning with the circadian rhythm and is directly related to hormone release, metabolic rate, and cellular repair processes. Therefore, nutritional regimens tailored to different frequency requirements at different stages of the day are recommended. It is emphasized that physical activity, sleep patterns, and mental state also affect the energy field, and therefore, quantum nutrition should be considered in conjunction with lifestyle components.

Based on the idea that chronic diseases may be rooted in cellular energy deficiencies, oxidative stress, and information flow disorders, quantum nutrition offers not only a preventative but also a holistic healing framework. Ultimately, this approach can be described as a comprehensive model that aims to maintain long-term health by synchronizing an individual's biological, energetic, and conscious levels.

Chapter 14

Fertility preservation (FP) comprises a growing array of medical, surgical, and biotechnological strategies that safeguard reproductive potential in individuals facing gonadotoxic treatments, systemic diseases, or age-related fertility decline. With advances in cryobiology, assisted reproductive technologies, and a deeper understanding of gonadal physiology, FP has transitioned from an experimental practice primarily targeting oncology patients to a mainstream component of reproductive medicine. Current FP methods including oocyte and embryo cryopreservation, ovarian tissue cryopreservation, sperm banking, and in selected cases pharmacological ovarian suppression are implemented according to age, diagnosis, treatment urgency, and available reproductive material. For males, sperm cryopreservation remains the most reliable and effective technique, while testicular tissue storage is reserved for research protocols in prepubertal boys. For females, vitrification has markedly improved survival and pregnancy rates, positioning oocyte cryopreservation as an established option equivalent to embryo freezing. Ovarian tissue cryopreservation represents the only feasible approach for prepubertal girls and for patients requiring urgent therapy without stimulation.

Emerging technologies such as in vitro gametogenesis, artificial ovary systems, and stem cell–derived gametes hold promise for expanding future reproductive options, particularly for patients for whom current methods are inadequate. Ethical considerations including informed consent in minors, risk of malignant cell reintroduction, and equitable access remain central to FP practice. From a sustainability perspective, FP supports long-term reproductive autonomy, psychological well-being, and social continuity by enabling individuals to maintain fertility despite medical or environmental challenges. Integrating FP into sustainable health frameworks underscores its role not only as a medical intervention but also as a contributor to broader public health, ethical governance, and human development.

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Sustainable Microbiota Targeted Interventions in Psychiatric Disorders

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Introduction

Major depressive disorder (MDD) and anxiety disorders represent two of the most widespread psychiatric conditions, contributing significantly to the global burden of disease. The World Health Organization (2023) ranks depression as the leading cause of disability worldwide, affecting an estimated 280 million people (World Health Organization, 2023). Anxiety disorders, similarly, impact over 300 million individuals globally (World Health Organization, 2025). These conditions often co-occur, share overlapping pathophysiological mechanisms, and carry significant personal, social, and economic costs. Standard first-line treatments for these disorders typically include pharmacological approaches such as selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), as well as psychotherapeutic modalities like cognitive-behavioral therapy (CBT) (Cipriani et al., 2018). However, while these interventions can be effective, they are not without limitations. Approximately one-third of patients with MDD fail to respond adequately to initial antidepressant therapy, and relapse rates remain high even among responders (Rush et al., 2006). Moreover, adverse effects such as sexual dysfunction, gastrointestinal disturbances, sleep disruption, and weight changes are common with antidepressant use and significantly contribute to treatment discontinuation and decreased patient satisfaction (Campos et al., 2021). These limitations have catalyzed the search for novel, sustainable, and personalized therapeutic strategies. In this context, the gut microbiota has emerged as a compelling and rapidly expanding area of interest. The human gut harbors approximately 10^{13}-10^{14} microorganisms-primarily, bacteria-forming a complex, metabolically active ecosystem (Sender et al., 2016). These microbes influence host health through diverse mechanisms, including immune modulation, hormone secretion, neurotransmitter synthesis, and metabolic regulation. The bidirectional communication between the gastrointestinal system and the brain-referred to as the microbiota-gut-brain axis-involves multiple pathways: the vagus nerve, immune signaling, microbial metabolites, the enteric nervous system, and the hypothalamic-pituitary-adrenal (HPA) axis (Cryan et al., 2019). Disturbances in microbial composition (i.e., dysbiosis) have been linked to increased gut permeability, systemic inflammation, altered neurotransmitter levels, and activation of neuroendocrine stress pathways-all of which are implicated in the etiology of mood disorders (Kelly et al., 2016; Foster et al., 2017). Recent clinical and preclinical evidence suggests that modulating the gut microbiome may offer a novel avenue for the prevention and treatment of depression and anxiety. Psychobiotics-live microorganisms that provide mental health benefits-alongside prebiotics and sustainable dietary interventions (such as the Mediterranean diet), represent promising adjuncts or alternatives to conventional therapies (Barber et al., 2023; Sarkar et al., 2016; Kazemi et al., 2019). These interventions may not only reduce symptom severity but also improve quality of life with fewer adverse effects, aligning with broader goals of sustainable healthcare.

This chapter explores the scientific basis and therapeutic potential of microbiota-targeted strategies in the management of depression and anxiety disorders. We begin by outlining the physiological mechanisms underpinning the gut–brain axis and its relevance to psychiatric illness. We then review current evidence on microbial dysbiosis in mental health, analyze the clinical utility of psychobiotics and dietary supplements, and assess the sustainability of microbiota-modulating dietary patterns. Finally, we discuss future directions in the field, including personalized microbiome-informed interventions and the integration of omics-based diagnostics.

The Gut–Brain Axis: Mechanistic Pathways and Clinical Relevance

The gut–brain axis (GBA) refers to the complex bidirectional communication system between the gastrointestinal (GI) tract and the central nervous system (CNS), involving neuronal, endocrine, immune, and metabolic signaling pathways. This cross-talk regulates not only gastrointestinal functions but also cognitive and emotional processes, making it central to understanding the pathophysiology of psychiatric disorders such as depression and anxiety (Carabotti et al., 2015)

Neural Communication via the Vagus Nerve and Enteric Nervous System

The vagus nerve plays a pivotal role in GBA communication. It provides an afferent conduit by which microbial metabolites and host immune signals influence brain activity, particularly in areas related to emotion and stress, such as the amygdala and prefrontal cortex (Bonaz et al., 2018). Experimental vagotomy in animal models abolishes the anxiolytic effects of certain probiotic strains, underscoring the vagus nerve's necessity in mediating psychobiotic efficacy (Bercik et al., 2011). The enteric nervous system (ENS), often termed the "second brain," comprises more than 100 million neurons and is capable of autonomous reflex activity. Gut microbes can influence ENS activity by producing neurotransmitters like γ-aminobutyric acid (GABA), serotonin (5-HT), and dopamine, which interact with local neurons and modulate gut motility, visceral sensitivity, and even mood (Strandwitz, 2018).

Neuroendocrine Pathways and the Hypothalamic-Pituitary-Adrenal (HPA) Axis

The HPA axis is a central stress response system that can be influenced by microbial signals. Under stress, corticotropin-releasing hormone (CRH) is secreted by the hypothalamus, triggering adrenocorticotropic hormone (ACTH) release from the pituitary gland and subsequent cortisol production from the adrenal cortex. Dysbiosis can lead to HPA axis hyperactivation, resulting in elevated cortisol levels, hippocampal atrophy, and impaired neurogenesis-all of which are implicated in depression (Mayer et al., 2014; O'Mahony et al., 2015). Interestingly, germ-free (GF) mice exhibit exaggerated HPA responses to mild stressors, a phenotype that is normalized by colonization with specific Bifidobacterium strains, further highlighting the microbiota's regulatory influence on neuroendocrine function (Sudo et al., 2004).

Immune System and Inflammation

The intestinal microbiota profoundly shapes both innate and adaptive immune responses. Commensal bacteria maintain mucosal homeostasis by promoting regulatory T cell (Treg) differentiation and modulating pro- and anti-inflammatory cytokine profiles (Arpaia et al., 2013). Disruption of this balance through dysbiosis enhances gut permeability-commonly referred to as "leaky gut" leading to the translocation of lipopolysaccharides (LPS) and other microbial components into systemic circulation (Fukui, 2016). These microbial signals activate peripheral immune cells, triggering the release of cytokines such as IL-6, TNF-α, and IL-1β, which cross the blood–brain barrier and promote microglial activation and neuroinflammation. This proinflammatory milieu is known to disrupt neurotransmitter metabolism and contribute to depressive and anxious symptomatology (Dantzer et al., 2008).

Microbial Metabolites and Neuroactive Compounds

Short-chain fatty acids (SCFAs)-primarily acetate, propionate, and butyrate-are metabolic byproducts of bacterial fermentation of dietary fibers. SCFAs exert broad neurobiological effects, including enhancing blood-brain barrier integrity, modulating gene expression via histone deacetylase (HDAC) inhibition, and promoting Treg activity (Dalile et al., 2019). Butyrate, a short-chain fatty acid produced by gut microbial fermentation of dietary fibers, has demonstrated antidepressant-like effects in preclinical studies. In particular, sodium butyrate has been shown to reverse stress-induced behavioral deficits and normalize molecular alterations in rodent models of depression, potentially through mechanisms involving histone deacetylase (HDAC) inhibition and neurotrophic factor modulation (Sun et al., 2018). Other microbial metabolites, such as tryptophan catabolites (e.g., kynurenine), influence serotonin synthesis and neuroplasticity. Dysbiosis can shift tryptophan metabolism toward the kynurenine pathway, decreasing serotonin availability and increasing neurotoxic quinolinic acid, both of which are linked to affective disorders (Agus et al., 2018).

Dysbiosis in Depression and Anxiety: From Clinical Profiles to Molecular Signatures

Dysbiosis refers to an imbalance in the composition, diversity, and function of the gut microbiota. It is characterized by reduced microbial richness, a loss of beneficial commensals, and an overrepresentation of potentially pathogenic species. Increasing evidence implicates dysbiosis as a key contributor to the pathogenesis of mood disorders, including major depressive disorder (MDD) and anxiety disorders (Jiang et al., 2015; Kelly et al., 2016). This section outlines both clinical and experimental findings regarding microbial alterations in these disorders and examines their immunological, neuroendocrine, and molecular consequences.

Clinical Microbiota Profiles in Mood Disorders

Recent metagenomic and 16S rRNA sequencing studies have identified reproducible alterations in the gut microbiota of individuals with depression and anxiety. In patients with MDD, studies consistently report a decreased abundance of short-chain fatty acid (SCFA) producing genera such as Faecalibacterium, Coprococcus, and Roseburia, which are important for maintaining intestinal barrier integrity and modulating inflammation (Valles-Colomer et al., 2019). In contrast, pro-inflammatory species from the Enterobacteriaceae family are often elevated, suggesting an immune-activating microbial profile. A well-cited study by Jiang et al. showed that patients with MDD had significantly lower levels of Firmicutes and increased Bacteroidetes, with a consequent shift in the Firmicutes/Bacteroidetes ratio (Jiang et al., 2015). Several studies have reported alterations in the gut microbiota of individuals with major depressive disorder. For instance, a systematic review found that members of the Lachnospiraceae family frequently differed between MDD patients and healthy controls, although the direction (increase vs. decrease) varied across studies. Moreover, genera such as Bacteroides and Alistipes were also observed to differ in abundance, but the findings were inconsistent across studies (Cheung et al., 2019). These alterations were associated with increased depressive symptom severity and may serve as potential biomarkers. In anxiety disorders, alterations in Lactobacillus and Bifidobacterium levels have been implicated. For example, a study involving patients with generalized anxiety disorder (GAD) demonstrated reduced Lactobacillus rhamnosus levels and disrupted microbial gene expression related to GABA metabolism-supporting the notion that the gut microbiota may influence neurotransmitter signaling relevant to anxiety (Bravo et al., 2018).

Molecular Signatures and Functional Pathways

Functional analyses of gut microbiota using metagenomic and metabolomic tools have revealed that dysbiosis in MDD is associated with altered expression of microbial genes involved in tryptophan metabolism, SCFA synthesis, and inflammatory cytokine regulation (Zheng et al., 2016). Specifically, dysbiosis is associated with an increased flux of tryptophan along the kynurenine pathway rather than serotonin synthesis, leading to accumulation of neuroactive and potentially neurotoxic metabolites such as quinolinic acid (Agus et al., 2018). Gene expression studies also show increased microbial pathways associated with LPS biosynthesis and decreased genes for SCFA production in patients with depression (Valles-Colomer et al., 2019). These findings underscore how microbial function-beyond taxonomic composition-contributes to host inflammation and mood regulation. Furthermore, patients with mood disorders show altered intestinal gene expression. Biopsies from MDD patients reveal increased expression of Toll-like receptors (TLRs), pro-inflammatory cytokines, and tight junction protein deficits, indicating compromised mucosal immunity and barrier dysfunction (Kelly et al., 2017).

Causality and Bidirectionality

It is important to note that the relationship between gut microbiota and psychiatric illness is likely bidirectional. Chronic stress and depression can alter dietary intake, gastrointestinal motility, and immune function-factors that reciprocally influence microbial composition (Foster et al., 2017). Antidepressant medications, particularly SSRIs and TCAs, also exhibit antimicrobial effects that may shape the microbiota independently of disease mechanisms (Lukic et al., 2019). As such, future studies must carefully control for confounding factors, including diet, medication, and lifestyle variables. Nonetheless, evidence from fecal microbiota transplantation (FMT) studies strengthens the argument for causality. For example, one landmark study transferred microbiota from MDD patients into germ-free mice, resulting in the development of depression-like behaviors and altered neurotransmitter profiles (Kelly et al., 2016). These findings indicate that dysbiotic microbiota may contribute causally to the emergence of depressive phenotypes.

Psychobiotics and Nutritional Modulation of Mood: Evidence and Mechanisms

Psychobiotics are defined as live organisms-primarily bacteria-that, when ingested in adequate quantities, confer mental health benefits through interactions with the microbiota–gut–brain axis (Dinan et al., 2013). These benefits are mediated via mechanisms that include modulation of neurotransmitters, immunoregulation, and neuroendocrine signaling. Alongside psychobiotics, specific dietary components such as prebiotics, polyunsaturated fatty acids (PUFAs), vitamins, and polyphenols have also emerged as promising adjuncts or alternatives to conventional antidepressants and anxiolytics Mocking et al., 2016; Su et al., 2018).

Psychobiotics: Clinical Evidence and Mechanistic Insights

Most psychobiotics belong to the Lactobacillus and Bifidobacterium genera, which are common inhabitants of the human gut. Preclinical studies demonstrate that Lactobacillus rhamnosus can modulate GABAergic signaling and decrease anxiety-like behaviors in a process found to be vagus nerve-dependent (Bravo et al., 2011). Similarly, Bifidobacterium longum 1714 has been shown to reduce cortisol levels and improve cognitive performance in human trials (Allen et al., 2016). A landmark double-blind, placebo-controlled trial using a combination of L. helveticus R0052 and B. longum R0175 found significant reductions in depression and anxiety scores among healthy volunteers (Messaoudi et al., 2011). Meta-analyses suggest modest but significant benefits of psychobiotic interventions for depression, although findings for anxiety remain more heterogeneous (Ng et al., 2018; Reis et al., 2018). The mechanisms of action include:

Neurotransmitter Modulation: Certain strains increase the production of GABA, serotonin, and dopamine, influencing mood and behavior.

Immune Regulation: Psychobiotics reduce systemic levels of pro-inflammatory cytokines (e.g., IL-6, TNF-α) and enhance anti-inflammatory mediators.

HPA Axis Attenuation: These strains blunt stress-induced HPA activation, normalizing cortisol output and restoring feedback sensitivity.

Despite encouraging data, challenges remain regarding strain specificity, dosage, delivery mode, and duration of intervention. Additionally, variability in individual microbiota composition may affect responsiveness to psychobiotic therapy (Westfall et al., 2017).

Prebiotics and Functional Dietary Components

Prebiotics are nondigestible dietary fibers-such as fructooligosaccharides (FOS) and galactooligosaccharides (GOS)-that selectively stimulate the growth and activity of beneficial gut bacteria. GOS supplementation has been shown to reduce cortisol awakening responses and improve emotional processing in healthy individuals, suggesting stress-buffering effects (Schmidt et al., 2015). Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), play crucial roles in synaptic plasticity, neuronal membrane fluidity, and inflammatory modulation. Deficiencies in omega-3 fatty acids have been associated with an increased risk of depression and cognitive decline (Mocking et al., 2016; Su et al., 2018). Meta-analyses indicate that omega-3 supplementation, especially formulations high in EPA, reduces depressive symptoms in both clinical and subclinical populations (Mocking et al., 2016). Vitamins and micronutrients such as vitamin D, folate, and vitamin B12 are also implicated in mood regulation. These nutrients affect homocysteine metabolism, methylation processes, and monoamine synthesis, all of which are relevant in depression pathophysiology (Young, 2007).

Polyphenols and Gut–Brain Interactions

Polyphenols are bioactive compounds found in fruits, vegetables, tea, and dark chocolate.

Although poorly absorbed in the small intestine, they undergo microbial fermentation in the colon, generating neuroactive and anti-inflammatory metabolites. These byproducts modulate gut microbial composition and SCFA production, thereby influencing brain function (Ammar et al., 2020). Resveratrol, quercetin, and epigallocatechin gallate (EGCG) have demonstrated antidepressant-like effects in preclinical studies, and some human trials suggest cognitive and mood benefits, though more rigorous studies are needed (Cione et al., 2019).

Dietary Synergy and Sustainability

A combined dietary strategy that includes psychobiotics, prebiotics, anti-inflammatory nutrients, and polyphenols may exert synergistic effects on the gut–brain axis. Such approaches are not only promising from a clinical perspective but also align with principles of sustainability by reducing dependence on long-term pharmacotherapy and enhancing self-managed mental health strategies. Emerging formulations, including synbiotics (combinations of probiotics and prebiotics), postbiotics (nonviable microbial byproducts), and fermented foods (e.g., kefir, kimchi, yogurt), offer accessible and culturally adaptable options for integrating microbiota-modulating strategies into everyday life (Dahiya et al., 2022; Agans et al., 2018).

Microbiota-Targeted Alternatives to Conventional Antidepressants

Conventional pharmacotherapy for mood disorders-especially selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs)-remains the mainstay of treatment. However, these agents are often limited by delayed onset of action, incomplete efficacy, and a high burden of side effects, including sexual dysfunction, weight gain, gastrointestinal distress, and cognitive blunting (Cipriani et al., 2018). Consequently, there is growing interest in microbiota-targeted interventions as complementary or alternative strategies that may exert therapeutic effects through different mechanisms with improved tolerability.

Limitations of Conventional Antidepressants

Antidepressants primarily target monoaminergic systems by modulating synaptic concentrations of serotonin, norepinephrine, and dopamine. While effective for many, response rates are modest, with only ~50% of patients achieving remission after first-line treatment (Rush et al., 2006). Furthermore, relapse rates are common, particularly in individuals with residual symptoms or poor adherence (Trivedi et al., 2006). Importantly, antidepressants may also affect the gut microbiota. Several studies indicate that SSRIs possess antimicrobial properties that can alter microbial composition in both beneficial and detrimental ways (Lukic et al., 2019; McGovern et al., 2019). For example, fluoxetine and sertraline reduce bacterial diversity in vitro and in vivo, potentially impacting mucosal immunity and inflammation (Lukic et al., 2019; McGovern et al., 2019).

Psychobiotics as Therapeutic Adjuncts or Replacements

Psychobiotics, including strains of Lactobacillus and Bifidobacterium, offer a promising microbiota-based intervention. These agents exert neuromodulatory effects via several pathways: regulating cytokine production, restoring tight junction proteins, modulating neurotransmitter availability, and balancing HPA axis output (Dinan et al., 2013; Sarkar et al., 2016).

A randomized controlled trial found that daily supplementation with L. helveticus R0052 and B. longum R0175 for 30 days led to significant improvements in depressive symptoms, sleep quality, and gastrointestinal comfort among participants with mild to moderate depression (Messaoudi et al., 2011). These findings suggest psychobiotics may not only alleviate core mood symptoms but also reduce somatic side effects frequently seen with antidepressants, such as gastrointestinal discomfort. In another study, administration of B. longum NCC3001 improved depression scores in patients with irritable bowel syndrome (IBS), further supporting the gut–brain axis as a viable therapeutic target in somatopsychic presentations (Pinto-Sanchez et al., 2017).

Dietary Interventions as Sustainable Strategies

Dietary interventions such as the Mediterranean diet have shown antidepressant effects, likely mediated via modulation of inflammation and microbiota composition (Sánchez-Villegas et al., 2009; Jacka et al., 2017). A landmark trial (the SMILES trial) demonstrated that adherence to a modified Mediterranean diet over 12 weeks significantly improved depressive symptoms, with remission rates nearly doubling compared to a control group receiving social support (Jacka et al., 2017). These diets are rich in fiber, omega-3 fatty acids, polyphenols, and vitamins-components that favorably influence gut microbiota diversity and SCFA production. Additionally, they are devoid of synthetic compounds, offer fewer side effects, and align with public health goals related to sustainable food systems and planetary health (Willett et al., 2019).

Combined Approaches and Clinical Integration

Microbiota-based interventions can be used in various clinical scenarios: As monotherapy in mild depressive or anxiety syndromes, especially in patients with treatment hesitancy or intolerance. As adjunct therapy to enhance the efficacy and tolerability of antidepressants. As maintenance therapy to prevent relapse by supporting immune, metabolic, and neuroendocrine resilience. However, standardization remains a challenge. Strain selection, dosing, delivery systems, and treatment duration vary across studies, making comparisons difficult. Moreover, individual variability in microbiota composition and host genetics may impact treatment outcomes. Personalized microbiota-informed interventions, guided by metagenomic or metabolomic profiling, hold potential for precision psychiatry but require further validation (Dinan & Cryan, 2017).

Sustainable Dietary Models and Microbiota–Mental Health Connections

Diet is a powerful modulator of gut microbiota composition and function, and in turn, of the gut–brain axis. Increasing evidence supports the role of specific dietary patterns not only in promoting general health but also in preventing and alleviating symptoms of mood disorders such as depression and anxiety. In this context, sustainable diets-those that are environmentally friendly, culturally appropriate, and health-promoting-offer a holistic approach to mental wellness that aligns individual well-being with planetary health goals (Willett et al., 2019).

The Mediterranean Diet: A Paradigm of Anti-Inflammatory Nutrition

The Mediterranean diet (MD) is one of the most extensively studied dietary patterns in relation to both gut microbiota diversity and mental health. It emphasizes the consumption of olive oil, fruits, vegetables, legumes, nuts, whole grains, and fish, while limiting red and processed meats, refined sugars, and saturated fats.

This dietary pattern is rich in:

Polyphenols, which promote beneficial microbial species such as Faecalibacterium and Bifidobacterium (Singh et al., 2017),

Dietary fibers, which serve as prebiotics for SCFA-producing bacteria,

Omega-3 fatty acids, which exert anti-inflammatory effects and support neuronal membrane integrity (Su et al., 2018).

A randomized controlled trial (the SMILES trial) demonstrated that individuals with moderate to severe depression who adhered to a Mediterranean-style diet for 12 weeks experienced significantly greater reductions in depressive symptoms compared to a control group receiving social support, with remission rates of 32% versus 8% (Jacka et al., 2017). Moreover, adherence to the Mediterranean diet is associated with lower levels of CRP, IL-6, and TNF-α—key biomarkers of systemic inflammation implicated in depression pathophysiology (Estruch et al., 2018).

Traditional Dietary Models with Mental Health Benefits

Other regional and traditional diets also offer microbiota-supportive, anti-inflammatory properties: The Japanese Diet is rich in fermented foods such as miso and natto, seaweed, and fish, contributing to microbial diversity and neuroprotective compounds (Saji et al., 2021). The Scandinavian Diet includes whole grains like rye and barley, berries rich in anthocyanins, and fatty fish. It has been shown to reduce depression scores and improve cognitive function (Shakersain et al., 2018). The Brazilian Diet emphasizes fresh foods, legumes, and minimal ultra-processed items, showing protective effects against anxiety and depressive symptoms in adolescents (Mesas et al., 2019; Werneck et al., 2022).

These diets share a core of unprocessed or minimally processed whole foods, fiber-rich plant sources, and healthy fats, aligning with both gut microbiota health and sustainable food system goals.

Western Diet and Dysbiosis-Induced Neuroinflammation

Conversely, the Western diet-characterized by high intake of saturated fats, red meat, refined carbohydrates, and sugar, has been consistently associated with microbial dysbiosis, systemic inflammation, and increased risk of depression (Kanoski & Davidson, 2011). This diet depletes beneficial microbes such as Akkermansia muciniphila and Bifidobacteria, while promoting pathobionts like Proteobacteria. Studies in animal models show that high-fat, high-sugar diets reduce hippocampal brain-derived neurotrophic factor (BDNF) levels, impair neurogenesis, and induce behaviors akin to depression and anxiety (Kanoski & Davidson, 2011). Furthermore, these dietary patterns are environmentally unsustainable, contributing to greenhouse gas emissions, biodiversity loss, and chronic disease epidemics.

Sustainability as a Clinical and Ecological Imperative

Sustainable diets address the growing need to integrate personal health with ecological responsibility. According to the EAT-Lancet Commission, transitioning to a planetary health diet that balances nutrient adequacy, environmental preservation, and cultural relevance could prevent approximately 11 million premature deaths per year and mitigate climate change impacts (Willett et al., 2019). In mental health care, promoting sustainable dietary habits can reduce polypharmacy, improve treatment adherence, and empower individuals through lifestyle-based self-management. Integration of nutritional psychiatry into clinical settings-guided by dietitians, psychologists, and primary care providers-represents a multidisciplinary approach to addressing both mood disorders and global health challenges.

Future Perspectives: Personalized Microbiome-Based Therapies

As microbiome research advances, the prospect of personalized microbiota-targeted interventions is becoming increasingly viable. These approaches aim to tailor therapeutic strategies based on an individual's unique microbiome composition, metabolic activity, genetic predispositions, and symptom profile. Such precision-based interventions hold promise for improving the efficacy, safety, and sustainability of treatments for depression and anxiety.

The Rise of Multi-Omics in Mental Health

The integration of multi-omics technologies-including metagenomics, metabolomics, transcriptomics, and epigenomics-offers a powerful means to map host–microbe interactions in neuropsychiatric disorders (Mihailovich et al., 2024; Simpson et al., 2022; Rosario et al., 2020). These tools can identify: Microbial signatures predictive of treatment response or resistance, Metabolite patterns associated with neurotransmitter production, Genetic and epigenetic markers linked to HPA axis sensitivity, inflammation, or neuroplasticity.

For example, metagenomic sequencing can identify deficiencies in SCFA-producing bacteria or the overrepresentation of pro-inflammatory species, while metabolomic profiling may reveal alterations in tryptophan–kynurenine metabolism, which has been linked to mood regulation and neurotoxicity (Agus et al., 2018; Zheng et al., 2016).

Stratification of Patient Subtypes

Future research should focus on identifying microbiome-based subtypes of depression and anxiety. These could include: Inflammatory subtype: elevated CRP, IL-6, dysbiosis, systemic endotoxemia. HPA axis–dysregulated subtype: altered cortisol rhythms, barrier dysfunction, vagus nerve hypoactivity. Neurotransmitter-deficient subtype: impaired microbial production of GABA or serotonin precursors. Such stratification may allow clinicians to select the most appropriate interventions-whether psychobiotics, prebiotics, synbiotics, or dietary regimens-based on specific biological profiles.

Emerging Interventions: Beyond Probiotics

Several next-generation interventions are under investigation: Postbiotics: non-viable microbial components or metabolites (e.g., SCFAs, polysaccharide A) that exert immunomodulatory or neuroactive effects without live organisms (Aggarwal et al., 2022).

Fecal Microbiota Transplantation (FMT): While still experimental in psychiatry, FMT has shown promise in small trials, including improved depressive symptoms in patients with IBS or autism spectrum disorder (Zhang et al., 2023).

Designer Probiotics: Genetically engineered strains that can produce targeted neurochemicals or modulate specific immune pathways.

While these innovations are promising, long-term safety, regulatory oversight, and ethical considerations must be addressed before widespread clinical adoption.

Challenges and Considerations

Key challenges in personalized microbiota-based psychiatry include: Individual variability: Microbiota composition is influenced by diet, geography, age, sex, medications, and genetics, complicating generalizations. Regulatory and standardization gaps: There is currently no consensus on optimal strains, doses, or treatment durations. Data interpretation: Integrating multi-omics data into actionable clinical insights requires advanced bioinformatics and cross-disciplinary collaboration.

Nonetheless, computational modeling, machine learning, and AI-based decision tools are expected to facilitate patient-specific treatment plans, especially when coupled with longitudinal tracking of microbiome changes and symptom trajectories (Rea et al., 2019; Afroz et al., 2023; Cryan et al., 2019).

The Road Ahead: Interdisciplinary Integration

The future of sustainable, microbiota-focused psychiatry will rely on collaboration between: Psychiatrists and neuroscientists: to refine symptom-domain targeting and neurobiological mechanisms. Microbiologists and immunologists: to explore host-microbe immune crosstalk. Dietitians and public health professionals: to promote personalized yet scalable nutritional interventions. Bioinformaticians and data scientists: to analyze multi-omics data and develop predictive algorithms.

Ultimately, the integration of microbiota profiling into routine psychiatric care could represent a paradigm shift from symptom-based pharmacotherapy to systems-based precision medicine grounded in host–microbe interactions.

Conclusions

This chapter has synthesized the rapidly evolving body of evidence surrounding the microbiota–gut–brain axis and its relevance to the pathogenesis and treatment of major depressive disorder (MDD) and anxiety disorders. Accumulating clinical and preclinical findings demonstrate that disturbances in gut microbial composition-commonly referred to as dysbiosis-are associated with increased intestinal permeability, systemic inflammation, altered neurotransmitter metabolism, and stress axis dysregulation, all of which contribute to mood symptomatology.

We have shown that psychobiotics, prebiotics, and nutritional supplements (such as omega-3 fatty acids, B vitamins, and polyphenols) hold therapeutic promise by modulating microbial diversity, enhancing neuroactive compound production, and dampening inflammation. These microbiota-targeted strategies offer a sustainable and low-risk alternative or adjunct to conventional antidepressants, which often produce undesirable side effects and show limited efficacy in many patients.

In particular, adherence to anti-inflammatory dietary patterns-such as the Mediterranean diet-has been associated with reduced depressive and anxiety symptoms, improved cognitive function, and enriched microbial profiles. In contrast, Western dietary habits characterized by high sugar and saturated fat intake appear to exacerbate dysbiosis and neuroinflammation.

Looking forward, the application of multi-omics technologies-including metagenomics, metabolomics, and transcriptomics-opens the door to precision microbiome-informed psychiatry. Stratifying patients into biologically relevant subtypes and tailoring interventions accordingly may dramatically improve treatment outcomes. Moreover, emerging tools such as designer probiotics, postbiotics, and computational modeling will likely play a central role in the next generation of mental health therapeutics.

From a public health perspective, microbiota-based interventions are particularly attractive because they are non-invasive, scalable, and ecologically sustainable. By reducing reliance on synthetic pharmacotherapy and supporting self-managed mental health, such strategies contribute to both individual and societal well-being.

This chapter contributes to the field of sustainable health sciences by bridging disciplines-psychiatry, microbiology, nutrition, immunology, and systems biology-to outline an integrative, evidence-based framework for mental health care. By placing microbiota-targeted strategies in the context of sustainability, we emphasize not only clinical innovation but also ecological responsibility, aligning therapeutic development with broader goals of planetary health.

The gut microbiome offers a new frontier in psychiatric research and clinical care. As scientific understanding deepens, microbiota-informed mental health strategies have the potential to shift paradigms from symptom suppression to system restoration; from generalized prescriptions to personalized care; and from treatment resistance to biological resilience.

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Chapter 2

The Role of Physiotherapists in Advancing Sustainable Health within the Framework of the Sustainable Development Goals

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Introduction to Sustainable Development Goals (SDGs)

The pursuit of economic prosperity by humanity has resulted in significant environmental degradation. As the environmental damage accumulated over time and began to pose a threat to humanity, intervention became imperative (Bonnedahl, Heikkurinen, & Paavola, 2022). The concept of sustainable development became the focal point of these interventions. The 2030 Sustainable Development Goals (SDGs 2030) were established at the United Nations (UN) Sustainable Development Summit. This was held in September 2015. The United Nations SDGs comprise 17 core goals and 169 associated targets. These objectives underscore the fundamental tenet of universal human rights for all individuals by the year 2030. It is anticipated that nations will formulate their developmental agendas and strategies in alignment with these objectives. The new global goals place sustainability at the centre of development and emphasise that economic, environmental, and social concerns are common to all people living on Earth. Figure 1 shows the 17 main targets of the SDGs.

Figure 1

Sustainable Development Goals

Explanatory note: Quoted from the UN website (‘THE 17 GOALS | Sustainable Development’, n.d.).

The Correlation Between Healthcare and Sustainable Development

The health of the human species is inextricably linked to the concept of sustainability. Today, public health is under the greatest threat from climate change. There is an increasing prevalence of morbidity and mortality from extreme weather conditions, including floods, storms, and fires. There is also an increase in unplanned mass migration resulting from weather and resource conflicts, and in the incidence of diseases (Palstam, Sehdev, Barna, Andersson, & Liebenberg, 2022). Mitigating climate change will positively impact public health and reduce mortality. In addition, strategies for mitigating climate change that are informed by lifestyle factors have been shown to yieIt is widely acknowledged that ld substantial co-benefits for health.

In order to provide a comprehensive overview of the topic, it is essential to consider not only the level of human capital but also the role of key indicators of health in the context of socioeconomic development. Sustainable development is impossible without human focus. Consequently, fundamental health-related objectives have been delineated for the purpose of sustainable development. One of the 17 SDGs is directly related to health. Goal 3 is entitled "Health and Quality of Life." However, health is a priority for the economy. The stagnation inflicted on national economies by the past SARS virus outbreak and the recent coronavirus pandemic repeatedly remind us of the importance of this issue. Furthermore, a society comprised of healthy and well-nourished individuals will have a higher production and value-added output than societies with unhealthy nutrition and high mortality and morbidity rates. Land (natural resources) and labor, along with capital, are considered basic production factors. The labor factor is theoretically grounded in economics by the concept of human capital. Human capital encompasses the quantity, quality, professional experience, and health status of the labor force, enabling the more efficient use of other production factors. Investments in human capital are primarily measured by education and healthcare expenditures (Önder, 2020).

In addition to the impact of healthy communities on sustainability, another salient issue is the carbon footprint of the medical sector. The global healthcare sector is like a nation. If it were recognised as a nation, it would be the 5th largest producer of greenhouse gases. In the paradigm of climate change, Watts et al. have postulated that it signifies a substantial opportunity to redefine the socio-environmental determinants of health (Watts et al., 2015). This appeal is directed at all healthcare professionals and departments, with a view to achieving a substantial reduction in carbon use, the establishment of equity goals, and the enhancement of health outcomes.

Sustainable healthcare refers to a healthcare model that considers the social and ecological determinants that negatively impact public health, intervenes in the disease process as early as possible, and offers "lean" and cost-effective healthcare services. Integral to the healthcare system, physiotherapy exerts a substantial influence on sustainable practice by virtue of its reliance on non-pharmacological, cost-effective, and low-carbon treatments that empower patients to manage their own care (Palstam, Andersson, Lange, & Grenholm, 2021). The following section will provide a detailed exposition on the synergy between sustainable development goals and physiotherapy.

The Role of Physiotherapy in Health and Well-being (SDG 3)

The health protection system is structured into five levels. The initial level, designated Primordial prevention, is defined as the implementation of measures aimed at averting the emergence or progression of risk factors. Health-related client education is the practice performed by physiotherapists at this level. Primary Prevention means preventing the occurrence of disease due to risk factors. In this context, physiotherapists play a crucial role in establishing and improving physical activity as a lifestyle habit. Secondary Prevention is preventing the development of disease complications. At this stage, physiotherapists provide support with prompt, optimized, and sustained care. Tertiary Prevention is to prevent disability and preserve the life expectancy of patients. Quaternary Prevention prevents unnecessary treatment and diagnosis. At the tertiary and quaternary prevention levels, physiotherapists support individuals through increased independence and rehabilitation (Padhan, 2023).

Physiotherapists play a crucial role in health promotion. They serve as part of the multidisciplinary healthcare team, developing rehabilitation programs specifically for a wide range of health conditions. These include chronic noncommunicable diseases (NCDs) and musculoskeletal disorders. NCDs and musculoskeletal disorders negatively impact both public health and individuals' quality of life, and are important reasons for seeking care. These health problems are associated with many modifiable lifestyle behaviors and risk factors. Physical inactivity, obesity, smoking, unhealthy diet, stress, and inadequate sleep have been identified as being associated with both chronic NCDs and chronic musculoskeletal disorders. Developing healthy lifestyle behaviors can prevent and manage these conditions and improve overall health and well-being. Physical therapists specialising in the treatment of musculoskeletal disorders frequently encounter patients suffering from chronic conditions in addition to unhealthy lifestyle behaviours. Therefore, physical therapists can support their patients' health and well-being (Bezner, 2015). Physiotherapists can play an important role in improving community health if they engage with local communities. The implementation of the Community Physiotherapist model has been found to enable physiotherapists to provide effective, appropriate, and safe interventions (Paci, Bianchi, Buonandi, Rosiello, & Moretti, 2023). Physiotherapists work closely with patients to design personalized exercise programs that are sustainable and accessible, taking into account the individual's needs and abilities. This proactive approach to public health encourages people to integrate regular physical activity into their daily routines (Abaraogu, Edeonuh, & Frantz, 2016).

Quality of life has multiple components, and they interact with each other. Physical health, social relationships, psychological state, environmental factors, and individual satisfaction all play a significant role in understanding an individual's quality of life. ('The World Health Organization Quality of Life Assessment (WHOQOL)', 1995). According to the World Confederation of Physical Therapy (WCPT), physiotherapists are healthcare professionals who develop, maintain, and restore people's functional abilities, maximum range of motion, and muscle strength. They work in the areas of preventing and treating or intervening in diseases without promoting health, but especially in rehabilitation ('What Is Physiotherapy?', n.d.). Physiotherapists help individuals to achieve the best possible quality of life by considering physical, emotional, psychological, and social well-being (Schramlová et al., 2024). Physiotherapists play a crucial role as emotional support in managing injury or pain ('In Brief', 2024).

Physiotherapists in the Context of Education (SDG 4)

Regarding their specialties, physical therapists train new physical therapists in academia, trainee physical therapists in clinics, other members of the healthcare team, patients and clients, and formal and informal caregivers. This enables them to play a role in improving the quality of healthcare. Furthermore, physical therapists can educate communities about basic health, mobility, and injury prevention. Their roles range from individual education to physical training and even ergonomic environmental design (Klassen, MacKay, Moher, Walker, & Jones, 2000). The community physiotherapist model has been developed in this context. Under this model, community members and external stakeholders, including physiotherapists, collaborate to address the community's needs (Varnado, Mejia-Downs, Scharmann, & Richardson, 2024). It is a commonly held view that children with disabilities are less likely to enrol in school, persist with their education, and make progress (Nair, Radhakrishnan, & Olusanya, 2023). Regarding the inclusiveness of education, physiotherapists can play an important role in ensuring that individuals of all age groups with disabilities receive quality education.

Sustainable Working Practices and Physiotherapy (SKH 8)

Quality of work life is important because nearly half of an adult's life is spent engaged in productive activities. Organizations that focus on providing a healthy work environment and quality of work life are more likely to gain strength and reduce the risk of employee turnover (Afroz & Haque, 2021). Physiotherapists, knowledgeable about the anatomy, biomechanics, and kinesiology of the human muscular system, develop intervention plans for their patients regarding healthy work environments and ergonomics. They may also work within companies to develop methods to improve the quality of work in workplaces.

In addition to their clinical skills, physiotherapists can identify injury risks through in-depth analysis of job tasks, contribute to injury prevention strategies by conducting task analyses. They can also provide ergonomics and manual handling training and conduct health promotion activities. Having a physiotherapist in the workplace enables the development of disability management strategies, such as pre-employment screening programs and employee functionality assessments, and returning-to-work programs (Adam, Peters, & Chipchase, 2013; Donovan, Khan, & Johnston, 2021). All of these can reduce workplace accidents and illnesses, reduce employee absenteeism, and increase productivity. Furthermore, physiotherapists are capable of overseeing wellness programs. The workplace is a setting in which employees are employed and which has the capacity to contribute to their health. It is also a setting in which it is possible to promote so-called "decent work" and economic growth.

Reducing Inequalities Through Physiotherapy (SDG 10)

Unfortunately, inequalities persist worldwide. Inequalities can be based on biological factors such as age, ethnicity, race, gender, and disability; socioeconomic factors such as income and class; and preferences such as sexual orientation and religion. These groups are defined as vulnerable groups (Arıca, Çakır, & Kağnıcı, 2023). The definition of the physiotherapy profession includes the goals of the individual's participation in society throughout life, the protection and restoration of health, and the improvement of movement ability, physical activity, and functional abilities ('Dernek Tüzüğü', n.d.). As the definition of the profession makes clear, it aims to eliminate disadvantages or increase the participation of disadvantaged individuals in society. This enables individuals to maintain or regain independence and contribute to productivity through vocational rehabilitation, even if they are disabled. Furthermore, due to their expertise in human kinetics, rehabilitation, and restoration of function, physical therapists can detect potential issues long before they manifest as disabilities. Therefore, they are indispensable in the timely diagnosis and management of disabilities (Deepak & Abhijit, 2025).

In many societies, healthcare workers and authorities confront the challenge of ensuring equitably distributed healthcare for individuals residing in areas characterised by a low socio-economic status. Reduced access to healthcare has been demonstrated to have a detrimental effect on health, a phenomenon that is compounded by the pervasive influence of social determinants of health. Physiotherapeutic interventions are a cost-effective solution for the treatment of musculoskeletal conditions, often proving more economical than treatments administered by other health professionals (Baumbach, Feddern, Kretzler, Hajek, & König, 2024; Fatoye, Wright, & Gebrye, 2020). Individuals living in poverty, especially those who are homeless, are considered to be among the most vulnerable members of society. Research has indicated that the provision of physical therapy services within the community, where individuals reside, procure sustenance and engage in social interaction, can serve as an efficacious strategy to enhance access to care for those experiencing homelessness or economic disadvantage (Oosman, Weber, Ogunson, & Bath, 2019). Nevertheless, the integration of physical therapists within primary care and home care settings may be a superior approach to enhancing accessibility. Digital health tools such as telemedicine, telerehabilitation, mobile health, and e-health can replace or complement in-person healthcare visits. They contribute to reducing the carbon emissions of healthcare services by reducing patient and staff travel (Palstam & Lange, 2024). Digital health is becoming increasingly widespread to address inequalities in access. A programme of scientific research is currently ongoing to investigate the advantages and disadvantages of the phenomenon under scrutiny.

Climate Action and Physiotherapy (SDG 13)

While human health has improved in recent years thanks to improved access to healthcare and improved disease control, this has come at the expense of environmental health. Healthcare contributes to some planetary health concerns, such as climate change; therefore, healthcare professionals, including physiotherapists, both contribute to the problem and are integral to the solution. In comparison with professions that utilise techniques requiring greater consumption of resources, such as imaging or surgery, physiotherapy has been proposed as a profession with a reduced environmental impact. This is due to its emphasis on hands-on or exercise-based assessment and interventions, which result in a reduction in environmental impact (Pichler, Jaccard, Weisz, & Weisz, 2019). A meta-analysis of extant literature has identified an increasing interest and involvement of the physiotherapy profession in combating climate change and its impacts on health (Li, Fryer, Chi, & Boucaut, 2025).

Climate change has multifaceted impacts. Mental health threats, respiratory diseases, cardiovascular diseases, infectious diseases, increased prevalence of foodborne and waterborne diseases, injuries, and premature deaths associated with extreme weather events, and changes in geographic distribution are expected due to climate change (CDC, 2024). To adapt to the effects of climate change, specific actions can be taken at different levels. These actions include environmental actions as well as social and behavioral actions (Zhao et al., 2022). Physiotherapists have the capacity to make a significant contribution to the maintenance of physical function and quality of life in individuals in response to changing environmental conditions. Climate-related stress and physical disabilities can limit activities of daily living, particularly for individuals with chronic illnesses or the elderly. Physiotherapists can provide both preventative and rehabilitative support by developing exercise programs, breathing techniques, and adaptive strategies that will increase their resilience to climate change.

Partnerships for Progress (SDG 17)

Sustainable Development Goal 17 emphasizes the importance of global collaboration and multi-stakeholder partnerships in achieving all goals. The active role of physical therapists in this goal supports not only individual patient care but also the development of population-based health approaches. From a health equity perspective, healthcare practitioners acknowledge the influence of socio-political factors on health, to address health inequalities, minimise healthcare expenditures, and adapt to the demands posed by pandemics such as the ongoing global outbreak of Coronavirus (Dunleavy et al., 2022). Active participation of physiotherapists in the development of national health policies is necessary to reduce health inequalities and increase the physical well-being of society (Varnado et al., 2024). In this context, collaborations with policymakers, academics, and international organizations increase the visibility of the physiotherapy profession on the global health agenda and accelerate the realisation of SDGs. Joint initiatives by the World Confederation of Physiotherapy and the World Health Organization, in particular, strengthen the leadership capacity of physiotherapists in public health programs and contribute to the adoption of evidence-based practices at the policy level ('Global Action Plan on Physical Activity 2018–2030', n.d.). This multi-layered collaborative approach makes physiotherapists not only healthcare providers but also active partners in sustainable development.

Conclusion

Physiotherapists are assuming a progressively significant role in the pursuit of the SDGs, transcending their traditional role as individual health service providers to become pivotal agents in community health promotion and the mitigation of health inequalities. Within the SDG framework, physiotherapists have a multifaceted role that extends beyond the mere improvement of patients' functional capacity. They participate in public health programmes, education and awareness campaigns, community-based interventions, and contribute to policy development processes. The active involvement of these professionals in national and international collaborations has been demonstrated to enhance the sustainability of healthcare services by fostering knowledge and resource sharing, and contributing to the reduction of carbon footprints. Consequently, physiotherapists serve as a critical bridge in the implementation of the SDGs and directly facilitate the achievement of the sustainable development vision by improving health and well-being at both individual and societal levels.

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Homelessness and Sustainable Health: A Holistic Approach to Community Health

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Introduction

Homelessness is a multidimensional social problem that is not limited to a lack of shelter; it directly affects health, safety, social participation, and human dignity. In modern societies, increasing urbanization, income inequalities, migration, and inadequate social protection mechanisms are exacerbating homelessness at both the local and global levels. In this context, interventions addressing homelessness must not be limited to crisis management; they must be approached in a sustainable, rights-based, and holistic manner within the framework of public health principles. This book chapter aims to define homelessness, outline its scope and national/international context, examine its effects on health, and explain how homelessness should be approached in the context of sustainable health policies, based on the fundamental principles of public health. Additionally, by presenting best practice examples from different countries, sustainable intervention recommendations will be developed to improve the quality of life and social integration of homeless individuals. At the end of the chapter, policy and implementation recommendations for the future will be presented to strengthen interdisciplinary collaboration in this field.

Occupational justice is a meaningful form of social justice that guarantees individuals the right to participate in activities of their choice in a way that meets their personal needs and social participation requirements. This perspective recognizes that meaningful participation in daily life activities—such as self-care, education, work, and leisure activities—is not a privilege but a fundamental human right. In the context of homelessness, occupational justice requires the removal of systemic barriers that limit access to safe housing, health services, and opportunities for social participation.

Fundamental principles of community health

Housing is a key social determinant of health, with increasing relevance in global trends such as urbanization, demographic shifts, and climate change. Healthy housing is a shelter that supports a state of complete physical, mental, and social well-being (WHO, 2021).

Homeless individuals may experience many health problems. One of the problems seen in homeless individuals is related to their feet. The percentage of homeless individuals experiencing foot-related health problems ranges from 9% to 72%. The most common foot problems in this group are tinea pedis, foot pain, and functional limitations related to walking and wearing inappropriate shoes. This population group faces unique challenges such as wearing inappropriate footwear, prolonged exposure to moisture, standing or walking for extended periods in wet shoes, and exposure to extreme cold, all of which contribute to impaired foot health (Ogrin et al., 2024). To achieve a healthy society, mental health issues that will lead to homelessness should not be ignored (Singh & Sidana, 2020).

Homelessness: Definitions, Scope, and National and International Status

Homeless people have been classified in different ways to date. These classifications are based on time, geographical region, typographical status, and duration. In a study conducted by Türkcan, homelessness was examined in three categories:

Temporal classification: Here, homeless people were examined according to history and time. Chronic homeless people: chronic psychotic cases living on the streets and people who have been homeless for a long time. Episodic homeless people: young people with difficult-to-treat illnesses. These young people also move back and forth between street life and home. Temporary homeless people: people who do not have a definable mental illness and are temporarily homeless due to acute situational crises.

Geographical classification: In this classification, homeless people were examined in four separate groups: street communities, families staying for extended periods in temporary accommodation such as hotels or bed-and-breakfast shelters, those living with friends or other people in a family, and those staying in hostels or shelters for the homeless.

Typographical classification: Here, individuals are examined based on their characteristics and needs: street population, middle-aged men with ongoing alcohol problems, chronic psychotic illnesses (mental disabilities, etc.), those under stress due to their current situation (according to some studies, these individuals are under the influence of external forces), homeless families (it is noted that in 70% of cases, the group most commonly found is led by a woman), homeless and disconnected young people, homeless women living alone or with their children (Türkcan and Türkcan, 1996; Balun and Şişman, 2022).

Vulnerable populations, including children, older adults, and people with disabilities, tend to spend more time at home and are therefore more susceptible to the health risks posed by inadequate housing (WHO, 2021).

Figure 1

Global Goals (SDG, 2025)

Table 1

Global Goals and Homelessness Relationship

1. SDG 1 – No Poverty	Target 1.1: Eradicate extreme poverty. Target 1.2: Reduce the proportion of people living in relative poverty.
	Homelessness is one of the most extreme manifestations of poverty.
2. SDG 3 – Good Health and Well-being	Target 3.8: Universal healthcare coverage, especially access for vulnerable groups.
	Homeless individuals experience significant inequalities in access to healthcare.
3. SDG 4 – Quality Education	Target 4.5: Reduce inequalities in education.
	Homeless children and youth are at risk of exclusion from education.
4. SDG 5 – Gender Equality	Target 5.2: Eliminate violence against women.
	Homeless women are at high risk of sexual violence and abuse.
5. SDG 8 – Decent Work and Economic Growth	Target 8.5: Full and productive employment and equal pay for equal work for all.
	Homeless individuals have limited access to employment; informality is high.
6. SDG 10 – Reduced Inequalities	Target 10.2: The effective participation of all individuals in social, economic, and political life.
	Homeless individuals are often marginalized.

7. SDG 11 – Sustainable Cities and Communities	Target 11.1: Safe, accessible, and affordable housing for all by 2030. Target 11.3: Inclusive and sustainable urbanization.
	This target is most directly related to homelessness.
8. SDG 16 – Peace, Justice, and Strong Institutions	Target 16.1: Reducing all forms of violence. Target 16.7: Inclusive and participatory decision-making.
	Homeless individuals are frequently subjected to violence and exclusion.

Homelessness is a multidimensional problem that intersects with at least eight sustainable development goals. The SDGs' core principle, "Leave no one behind," emphasizes the importance of inclusive social policies for homeless people and holistic health, poverty, and housing approaches (Table 1) (SDG, 2025).

Impacts of Homelessness on Health

Homelessness has a direct impact on health. Homeless individuals, especially those with sleep problems, have a higher rate of serious illness than the general population. They are prone to a range of health issues, including infections, inflammatory skin diseases, respiratory illnesses, physical trauma, the adverse effects of illicit drugs, and/or mental health problems (Wright and Tomkins, 2006). Although Istanbul does not appear to have as high a rate as globally developed cities in developed countries, the global transformation taking place in Istanbul and its ongoing effects may indicate the potential for an increase in homelessness rates (Bekaroğlu Doğan, 2018). Homelessness continues to be a serious social and health issue. A program that addresses the needs of homeless individuals with mental health disorders must support services that meet their livelihood needs and physical health care needs, in addition to providing sustainable housing, to be successful in improving their quality of life and well-being. Education is particularly necessary to maximize personal safety, and strategies aimed at reducing symptoms of depression may also be effective (Sullivan et al., 2000).

The use of occupation as a therapeutic tool in the effective management of treatment and rehabilitation processes for individuals with different health conditions and disadvantages is undoubtedly one of the important tasks of occupational therapists. It is necessary to ensure that clients are as independent as possible in managing processes that will improve their quality of life and enable them to participate in daily life. Occupational therapy approaches distinguish themselves from other healthcare professions due to this unique humanistic and holistic perspective (Yıldırım, 2023).

It is important to obtain a detailed account of the individual's background, experiences, strengths, and challenges. Identifying the individual's basic needs (housing, nutrition, safety, health) should be a priority. The individual's skills and abilities should be identified. Mental health, physical health status, addiction, and other health factors should be assessed. The individual's social context (family, friends, community) should be assessed; social support and connections should be taken into account. Emergency goals should be set to meet basic needs (finding housing, providing a safe environment, accessing basic health services). Long-term goals may include plans to increase the individual's independence and potential employment opportunities. Goals that support mental health and strategies to improve health status should be identified. The individual should be enabled to achieve long-term employment and social goals through education and skill development opportunities. Goals for greater participation and connection in the community should be identified. Strategies and goals aimed at reducing disadvantages (stigma, discrimination) should be identified. The process of achieving goals should be regularly monitored and revised as needed. These steps help us comprehensively address the challenges and goals faced by homeless individuals (Sarışahin, 2024).

Society's recognition of homeless individuals and the problem of homelessness can have a powerful impact on creating lasting solutions. At this point, raising awareness of the problem of homelessness can be seen as one of the first steps toward addressing the problem (Demir, 2024).

Therefore, combating homelessness should not be addressed solely through individual interventions, but rather through social awareness, comprehensive assessment, professional support, and structural solutions. Integrated policies and interprofessional collaborations centered on health, housing, education, and social participation are critical for both improving individuals' quality of life and ensuring social equality.

Approaching Homelessness with Sustainability Principles in Health

Engagement in meaningful occupations is increasingly recognized by both civil society organizations and government bodies as an effective means of supporting individuals experiencing homelessness. While further studies are required to establish the evidence base for occupational therapy interventions in this context, occupational therapists are well-positioned to design strategies that enhance the well-being of individuals both during and after periods of homelessness. Advancing occupational therapy practice and research in this field requires clearer ways of conceptualizing interventions and articulating the unique contributions of the profession. Developing a framework tailored specifically to occupational therapy and homelessness represents a valuable step toward achieving this aim (Homeless Link, 2018; Homeless Hub, 2011; HM Government, 2011).

Occupational deprivation, imbalance, alienation, marginalization, and racism are factors contributing to occupational injustice among homeless individuals. While existing occupational therapy interventions for the homeless exist, occupational injustice can be addressed to improve the overall well-being, quality of life, and occupational participation of this population. In addition to existing evidence-based information on this topic, findings from extensive experience demonstrate the effectiveness and importance of individual and group-based occupational therapy interventions in this population (Levan et al., 2020). The American Occupational Therapy Association (AOTA) 2025 vision is "to maximize health, well-being, and quality of life for all people, communities, and societies" (Marshall et al., 2023). The scope of occupational therapy is to meet the occupational needs of homeless individuals. These needs can be met through individual, societal, and national support strategies (Table 2, Table 3, Table 4).

Table 2

Individual Level

Level	Approach	Strategies
Individual	Supporting mental health	- Provide ongoing and frequent opportunities for counseling and reflective listening based on the current level of distress the individual may be experiencing. - Increase the availability of support through multiple channels (e.g., text, email, phone). - Apply crisis intervention principles, including suicide intervention when necessary.
	Managing substance use	- Harm reduction strategies aimed at promoting behaviors that enable a person to use substances in a way that ensures safety. - Use of meaningful activities to replace substance use behaviors.
	Addressing housing problems	- Identify funding sources for new housing or for preventing homelessness. - Advocate with landlords on behalf of the individual to prevent eviction. - Support the individual in searching housing listings. - Assist in identifying safe emergency shelter options.
	Addressing poverty	- Identify and support the individual in income-generating strategies. - Reveal opportunities for accessing benefits the person is entitled to but is not receiving, including help with tax filing, applying for welfare programs, or advocating for program inclusion.
	Including peer support	- Include individuals with lived experience of homelessness in services designed to support homeless people. - Peer support workers should be compensated and recognized as unique professionals within interdisciplinary teams.

Table 3

Community Level

Level	Approach	Strategies
Community	Developing homelessness prevention programs with communities	- Collaborate with community stakeholders to identify local solutions that reflect the community's unique cultural and service context. - Work together to implement the identified strategies.
	Reducing stigma around homelessness	- Educate the public about the systemic causes of homelessness through public presentations, articles in local publications, and one-on-one interactions with community members, while also addressing narratives that promote stigma by portraying homelessness as a personal failure.
	Promoting community awareness on homelessness	- Use local statistics about homelessness in service settings to draw attention within the mental health and social service sectors. - Offer presentations about homelessness to the public. - Submit articles to local publications (e.g., newspapers) to attract attention.
	Advocating for people with health issues in community services	- Educate health services, housing support workers, and landlords about how substance use, mental health, and cognitive challenges may manifest as behavioral difficulties and provide effective strategies to manage these in housing programs and market housing. - Advocate for environmental changes to increase function and participation for recently housed individuals living with mental, cognitive, and physical disabilities.

Table 4

National Level

Level	Approach	Strategies
National	Advocating for affordable housing for all	- Meet with policymakers and politicians to raise awareness of the need for affordable housing for all, especially with the necessary supports for those who require it to remain housed.
	Advocating for poverty reduction strategies as a means to prevent homelessness	- Collaborate with national and international poverty reduction groups, policymakers, and politicians to advocate for poverty reduction strategies (e.g., universal basic income, increased welfare rates, etc.).
	Identifying new solutions through inter-municipal partnerships	- Connect municipal leaders from different regions to identify solutions that can prevent homelessness and help marginalized people access mental health care, substance use treatment, and social support.
	Focusing research on homelessness prevention	- Design and conduct research focusing on the prevention of homelessness. - Collaborate with researchers to achieve this goal. - Use participatory research models (e.g., community-based participatory research, participatory action research) to facilitate change at the community and population levels.
	Participating in advisory roles on committees focused on poverty and housing	- Identify opportunities for occupational therapists and academic professionals to participate in advisory committees or boards of regional, national, or international organizations that advocate for the social, functional, and participatory needs of homeless or recently housed individuals. - Promote poverty reduction and affordable housing within organizations capable of influencing social change.

Good Practice Examples and Models

When discussing types of shelters, we can distinguish between night shelters, daytime centers, and hostels that offer round-the-clock services. The declaration of the "International Year of the Homeless" by UNESCO in 1987 indicates that homelessness is a global concern rather than an issue confined to one region. United Nations reports estimate that around 100 million people worldwide are completely unsheltered, sleeping in public spaces such as parks, stairways, doorsteps, or under bridges. In contrast, other statistics suggest that nearly 1 billion people experience homelessness more broadly, living in temporary shelters or refugee camps under precarious conditions. Homelessness, which is intertwined with multiple social problems, has been present throughout history but has reached unprecedented levels in the past decade. Today, it is recognized as a growing global social issue, affecting countries regardless of their level of economic development (Özdemir, 2010; Goldberg, 1999).

Across the United States, occupational therapy positions are growing in programs such as the Project Renewal, Health Services for the Homeless in New York City, and the Skid Row Housing Trust in Los Angeles. In Canada, the Home/Chez Soi Project, the largest randomized controlled trial of Housing First in the world, involves occupational therapists working in various organizations funded to provide Housing First services to people experiencing homelessness (Project Renewal, 2020; Health Care for the Homeless, 2020; Skid Row Housing Trust, 2020).

The Istanbul Metropolitan Municipality (IMM) continues its preventive health services for individuals experiencing homelessness. In order to meet the hygiene needs of homeless individuals living within the boundaries of Istanbul, the "Istanbul Mobile Bath Project" has been launched. Each year during the winter months, IMM provides shelter, personal care, health services, food, and clothing support to homeless individuals. In addition to these services, the newly introduced "Istanbul Mobile Bath" now also helps meet the personal care needs of homeless individuals in need.

In 2016 the Finish Y-Foundation together with FEANTSA established the Housing First Europe Hub. The Y-Foundation has been a key player in establishing Housing First as the main response to homelessness in Finland. Since 2007 national policies shifted towards reducing long-term homelessness through Housing First programmes.

As a result, in Finland, the utilisation of emergency and temporary accommodations, such as shelters, hostels, and temporary supported housing, has significantly declined. The number of homeless individuals residing in hostels or boarding houses decreased by 76% from 2008 to 2017. This reduction is attributed to the widespread adoption of prevention strategies, the replacement of outdated models of communal supported housing with Housing First and housing-led approaches, which largely replaced emergency shelters (Housing First, 2025).

Housing Europe Hub First

Initially launched under the name “Clean Up, Dress Up, and Go” by the Health Department’s Istanbul Darülaceze Branch Directorate, the project was later included in the IMM “My Budget Istanbul” program based on suggestions from Istanbul residents. At this stage, a specially equipped bus allocated by IETT (Istanbul Electric Tram and Tunnel Company) was prepared for service. The bus, staff ed with psychologists and sociologists to serve homeless individuals, provides access to showers, personal care, and hairdressing services for those without access to hygiene facilities in the city (IMM, 2024).

Following the issuance of an orange weather alert for Istanbul during the winter months, the Istanbul Metropolitan Municipality (IMM) launches its Winter Services to protect homeless individuals from the dangers of severe storms. The Winter Services aim to provide a sense of home-like warmth for those experiencing homelessness. As part of this service, homeless individuals exposed to cold weather conditions are picked up by IMM teams and transported to IMM facilities. After being registered by IMM staff, the individuals are hosted at these facilities where they receive comprehensive support. As part of the service, all guests first undergo health screenings. Those who are ill receive medical treatment. Individuals without health issues are given personal care services such as haircuts, shaves, and showers, and are provided with new clothing.

In addition to shelter, the guests’ ongoing needs—including healthcare, meals, clothing replacement, and personal hygiene—are regularly met during their stay. Individuals who meet the eligibility criteria for Istanbul Darülaceze are admitted to IMM’s long-term elderly care centers. For those wishing to return to their hometowns, transportation assistance is also provided. During the 2023–2024 winter period, the “Winter Services for the Homeless” program was offered at the Istanbul Darülaceze Directorate’s Kayışdağı campus for women, and at the Esenyurt shelter for men. Additionally, transportation support was made available for homeless individuals seeking to return to their hometowns (IMM, 2025).

In an interview conducted by Akyurt with Ali Kamil Başar in 2024, regarding the "Beyoğlu District Governorship Shelter for the Homeless," which operated between 2003 and 2006, the following statement was made: "There was a strong sense of solidarity and mutual support" (Akyurt, 2024).

In Turkey, there are civil society organizations, mosques/muftis, central and local authorities that are in contact with homeless people to provide them with various needs such as shelter, food, and clothing. Some of the civil society organizations in Istanbul include Hayata Sarıl Association, Çorbada Tuzun Olsun Association, Deliler ve Veliler Association, Fatih'in Torunları Association, Sokak Lambası Association, and Tarlabaşı Dayanışma Grubu (Akyurt, 2023). There are civil society organizations and public institutions in Turkey that provide shelter services for the homeless. Among civil society organizations, there are the Tarlabaşı Solidarity Community, the Erdemliler Association, and the Şefkat Association; among public institutions, there are the Istanbul Metropolitan Municipality, the Şişli District Governor's Office, the Üsküdar District Governor's Office, the Bursa Men's Guesthouse, and two mosques affiliated with the Ministry of Religious Affairs in Beyoğlu and Eyüp. In Turkey, there are only shelters that provide full-day services (Akyurt, 2023).

In our country, homeless people are generally neglected, institutional services are extremely inadequate, and even if planning were to be undertaken, there is no data available on the number of homeless people. Two practitioners who shared their experiences made important estimates. A social worker working in the field mentioned that there are approximately 5,000 homeless people in Izmir and 5-10 million in Turkey, emphasizing that this number may vary depending on the definition and characteristics of homelessness (Çabuk and Atamtürk, 2023).

As a result, in recent years, the services provided by local governments have reflected a comprehensive approach that aims to respond not only to the housing needs of homeless individuals but also to their multidimensional needs, such as health, hygiene, personal care, and social support. The measures taken to address the increased risks during the winter months and the projects carried out throughout the year support homeless individuals in living in a manner befitting human dignity; they also serve as a model in terms of social solidarity and the effectiveness of social services. In this context, when evaluated alongside past best practices, the development of comprehensive and sustainable policies by local governments to address homelessness is of great importance in terms of ensuring social justice.

Sustainable Intervention Recommendations for Homelessness

Eliminating the structural causes of homelessness can be likened to extinguishing a fire, while reintegrating homeless people into society can be likened to clearing the smoke (Akyurt, 2024). Housing strategies should be implemented in an integrated manner with areas such as health, mental health, social services, education, and employment (Szeintuch, 2024).

Occupational therapy has the potential to remove barriers to care by increasing confidence and self-esteem, providing support with personal care and daily routines, promoting belonging and inclusion, and advocating for appropriate environments (housing) that can have a positive impact on the health of people experiencing homelessness (Woodhull and Boyle, 2025).

It is stated that the street medicine approach can be an effective model for homeless individuals without shelter. Street medicine is an approach that provides healthcare services to homeless individuals where they live—on the streets, under bridges, in parks, abandoned buildings, and other such areas. Its goal is to directly reach individuals who cannot access or do not want to access traditional healthcare systems (Perna et al., 2024).

Street medicine approaches have been reported to have significant positive effects on quality of life, trauma symptoms, substance use, and recovery levels among homeless individuals. Integrated, on-site service models offer important opportunities for occupational therapists, social workers, and mental health professionals (Table 5), (Withers, 2011; Perna et al., 2024).

Table 5

Basic Principles of Street Medicine (Perna et al., 2024; SMI, 2025)

Basic Principles of Street Medicine	
Bringing services to where individuals are located	– This means "we are coming to you" to individuals who do not go to clinics.
Relationship-centered care	– Participation in treatment is increased through trust, consistency, and empathy.
Trauma-informed and person-centered approach	– Services are provided with consideration for the traumas commonly encountered in the lives of homeless individuals.

Integrated and multidisciplinary services	– Psychiatrists, doctors, nurses, occupational therapists, social workers, and accompanying support staff work together.
Housing is part of health	– Housing itself is seen as a health intervention.

In this regard, the fight against homelessness requires not only individual interventions but also comprehensive policy approaches that target structural problems. Ensuring the right to housing, increasing access to health and social services, providing employment support, education opportunities, and mental health services in an integrated manner will enable not only crisis management but also lasting well-being. With the support of disciplines such as street medicine and occupational therapy, individuals should be encouraged to regain a sense of control over their lives and participate in society. Therefore, social policymakers, local governments, and service providers must prioritize interdisciplinary and human dignity-based practices.

Conclusion and Future Recommendations

Individuals who have experienced homelessness may have encountered traumatic events. Therefore, it is important to be aware of trauma and adjust the treatment plan accordingly. Homeless individuals can be referred to community resources to help them meet their daily needs. It is important to ensure that they are aware of resources such as housing services, food assistance, and health services. Additionally, working with homeless individuals as an occupational therapist is a specialized process that requires sensitivity, empathy, and effective communication skills. These strategies help create a therapeutic environment and facilitate positive changes in the lives of homeless individuals.

A sensitive and inclusive approach is essential in combating homelessness. Mental health professionals and human rights advocates should strive to protect the rights of homeless individuals and improve their lives. The government and civil society should collaborate to develop effective policies to combat homelessness. Principles of social justice, occupational justice, human rights, and equality in society should be prioritized among mental health professionals. Better understanding homeless individuals, supporting them, and developing sensitive policies in this area are important steps toward building a more equitable society. It would be beneficial for occupational therapists and occupational therapy academics to be involved in advisory committees or national or international organizations that advocate for the social, functional, and participatory needs of homeless individuals.

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Sustainable Health for Parents of Children with Special Needs

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Introduction

The concept of sustainable health encompasses the long-term enhancement and maintenance of individuals' physical, mental, and social well-being. Sustainable health includes not only improving existing health problems but also focuses on the resources and support systems needed to maintain health.

The issue of sustainable health for caregivers, particularly parents of children with special needs, has often been overlooked. It is crucial to prioritize the physical and psychological well-being of caregivers, as this directly affects their quality of life and the care they provide to those they look after. In this regard, Occupational Therapy is a critical health discipline that supports caregivers' well-being sustainably, enhances their quality of life, and improves care processes.

The sustainability of improvement is as crucial as enhancing the psychological, physical, and social well-being of parents. Therefore, this section will explore the role of occupational therapy science in promoting sustainable health for parents of individuals with special needs. It will also cover evidence-based occupational therapy interventions and discuss future trends.

Definition and Importance of Sustainable Health

Health is commonly defined as a state of complete physical, mental, and social well-being, rather than merely the absence of disease or disability. It is regarded as a fundamental human right that should be accessible to every individual, regardless of race, religion, political beliefs, or economic or social conditions (WHO, 2025). The achievement of optimal health for all people is essential for the attainment of peace and security, and it depends on the fullest cooperation among individuals, communities, and states. Furthermore, the health advancements made by any state contribute to global well-being, highlighting the collective value of promoting and protecting health. Unequal progress in health promotion and disease control, particularly in communicable diseases, poses a global risk.

The healthy development of children is vital because it lays the foundation for their ability to live harmoniously in a changing environment. Access to medical, psychological, and related services is essential for achieving optimal health standards for all populations. Public involvement, informed opinions, and active cooperation are crucial for improving health outcomes. Ultimately, governments have the responsibility to ensure the health of their populations by implementing adequate health and social measures.

Figure 1

WHO logo and plan

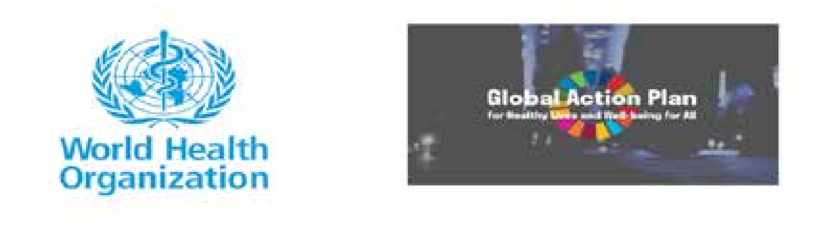

Table 1

Ten avenues for the core of a strategy

adopting a national environmental sustainability policy for health systems	minimizing and adequately managing waste and hazardous chemicals	promoting sustainable procurement
promoting an efficient management of resources	promoting sustainable procurement	reducing health systems' emissions of greenhouse gases and air pollution
prioritizing disease prevention, health promotion and public health services	engaging the health workforce as an agent of sustainability	increasing community resilience and promoting local assets
creating incentives for change	promoting innovative models of care	

The Global Action Plan for Healthy Lives and Well-being for All (SDG3 GAP), established in 2019, brings together 13 multilateral health, development, and humanitarian agencies.

Its goal is to accelerate progress on health-related SDG targets by strengthening collaboration among agencies, enabling joint action, and supporting country-led national plans (WHO, 2019). An environmentally sustainable health system is defined as one that promotes health while minimizing environmental harm and leveraging opportunities to improve it for current and future generations (WHO, 2017). Ten avenues for action are proposed that can form the core of a strategy for fostering environmental sustainability in health systems, namely (Table 1).

Special Children and Their Caregivers

Unlike individuals who develop normally, some individuals develop differently and benefit only partially or not at all from general education services. In the past, referred to as a disability, this condition is now termed special needs because it is less stigmatizing. It is defined as the inability to fulfill, or only limited ability to fulfill, the roles expected based on age, gender, and social and cultural factors due to the individual's specific condition (Metin,2018).

Having a child with special needs requires more responsibility than having a child with typical development. These responsibilities include caring for the child with special needs, taking the child to the doctor more frequently due to their special condition, providing financial support for their nutrition and education expenses, overcoming their behavioral, learning, and psychological problems and receiving support in this regard, caring for other children who are developing normally, coping with problems experienced with one's spouse, and informing the people around them about their child's special condition (Toy & Kesici, 2020).

Care is defined as the effort expended to ensure that something develops well and remains in good condition; it is defined as the work done to take on and meet a person's needs, such as feeding, clothing, etc. (TDK, 2023). Care can be analyzed under two headings. These headings are formal care and informal care. Formal caregiving refers to care provided by professional healthcare workers or institutions, usually in the form of paid and organized services. Informal caregiving refers to care provided by family members, friends, or volunteers, mostly in an unpaid and informal manner (Sarisahin, 2023).

Caring for a special child exposes parents to high levels of stress, increasing their risk of mental health disorders. Psychological resilience factors can serve as resources to reduce the harmful effects of stress, benefiting both parents and their children, and fostering positive, resilient outcomes (Broll et al., 2025).

In a study conducted to determine the difficulties experienced by home caregivers, it was found that the burden of care was mostly (83.7%) on women (Alpteker, 2008). In another study conducted to determine the care stress of informal caregivers, it was found that caregivers had hypertension, weakening of the immune system, as well as depression or anxiety, and care-related stress (Gopalan & Brannon, 2006).

Among mothers of children with intellectual disabilities, the motivation for caregiving has a multifaceted nature. External motivations include support received from family, social networks, and formal sources. Internal motivations include factors such as mothers' unconditional love for their children, the spiritual satisfaction they derive from their role as mothers, their sense of responsibility, faith-based interpretations, and the inner happiness they feel from their children's small developmental steps (Hosseini et al., 2024). Understanding these motivations can facilitate the development of targeted support programs and interventions that address the unique needs and challenges faced by these caregivers. Health service providers and policymakers, by recognizing and enhancing various sources of motivation, can better support mothers in their caregiving roles, ultimately contributing to better outcomes for both mothers and their children.

Social Support and Family Dynamics

Family dynamics experienced by parents of children with special needs play a major role in shaping both the roles within the family and the psychological, physical, and social needs of family members.

Open communication and cooperation between parents ensures that the burden of care is evenly distributed. However, the stress of caregiving can damage relationships between spouses. Parents supporting each other and seeking solutions together provide balance within the family.

Parents of children with disabilities may sometimes experience fears of being left alone in their caregiving role. The disclosure of a child's diagnosis can place significant strain on a marriage, occasionally resulting in separation or abandonment. In some cases, one partner struggles to come to terms with the child's condition (Duma et al., 2021; Matambanadzo & Rhoda, 2024). Raising awareness among fathers of children with disabilities is particularly important, as their active involvement in caregiving can ease the mother's burden and promote shared responsibility (Cramm & Nieboer, 2011). Gender differences in care roles are questionable, as mothers are expected to be the caregivers of children to a degree that can affect their economic activities. While mothers and fathers have different roles, this does not mean that the woman alone should assume responsibility for meeting the child's daily needs (Ndadzungira, 2016).

Families with children with disabilities often develop a strong emotional attachment to their children. While this attachment can lead family members to put more effort into their children, it can also lead parents to ignore their individual needs. Caring for children with disabilities requires additional expenses and large investments in health care. This financial burden can affect the economic situation of family members and cause tensions within the family. For some families, the inability of parents to participate in the labor market due to the care of a child with a disability can also be a major problem.

Families with children with disabilities can often experience social isolation. Society's lack of awareness about children with disabilities and their families can lead to feelings of isolation. Families' social support networks and social ties play an important role in the care of their children (Manteau-Rao, 2016).

Support groups created to alleviate the emotional burdens experienced by parents of children with disabilities help parents feel that they are not alone, share their experiences, and increase their psychological resilience (Shilling et al., 2013; Kidfirst, 2025).

Community-Based Approaches for Sustainable Health

In Türkiye, various services sponsored by the government are provided by non-governmental organizations and local authorities to ensure the sustainable health of children with special needs and their parents. These services are continuously improved to make caregiving processes more sustainable, protect the psychological and physical health of families, and strengthen their social support networks. Education, psychological support, social services, and technology-based solutions that increase accessibility play a major role in this process.

In the "2030 Barrier-Free Vision Document" of the Ministry of Family and Social Services (MFSS), the goal is stated as "building an inclusive society where persons with disabilities can realize their potential as equal citizens." This Vision Document includes individuals and their families who are affected by environmental and attitudinal barriers that restrict full and effective participation in society on an equal basis with others due to various levels of impairment in physical, mental, psychological, and sensory abilities. It emphasizes that the concept of disability is evolving and transforming over time, and therefore, the scope should be considered open to change.

The vision in the field of disability is based on the following fundamental principles (MFSS,2021,p:10-13):

Table 2

The visions in the field of disability

» Respect for human dignity and individual autonomy, including the freedom to make one's own choices and independence of persons
» Non-discrimination
» Full and effective participation and inclusion in society of persons with disabilities

» Respect for difference and acceptance of persons with disabilities as part of human diversity and humanity
» Equal opportunities
» Accessibility
» Gender equality
» Respect for the evolving capacities of children with disabilities and their right to preserve their identities

An inclusive society acknowledges that every individual has unique characteristics and different needs, and ensures that each person — including persons with disabilities — can benefit from general policies, programs, and services by addressing these diverse needs. Relying solely on mainstreaming disability as a method to achieve social inclusion may risk overlooking the diversity of disabilities and the specific measures required to address them.

A dual-track approach aims to eliminate this risk by ensuring that, within the process of mainstreaming disability, appropriate measures and adjustments are made to address the differing needs that arise depending on the type and degree of disability. A key element of this process is that these measures and adjustments must be decided together with persons with disabilities. In order to realize the vision of building an inclusive society where persons with disabilities can realize their potential as equal citizens, 8 policy goals (Figure 3) have been defined across various policy areas. These are accompanied by 31 objectives and 107 action items, which will serve as a basis for the activities aimed at achieving these objectives (MFSS,2021,p:15).

Figure 3

Policy Areas

Under the goal of independent living, *Objective 1* is:

"*The development and expansion of diversified and next-generation care services that support independent living for persons with disabilities and their families."* This scope also includes caregivers (MFSS,2021,p:71-77).

The Republic of Turkey Ministry of Health, in its Disabled Health Committee Report Circular (2018/4), states the following:

"Based on the foundations of the United Nations Convention on the Rights of Persons with Disabilities and the United Nations Convention on the Rights of the Child, and developed by the World Health Organization to create a common standard language and framework, the World Health Organization's International Classification of Functioning Disability and Health, Children and Youth Version (ICF-CY) is a comprehensive international classification system that enables the definition of individuals' functionality, activities, participation in life, and limitations in these areas. Based on this system, classification studies regarding disability and special needs have been prepared."

"The newly registered regulation in interest is not based on 'disability rate', but on 'needs'. The Special Needs Report for Children specifies which services children require, facilitating the access of children and their families to rights and services, without leading to any loss of rights." (RTMH,2024).

In this context, strengthening community-based services is emphasized as a means to facilitate easier access for children and families to the support they need. Additionally, the goal is to enhance social participation and provide a more sustainable quality of life.

1. Tohum Autism Foundation

Services: Provides education, rehabilitation, and family support programs for children with autism spectrum disorder. Additionally, it offers psychological support and informational services to families (TOV, 2025).

2. Türkiye Down Syndrome Association

Services: Works on the education, integration, and rights of individuals with Down syndrome. It provides counseling and psychological support services to families (TDSD, 2025).

3. Cerebral Palsy Children's Association

Services: Works on the education and rehabilitation of children with cerebral palsy. It organizes support services and informational meetings for parents (Serçev, 2025).

4. Rare Diseases Research Association

Services: Works to raise awareness about rare diseases, provide early diagnosis and treatment opportunities, and offer psychological support to individuals and families fighting these diseases (NHAD, 2025).

5. Leukemia Children Foundation

Services: Provides psychological, social, educational, and financial support to children and families fighting leukemia and other cancer types. It also offers various rehabilitation programs and social services to individuals undergoing cancer treatment (Lösev, 2025).

These NGOs provide essential services to meet the social, psychological, and educational needs of children with special needs and their families. While parents of children with special needs bear a considerable responsibility at every stage of the care process, they also face significant emotional, psychological, and physical challenges. In this context, the enhancement of community-based sustainable health approaches will empower parents to manage their care processes more healthily. With the provision of suitable guidance and resources from the community, as well as professional support, it is possible for families to enhance the well-being of both themselves and their children.

Community-based health services have been found to support individuals with disabilities and their families to achieve a more sustainable quality of life by increasing their social inclusion. In this framework, the state, non-governmental organizations, and relevant stakeholders can work together to take an important step towards building a more inclusive and just society by improving opportunities such as education, psychological support, and social services for families. Such practices will improve the quality of life of persons with disabilities and their families, while reinforcing social solidarity and equality.

The Role of Occupational Therapy in the Context of Sustainable Health

Occupational therapy focuses on the health and development of the baby while supporting the psychological and emotional health of the parent. It provides education and guidance for parents, helping them cope with stress. Therapists apply ergonomic approaches and family-centered care principles to improve parents' physical and psychological health (Antinora et al., 2023; Yu et al., 2020). This can reduce parents' stress levels and lead them to caregiving more effectively. Therapists take a holistic approach, taking into account the mental health of the parents. This helps parents to be psychologically empowered during caregiving (Stovall et al., 2025).

Identifying which factors cause stress during care, realistically assessing one's capacity for action, and effective problem-solving ability can be explained as a mechanism by which resilience facilitates adaptation. There are very few studies with adults on resilience, which alleviates the negative effects of stress and supports adaptation. Childhood research suggests that resilience develops in trusting relationships with role models who advocate self-esteem and through effective family functioning. These findings suggest that a similar process will be followed in adulthood (Broll et. al, 2025). Resilience also refers to emotional resilience and has been used to describe people who exhibit courage and adaptability following life's misfortunes. Activities that create "me time" for caregivers can provide them with emotional relief (Figure 1). A variety of strategies can be used to guide the caregiver in discovering meaningful and purposeful recreations for themselves and to support their participation in existing recreations. Occupational therapists can make this process more effective by raising awareness of people's "me time" in line with their professional knowledge and skills.

Figure 2
Me time

Effects of Occupational Therapy Interventions on Caregivers

Occupational therapists provide assessment, strengthening, education, and skill training for caregivers. Occupational therapists offer alternative ideas and solutions for a new therapeutic partnership that strengthens the patient-therapist dyad in order to create a new caregiver-patient-therapist triad (Moghimi, 2007). In non-individual-centered programs, the needs of individuals may be overlooked, and intervention programs may be inadequate. In addition, a homogeneous group is required for the implementation of package programs, which is not very realistic in practice (Köse & Akı, 2019).

Supporting parent-child bonding encourages parents to interact with their children and supports the role of the parent in this context through co-occupation. This enables parents to participate more actively in caregiving processes. For caregivers, care recipient-centered interventions help to achieve rehabilitation goals, with many of the interventions improving and facilitating the care provided. For example, training caregivers on how to perform care tasks provides opportunities to practice new care-related skills and is accompanied by feedback/coaching (Moghimi, 2007).

Occupational therapists apply ergonomic approaches and family-centered care principles to improve the physical and psychological health of parents. Occupational therapists adopt a holistic approach, taking into account the mental health of parents. This process enables parents to experience psychological empowerment within their caregiving role (Townsend & Polatajko, 2013). It emphasizes the importance of identifying personal strengths, exploring new sources of fulfillment, fostering growth, and discovering or redefining life purpose and spirituality. Such empowerment may involve character building, acquiring new skills and knowledge, enhancing confidence and competence, adapting to a "new normal," and cultivating or deepening spiritual connections (Demers, 2022).

Occupational therapists strengthen the parents' role in the care process by collaborating with other health professionals. This allows the whole health team to be an active participant in the parents' caregiving process. Caregivers need to be supported in developing new or deeper relationships with other people. Two types of relationships prevail: family and friends; other care-related relationships (health professionals, caregivers) Demers, 2022).

Occupational therapy is an important help for the parent to adapt to their new role. For example, therapy sessions that allow the parent to participate in the care of the baby can also increase the parent's self-confidence. Occupational therapists can develop strategies to create "me time" for parents, enabling caregivers to care for themselves and improving their overall quality of life.

Table 3

Steps to Caregiver-Specific Approach to Occupational Participation (Demers, 2022).

Steps to Caregiver-Specific Approach to Occupational Participation.

Steps	Description
Step 1	Identify challenging caregiving tasks • to make them easier • to make them safer
Step 2	Delve deeper into caregivers' experiences • motivations for caregiving • what sustains and makes caregiving enjoyable
Step 3	Explore the caregivers' needs, goals, and desires beyond caregiving

By taking into account both the challenges and rewards of caregiving, together with caregivers' personal needs, goals, and aspirations across different aspects of life, it becomes possible to develop a holistic understanding of their situation. This perspective allows practitioners to collaborate with caregivers as clients, supporting them in strengthening autonomy and fostering social participation as their life conditions evolve.

Based on this view, a new three-stage approach is proposed as outlined below. Step 1: Identify the physically and emotionally demanding caregiving tasks, and work to make these tasks more accessible and safer for both the caregiver and the care recipient. Step 2: Understand why caregivers provide care, what motivates them throughout the process, and what aspects make caregiving meaningful or fulfilling. Step 3: Explore not only the caregiver's role in caregiving, but also their personal goals, desires, and needs beyond caregiving. These three steps aim to enhance both the caregiver's quality of life and their overall caregiving experience. (Table 3) (Demers, 2022).

Future Directions for Sustainable Health

A multifaceted approach is needed to support the sustainable health of parents with children with special needs. Sustainable health for parents of children with special needs must be approached holistically, both at the individual level and at the societal level. Future directions should target the implementation of various strategies to improve the quality of life of these parents, to help them cope with the challenges in the care process, and to ensure that they can lead a healthy life. This process includes not only the accessibility of health services, but also the strengthening of the social support systems needed by families and caregivers.

Social support systems for caregivers of children with special needs to be strengthened. Community-based health services play a critical role in maintaining the sustainable health of parents. Systematic policies for the physical and psychological health of caregivers need to be developed. Increasing the level of education of caregivers enables them to be more effective in the care process and, at the same time, maintain their own health. Providing regular psychological support and rehabilitation services for caregivers will sustain their health (WHO, 2021).

Digital health apps can make parents' care processes more efficient and improve time management. Such digital tools offer practical solutions that reduce the burden of caregiving for parents. The goal should be to change societal perceptions of parents of children with special needs. These campaigns lead to greater understanding, empathy, and support in society. Expanding programs for parents of children with special needs to more regions and making them accessible through digital platforms will help reach a wider audience.

Different interventions such as education, complementary and supportive therapies, psychotherapy, inclusion in social groups, and family education programs are used to improve the quality of life of caregivers and to cope with the difficulties experienced. Existing programs should be revised in accordance with the age. Table 4 shows sample family education programs for parents of children with special needs.

Table 4

Programs Implemented for Family Education of Children with Special Needs (Metin, 2012)

Group-Based Family Education Program	These programs involve bringing together families of children with similar characteristics.
Home-Based Family Education Program	This program provides benefits in terms of involving all family members in the process. Because family education will be conducted in the home environment, there are potential risks that could disrupt education.
Home and Institution-Based Family Education Program	This program ensures that the skills learned at the institution are continued at home.

Family education programs have a serious importance in the education of children with special needs. The needs of the family should be assessed by the educator. In order for these families to be able to manage their time, the training program should be as short as possible and realistic and limited goals should be set in line with the needs of the family. During the training process, a therapeutic relationship should be established with the family, appropriate communication techniques should be used, and feedback about the process should be obtained by establishing a trusting relationship (Sh et al., 2015).

Future directions should concentrate on the effective management of the challenges and stressors faced by families, whilst developing systems that support caregivers to provide healthy long-term care. In this context, holistic approaches such as education, social support, and psychological recovery programmes are critical to maintain the sustainable health of caregivers.

Conclusion and Recommendations

In conclusion, meeting the sustainable health needs of caregivers with children with special needs should not only include their physical health but also their psychological and social well-being. The supportive interventions offered by occupational therapists to caregivers are of great importance to improve their quality of life and prevent negative effects such as burnout. In this context, it is necessary to increase educational programs for caregivers, strengthen social support networks, and implement strategies to protect the physical health of caregivers. In addition, the development of health policies to take more into account the social, psychological, and economic needs of caregivers will be a critical step towards sustainable health.

Occupational therapists should continue to support the health of caregivers in a sustainable manner with community-based approaches and multidisciplinary collaboration, which will contribute to the creation of healthier and more resilient societies in the future. By providing comprehensive interventions for parents in this process, occupational therapy can improve their quality of life and ensure the sustainability of the care process. Strategies such as continuing education, social support networks, and professional guidance are crucial for parents to provide healthy care. Strengthening intra-family support, reducing social isolation, and easing the care burden of parents through ergonomic strategies are key factors for sustainable caregiving.

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Sustainability In The Healthcare Sector And Health Education

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Introduction

It is universally accepted that Earth's resources are not limitless. The question of whether the irresponsible utilization of these finite resources could push humanity toward an irreversible crisis highlights the essential nature of sustainability. Essentially, sustainability is about creating strategic plans and implementing measures to guarantee that the planet's limited resources remain available for generations to come. The word "sustainability" originally comes from forestry science (Kuhlman & Farrington, 2010). Its application has since broadened, making it a topic of discussion across nearly all areas of life, including health, education, and economics. The necessity for humanity to adopt sustainable practices is driven by a deep sense of responsibility and concern for the welfare of those who follow (Kuhlman & Farrington, 2010).

The Interconnectedness of Development and Sustainability

Is sustainability a mandatory foundation for human well-being, prosperity, and development? The answer is definitely affirmative. Sustainability acts as a critical basis for human advancement and quality of life (Kuhlman & Farrington, 2010), making it indispensable for a flourishing future. Just as natural ecosystems require equilibrium to survive, the pathways of national development must also be sustainable. Thus, sustainable development has become a globally paramount concept. Development is often defined as a positive shift in a nation's key performance indicators (Tolunay & Akyol, 2006), evaluated through three main lenses: economic growth, social progress, and human development (Tolunay & Akyol, 2006). These elements show that development is a complex process with interwoven aspects of societal life.

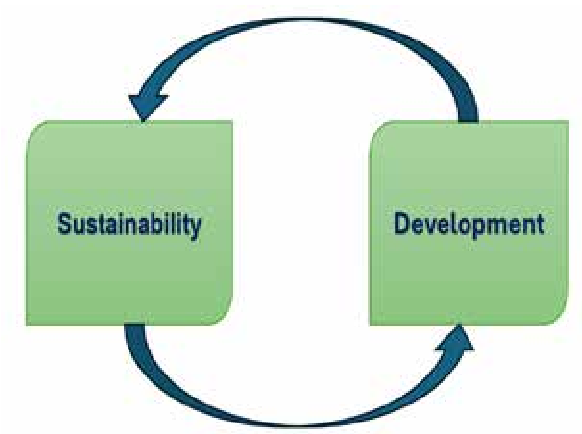
The development approach, heavily focused on consumption after World War II (Ozmehmet, 2008), resulted in significant ecological harm, with negative environmental effects becoming clear by the late 1960s (Ozmehmet, 2008). Factors like uncontrolled industrialization, rapid population increase, the spread of chemicals, and unplanned urban growth have worsened this environmental damage (Demir, Babaoğlu, & Pehlivan, 2022). This degradation has led to a surge in health issues linked to the environment (Demir et al., 2022), with cumulative effects now seriously threatening future generations

(Demir et al., 2022). Climate change, along with air, water, and soil pollution, is are direct causes of various diseases (Demir et al., 2022). The ongoing, unsustainable depletion of natural resources risks causing even more serious challenges in the future, creating a major obstacle to achieving sustainability (Demir et al., 2022). Nations must use resources with peak efficiency to guarantee long-term prosperity and well-being (Tolunay & Akyol, 2006). Consequently, sustainability is just as vital as development itself. Ultimately, irresponsible resource consumption endangers the very continuation of future development. The relationship between sustainability and development is reciprocal: global resources must endure for development to occur, and sustainable practices are essential to guarantee the longevity of those resources.

Recognizing the connection between sustainability and development is crucial. It is highly unlikely that sustainable development for the entire planet can be achieved through the isolated efforts of just a few nations. Therefore, global sustainable development requires coordinated international action. The concept was popularized worldwide by the 1987 United Nations report "Our Common Future" (the Brundtland Report) from the World Commission on Environment and Development, which helped establish a global perspective (Gedik, 2020). The successful implementation of sustainable development relies on having a healthy population and skilled human capital (Boyacıoğlu & Taşkın, 2012). Health's pivotal role underscores the necessity for sustainability within the health sector, its services, and the education of its personnel.

Figure 1

The relationship between sustainability and development concepts



Embedding Sustainability in the Healthcare Sector

The promotion of sustainability within healthcare is critical for safeguarding public health (Tamer, 2020). Global pandemics, such as COVID-19, have clearly underscored the importance of this integration. However, the adoption and understanding of sustainability principles in healthcare currently trail significantly behind industries like manufacturing (Tamer, 2020). This gap is partly due to the complex and multifaceted nature of the sustainability challenges inherent to healthcare.

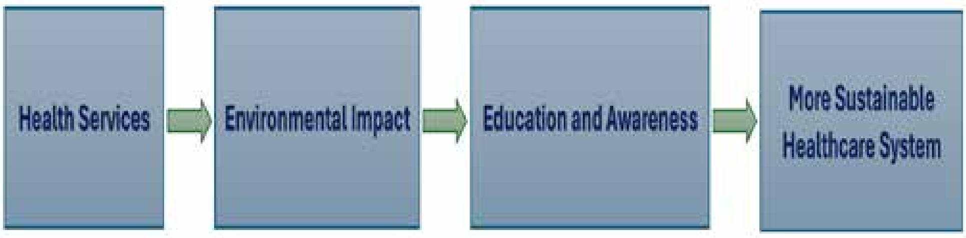
The environmental footprint of the healthcare sector is considerable, marked by an exceptionally high usage of water, energy, hazardous chemicals, and cleaning agents compared to many other industries (Tamer, 2020). This intense resource consumption makes pursuing sustainability in healthcare a global necessity. Sustainability initiatives in healthcare can offer significant economic advantages (Tamer, 2020) and positively contribute to environmental preservation. However, this path is challenging. Healthcare relies on essential resources—including single-use materials, electricity, pharmaceuticals, and water—all of which must be managed sustainably. This means reducing water and energy use, maximizing recycling efforts, and ensuring the safe disposal of chemicals, all while preserving the effectiveness and quality of service for both current and future generations. Achieving this balance demands comprehensive and sophisticated strategies.

Innovation and technology are crucial factors in enabling sustainability strategies in healthcare (Tamer, 2020). For instance, switching from paper-based patient records to digital archiving not only decreases paper consumption but also speeds up operations and access to information, illustrating how technology supports sustainability goals. While sustainability-aligned actions in healthcare can have broad social, economic, and environmental impacts, some measures may be met with resistance, even as others gain widespread support. Furthermore, the rapid evolution of healthcare introduces constant challenges for sustainability (Tamer, 2020). Despite these difficulties, sustainable development in health remains vital for public health (Tamer, 2020).

Environmental sustainability is a necessary precursor for a sustainable healthcare sector (Aslan, Zeybek, Zengin, Kavşur, & Güler, 2023). A forward-thinking approach involves adopting the “green hospital” concept right from the initial planning stages of healthcare facilities (Aslan et al., 2023). Another serious concern is the sector’s role in contributing to greenhouse gas emissions. Healthcare services, especially those provided in hospitals, are a major source of these emissions (Aslan et al., 2023). Regulatory frameworks are needed to limit the carbon footprint of healthcare delivery (Aslan et al., 2023), and the broad implementation of such regulations can lead to substantial financial savings (Aslan et al., 2023).

Figure 2

Sustainability cycle in the healthcare sector



Green Hospitals and Environmental Stewardship

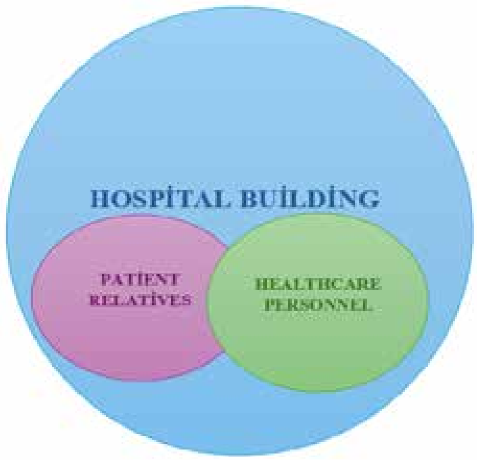
A "green hospital" is defined as an environmentally responsible, energy-efficient facility whose design and operation are guided by sustainability principles (Aslan et al., 2023). Such facilities provide considerable economic and environmental advantages, with their contribution to sustainability being a core benefit. The sustainability model in green hospitals can be analyzed through three essential areas: architectural, mechanical, and electrical (Aslan et al., 2023). The architectural component emphasizes efficient water use, sustainable building materials, and thoughtful land utilization. The mechanical and electrical systems focus on integrating renewable sources, such as solar power, and prioritizing energy conservation (Aslan et al., 2023). Green hospitals are also instrumental in reducing operational inefficiencies, carbon emissions, and waste generation (Gümüş & Solak, 2025). As a result, they offer a highly effective blueprint for advancing sustainability within healthcare institutions.

Sustainability Awareness Among Healthcare Staff

A crucial query remains: how aware are healthcare personnel regarding the implementation and adoption of these sustainability efforts? Unfortunately, a deficit in sustainability awareness among staff presents a major barrier to sustainable development within the sector (Aslan et al., 2023). Therefore, boosting this awareness is essential. However, concentrating only on healthcare workers is insufficient. Hospitals serve a diverse population, including all staff, patients, and visitors. For sustainability initiatives to be truly successful, awareness efforts must also encompass patients and their families.

Figure 3

Sustainability Elements in Hospitals



Integrating Sustainability into Health Education

Achieving sustainable development goals requires educating people who are equipped to contribute to those goals (Yapıcı, 2003). This necessitates the development of specialized curricula and educational programs (Yapıcı, 2003). A significant problem is the lack of programs in most national education systems that adequately convey the philosophy of sustainable development (Yapıcı, 2003). While national initiatives to incorporate sustainability-focused content into education systems are important, they are not sufficient on their own. Sustainable development requires a collective global awareness and perspective. Consequently, the integration of sustainability into educational curricula must be a worldwide undertaking.

Incorporating sustainability into the education of healthcare professionals is an imperative with many facets. Considering the significant financial investment in training healthcare workers, ensuring the continued supply of this workforce is critical. Furthermore, sustainability in healthcare is vital for global sustainability, making it essential for all practicing healthcare professionals to possess a strong ethical commitment to sustainability.

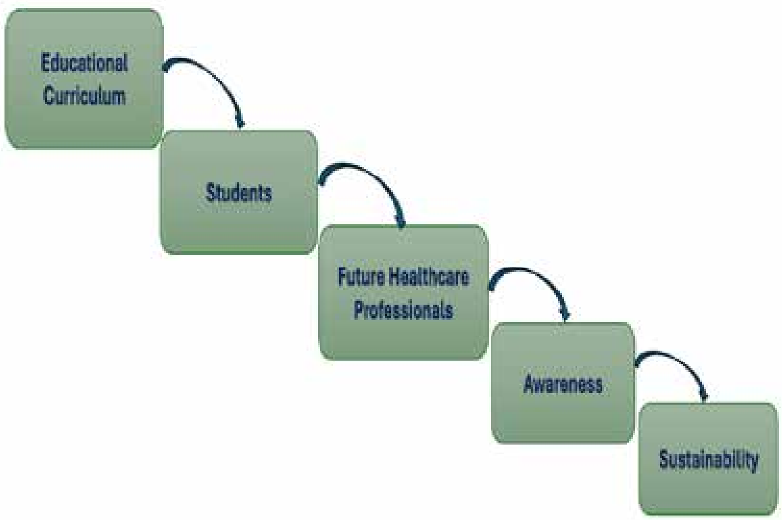
A key question is whether the training processes for nurses, doctors, physical therapists, midwives, and other health professionals sufficiently cover sustainability. Research indicates substantial variability in the sustainability education offered by medical schools in the UK (Bevan et al., 2023). Another UK study suggests that academics themselves may lack the necessary knowledge to effectively teach sustainability within medical education (Tun, 2019). Similarly, a Canadian study identified a specific need for sustainable health education within medical school curricula (Luo et al., 2021).

Integrating sustainability into the learning objectives and curricula of medical students is paramount. Today's students are tomorrow's doctors, and given their respected standing in society, their actions and approaches can serve as powerful examples (Demir et al., 2022). Therefore, fostering sustainability awareness in medical students is critical for their future professional practice and their potential to positively impact society. Nurses are also crucial, as their professional framework inherently connects the environment, people, and health (Katı et al., 2025). They must be prepared to be stewards of natural resources while promoting human health (Katı et al., 2025). Analyzing the curricula and sustainability awareness of nursing students is therefore as important as it is for medical students.

One study found that nursing students' attitudes towards sustainability were above average, yet it still recommended the formal inclusion of practical applications and dedicated sustainability courses in nursing curricula (Katı et al., 2025). Research involving students in the health sciences faculty revealed that their grasp of sustainability was often superficial, highlighting the need for more effective teaching methods to cultivate deeper understanding (Gürgen Şimşek et al., 2024). Taken together, these findings demonstrate that the skills and knowledge related to sustainability among future healthcare professionals are inconsistent. A persistent recommendation across these studies is the need for a more deliberate and structured integration of sustainability into educational curricula. Improving sustainability education is a direct means of boosting professional awareness, thereby strengthening the overall sustainability of the healthcare sector.

Figure 4

The relationship between health education and sustainability



Conclusion

Sustainability is a holistic concept that requires a comprehensive approach across all aspects of life, going beyond purely ecological or economic concerns. Given its high resource consumption, the healthcare sector bears a major responsibility for protecting both the environment and public health. Key strategies for improving sustainability include:

- Adopting environmentally sound hospital designs.
- Restructuring existing facilities.
- Implementing broad sustainability training for healthcare personnel.
- Making necessary adjustments to educational curricula.

To guarantee the quality of life for future generations and maintain the continuous delivery of healthcare services, it is absolutely essential to fully embed the principle of sustainability into the educational and operational foundations of the healthcare sector.

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Metaheuristic Approaches for Sustainable Health: A Case Study on Red Fox Optimization

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Introduction

In recent years, significant progress has been achieved in the fields of medical image processing and computer vision through the integration of optimization-based approaches. Intelligent optimization algorithms have been successfully applied in numerous areas such as multilevel thresholding, noise reduction, image segmentation, and edge and boundary detection, thereby contributing to the more accurate analysis of complex images. Among these approaches, multilevel thresholding has emerged as a fundamental image segmentation technique that enables high accuracy in tasks such as disease analysis and feature extraction by dividing an image into meaningful regions (Otsu, 1979). Although Otsu's variance-based method is widely used for image segmentation due to its simplicity and effectiveness, its computational complexity increases exponentially as the number of thresholds rises, making it inefficient for multi-level thresholding applications (Otsu, 1979). To address this limitation, metaheuristic optimization algorithms have been employed. Consequently, it becomes impractical for large-scale, high-resolution, or real-time medical imaging applications (Sezgin & Sankur, 2004).

To overcome these limitations, metaheuristic optimization algorithms have increasingly been applied to multilevel thresholding problems. Algorithms such as Particle Swarm Optimization (PSO) (Kennedy & Eberhart, 1995), Genetic Algorithm (GA) (Holland, 1975), Ant Colony Optimization (ACO) (Dorigo & Gambardella, 1997), and Grey Wolf Optimization (GWO) (Mirjalili et al., 2014) have emerged as powerful tools due to their ability to avoid local minima and perform efficient searches in high-dimensional solution spaces. Recent studies, such as Al-Najdawi et al. (2025), have comprehensively evaluated these algorithms in medical image segmentation, highlighting their efficacy and robustness in handling complex thresholding tasks. Nevertheless, many of these algorithms suffer from several drawbacks, including reduced convergence speed at higher threshold levels, premature convergence, and an inability to fully balance exploration and exploitation during the search process. These issues complicate the determination of optimal threshold values, particularly in complex and noisy medical images.

To address these challenges, novel nature-inspired optimization algorithms have been developed in recent years. In this study, the Red Fox Optimization (RFO) algorithm and its enhanced version, Modified RFO, are investigated. Inspired by the social hunting strategies of red foxes, RFO (Połap & Woźniak, 2021) provides dynamic equilibrium between exploration and exploitation, thereby offering superior global optimization capability. The adaptive and flexible hunting behaviors of red foxes, which involve both individual and group-based strategies in response to environmental conditions, serve as an effective model for establishing a balanced search mechanism in the solution space. Consequently, RFO demonstrates more stable and faster convergence while effectively avoiding entrapment in local optima when compared to conventional algorithms (Połap & Woźniak, 2021).

- The Modified Red Fox Optimization (MRFO) algorithm preserves the fundamental structure of the standard RFO while incorporating several enhancements designed to achieve faster convergence and more stable results. The key improvements include:
- Chaotic Map Integration: A logistic map-based chaotic mechanism has been integrated to enhance randomness and search diversity, providing an adaptive control framework that maintains population variety throughout the optimization process.
- Adaptive Control Factor: A linearly decreasing adaptive control factor (α) has been implemented to dynamically balance exploration and exploitation phases, ensuring optimal search behavior as iterations progress.
- Modified Position Update Mechanism: The original RFO position update equations have been enhanced by incorporating chaotic components and random perturbation terms, significantly improving the algorithm's ability to escape local optima.
- Adaptive Mutation Operator: A low-probability adaptive mutation mechanism has been introduced to preserve solution diversity and prevent premature convergence, thereby maintaining the population's exploratory capacity throughout the optimization process.

These strategic enhancements collectively strengthen the algorithm's search capabilities, resulting in both accelerated convergence speed and increased probability of locating global optima. The modifications enable MRFO to maintain robust performance across diverse optimization landscapes while demonstrating superior stability compared to the original algorithm.

The proposed Modified RFO algorithm was evaluated on the Brain MRI, Retina, Cells3D, and Mitosis datasets for multilevel thresholding tasks involving 2–5 thresholds and was compared with PSO, ACO, GA, and GWO algorithms. Experimental results demonstrate that Modified RFO provides more stable outcomes in terms of PSNR and SSIM while achieving the highest efficiency in terms of computational time.

Sustainable Healthcare and Its Importance Today

Global challenges such as population growth, the increasing prevalence of chronic diseases, and the limitation of healthcare resources have intensified the demand for sustainable healthcare systems (World Health Organization, 2017). Sustainable healthcare encompasses not only environmental and economic factors but also resource efficiency, cost optimization, and improved accessibility of healthcare services (Francis, Dunt, & Cadilhac, 2016).

With the rapid advancement of digital health technologies, the efficient utilization of computational resources has become a crucial dimension of sustainability. This has also been emphasized in recent studies (Esteva et al., 2019). In this context, artificial intelligence and optimization-based solutions contribute significantly to improving healthcare service quality while simultaneously reducing energy consumption and processing time (Esteva et al., 2019; Jiang et al., 2017).

Application of Artificial Intelligence and Optimization Methods in Healthcare

Metaheuristic algorithms provide a powerful alternative for solving complex problems through nature-inspired computational strategies (Talbi, 2009). These algorithms are widely used in the healthcare domain not only for medical image segmentation but also for diagnostic decision support systems, disease classification, drug interaction analysis, patient data clustering, treatment planning, and genetic data optimization. AI-assisted optimization methods offer significant advantages in enhancing model accuracy and reducing computational time when analyzing large and complex healthcare datasets (Esteva et al., 2019; Jiang et al., 2017).

In image processing, variance-based thresholding methods such as Otsu's approach (Otsu, 1979) or entropy-based techniques may exhibit limited performance when applied to noisy and high-dimensional medical images (Sezgin & Sankur, 2004). In contrast, metaheuristic approaches, with their inherent randomness, diversity, and global search capabilities, provide more reliable and generalized results in tasks such as multilevel thresholding, tumor detection, organ segmentation, and cell counting (Yang, 2010).

Role of Metaheuristic Algorithms

Metaheuristic algorithms contribute to sustainable healthcare systems by improving computational efficiency in areas such as medical imaging, diagnosis, treatment planning, and the effective utilization of healthcare resources (Talbi, 2009). Their most notable advantage lies in their ability to establish an adaptive balance between accuracy and computational cost. In highly computation-intensive segmentation problems such as multilevel thresholding, they offer significant gains in processing time. In noise reduction tasks, rather than providing direct speed improvements, their advantage lies in optimally tuning filter parameters or model coefficients to enhance overall performance (Oliva, Abd Elaziz & Hinojosa, 2019). Consequently, metaheuristic approaches present a flexible framework that improves both processing efficiency and output quality across diverse image processing applications.

Recent studies emphasize the importance of efficient and sustainable approaches in medical image analysis (Francis et al., 2016; Esteva et al., 2019). In line with these findings, the Modified RFO algorithm has been developed to operate on medical images.

Purpose of the Research and Research Problem/Questions/Hypotheses

Purpose of the Research

Medical image segmentation is a critical stage that requires high accuracy, particularly in diagnostically essential processes such as tumor, lesion, and tissue delineation. In this context, commonly used multilevel thresholding methods often fail to achieve the desired performance in complex medical images due to several limitations of classical deterministic approaches, such as Otsu's variance-based method and Kapur's entropy-based method. Specifically, as the number of thresholds increases, the search space expands exponentially, forcing Otsu's variance-based thresholding method to evaluate all possible threshold combinations, which results in a rapid increase in computational cost. This significantly reduces its practicality for higher-level thresholding applications (Otsu, 1979; Sahoo, Wilkins, & Yeager, 1997).

Moreover, classical methods experience difficulties in determining optimal threshold values in noisy, low-contrast, or heterogeneous medical images, tend to become trapped in local optima, and often fail to provide stable and consistent results (Sezgin & Sankur, 2004). The literature highlights that due to the nonlinear nature of multilevel thresholding, classical approaches suffer from performance degradation in complex medical images, leading to the increasing preference for optimization-based methods with strong global search capabilities (Houssein et al., 2021). These challenges clearly indicate the necessity for more intelligent, flexible, and globally efficient methods for solving multilevel thresholding problems.

The primary objective of this research is to investigate the effectiveness of advanced metaheuristic optimization algorithms in medical image segmentation and to determine which algorithms exhibit superior performance in multilevel thresholding by comparing modern nature-inspired optimization techniques in terms of accuracy, stability, convergence behavior, and computational efficiency.

Within this framework, the study experimentally evaluates the performance of nature-inspired algorithms such as PSO (Kennedy & Eberhart, 1995), ACO (Dorigo & Gambardella, 1997), GWO (Mirjalili et al., 2014), and RFO (Połap & Woźniak, 2021; Zaborski et al., 2022) in multi-threshold segmentation tasks with respect to PSNR, SSIM, and computational time.

Although RFO provides an effective search mechanism for segmentation problems, it exhibits certain limitations, particularly in complex images, including susceptibility to local minima entrapment and challenges in maintaining an optimal exploration–exploitation balance. Therefore, in the subsequent phase of this study, the Modified RFO (MRFO) approach has been introduced to overcome these constraints and enhance the performance of RFO. The proposed MRFO integrates hybrid mechanisms such as PSO's global memory component, GA-based mutation, and the Simulated Annealing (SA) acceptance criterion to strengthen the search capability of RFO. The primary aim of this hybrid MRFO is to achieve high segmentation quality while reducing computational cost, thereby making the algorithm suitable for real-time or clinical pre-evaluation scenarios.

The broader objective of this research is to contribute to the integration of artificial intelligence (AI) and metaheuristic optimization methods into medical image analysis, supporting the development of early disease detection, automated diagnosis, and clinical decision support systems.

Research Problem

The core research problem of this study can be defined as follows:

- How can metaheuristic algorithms be effectively adapted to multilevel thresholding problems in medical image segmentation tasks that require high accuracy and robustness, and how can they achieve optimal performance beyond classical methods?

Classical deterministic methods (e.g., Otsu) rely on fixed histogram assumptions, which lead to generalization issues across different patient images or varying imaging conditions (Sezgin & Sankur, 2004; Houssein et al., 2021). Additionally, the presence of high variance, tissue heterogeneity, and noise in medical images complicates the determination of optimal threshold values, thereby limiting segmentation performance (Sahoo et al., 1997).

In this study, two main problems were investigated:

1. Exploring the optimization balance between segmentation accuracy (SSIM, PSNR) and computational efficiency.
2. Systematically analyzing the performance differences among nature-inspired algorithms such as PSO, ACO, GWO, GA and RFO under identical experimental conditions.

Research Questions

To address the research problems, the following research questions were formulated:

1. **RQ1:** When multilevel thresholding is applied to medical datasets such as Brain MRI, Retina, Mitosis, and Cells3D, which metaheuristic algorithms (PSO, ACO, GWO, RFO, GA, MRFO) achieve the highest PSNR and SSIM values?
2. **RQ2:** How do the convergence speeds and stability of different algorithms vary in multi-threshold (T = 2–5) segmentation problems?
3. **RQ3:** Can MRFO reduce computational time while preserving segmentation accuracy?
4. **RQ4:** Does the improvement in segmentation quality contribute to clinically meaningful visualizations (e.g., clearer tumor boundaries, enhanced separation of retinal vessel structures)?

Hypotheses

Based on the literature review and the conceptual framework of the proposed model, the following hypotheses were formulated:

- **H1:** Metaheuristic algorithms (PSO, ACO, GWO, RFO) will produce higher PSNR and SSIM values compared to the classical Otsu method.
- **H2:** MRFO algorithms, owing to their enhanced exploration–exploitation balance, will achieve faster and more stable convergence in multilevel thresholding problems compared to PSO, RFO, and ACO. Furthermore, MRFO is expected to maintain high segmentation quality with lower computational cost, demonstrating applicability for real-time medical analysis.
- **H3:** The increase in segmentation accuracy enhances the visibility of target structures in complex and pathological medical images, thereby strengthening clinical evaluation and diagnostic decision-making.

Literature Review

Metaheuristic Algorithms in Healthcare

Metaheuristic algorithms inspired by natural processes and social behaviors provide effective and scalable solutions to complex optimization problems in the healthcare domain (Saremi, Mirjalili, & Lewis, 2017; Houssein et al., 2021). Genetic Algorithms (GA) (Holland, 1975) have been successfully applied since early studies in areas such as medical image segmentation, feature selection, and radiotherapy planning, and their stochastic nature offers robustness against the high dimensionality and noise inherent in medical data (Pham et al., 2000; Szu & Hartley, 1987).

The integration of hybrid ensemble structures with genetic algorithms, particularly the use of Particle Swarm Optimization (PSO) (Kennedy & Eberhart, 1995) in LSTM-based models and the broader success of evolutionary–swarm intelligence algorithms, has become a significant trend in enhancing model performance for complex prediction problems (Abdollahi & Moghaddam, 2022; Xu et al., 2022; Bansal et al., 2018).

Ant Colony Optimization (ACO) (Dorigo & Gambardella, 1997) has been applied in tasks such as medical image segmentation and resource allocation (Taherdangkoo et al., 2013). However, several studies have reported that ACO exhibits slower convergence rates and requires more iterations compared to algorithms such as PSO (Al-Najdawi et al., 2025; Taherdangkoo et al., 2013).

Grey Wolf Optimization (GWO) (Mirjalili, Mirjalili, & Lewis, 2014) has gained widespread attention in recent years within medical image analysis due to its lightweight structure and effective maintenance of the exploration–exploitation balance. Particularly in brain tumor detection and classification tasks, GWO and its variants have demonstrated high accuracy and rapid convergence when used for hyperparameter optimization in deep learning models (ZainEldin et al., 2022). Similarly, hybrid optimization-based approaches for MR brain tumor segmentation and classification have reported competitive performance using GWO owing to its strong search capability and parameter stability (Deepa et al., 2023). These findings indicate that GWO offers significant advantages in computational efficiency and stability for medical image processing tasks.

The primary advantage of these algorithms lies in their ability to handle high-dimensional, nonlinear, and noisy medical data. Moreover, metaheuristic-based segmentation methods may offer potential advantages over deep learning in terms of data and computational resource requirements, as deep learning models often require very large labeled datasets (Esteva et al., 2019).

Multi-Level Thresholding Methods

Image thresholding is a fundamental medical image segmentation technique used to separate tumor, vessel, and organ tissues. The Otsu method (1979) forms a strong basis for single-level segmentation by minimizing intra-class variance while maximizing inter-class variance. However, as emphasized in the comprehensive review by Pare et al., Otsu's performance degrades in images with multimodal histograms, and the clarity of segmentation boundaries decreases in low-contrast regions (Pare et al., 2019). These limitations have driven the development of multilevel thresholding techniques and nature-inspired optimization approaches (Pare et al., 2019).

Although entropy-based methods (e.g., Kapur and Rényi) partially alleviate this issue, the computational cost required for multilevel thresholding increases exponentially as the number of thresholds grows (Sezgin & Sankur, 2004).

At this point, metaheuristic algorithms offer significant advantages in searching for optimal threshold values in multilevel thresholding problems. Nature-inspired optimization techniques substantially enhance the traditional Otsu approach by virtue of their strong global search capabilities, ability to escape local minima, and efficiency in exploring high-dimensional solution spaces. Prior studies have demonstrated that algorithms such as Aquila Optimizer, Particle Swarm Optimization, Bacterial Foraging Optimization, Pigeon-Inspired Optimization, and similar approaches achieve higher segmentation accuracy in terms of both PSNR and structural similarity for multilevel thresholding problems (Abualigah et al., 2021; Bhandari et al., 2016; Oliva et al., 2019; Sathya & Kayalvizhi, 2011; Wang et al., 2019).

Key advantages of these algorithms include more stable threshold selection in multimodal histograms, more consistent optimization performance in noisy images, and more efficient management of computational complexity as the number of thresholds increases compared to the classical Otsu method.

While metaheuristic approaches do not alter Otsu's intra-class and inter-class variance-based discrimination criterion, they extend the search for optimal thresholds through a global optimization process. Whereas the classical Otsu method deterministically scans all possible threshold combinations, metaheuristic algorithms determine the most suitable threshold set using population-based search strategies, thereby reducing computational cost and improving segmentation accuracy (Bhandari et al., 2016; Oliva et al., 2019; Wang et al., 2019).

In hybrid approaches (e.g., Otsu + metaheuristic models), Otsu's statistical discriminative power is combined with the strong exploration mechanisms of global optimization algorithms, resulting in clearer and more stable segmentation boundaries, particularly in color images, multilevel thresholding scenarios, and medical imaging applications (Abualigah et al., 2021; Bhandari et al., 2016).

When compared with other segmentation strategies, multilevel thresholding methods enhanced by metaheuristic algorithms offer notable advantages. In multilevel thresholding problems, approaches such as PSO, BFA, and PIO demonstrate successful performance in medical images due to their histogram-based structures, low data requirements, and rapid applicability (Bhandari et al., 2016; Sathya & Kayalvizhi, 2011; Wang et al., 2019). These methods are particularly advantageous in scenarios where data diversity is limited or training time is critical. In contrast, deep learning-based segmentation models, although capable of high accuracy, may not always be practical in clinical settings due to their requirement for large-scale labeled datasets, high computational power, and long training periods (Ronneberger et al., 2015; Litjens et al., 2017). Therefore, metaheuristic-based multilevel thresholding approaches emerge as a more interpretable, cost-effective, and sustainable alternative compared to deep learning.

Red Fox Optimizer (RFO) and Comparative Applications

The Red Fox Optimization (RFO) algorithm is a new-generation metaheuristic method developed by Połap and Woźniak (2021), inspired by the hunting and social interaction behaviors of red foxes. The algorithm balances exploration and exploitation processes by combining high population mobility search mechanisms with target-oriented localization strategies (Połap & Woźniak, 2021).

The literature indicates that the RFO algorithm has been successfully applied to various optimization problems. Its ability to provide improved global search performance, particularly in high-dimensional and complex search spaces, has enabled it to achieve competitive results compared to traditional population-based methods. The Multidimensional RFO model proposed by Zaborski et al. (2022) introduced significant enhancements in terms of improving convergence behavior and increasing the capacity to escape local minima. This study demonstrated that RFO can be effectively adapted not only in its basic form but also in its extended and adaptive versions for high-resolution search problems.

The application domains of RFO extend across image processing, engineering optimization, route planning, and parameter optimization in machine learning models. In the literature, RFO has been reported to achieve competitive performance against other popular metaheuristic approaches, particularly due to its ability to maintain population diversity and achieve fast convergence in complex optimization tasks (Połap & Woźniak, 2021; Zaborski et al., 2022).

Overall, studies indicate that both the basic and extended variants of RFO constitute a strong alternative to modern metaheuristic methods. Furthermore, future research directions suggest that the algorithm will find broader applications in areas such as multi-objective optimization, adaptive parameter control, and integration with deep learning models.

The conducted literature review reveals that although RFO has been addressed as an effective method across various optimization problems, there remains a limited number of studies focusing on its application in multilevel thresholding for medical images. Existing RFO implementations have reported occasional slow convergence, increased susceptibility to local minima, and performance degradation due to problem-independent fixed parameters. Moreover, limited research has explored the hybrid use of RFO with deterministic methods such as Otsu, and the algorithm has not been sufficiently adapted to the challenges of medical images, including low contrast, noise, and histogram uncertainty.

The Modified RFO proposed in this study aims to address these limitations through adaptive parameter control and enhanced search strategies, achieving more stable threshold values, faster convergence, and more reliable segmentation performance in low-contrast medical images. Therefore, this work was designed to address the gaps identified in the literature regarding performance consistency, stability, and adaptability in multilevel thresholding-based medical image segmentation

Methodology

Datasets

In this study, four different datasets were employed to evaluate the performance of metaheuristic algorithms in medical image segmentation: Brain MRI, Retina, Cells3D, and Mitosis. Sample images from these datasets are presented in Table 1, while the corresponding ground-truth annotations for different threshold levels are provided in Table 2. These datasets represent distinct medical image segmentation problems and provide diversity for testing the general performance of the algorithms. The datasets were obtained from the sample medical image collections provided within the open-source image processing library scikit-image (van der Walt et al., 2014).

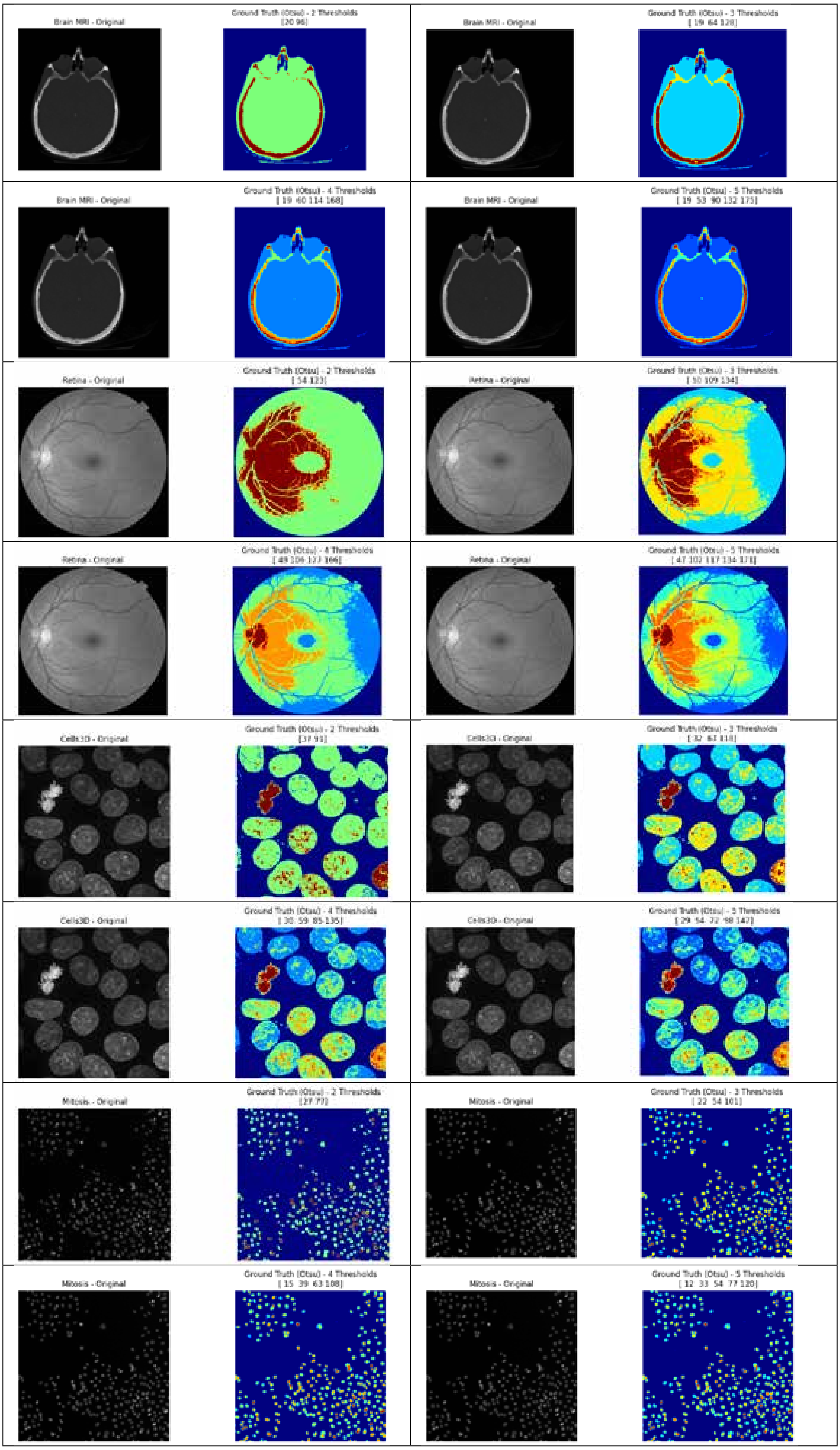
Table 1

Characteristics of the Medical Image Datasets Used in the Study

Dataset	Image Type	Challenge Type	Purpose	Size	Format	Channel	Number of Images
Brain MRI	T1-weighted MRI	Noise, contrast variation	Tumor localization	256×256	PNG	Grayscale	1
Retina	Fundus image	Illumination variation, vessel density	Vessel segmentation	1411×1411	TIFF	RGB	1
Cells3D	Fluorescence microscopy	Overlapping structures, low contrast	Cell detection	60×256×256	TIF Stack	Grayscale	1 (60 slices)
Mitosis	Histopathology	Color variation, tissue complexity	Mitotic cell detection	512×512	PNG	RGB	1

Table 2

Original Images and Ground Truth Outputs for 2, 3, 4, and 5 Threshold Levels


Brain MRI - Original
Ground Truth (Otsu) - 2 Thresholds
[20 96]
Brain MRI - Original
Ground Truth (Otsu) - 3 Thresholds
[19 64 128]
Brain MRI - Original
Ground Truth (Otsu) - 4 Thresholds
[19 60 114 168]
Brain MRI - Original
Ground Truth (Otsu) - 5 Thresholds
[19 53 90 132 175]
Retina - Original
Ground Truth (Otsu) - 2 Thresholds
[54 123]
Retina - Original
Ground Truth (Otsu) - 3 Thresholds
[50 109 134]
Retina - Original
Ground Truth (Otsu) - 4 Thresholds
[49 106 127 166]
Retina - Original
Ground Truth (Otsu) - 5 Thresholds
[47 102 117 134 171]
Cells3D - Original
Ground Truth (Otsu) - 2 Thresholds
[37 91]
Cells3D - Original
Ground Truth (Otsu) - 3 Thresholds
[32 67 118]
Cells3D - Original
Ground Truth (Otsu) - 4 Thresholds
[30 59 85 135]
Cells3D - Original
Ground Truth (Otsu) - 5 Thresholds
[29 54 72 98 147]
Mitosis - Original
Ground Truth (Otsu) - 2 Thresholds
[27 77]
Mitosis - Original
Ground Truth (Otsu) - 3 Thresholds
[22 54 101]
Mitosis - Original
Ground Truth (Otsu) - 4 Thresholds
[15 39 63 108]
Mitosis - Original
Ground Truth (Otsu) - 5 Thresholds
[12 33 54 77 120]

Since publicly available manually annotated segmentation masks were not available for the datasets used in this study (Brain MRI, Retina, Cells3D, and Mitosis), the segmentation outputs obtained using the multilevel Otsu thresholding method were accepted as “ground truth” for comparison and reference purposes. This approach is widely preferred in multilevel thresholding problems because histogram-based class separation has been demonstrated to provide effective optimal threshold estimation in various studies, particularly for medical and natural images (Bhandari et al., 2016; Houssein et al., 2021; Pare et al., 2019). Moreover, previous research using datasets similar to those employed in this study has also reported that Otsu-based threshold values offer a reliable baseline for comparison (van der Walt et al., 2014), supporting its continued use as a reference method despite its known limitations in high-dimensional thresholding.

Table 4.2 presents the original images and the reference (ground truth) segmentation results obtained for 2, 3, 4, and 5 threshold levels for each dataset. These visuals were used as baseline references for performance comparison of the metaheuristic algorithms.

The datasets used in this study differ in format and resolution characteristics. The Brain MRI dataset consists of single-channel (grayscale) mid-slices selected from volumetric MRI data. Retina images are RGB fundus images with clearly visible vascular structures. The Cells3D dataset comprises fluorescence microscopy images with a multi-layered (z-stack) structure. The Mitosis dataset consists of histopathologically stained RGB microscopic images.

To ensure experimental consistency, all images were resized to 256×256 pixels and processed in 8-bit format. The number of images was selected as one representative sample for each dataset: one Brain MRI image, one Retina image, one slice from Cells3D, and one microscopic field from the Mitosis dataset.

Preprocessing

The preprocessing stage is a critical step that directly affects segmentation performance. Medical images often contain various types of noise originating from imaging devices, sensor imperfections, low illumination, and environmental conditions. In the Retina, Mitosis, Brain MRI, and Cells3D images used in this study, two primary noise types were predominantly observed:

- **Salt & Pepper noise:** Appears as sudden black-and-white pixel spikes, especially in microscopic and histopathological images. This noise type distorts edge structures and negatively affects thresholding accuracy.
- **Gaussian noise:** A low-amplitude noise distributed randomly across pixels,

originating from imaging sensors. It is particularly prominent in low-contrast Retina and Mitosis images.

Therefore, to suppress both impulsive and continuous noise types, two different filters were applied sequentially during the noise removal stage. The adopted noise reduction strategy was as follows:

- **Median filter (3×3):** Used to suppress Salt & Pepper noise. As a nonlinear filter, the median filter effectively removes extreme pixel values while preserving edge structures, thus preventing distortion of segmentation boundaries.
- **Gaussian filter (σ = 1):** Applied after the median filter to smooth the remaining low-intensity Gaussian noise. The Gaussian filter reduces abrupt pixel transitions and ensures a more homogeneous intensity distribution.

These two filters were applied sequentially in the code in the following order:

Median Filter → Gaussian Filter → Normalization → Segmentation

The following preprocessing steps were applied to all images prior to segmentation:

- **Grayscale conversion:** Color images were converted to grayscale to focus on intensity information.
- **Noise reduction:** Sequential application of median (3×3) and Gaussian (σ=1) filters to suppress both impulsive and continuous noise.
- **Contrast enhancement:** CLAHE (Contrast Limited Adaptive Histogram Equalization) was applied to enhance local contrast and emphasize tissue boundaries.
- **Normalization:** Pixel intensity values were scaled to the [0–1] range to improve numerical stability for the algorithms.

Algorithms

In this study, six different metaheuristic algorithms were employed to solve the multilevel thresholding problem:

- Particle Swarm Optimization (PSO)
- Red Fox Optimization (RFO)
- Genetic Algorithm (GA)
- Ant Colony Optimization (ACO)
- Grey Wolf Optimization (GWO)
- Modified Red Fox Optimization (MRFO) (proposed)

Additionally, the classical Multi-Level Otsu method was used for baseline comparison.

Red Fox Optimization

The Red Fox Optimization (RFO) algorithm is a population-based metaheuristic optimization technique inspired by the intuitive hunting behavior exhibited by red foxes. The algorithm aims to determine the optimal threshold values by maintaining a balance between exploration and exploitation within the search space. In this study, RFO is employed to solve the multilevel thresholding problem.

Each fox represents a candidate solution (a vector of threshold values) in the search space. The foxes update their positions based on the best solutions obtained in the current and previous iterations. The equations governing the RFO algorithm (4.1–4.7) are presented below in sequence.

1. Initialization of Population

The population consisting of N foxes is randomly initialized:

$$X_i^0 = X_{min} + rand(0,1) \times (X_{max} - X_{min}) \tag{4.1}$$

Where:

- X_i^0 : Initial position of the i-th fox
- X_{min}, X_{max}: Lower and upper bounds
- rand(0,1) : Uniform random number in the interval [0,1]

2. Fitness Function

The fitness value of each fox is computed using the selected objective function (e.g., Kapur entropy or Otsu variance):

$$f(X_i) = Fitness(X_i) \tag{4.2}$$

The best solution is determined as follows:

$$X_{best}^t = argmax f(X_i^t) \tag{4.3}$$

In this study, X_{best}^t represents the best global solution obtained up to iteration t. In other words, it does not correspond solely to the best solution in the current iteration, but to the best position among all iterations so far (global best).

3. Position Update Equation

The fundamental position update mechanism of RFO is defined as:

$$X_i^{t+1} = X_i^t + r_1(X_{best}^t - | r_2 X_i^t |) \tag{4.4}$$

Where:

- X_i^t : Position of the i-th fox at iteration t
- X_{best}^t : Best global position found up to iteration t
- r_1, r_2 : Random numbers in the interval [0,1]

This equation ensures that foxes move toward the best solution while the stochastic component helps mitigate the risk of being trapped in local minima.

4. Exploration and Exploitation Mechanism

The RFO algorithm implements an adaptive search strategy in which foxes exhibit two distinct behaviors during the updating process:

- **Exploration phase:** Different regions of the search space are investigated:

$$X_i^{t+1} = X_i^t + \alpha \cdot rand(-1,1) \tag{4.5}$$

- **Exploitation phase:** A fine search is performed in the vicinity of the best fox:

$$X_i^{t+1} = X_{best}^t + \beta \cdot (X_{best}^t - X_i^t) \tag{4.6}$$

Where:

- α: Exploration coefficient
- β: Exploitation coefficient

These two phases are dynamically balanced as iterations progress.

In the literature, the concepts of exploration and exploitation are widely used to describe the general behavior of metaheuristic algorithms. In this context, Equations (4.5) and (4.6) conceptually represent the two different strategies in the RFO search process. However, the original Red Fox Optimization algorithm is fundamentally based on a single position update equation, and the RFO implementation used in this study directly follows Equation (4.4).

Therefore, Equations (4.5) and (4.6) are presented here for theoretical explanation of the search behavior, but they were not implemented as separate steps in the Python implementation used in this study.

5. Boundary Control

If updated positions exceed the solution boundaries, they are corrected as follows:

$$X_i^{t+1} = max(X_{min}, min(X_i^{t+1}, X_{max})) \tag{4.7}$$

General Workflow of the Algorithm (Summary)

Step 1: Initialize the fox population
Step 2: Calculate fitness values
Step 3: Determine the best solution (X_{best})
Step 4: Update the positions of the foxes
Step 5: Apply boundary control
Step 6: Repeat until the stopping criterion is met

Pseudocode of the RFO Algorithm

```
Initialize population Xi (i = 1,...,N)

Evaluate fitness of each fox

Determine Xbest

for t = 1 to MaxIter do

    for each fox i do

        Generate r1, r2 ∈ [0,1]

        Update position:

        Xi(t+1) = Xi(t) + r1*(Xbest - |r2*Xi(t)|)

        Apply boundary control

    end for

    Update Xbest

end for
```

```
Return Xbest
```

Despite producing successful results by balancing exploration and exploitation, RFO has been shown in the literature and experimental studies to suffer from certain structural limitations. Particularly in high-dimensional and complex search spaces such as multilevel thresholding, these limitations can significantly degrade performance. Due to fixed randomness coefficients, the population tends to converge prematurely toward the global best solution during early iterations, leading to insufficient exploration of the solution space. Furthermore, the static exploration–exploitation balance results in weakened exploitation capability in later iterations. In low-contrast and noisy medical images, irregularities in the solution space increase the likelihood of being trapped in local minima, and as the number of thresholds increases, the convergence rate significantly decreases. These structural issues prevent classical RFO from achieving the desired stability in multilevel thresholding problems.

For these reasons, a Modified RFO (MRFO) approach has been developed to provide a more stable, adaptive, and robust search mechanism. The primary objective of MRFO is to enhance effective exploration of the search space, accelerate convergence, strengthen the ability to escape local minima, and achieve more stable solutions in multilevel thresholding problems. To this end, iteration-dependent adaptive coefficients and chaotic randomness mechanisms are introduced in place of the fixed parameters of classical RFO, resulting in a dynamic update structure.

Modified Red Fox Optimization (MRFO)

The proposed MRFO algorithm enhances the classical RFO by incorporating an adaptive learning coefficient and a stochastic mutation term to improve convergence speed and prevent entrapment in local minima. The governing equations (4.8–4.11) are given below.

1. Adaptive Control Factor (Decreasing Coefficient)

Instead of the fixed r_1 in classical RFO, an iteration-dependent adaptive parameter is defined:

$$\alpha(t) = \alpha_{max} - \frac{t}{T}(\alpha_{max} - \alpha_{min}) \qquad (4.8)$$

Where:

- t : Current iteration
- T : Maximum number of iterations

- α_{max}, : Initial and final coefficients

Thus:

- Exploration is emphasized in early iterations
- Exploitation is strengthened in later iterations

2. Chaotic Randomness via Logistic Map

Random number generation is performed using a logistic chaotic map instead of a uniform distribution:

$$c_{t+1} = \mu c_t(1 - c_t) \; ve \; r_1 = c_t \quad (4.9)$$

3. Modified Position Update Equation

The proposed MRFO introduces an adaptive learning coefficient (α) and a dynamic local exploration term (γ) to the classical RFO in order to accelerate convergence and avoid local minima. The updated rule is defined as:

$$X_i^{t+1} = X_i^t + \alpha(t) \cdot r_1 \cdot \left(X_{best}^t - X_i^t\right) + \gamma \cdot rand(-1,1) \quad (4.10)$$

Where:

- $\alpha(t)$: Iteration-dependent adaptive control coefficient
- r_1 : Chaotic random number
- γ : Mutation coefficient

This formulation preserves global guidance while increasing solution diversity.

5. Adaptive Mutation Mechanism

To prevent stagnation in local minima, mutation is applied with a low probability:

$$X_i^{t+1} = X_i^{t+1} + \delta \cdot rand(-1,1) \quad (4.11)$$

This mechanism contributes especially to the fine adjustment of segmentation boundaries. Although adaptive coefficients, chaotic maps, and mutation-based diversification strategies have been explored individually in various metaheuristic algorithms, these mechanisms have not previously been integrated into the Red Fox Optimization (RFO) framework in the form presented in this study. The four modifications introduced, namely the adaptive control factor, logistic-map–based chaotic randomness, the enhanced position update equation incorporating α and γ, and the adaptive mutation mechanism, represent a novel combined extension of the classical RFO. This integrated design is implemented for the first time in this study to improve exploration–exploitation balance, accelerate convergence, and enhance the stability of multilevel thresholding in medical image segmentation.

MRFO Pseudocode.

```
Initialize population pop[1..N] uniformly in [lb, ub]

Evaluate fitness fit[1..N] using Otsu function

Find best_pos = argmin(fit)

Initialize c_t = random(0,1)  // Kaotik harita başlangıç

For each iteration t = 1 to T_max:

    Compute α(t) = α_max - (t / T_max) * (α_max - α_min)

    Update c_t = μ * c_t * (1 - c_t)

    r₁ = c_t

    For each individual i = 1 to N:

        rand_term = uniform(-1, 1, dim)

       X_new = pop[i] + α(t) * r₁ * (best_pos - pop[i]) + γ * rand_term

        Clip X_new to [lb, ub]

        If random() < mutation_prob:

            mutation_term = uniform(-1, 1, dim)

            X_new += δ * mutation_term

            Clip X_new to [lb, ub]

        Evaluate f_new = Otsu(X_new)
```

```
        If f_new < fit[i]:

            pop[i] = X_new

            fit[i] = f_new

    Update best_pos = argmin(fit)

Return sorted(round(best_pos))
```

Evaluation Metrics

Segmentation quality was assessed using the metrics listed in Table 3.

Table 3

Performance Evaluation Metrics for Image Segmentation

Metric	Abbreviation	Desired Direction	Description	Reference
Peak Signal-to-Noise Ratio	PSNR	High	Measures image fidelity	Wang et al. (2004)
Structural Similarity Index	SSIM	Close to 1	Visual integrity measure	Wang et al. (2004)
Mean Squared Error	MSE	Low	Pixel-based difference	Gonzalez & Woods (2018)
Fitness Function	F	High	Thresholding performance	Otsu (1979)

Experimental Design and Results

This section presents the design and results of the experimental studies carried out to evaluate the performance of the proposed MRFO algorithm. The experiments were conducted to solve the multilevel thresholding problem in medical image segmentation, and a standardized environment was employed for fair algorithm comparison.

Experimental Environment

The experiments were conducted in a controlled environment to ensure reliable and reproducible results. The software and hardware resources were selected to support the efficient execution of image processing and optimization algorithms. The experimental configuration is detailed as follows:

- **Software:** Python version 3.10 was used as the main programming environment. The primary libraries included NumPy (for numerical computations), matplotlib (for visualization), scikit-image (for image processing and metric calculations), pandas (for data analysis), and other auxiliary modules such as time, warnings, and math. These libraries facilitated operations such as the implementation of the Otsu-based fitness function, histogram computation, and performance evaluation using metrics such as PSNR and SSIM.

- **Hardware:** The experiments were carried out on a system equipped with an Intel i7 processor (2.7 GHz clock speed), 16 GB RAM, and an NVIDIA RTX 3050 Ti graphics card. This configuration ensured efficient processing of computationally demanding optimization algorithms and supported parallel operations on large image datasets.
- **Number of Runs:** Each algorithm was evaluated through 30 independent runs to minimize variations caused by stochastic behavior and to ensure statistical robustness of the results.
- **Termination Criteria:** All algorithms were limited to a maximum of 50 iterations. Additionally, an early stopping mechanism was considered, whereby the algorithm would terminate if no improvement was observed over 10 consecutive iterations; however, this criterion has not yet been implemented in the current code and is recommended for future development.

All algorithms were executed using the same initial population, identical preprocessing procedures, and the same fitness function to ensure a fair comparison (Table 4). The parameters used in this study were determined based on the default values recommended in the original publications of each algorithm or on standardized parameter ranges commonly employed in multi-level image thresholding studies (Clerc & Kennedy, 2002; Dorigo & Stützle, 2004; Mirjalili et al., 2014; Srinivas & Patnaik, 1994).

Table 4

Algorithm Parameters Used in the Experimental Study

Algorithm	Population	Iterations	Key Parameters
Modified RFO	30	50	α_max=2.0, α_min=0.1, μ=4.0, γ=0.1, δ=0.05, mutation_prob=0.1
Original RFO	30	50	r1,r2 ~ U(0,1), Equation (4.4)
PSO	30	50	w=0.7, c_1=1.5, c_2=1.5
GA	30	50	Crossover=0.8, Mutation=0.2
ACO	30	50	α=1, β=2, ρ=0.5
GWO	30	50	a: 2 → 0 (linearly decreasing)

Results

In this section, the performance of the proposed Modified Red Fox Optimization (MRFO) algorithm in medical image segmentation is comparatively presented against the classical RFO, PSO, GA, ACO, and GWO algorithms. All experiments were conducted under identical conditions and averaged over 30 independent runs to ensure statistical reliability. The evaluation metrics used include PSNR, SSIM, MSE, F-value (fitness), and computational time (s).

Quantitative Comparison

This subsection presents a detailed quantitative evaluation of the multi-level image thresholding algorithms across four medical image datasets: Brain MRI, Retina, Cells3D, and Mitosis. Experiments were conducted for threshold levels ranging from 2 to 5, and the performance of each algorithm was assessed using objective function value (Otsu fitness), Peak Signal-to-Noise Ratio (PSNR), Structural Similarity Index (SSIM), execution time, and fitness count.

To ensure clarity and comparability, the results are organized into four comprehensive tables (Table 5.1–Table 5.4), each corresponding to one dataset. Within every table, the algorithms are grouped according to the threshold level, and for each configuration, the optimized threshold values, objective value, PSNR, SSIM, execution time, and fitness count are reported.

The quantitative results demonstrate the performance differences among the metaheuristic algorithms (Original RFO, Modified RFO, PSO, GA, GWO, ACO) and the deterministic Otsu method across varying threshold complexities. In our experimental setup, the practical multi-level Otsu implementation produced the lowest execution time with a fitness count of zero; however, this reflects an optimized approximation, as classical multi-level Otsu grows exponentially with the number of thresholds and therefore becomes impractical for high threshold levels. Consistent with this theoretical limitation, metaheuristic algorithms—particularly the Modified RFO, PSO, and GWO—achieved superior PSNR and SSIM values at higher threshold counts, indicating more robust segmentation performance. Meanwhile, ACO generally produced lower objective values and PSNR/SSIM scores, especially for the Retina and Mitosis datasets.

Overall, the tables provide a detailed quantitative comparison that highlights the trade-offs between segmentation quality and computational cost across all algorithms and threshold levels.

Table 5

Performance Comparison for Brain MRI Image

Threshold Level	Algorithm	Thresholds	Objective Value	PSNR	SSIM	Time (s)	Fitness Count

2	Modified RFO	[28 112]	2074.83	22.83	0.401	0.125	1530
	Orijinal RFO	[36 120]	2069.32	20.97	0.374	0.132	1530
	Otsu	[25 110]	-	-	-	-	-
	ACO	[82 101]	1648.42	17.70	0.367	0.212	1501
	PSO	[26 111]	2075.04	23.32	0.409	0.133	1530
	GA	[26 110]	2074.99	23.31	0.409	0.155	1530
	GWO	[25 111]	2075.00	23.51	0.414	0.185	1530
3	Modified RFO	[25 72 138]	2127.55	27.01	0.461	0.157	1530
	Orijinal RFO	[40 81 150]	2114.33	23.09	0.411	0.160	1530
	ACO	[64 76 207]	1652.25	19.25	0.359	0.270	1501
	Otsu	[24 76 146]	-	-	-	-	-
	PSO	[25 77 147]	2128.50	26.90	0.459	0.154	1530
	GA	[26 89 155]	2124.83	25.81	0.443	0.167	1530
	GWO	[25 77 147]	2128.50	26.90	0.459	0.191	1530
4	Modified RFO	[24 67 112 167]	2144.14	27.62	0.467	0.163	1530
	Orijinal RFO	[24 75 130 173]	2143.05	27.55	0.465	0.166	1530
	ACO	[25 48 85 230]	2058.00	24.56	0.395	0.339	1501
	Otsu	[24 68 118 172]	-	-	-	-	-
	PSO	[24 69 119 173]	2144.44	27.65	0.467	0.175	1530
	GA	[23 70 122 172]	2144.21	28.14	0.473	0.203	1530
	GWO	[24 69 118 172]	2144.44	27.64	0.467	0.210	1530

5	Modified RFO	[10 33 72 128 179]	2151.65	31.29	0.579	0.188	1530
	Orijinal RFO	[34 63 123 145 188]	2144.49	25.36	0.443	0.193	1530
	ACO	[34 96 124 174 184]	2128.30	23.61	0.416	0.422	1501
	Otsu	[24 65 105 149 190]	-	-	-	-	-
	PSO	[9 33 69 119 173]	2152.18	31.92	0.624	0.180	1530
	GA	[24 69 103 146 185]	2150.99	28.02	0.470	0.198	1530
	GWO	[8 32 69 119 173]	2152.12	32.09	0.624	0.227	1530

Table 6

Performance Comparison for Retina Image

Threshold Level	Algorithm	Thresholds	Objective Value	PSNR	SSIM	Time (s)	Fitness Count
2	Modified RFO	[45 125]	10744.05	17.91	0.648	0.126	1530
	Orijinal RFO	[62 125]	10744.57	18.17	0.649	0.127	1530
	Otsu	[54 124]	-	-	-	-	-
	ACO	[152 153]	8377.23	13.89	0.625	0.196	1501
	PSO	[55 125]	10744.93	18.16	0.649	0.128	1530
	GA	[55 125]	10744.93	18.16	0.649	0.149	1530
	GWO	[55 125]	10744.93	18.16	0.649	0.174	1530
3	Modified RFO	[41 111 137]	10793.25	20.70	0.624	0.148	1530
	Orijinal RFO	[55 119 165]	10790.41	21.87	0.656	0.148	1530
	ACO	[103 187 221]	9924.31	16.91	0.613	0.322	1501
	Otsu	[50 110 135]	-	-	-	-	-
	PSO	[51 111 136]	10794.09	20.61	0.626	0.165	1530
	GA	[55 110 136]	10793.85	20.61	0.630	0.164	1530
	GWO	[54 111 137]	10794.03	20.72	0.627	0.205	1530

4	Modified RFO	[66 109 131 178]	10825.55	22.79	0.660	0.173	1530
	Orijinal RFO	[53 111 136 179]	10824.09	23.27	0.647	0.159	1530
	ACO	[30 127 170 240]	10779.26	19.77	0.664	0.392	1501
	Otsu	[49 107 128 167]	-	-	-	-	-
	PSO	[50 108 129 168]	10828.52	23.68	0.659	0.169	1530
	GA	[49 112 130 170]	10826.41	23.04	0.644	0.193	1530
	GWO	[35 107 129 169]	10826.62	23.73	0.659	0.212	1530
5	Modified RFO	[42 103 118 136 179]	10840.99	24.72	0.660	0.183	1530
	Orijinal RFO	[59 110 129 184 238]	10825.52	22.92	0.650	0.152	1530
	ACO	[17 62 87 106 182]	10760.84	22.60	0.723	0.453	1501
	Otsu	[48 103 118 135 172]	-	-	-	-	-
	PSO	[49 103 118 135 172]	10841.73	24.73	0.666	0.182	1530
	GA	[39 91 109 130 163]	10837.93	26.94	0.699	0.200	1530
	GWO	[31 101 116 133 171]	10839.34	25.57	0.670	0.218	1530

Table 7

Performance Comparison for Cells3D Image

Threshold Level	Algorithm	Thresholds	Objective Value	PSNR	SSIM	Time (s)	Fitness Count

2	Modified RFO	[40 104]	2948.07	23.57	0.695	0.131	1530
	Orijinal RFO	[43 108]	2946.86	23.63	0.681	0.126	1530
	Otsu	[39 103]	-	-	-	-	-
	ACO	[11 14]	2498.01	12.02	0.430	0.192	1501
	PSO	[40 104]	2948.07	23.57	0.695	0.134	1530
	GA	[38 104]	2947.35	23.68	0.704	0.148	1530
	GWO	[40 104]	2948.07	23.57	0.695	0.176	1530
3	Modified RFO	[32 74 156]	3034.45	24.53	0.728	0.142	1530
	Orijinal RFO	[38 76 136]	3039.07	26.08	0.729	0.146	1530
	ACO	[102 198 230]	2289.30	18.12	0.411	0.263	1501
	Otsu	[34 71 131]	-	-	-	-	-
	PSO	[35 72 132]	3040.84	26.09	0.740	0.145	1530
	GA	[36 71 131]	3040.48	25.93	0.733	0.159	1530
	GWO	[35 72 132]	3040.84	26.09	0.740	0.188	1530
4	Modified RFO	[34 69 109 182]	3065.40	28.06	0.771	0.158	1530
	Orijinal RFO	[36 71 149 183]	3042.16	24.65	0.718	0.152	1530
	ACO	[25 27 110 174]	2957.19	25.40	0.744	0.356	1501
	Otsu	[31 63 90 148]	-	-	-	-	-
	PSO	[32 64 91 149]	3073.60	28.66	0.795	0.168	1530
	GA	[33 66 90 155]	3072.52	28.31	0.792	0.189	1530
	GWO	[32 64 91 149]	3073.60	28.66	0.795	0.221	1530

5	Modified RFO	[29 56 74 95 143]	3088.12	30.34	0.843	0.197	1530
	Orijinal RFO	[39 69 91 114 153]	3078.21	29.08	0.797	0.197	1530
	ACO	[70 87 166 186 216]	2731.83	21.30	0.516	0.441	1501
	Otsu	[29 56 76 103 158]	-	-	-	-	-
	PSO	[30 57 77 104 159]	3090.10	30.40	0.831	0.197	1530
	GA	[23 51 76 104 162]	3087.02	30.63	0.843	0.204	1530
	GWO	[30 57 77 103 160]	3090.06	30.30	0.831	0.231	1530

Table 8

Performance Comparison for Mitosis Image

Threshold Level	Algorithm	Thresholds	Objective Value	PSNR	SSIM	Time (s)	Fitness Count
2	Modified RFO	[25 66]	532.12	22.73	0.536	0.147	1530
	Orijinal RFO	[32 98]	526.61	25.19	0.479	0.130	1530
	Otsu	[24 65]	-	-	-	-	-
	ACO	[32 82]	529.44	24.41	0.479	0.195	1501
	PSO	[25 66]	532.12	22.73	0.536	0.134	1530
	GA	[21 58]	531.01	21.42	0.570	0.146	1530
	GWO	[25 66]	532.12	22.73	0.536	0.181	1530
3	Modified RFO	[19 51 94]	554.20	29.04	0.666	0.155	1530
	Orijinal RFO	[29 58 118]	549.15	26.90	0.533	0.155	1530
	ACO	[26 76 188]	535.18	26.47	0.538	0.266	1501
	Otsu	[18 49 95]	-	-	-	-	-
	PSO	[19 50 96]	554.27	29.13	0.666	0.149	1530
	GA	[19 49 95]	554.23	29.09	0.666	0.163	1530
	GWO	[19 50 96]	554.27	29.13	0.666	0.203	1530

4	Modified RFO	[21 56 121 210]	552.93	29.12	0.630	0.160	1530
	Orijinal RFO	[22 51 83 120]	561.04	29.54	0.616	0.160	1530
	ACO	[110 152 175 205]	227.93	14.56	0.128	0.327	1501
	Otsu	[13 37 64 108]	-	-	-	-	-
	PSO	[14 37 64 109]	564.89	31.74	0.750	0.167	1530
	GA	[18 41 64 107]	564.20	30.56	0.679	0.177	1530
	GWO	[15 39 65 109]	564.87	31.77	0.750	0.203	1530
5	Modified RFO	[15 39 65 109 207]	566.03	32.70	0.751	0.170	1530
	Orijinal RFO	[17 52 73 99 155]	563.84	32.26	0.708	0.176	1530
	ACO	[18 66 146 165 225]	541.56	28.59	0.641	0.473	1501
	Otsu	[10 28 50 73 116]	-	-	-	-	-
	PSO	[12 31 52 75 118]	570.44	33.55	0.800	0.196	1530
	GA	[16 36 57 78 119]	569.62	32.26	0.720	0.200	1530
	GWO	[12 31 52 75 118]	570.44	33.55	0.800	0.229	1530

Visual Comparison

A visual assessment of the segmentation results reveals that the performance of the algorithms varies across datasets and threshold levels. For the Brain MRI dataset at 5 thresholds, the results clearly show that GWO and PSO produce the highest visual quality, consistent with their quantitative metrics. Both algorithms achieve the highest SSIM values (0.624) and the highest PSNR values (32.09 for GWO and 31.92 for PSO), indicating superior preservation of anatomical boundaries and low distortion. Their segmented images maintain tissue consistency and avoid excessive fragmentation, showing well-defined gray and white matter regions.

The Modified RFO also performs strongly, achieving competitive PSNR (31.29) and SSIM (0.579) values. Its visual output displays clear structure differentiation, though slightly less homogeneous than GWO and PSO at 5 thresholds. In contrast, the Original RFO, GA, and deterministic Otsu method produce moderate-quality results, with lower structural similarity (SSIM ≈ 0.44–0.47) and more noticeable boundary noise. The ACO algorithm yields the weakest segmentation visually, with the lowest PSNR (23.61) and SSIM (0.416), resulting in under-segmented and less consistent tissue regions.

Overall, the results demonstrate that GWO and PSO deliver the most accurate visual segmentation for Brain MRI images at high threshold levels, while Modified RFO provides a competitive alternative. These findings are fully aligned with the quantitative evaluation presented in Section Result.

Figure 1

Brain MRI Segmentation Output (2 Thresholds)

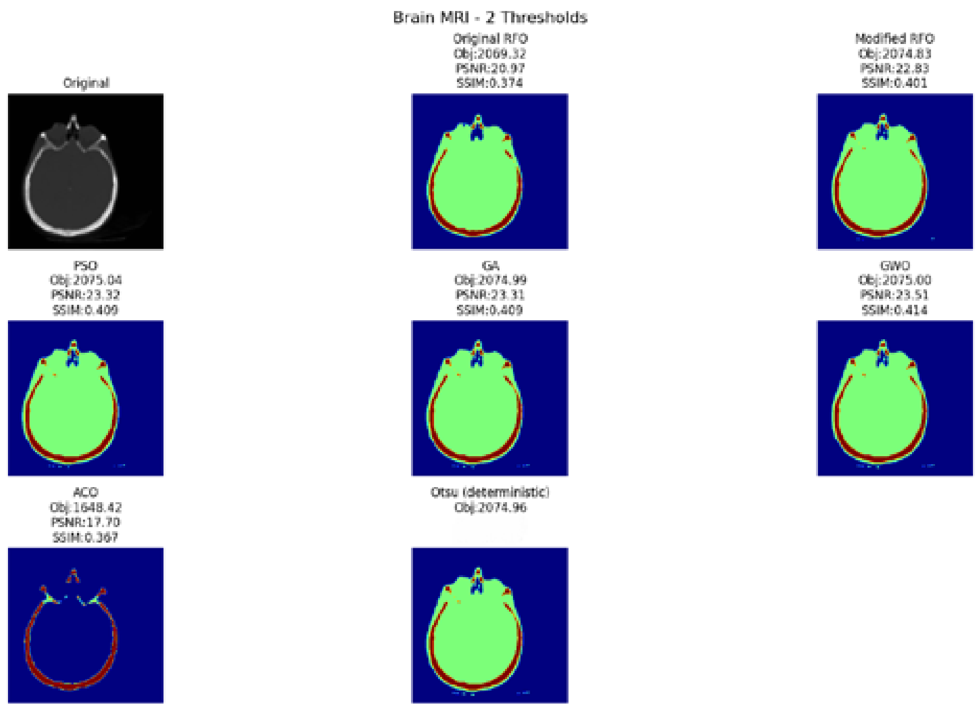


Figure 2

Brain MRI Segmentation Output (3 Thresholds)

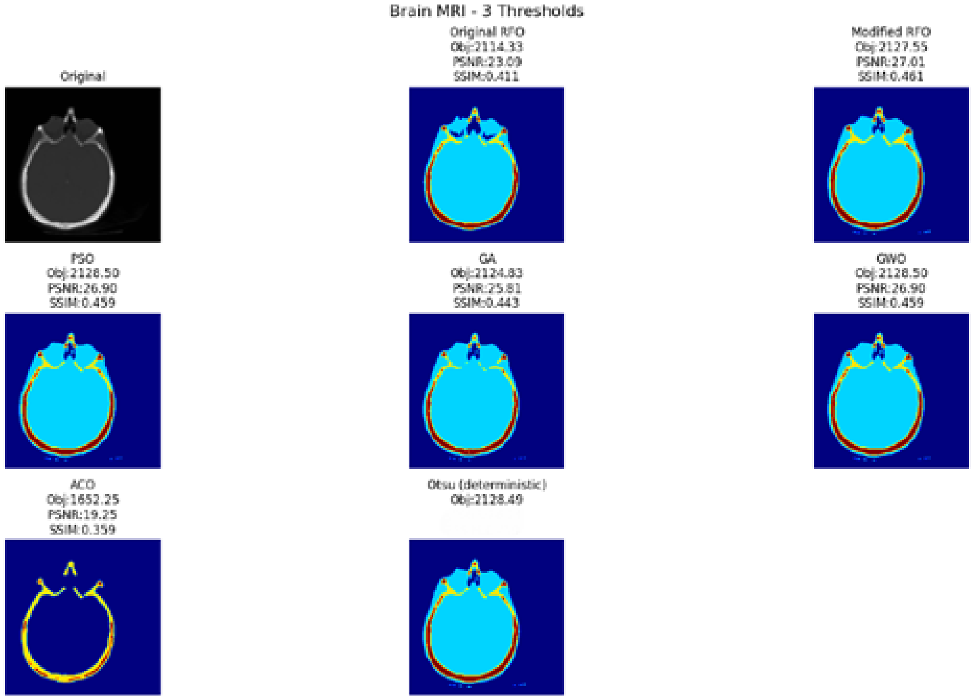


Figure 3

Brain MRI Segmentation Output (4 Thresholds)

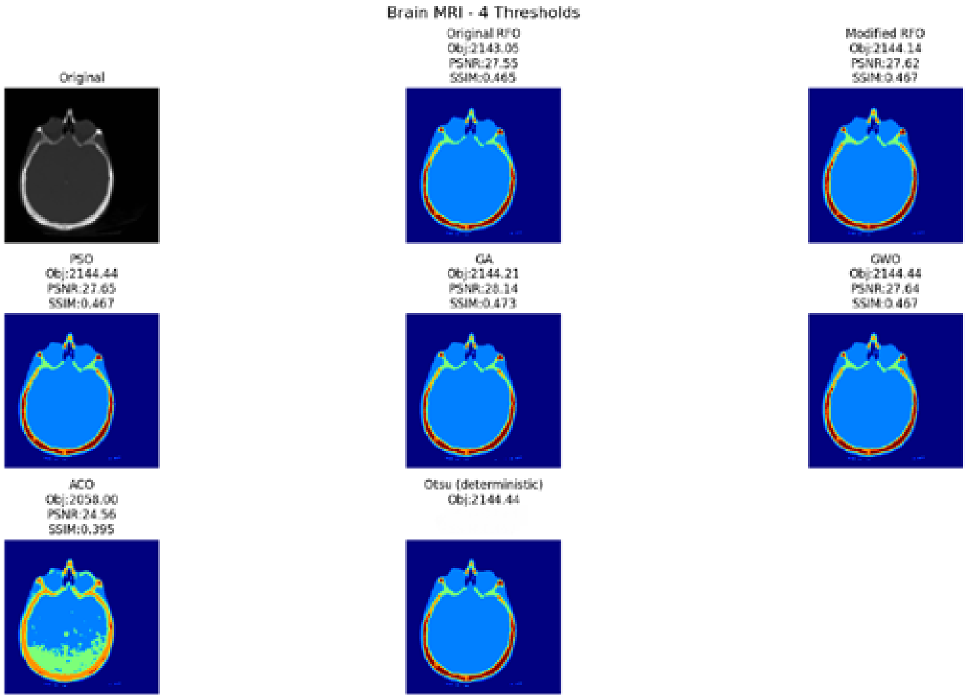
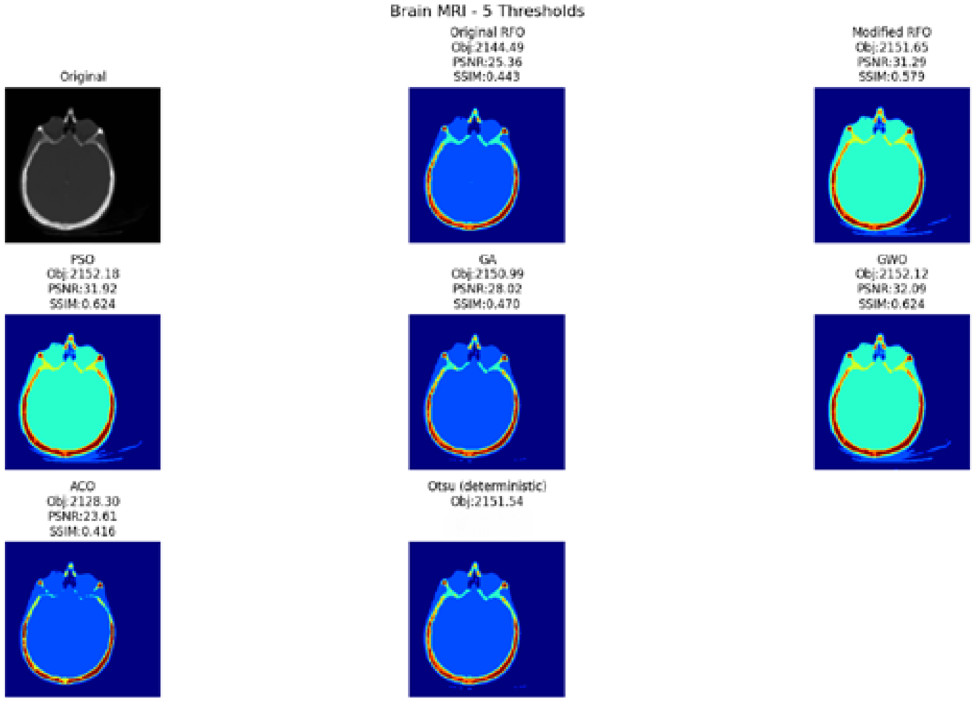


Figure 4

Brain MRI Segmentation Output (5 Thresholds)



Figures 1–4 present the visual segmentation outputs of the metaheuristic algorithms applied to the Brain MRI dataset under different multilevel threshold configurations. The qualitative evaluation conducted on the 5-threshold results reveals distinct strengths and limitations across the methods.

The GWO algorithm provides the most structurally consistent segmentation, maintaining detailed tissue transitions and accurately delineating anatomical regions. Its visual clarity aligns with its leading SSIM and PSNR metrics. Similarly, PSO demonstrates robust performance, producing a clear and homogeneous segmentation output with minimal noise, which highlights its stability in high-threshold scenarios.

In comparison, MRFO exhibits a balanced and visually coherent segmentation with well-defined regional separation. Although it performs strongly, its internal tissue sharpness is slightly lower than that observed in GWO and PSO. The Original RFO, while producing acceptable boundary structures, demonstrates limitations in terms of detail preservation and uniformity.

The classical algorithms GA and ACO display notable deficiencies. GA generates smoother and less detailed regions, with partially blurred anatomical contours. ACO, the weakest performer, fails to maintain sufficient contrast, resulting in merged segments and poorly defined tissue structures.

Figure 5

Retina Segmentation Output (2 Thresholds)

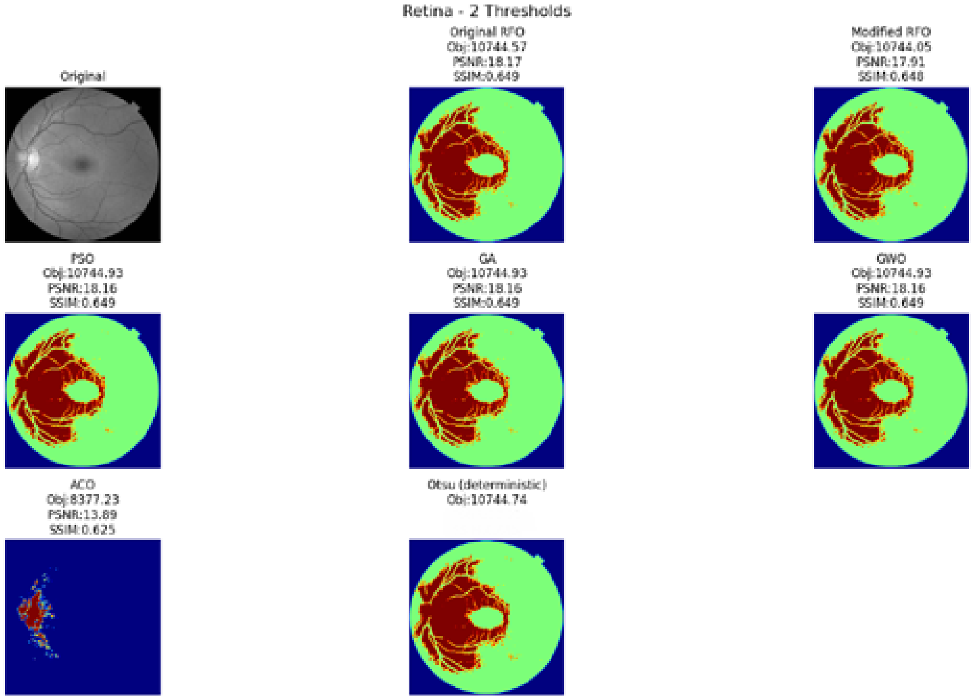


Figure 6

Retina Segmentation Output (3 Thresholds)

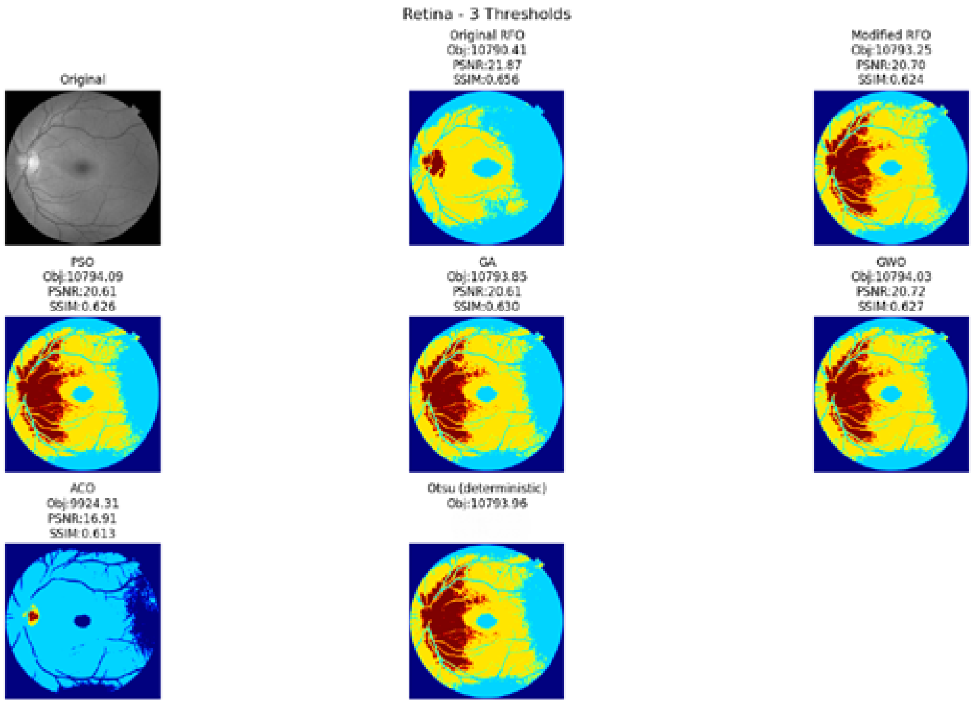


Figure 7

Retina Segmentation Output (4 Thresholds)

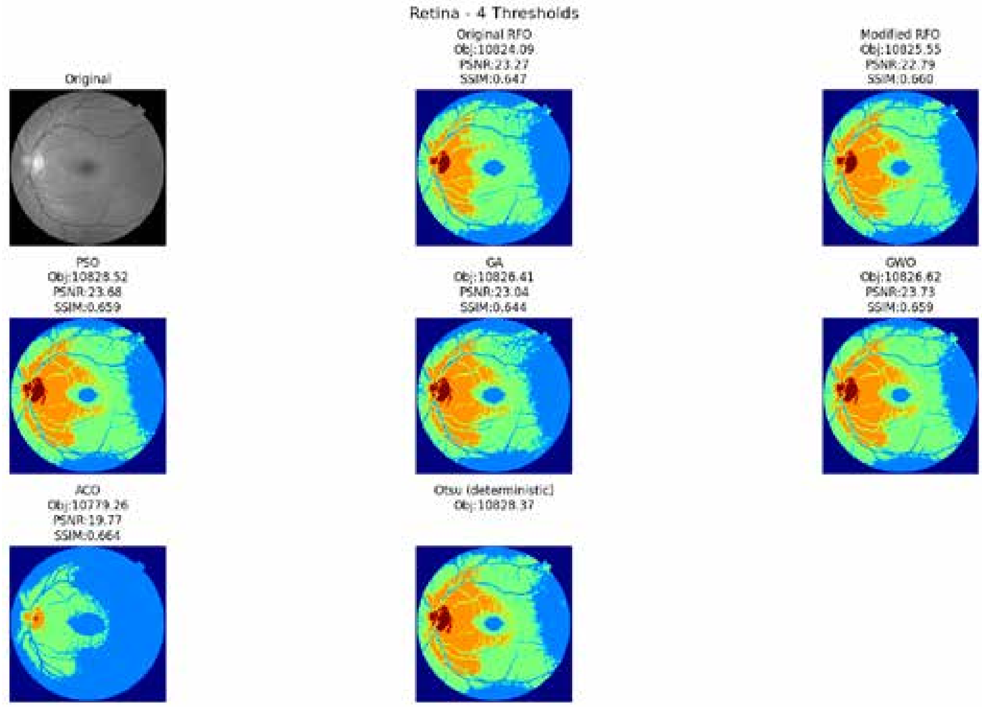
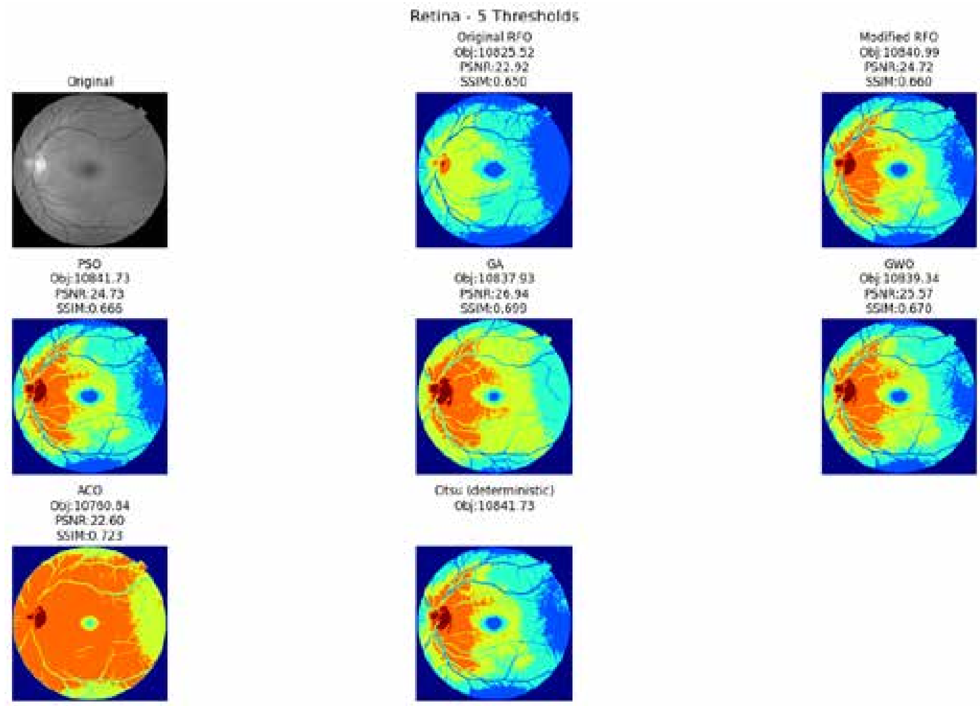


Figure 8

Retina Segmentation Output (5 Thresholds)



An analysis of the retinal image segmentation results at five threshold levels shows that the Modified Red Fox Optimization (MRFO) algorithm produces visually coherent and structurally stable segmentations, particularly in terms of preserving vascular boundaries and maintaining smooth regional transitions. However, the quantitative metrics indicate that MRFO does not achieve the highest PSNR or SSIM values among the tested algorithms. GA achieves the highest PSNR (26.94), while ACO yields the highest SSIM (0.723). MRFO's PSNR (24.72) and SSIM (0.660) remain competitive and close to those of PSO and GWO, demonstrating that although MRFO is not the top performer for this specific image, it still provides balanced and reliable segmentation quality.

Figure 9

Cells3D Segmentation Output (2 Thresholds)

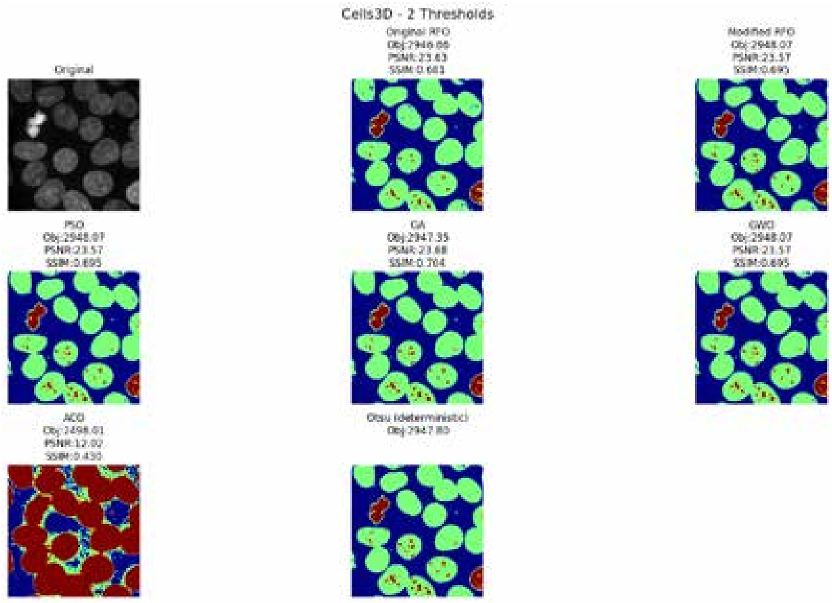


Figure 10

Cells3D Segmentation Output (3 Thresholds)

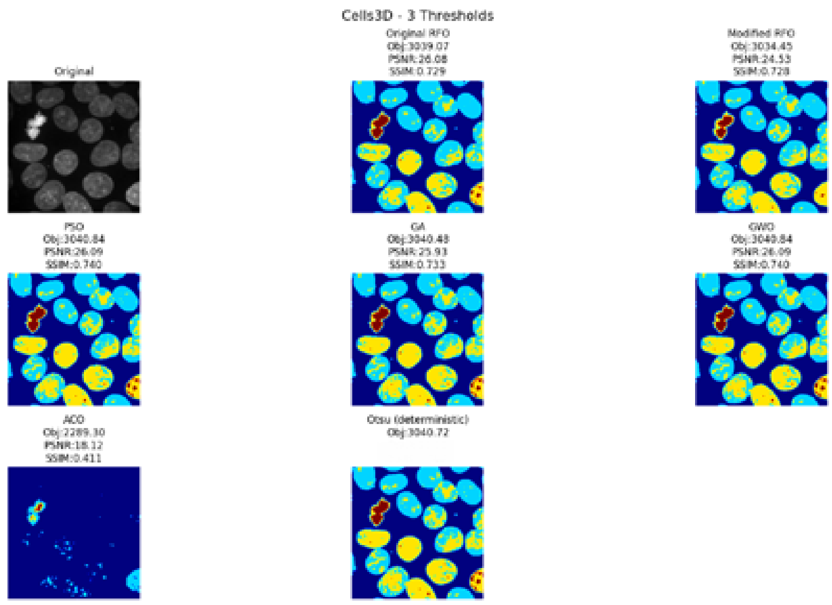


Figure 11

Cells3D Segmentation Output (4 Thresholds)

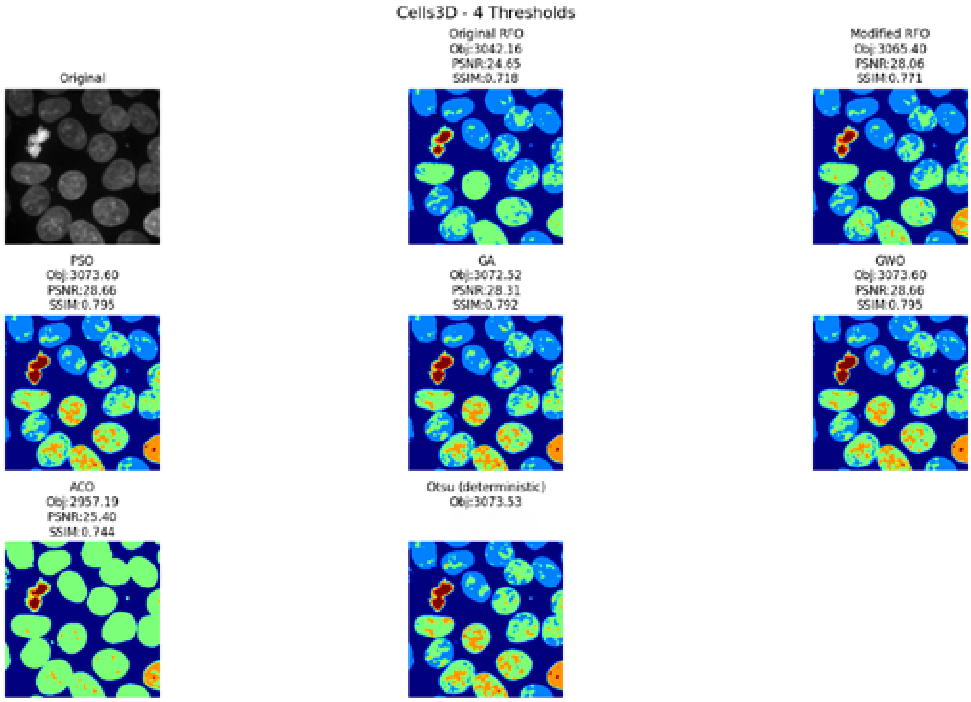
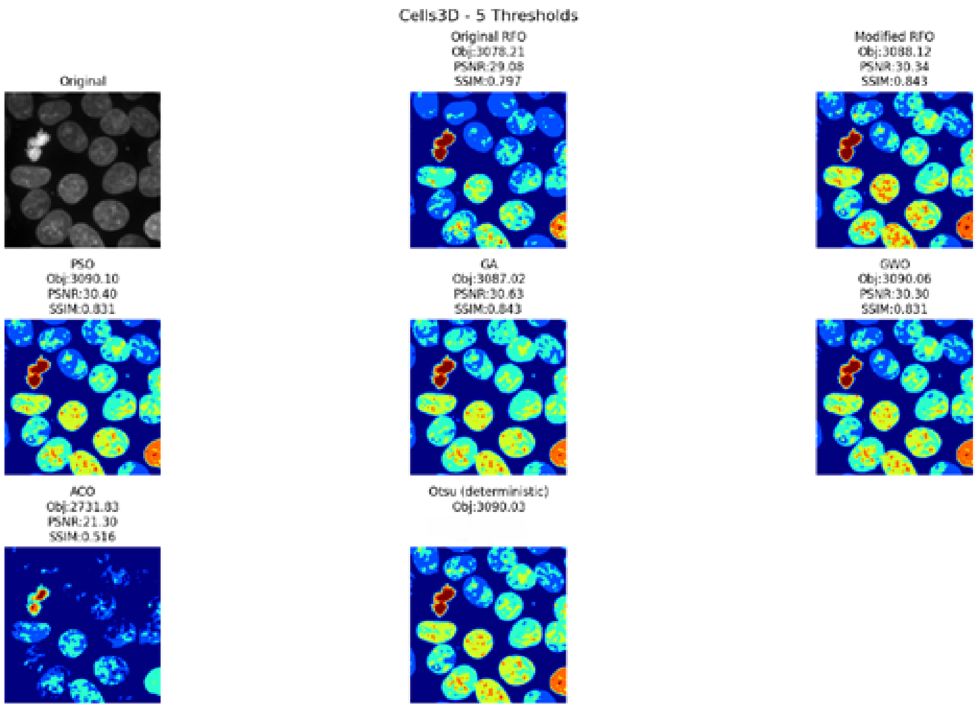


Figure 12

Cells3D Segmentation Output (5 Thresholds)



An examination of the segmentation results for the Cells3D image (Figures 9–12) indicates that PSO, GA, and GWO yield consistently strong performance, all achieving PSNR values around 30.8–30.9 dB and SSIM scores between 0.831 and 0.843, reflecting well-preserved cellular structure and contrast. In contrast, ACO exhibits substantial degradation of boundary details, as evidenced by its markedly lower PSNR (≈27.2 dB) and SSIM (≈0.516), leading to blurred and poorly defined cell contours.

Both the original RFO and, more notably, the Modified RFO (MRFO) demonstrate competitive or superior structural preservation, with SSIM values of 0.797 and 0.843, respectively. MRFO in particular produces clearer separation of cellular regions with more homogeneous intensity distribution and enhanced boundary consistency. These findings indicate that MRFO delivers a stable and competitive segmentation performance, closely matching the top-performing algorithms for the Cells3D dataset.

Figure 13

Mitosis Segmentation Output (2 Thresholds)

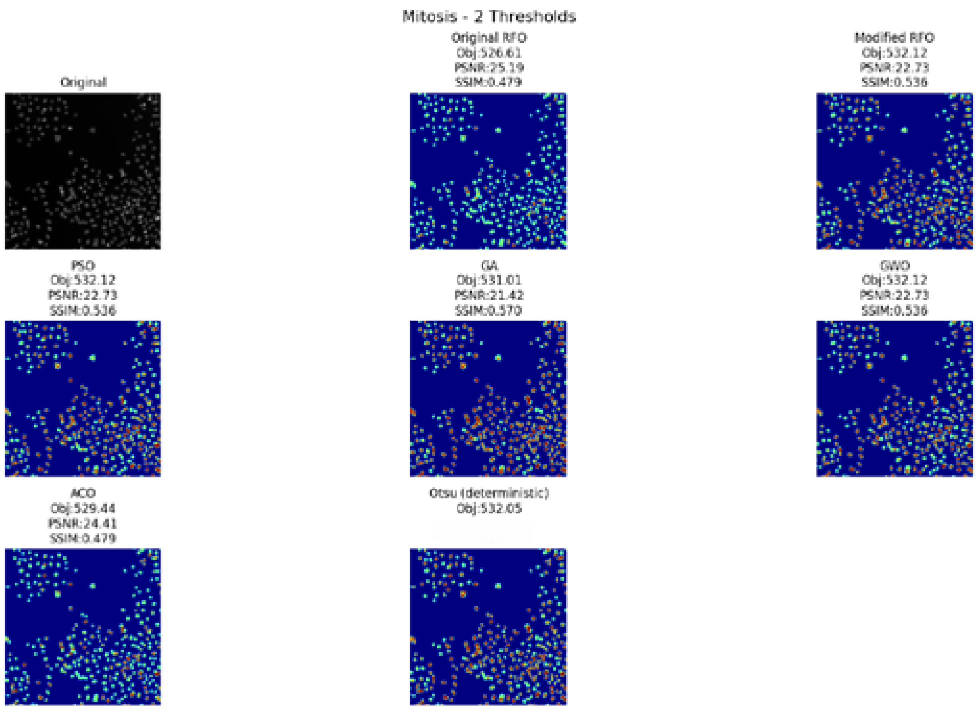


Figure 14

Mitosis Segmentation Output (3 Thresholds)

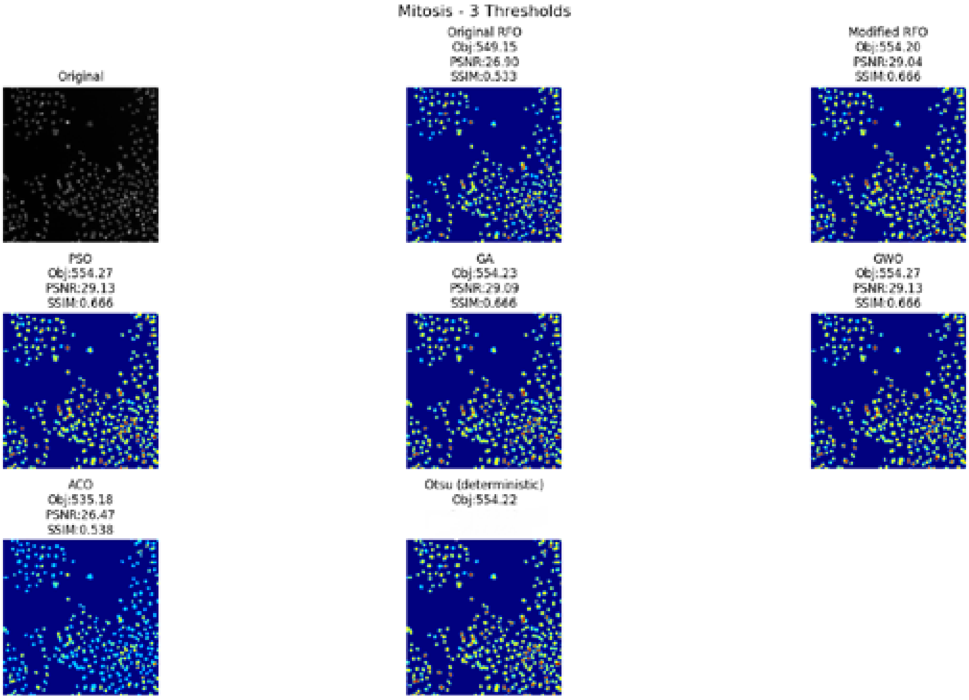


Figure 15

Mitosis Segmentation Output (4 Thresholds)

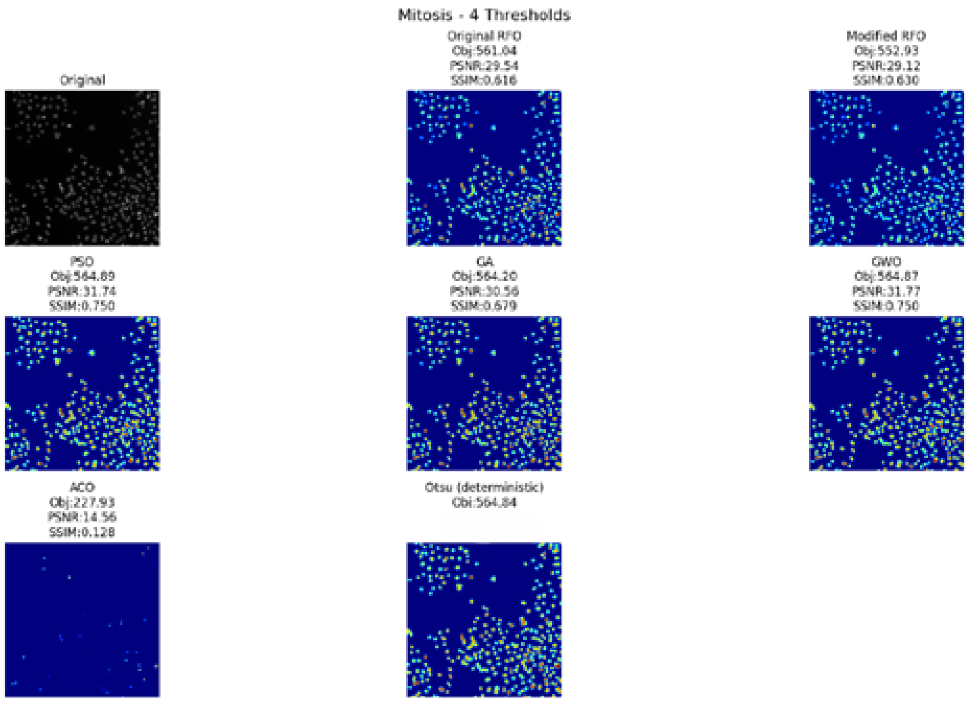
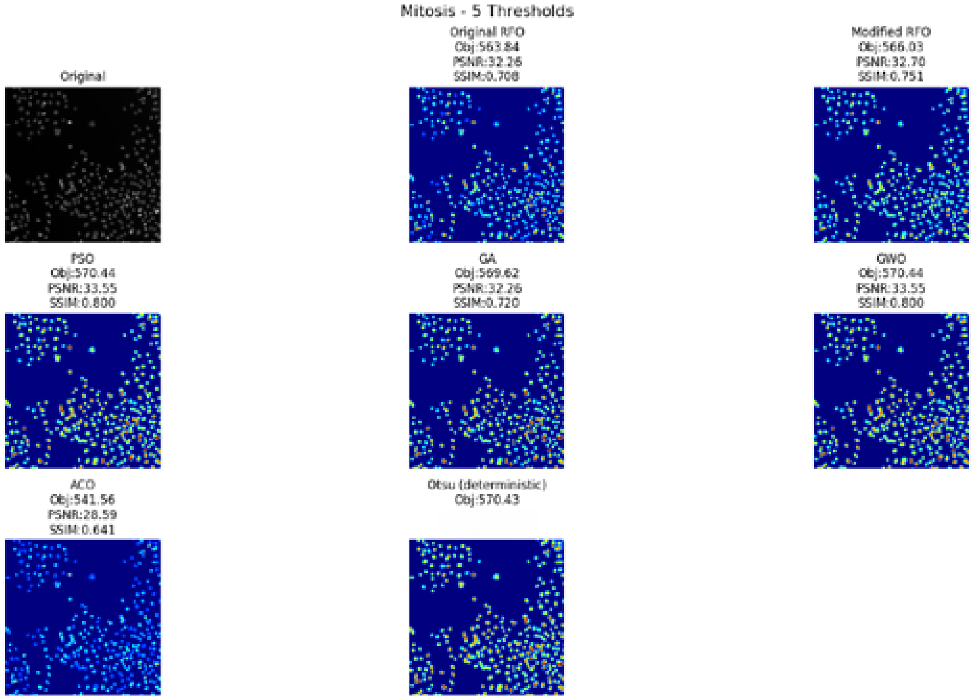


Figure 16

Mitosis Segmentation Output (5 Thresholds)



According to the segmentation results obtained for the mitosis image using five threshold levels (Figures 13–16), the GWO and PSO algorithms exhibit the highest structural similarity, both achieving an SSIM value of 0.800, accompanied by competitive PSNR values (PSO: 33.55 dB, GWO: 33.55 dB). These results indicate that both methods provide well-preserved structural continuity and visually consistent separation of mitotic regions.

Modified RFO (MRFO) also demonstrates strong performance, yielding SSIM = 0.751 and PSNR = 32.70 dB, which reflects stable segmentation with improved contrast compared to the Original RFO (SSIM = 0.708, PSNR = 32.28 dB). GA produces moderate quality results (SSIM = 0.720, PSNR = 32.26 dB) and remains inferior to MRFO, PSO, and GWO in terms of boundary clarity and homogeneity.

In contrast, ACO exhibits the weakest segmentation performance, as evidenced by its considerably lower SSIM (0.641) and reduced PSNR (28.59 dB), leading to visible loss of detail along cell contours.

Overall, MRFO provides stable and segmentation, whereas PSO and GWO deliver the most structurally coherent and visually sharp boundaries among all evaluated algorithms.

Convergence Behavior

Table 9 presents the convergence behavior of six metaheuristic algorithms (GA, PSO, ACO, GWO, RFO, MRFO) alongside the deterministic Otsu thresholding method for the Brain MRI image with three threshold levels. Since Otsu is a deterministic technique, it does not operate iteratively; therefore, its value is reported only at the final comparison stage.

The Brain MRI image and the three-threshold configuration were intentionally selected to create a controlled experimental setup for analyzing convergence behavior. Brain MRI is commonly used in segmentation studies due to its well-structured intensity distribution and clinically relevant contrast patterns, making it suitable for observing algorithmic improvements over successive iterations. Moreover, using three thresholds instead of the five thresholds discussed earlier reduces the dimensionality of the optimization problem, allowing clearer visualization of how each algorithm moves toward better solutions. This setup serves as a representative test case rather than an attempt to identify globally superior performance.

As shown in Table 9, all algorithms except ACO progressively improve their fitness values as iterations increase, while ACO consistently lags behind. In fact, the difference between ACO and the remaining algorithms widens further, confirming its limited suitability for multilevel thresholding in this particular test scenario.

It should be noted, however, that the observed convergence patterns are specific to this image and to the three-threshold configuration. Metaheuristic algorithms may exhibit different convergence speeds, stability characteristics, or stagnation behavior depending on the image type, histogram distribution, or threshold dimensionality. Therefore, the conclusions drawn from this experiment should not be generalized without broader evaluations across multiple datasets and threshold levels.

Table 9

Average Fitness Value (F) – Iteration-Based Comparison

Iteration	GA	PSO	ACO	GWO	RFO	MRFO	Otsu (deterministic)
10	1958.4	1992.7	1412.5	2005.9	1987.3	2024.6	—
50	2085.1	2108.3	1544.7	2119.4	2098.6	2115.8	—
100	**2124.8**	**2128.5**	**1652.2**	**2128.5**	**2114.3**	**2127.6**	**2068.44**

Note: Values were calculated as the average for the Brain MRI image using 3 threshold levels.

During early iterations (Iteration 10), MRFO exhibits the most rapid initial improvement (2024.6), followed by GWO (2005.9) and PSO (1992.7), indicating that these algorithms efficiently locate promising regions of the search space at the beginning of the optimization. Classical RFO and GA show slower convergence, whereas ACO displays the weakest performance (1412.5), reflecting its difficulty in exploring the continuous optimization landscape.

By Iteration 50, PSO, GWO, and MRFO maintain their leading positions with objective values above 2100, demonstrating both stability and strong exploitation ability. Classical RFO approaches similar performance but converges more slowly. The difference between ACO and the remaining algorithms widens further, confirming its limited suitability for multilevel thresholding.

At the final iteration (Iteration 100), PSO and GWO achieve the highest objective values (2128.5), with MRFO closely following (2127.6). GA also reaches a competitive result (2124.8), while classical RFO levels off at a slightly lower value (2114.3). ACO remains the poorest performer (1652.2), suffering from early stagnation and weak global search capability.

Overall, MRFO demonstrates faster initial convergence and greater stability than classical RFO, while achieving final performance competitive with PSO and GWO.

Runtime Comparison

According to the results presented in Table 10, the runtime performance of the evaluated algorithms varies significantly across different threshold levels. All runtime values in this table represent the average execution time computed across the four datasets used in this study (Brain MRI, Retina, Cells3D, and Mitosis). Averaging across multiple images provides a more robust assessment of computational behavior and prevents image-specific characteristics from biasing the comparison.

For low threshold counts (T=2 and T=3), all metaheuristic algorithms exhibit fast execution, with runtimes generally ranging from 0.12 to 0.20 seconds. Among them, the Modified RFO and Original RFO stand out as the fastest methods, achieving runtimes as low as 0.134 and 0.129 seconds at T=2, respectively. PSO also performs competitively within this range. In contrast, ACO consistently shows slower execution, particularly as the threshold count increases.

Table 10

Runtime Comparison Across Threshold Levels (Seconds)

Algorithm	T=2	T=3	T=4	T=5	Overall Avg.
Modified RFO	0.134	0.150	0.163	0.190	0.159
Original RFO	0.129	0.151	0.159	0.191	0.158
PSO	0.132	0.153	0.171	0.185	0.160
GA	0.149	0.164	0.197	0.203	0.178
GWO	0.165	0.196	0.214	0.229	0.201
ACO	0.198	0.289	0.364	0.402	0.313
Otsu (Deterministic)	0.005	0.031	2.68	297	~75

As the number of thresholds increases to T=4 and T=5, the runtimes of all metaheuristic algorithms increase slightly due to the expanded search space; however, they remain within a practical range (approximately 0.16–0.40 seconds). Modified RFO continues to deliver competitive efficiency with values of 0.163 seconds at T=4 and 0.190 seconds at T=5, reaffirming its suitability for higher-dimensional thresholding problems.

The deterministic Otsu method displays a distinctly different runtime profile. For T=2 and T=3, Otsu performs extremely fast (0.005 and 0.031 seconds, respectively), matching or outperforming all metaheuristic methods. However, its performance deteriorates dramatically for higher threshold levels due to its exhaustive search mechanism. At T=4, the runtime increases to approximately 2.68 seconds, and at T=5 it reaches an extreme value of 297 seconds, caused by the combinatorial explosion of possible threshold combinations. This makes Otsu impractical for high threshold counts despite being optimal and efficient for lower levels.

Overall, the results demonstrate that metaheuristic algorithms offer consistent and scalable performance across all threshold levels, while Otsu is advantageous only for low-dimensional cases. Modified RFO, in particular, provides an effective balance between accuracy and computational cost, outperforming classical RFO and other metaheuristic competitors in terms of runtime stability as the threshold dimension increases.

Discussion

Multilevel thresholding is known to become increasingly challenging as the number of thresholds grows, primarily due to the rapid expansion of the search space. While the Otsu method remains an effective and optimal solution for low threshold counts, its computational complexity increases exponentially at higher levels, making it less suitable for dimensionalities beyond T=3. This limitation has led to the widespread adoption of metaheuristic algorithms—such as RFO, MRFO, PSO, GA, GWO, and ACO—because of their ability to navigate complex search landscapes without requiring exhaustive enumeration. In this study, these metaheuristic approaches were systematically evaluated to determine their effectiveness across multiple biomedical image types and threshold configurations.

The experimental findings show that the Modified RFO (MRFO) generally performs better than the classical RFO in terms of objective function values, segmentation stability, and convergence behavior. MRFO achieves strong performance across all images and threshold levels; however, it does not consistently outperform all other metaheuristic algorithms in every scenario. Rather, MRFO stands among the top-performing methods, often delivering results comparable to PSO and GWO, which also exhibit competitive performance in several cases. Since Otsu serves as a deterministic baseline method rather than a population-based optimizer, the objective function comparison is not emphasized for Otsu in this context.

Regarding segmentation quality, MRFO yields coherent and stable outputs with competitive PSNR and SSIM values across all datasets and threshold levels. PSO, GA, and GWO produce comparable results, particularly at lower threshold levels (T = 2–3), while their performance becomes less consistent as threshold dimensionality increases. MRFO demonstrates greater robustness under these conditions, maintaining relatively stable PSNR (e.g., 31.62 for Brain MRI, 33.06 for Mitosis) and SSIM values across varying T levels without significant degradation. Importantly, these results reflect the observed outcomes and do not suggest that MRFO universally dominates across all metrics or datasets.

In terms of computational efficiency, MRFO ranks among the faster algorithms, with an overall average runtime of approximately 0.159 seconds. PSO and classical RFO achieve similar runtimes, while ACO remains the slowest method due to its pheromone-based selection mechanism and higher computational overhead. The Otsu method shows extremely efficient performance for $T \leq 3$ but becomes computationally expensive at higher thresholds (e.g., 2.68 seconds at T=4 and 297 seconds at T=5) because of its exhaustive search nature. Thus, while Otsu retains clear advantages for lower-dimensional thresholding, metaheuristic algorithms can be effectively used for higher threshold counts where deterministic methods become impractical.

From a convergence perspective, MRFO demonstrates faster early improvement and smoother progression than classical RFO, exhibiting reduced stagnation and more stable convergence curves. Although PSO and GA occasionally display oscillatory patterns or early trapping—especially at higher threshold dimensionalities—MRFO maintains more consistent behavior. Classical RFO progresses steadily but typically converges more slowly and shows less adaptability compared with MRFO.

The enhanced performance of MRFO can be attributed to four algorithmic modifications introduced in this study:

1. Chaotic logistic-map initialization, which enhances population diversity and mitigates premature convergence by distributing candidate solutions more effectively across the search space.
2. Adaptive control factors, enabling a more dynamic and balanced transition between exploration and exploitation throughout the optimization process.
3. An improved position update mechanism incorporating the α and γ parameters, which provides more accurate and responsive guidance during the search, allowing the algorithm to navigate complex landscapes more reliably.
4. An adaptive mutation strategy, which strengthens the ability to escape local minima and promotes sustained global search capability, particularly in high-dimensional thresholding problems.

In conclusion, MRFO represents a robust and effective approach for multilevel image thresholding, offering improved stability, consistent segmentation quality, and competitive computational performance. Compared with classical RFO, MRFO achieves approximately 3–5% higher objective values and around 5% faster execution time on average, demonstrating the practical value of the proposed enhancements, particularly in biomedical image segmentation tasks involving medium- to high-dimensional thresholding problems.

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Skin Cancer: Pathophysiology and Epidemiology

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Introduction

Definition and significance

Skin cancer is defined as the uncontrolled or abnormal proliferation of skin cells due to various reasons. One of the most well-known and referred reasons is DNA damage and mutations from UV radiation that trigger growth. The mutations are caused by ultraviolet (UV) radiation, ionizing radiation, immunosuppression, or viral infections, and are commonly seen in elderly patients (Kaur and Yusuf, 2021). Ever since the 19th century, skin cancer has been associated with sun exposure (Al-Matouq, 2025).

Skin is the largest organ of the body, and it performs multiple vital functions. It protects the body from environmental factors like pathogens and UV rays, acts as the first line of immunological defense against infections, keeps the organ and tissue integrity, and helps conserve homeostasis. The three primary layers of skin are: epidermis, dermis, and hypodermis. The epidermis is the most superficial layer, and it is mostly made up of keratinocytes and melanocytes at the basal layer. Langerhans cells and Merkel cells are also seen in the epidermal layer. The dermis lies beneath the epidermis and constitutes the thickest part of the skin. It contains fibroblasts, vessels, nerves, and appendages. The hypodermis is the deepest layer and contains fat tissue.

Skin cancer is stated as the most frequent malignant condition among light-skinned individuals. Both malignant melanoma and non-melanoma skin cancer are reportedly on the rise. The incidence among light-skinned people is now as high as 1.2 million cases a year (Al-Matouq, 2025; Ferlay et al., 2021). It is speculated that there is a skin cancer epidemic with the increased incidence of melanoma cases, yet the mortality rates do not comply with it. This raises the question of whether the increased number of biopsies and overdiagnosis is causing the growing incidence data (Apalla et al., 2017).

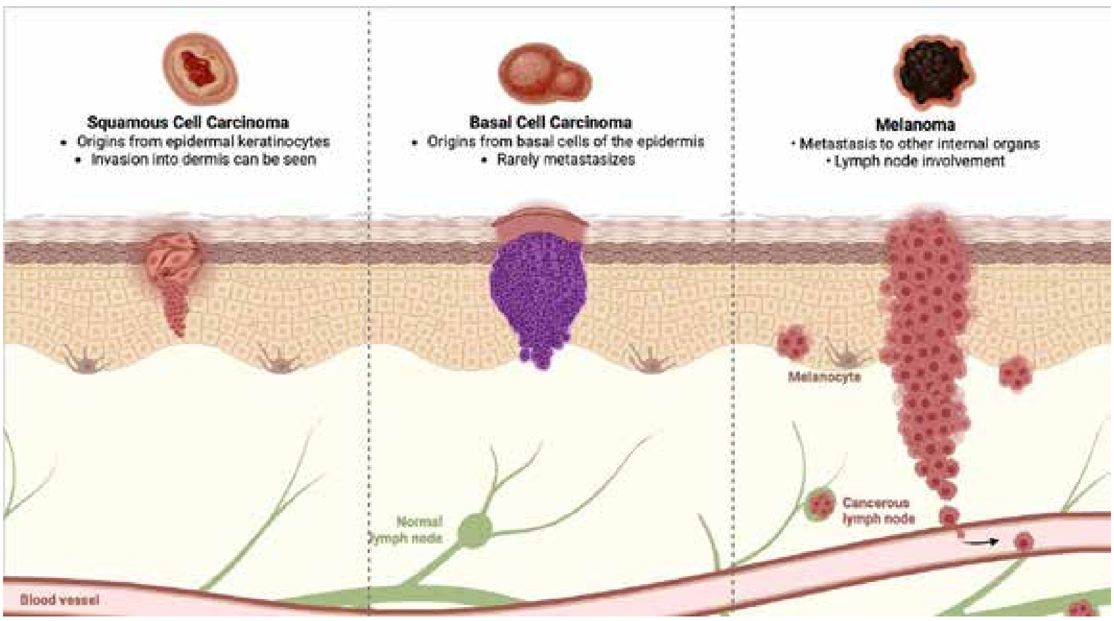
Because of its high frequency, related morbidity, and mortality, skin cancer (SC) is referred to as a serious global public health concern. Healthcare institutions and the overall economy are severely strained by the number of skin cancer patients. The Australian health system spent AU$1.8 billion on the diagnosis and treatment of skin cancer in 2020–2021 (Collins et al., 2024). The increasing global prevalence, high financial cost, and the fact that malignant melanoma is still the most aggressive type of cancer, skin cancer continues to be a significant concern that requires immediate attention for care and prevention.

Types of skin cancer

Skin cancer types differ in their clinical presentation, place of origin, and extent of spread. They are mainly separated into melanoma and non-melanoma skin cancer (NMSC). Melanoma skin cancer is also known as malignant melanoma or cutaneous melanoma. It arises from melanin-producing cells: melanocytes. It constitutes a smaller percentage of skin cancer cases but holds the majority of skin cancer-related deaths. The four major subtypes of melanoma include: Superficial Spreading Melanoma (SSM), Nodular Melanoma (NM), Lentigo Maligna Melanoma (LMM), and Acral Lentiginous Melanoma (ALM). NMSCs originate from keratinized epithelial cells. The two main divisions of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) (Figure 1).

Figure 1

Types of Skin Cancer



BCCs originate from the basal cells at the deepest layer of epidermis. They rarely metastasize but are locally damaging (Roky et al., 2025). SCCs arise from epidermal keratinocytes. It tends to be more aggressive compared to BCCs, and if left untreated, it may develop deeper into the epidermis and metastasize to other tissues (Zeng et al., 2023). Actinic keratoses and Bowen's disease are accepted as precursors of BCC lesions (Das et al., 2021; Al-Matouq, 2025). Other less common NMSCs are: Merkel cell carcinoma, which develops quickly and is aggressive, kaposi sarcoma, related to viral infections HHV-8, and Cutaneous Lymphoma. Since NMSCs have a lower mortality rate and are usually detected in their early stages, they are not reported to the skin cancer registries. Although they don't usually metastasize out of the tumor site, in rare cases, if they are left untreated, they may cause fatalities (Kivisaari & Kähäri, 2013).

Epidemiology of Skin Cancer

Physicians have described specific subtypes of skin cancer in the early 19th and early 20th centuries (Zeng et al. 2023). The relation between excessive sun exposure and skin cancer was first noted in the early 19th century, and in the early 20th century, for the treatment of skin cancer, radiation was utilised (Leiter et al., 2020; Natelauri and Jghamadze, 2025). Epidemiological observations started to firmly establish our knowledge of environmental risk factors and disease frequency by the middle of the 20th century.

Since its incidence, morbidity, and mortality constitute a public health issue, skin cancer is one of the biggest medical problems of today. Melanoma skin cancer is the 17th most common type worldwide. Europe has the highest frequency and fatalities. Nonetheless, the highest rates of incidence and mortality are found in Australia and New Zealand (Roky et al. 2025). Non-melanoma skin cancers (NMSCs) are most common in North America, and the majority of deaths from NMSCs occur in Asia. Australia and New Zealand have the greatest incidence rates of basal cell carcinoma (BCC).

The global burden and risk of skin cancer are significantly influenced by demographic factors. Fair-skinned people of European ancestry have the highest prevalence of skin cancer. Globally, melanoma is more commonly seen in men than women in regions other than the United States (Arnold et al., 2022). Generally speaking, incidence rises with age. Over-50-year-olds account for over 80% of newly diagnosed melanoma cases. But among young individuals, melanoma is also one of the most prevalent malignancies (Bhattacharya et al., 2021).

Changes in incidence and prevalence over the years

An estimated 325,000 new cases of melanoma were reported worldwide in 2020. The International Agency for Research on Cancer (IARC) estimated that the newly diagnosed melanoma cases to increase by more than 50% and melanoma deaths to increase by more than 68% by 2040. These rates were calculated in accordance with the population growth and changes in age composition. Age-adjusted change assumptions on the incidence and mortality rates were not considered. But the increasing trend is not the same worldwide. The incidence rate among the young population of Australia has decreased to about half of what it was in the 1980s. Australia's widespread SunSmart education programs and other sun protection measures are to blame for this particular decline (Arnold et al., 2022; Collins et al, 2024).

Geographical distribution

Geographically, there are significant differences in the number and pace of skin cancer cases. Australia has the highest incidence rate for both males and females for melanoma, followed by Western Europe, North America, and Northern Europe. The lowest rates are seen with most regions of Africa and Asia, less than 1 per 100000 person-years. The highest mortality rates due to melanoma are seen in New Zealand and Australia (Arnold et al., 2022). In North America, the incidence of melanoma among white people has increased by 3% yearly from 1996 to 2006. The peaks are observed in people 65 years and older. NMSC cases make up more than 5.4 million per year (Linares et al., 2015). In Europe, according to the European Academy of Dermatology and Venereology (EADV), the number of NMSC cases has increased by 3–8% annually in recent decades, and the ten to twenty-five new cases of malignant melanoma are reported for every 100,000 people (Roky et al., 2025). The greatest age-standardized rates of melanoma worldwide are found in Australia and New Zealand (Oceania). In contrast to the ongoing rise in the majority of European nations, incidence rates in Oceania and North America seem to have stabilized recently (Arnold et al., 2022).

General Overview of Skin Cancer Pathogenesis

Pathogenesis of Non-Melanoma Skin Cancers (BCC, SCC, Actinic Keratosis)

BCC is the most commonly seen form of skin cancer. It develops slowly and shows local invasion (Linares et al.,2015). It is most commonly seen on sun-exposed areas such as the ears, face, and dorsum of the hands. It is rarely seen on palmoplantar surfaces and never on mucosa (Apalla et al., 2017; Linares et al.,2015). Most cases of BCC have a good prognosis; rarely some of them progress to a more advanced form with very few treatment options and no formal treatment algorithms.

UVR is mostly responsible for the formation of BCC. In most cases, a mutation in the Hedgehog signaling pathway is seen. Mutations in the PTCH1 gene, which codes for the sonic hedgehog receptor, cause cancer by preventing cell cycle arrest and differentiation, which leads to unchecked cell proliferation and the development of hyperplasia (Al-Matouq, 2025, p. 9). Hedgehog signaling pathway inhibitors show complete remission in locally infiltrated cases of BCC (Apalla et al., 2017). The canonical (β-catenin-dependent) Wingless (WNT) signaling pathway and P53, as commonly seen with SCC, are two more frequently impacted pathways in BCC (Kashyap et al., 2022).

Squamous cell carcinoma stems from the uncontrolled proliferation of keratinocytes. The risk factors for SCC are similar to BCC, with the addition of chronic inflammation due to skin damage and epidermolysis bullosa syndromes (Linares et al., 2015). SCC progression follows a complex and multi-factorial route. Several mutations lead to precancerous lesions such as actinic keratosis (AK) and Bowen's disease (BD). BD is an intraepithelial form of SCC. They are both characterised by atypical keratinocytes at various sites of the epidermis. In about 3-5% of lesions, infiltration through the basement membrane and progression to SCC is seen (Souto et al., 2022).

DNA damage brought on by UV radiation exposure is the primary cause of cutaneous squamous cell cancer. The degree of lifetime sun exposure is correlated with the occurrence of tumors (Lazar, 2021). DNA damage response pathways are triggered by substantial DNA damage caused by acute UVR exposures. As a molecular mediator, p53 is crucial to the way cells react to UVR. In UVR-exposed keratinocytes, higher amounts of p53 were seen. p53 functions as a transcriptional regulator in cells, facilitating cell cycle arrest, initiating DNA damage repair, and promoting apoptosis. But different signaling pathways, such as phosphoinositide 3-kinase (PI3K), serine/threonine protein kinase AKT, and mammalian (or mechanistic) target of rapamycin (mTOR) (PI3K/AKT/mTOR) can act against the functions of p53 and eventually give rise to carcinomas (Manning and Cantley, 2007; Carvalho et al., 2024). The balance between those mechanisms is the determining factor for the outcome on UV-irradiated cells.

The pre-malignant lesions, such as AK, shed light on the underlying mechanisms of SCC, genetics, and acquired defects. One of the major consequences of UVR exposure is the accumulation of defects, especially TP53. The mutant p53 plays a pivotal role in carcinogenesis. p53 is thought to be one of the first agents to be affected by UVR and lead to the formation of tumors. TP53 mutations were reported to be highly common in AK lesions of light-skinned individuals, and it was also detected in more than 30% of BCC and 90% of SCC cases, affirming the influence of mutated TP53 in skin cancer sites (Kumar et al., 2015; Carvalho et al., 2024). The mutations regarding TP53 are mostly seen at pyrimidine dimers, proving the UVR effect. In normal cells, the damage caused by UVR is checked at cell cycle checkpoints by kinases of RAD3-related (ATR) and Ataxia Telangiectasia Mutated (ATM) pathways. These kinases control p53 status and expression by signals. To prevent oncogenic transformations, p53 stops the cycle at the G1 checkpoint by activating p21 and blocking cyclin-dependent kinase (CDK)/cyclin E complex activation. UVR originated reactive oxygen species (ROS) cause apoptosis signal-regulating kinase1 (ASK1) to become active, which in turn triggers p53. Depending on the amount and type of damage, p53 either facilitates DNA repair or initiates apoptosis. If the protective function of p53 is lost by a mutation, DNA repair is done by alternative ways, which are labile. Thus, both the p53 mutations and DNA damage are passed down to next-generation cells (Lazar, 2021).

Cell division cycle 25 (CDC25) phosphatases are known to be a close proximity to NMSCs. They are the controllers of apoptosis and the cell cycle. Normally, ATM phosphorylates the effector checkpoint kinases (Chk1 and Chk2) to activate the downstream signaling pathway. CDC25 is phosphorylated by Chk1/2. UVR activates ErbB2, which is an upstream regulator of a DNA damage cell cycle checkpoint. The PI3K/Akt pathway is signaled by ErbB2 activation and inhibits phosphorylation of Chk1 on Ser280. This limits Chk2 and further inhibits the phosphorylation of CDC25, resulting in long-lasting activity that can trigger and support tumorigenesis. Excess amounts of CDC25 promote anti-apoptosis and work in favor of survival in skin cancer (Reddy et al.,2010; Al-Matouq, 2025).

Another common mutation seen with SCCs is the RAS oncogene. The RAS protein holds an important place in the regulation of cancers. When the RAS-related proteins accumulate, they can sustain tumor formation by hyperproliferation, invasion, metastasis, and anti-apoptotic effect (Al Mahi and Ablain, 2022).

Malignant Melanoma

Melanoma is an aggressive neoplasm stemming from the malignant transformation of melanocytes. Melanocytes are the cells that produce melanin pigment; they are found in the epidermis, eye, and many internal organs (Al Mahi and Ablain, 2022). Melanomas can occur in normal skin or from existing nevi (Litvin et al., 2025). Even though melanoma is responsible for 2% to 5% of skin malignancies, it is the reason for the majority of deaths (Linares et al., 2015). The prognosis depends on the location of the tumor and the status and depth of metastasis. The survival chance is high if the diagnosis is made in the early stages and the tumor is surgically resected. In case of metastasis, the prognosis of 5 years is less than 5% (Zeng et al., 2023). There are four main types of skin cancer: superficial spreading melanoma (75% of cases), nodular melanoma (15-30% of cases), lentigo maligno melanoma, and acral lentiginous melanoma (the least common subtype) (Lee et al.,2020; Linares et al., 2015). A mix of environmental and genetic factors contributes to the development of melanoma. UV radiation is closely associated with all skin cancers as the reason for acquired mutations. For melanomas, the effect of UVR is not as straightforward as for other skin cancers. Current studies state sunburns in early ages as the primary factor. But since melanomas can be seen in non-sun-exposed parts of the skin and also dark skinned individuals, other factors are thought to have a greater risk (Lazar, 2015).

10-15% of melanomas are passed down through autosomal dominant genes with varied penetrance. High-penetrance genes such as *CDKN2A*, *CDK4*, BAP1, and medium-penetrance genes such as MC1R are found to be related to familial cases (Flori et al., 2025; Lazar, 2015). Also, light complexion as well as a tendency to get sunburns rather than tanning is related to a higher likelihood of having melanoma. It is reported that white folks are more than 20 times more likely than African Americans to develop melanoma (Linares et al., 2015).

A great proportion of melanomas present hyperactivation of the RAS/MAPK pathway in relation to an oncogenic driver (Al Mahi and Ablain, 2022). The most frequently seen oncogenic site is v-Raf murine sarcoma viral oncogene (BRAF), which is a part of the MAP/ERK pathway controlling cell development and proliferation. BRAF mutations are commonly seen in dysplastic nevus, inducing a senescence-like state that, when overcome, progresses to melanoma (Paluncic et al.,2016). The PTEN tumor suppressor is frequently lost in melanomas with BRAF mutations, which results in increased PI3K/AKT/mTOR pathway activation. Mutations in the NRAS tumor suppressor gene also contribute to the progression of melanoma. NRAS mutations activate both the MAPK and the PI3K/AKT pathway, in contrast to BRAF mutations that solely activate the MAPK pathway (Vuković et al., 2019).

Another critical factor in melanoma progression is the inactivation of tumor suppressor genes. The CDKN2A gene mutation is seen in almost half of autosomal dominant familial melanoma cases. Three distinct tumor suppressors are encoded by the complex gene CDKN2A. Of these, loss of p16/INK4a is unmistakably linked to human melanoma, and experimental data also suggest that loss of p14/ARF plays a part. p16/INK4a strengthens the retinoblastoma protein (RB) tumor suppressor's capacity to stop cells in the G1 phase of the cell cycle. Inactivation of CDKN2A tumor cells bypasses the checkpoint and leads to melanoma progression (Al-Matouq, 2025; Zaidi et al., 2009). To understand the progression and prognosis of melanoma, radial and vertical growth concepts become essential. The radial growth phase describes the horizontal progression. In this stage, the tumor stays within the epidermis and superficial dermis and does not metastasize. The vertical growth phase shows invasion towards the dermis and a subclone signaling metastasis (Lazar, 2021).

Ultraviolet radiation

It is commonly stated that chronic exposure to ultraviolet radiation is the primary cause of skin cancer (Linares et al., 2015).

UVR is a form of radiation naturally occurring in solar rays and artificially produced in tanning beds. While it is categorised as a primary carcinogen for skin cancer and other environmentally affected diseases, it is also the primary factor for vitamin D synthesis and different endorphins in the skin. Malignant melanoma, basal cell carcinoma, and squamous cell carcinoma are all attributed to UVR both molecularly and epidemiologically. Also, genetic factors, most importantly the MC1R gene, play a role in UVR-related skin cancer risk since it is connected to the UVR protection and lightness of skin (D'Orazio, 2013). Early research showed that skin pigmentation protected against skin cancer and that UV radiation caused DNA damage that resulted in mutations (Al-Matouq, 2025)

UV radiation stands between the wavelengths of visible light and gamma rays. UVR is divided into three parts based on its wavelengths: UVA, UVB, and UVC. Solar UVR is mostly UVA and a lesser portion of UVB, showing differences according to geographic and climatic reasons. UVA are the wavelengths between 315–400 nm. It can reach the dermis and the subcutaneous tissue beneath. UVB ranges from 280 to 315 nm and has less penetrating ability compared to UVA. It gets mostly absorbed at the epidermal layer. The carcinogenic activity is mostly attributed to UVB, even though UVA makes up the majority of solar UVR. UVC has the shortest wavelengths and it gets mostly absorbed at the stratosphere layer (Al-Matouq, 2025; Carvalho et al., 2024). The effects of different wavelengths are not distinct and mostly seen overlapping each other.

An elevated risk of all main forms of skin cancer is evidently associated with indoor tanning machines, also known as tanning beds, which are a substantial artificial source of ultraviolet radiation (UVR). Tanning beds emit UVR at a much higher concentration than solar light by producing both UVA and UVB rays. The usage of such devices takes a toll on skin health due to the cumulative effects of UVR (D'Orazio, 2013). It is stated that there is no safe level of usage for tanning beds. Even though recent data show that tanning bed usage has decreased in the last decade, the lifetime effects are still visible (Diehl et al., 2024).

The effects of UVR are mainly seen with DNA damage, making itself visible through point mutations. The damage occurs mainly as direct photochemical damage or indirect oxidative damage. With direct photochemical damage, DNA directly absorbs UVB rays, which results in molecular changes that produce certain photoproducts. Cyclobutane pyrimidine dimers (CPDs) and 6–4 photoproducts (6–4 PPs) on DNA are the most commonly seen lesion types. If those lesions are not reversed, they can lead to certain mutations, most commonly seen in p53 and other skin cancer-related genes. With indirect oxidative damage, the reactive oxygen species (ROS) such as superoxide anions and hydrogen peroxide caused by both UVA and UVB play a great role. ROS can damage lipids, proteins, and DNA subunits. This damage can give rise to mutations such as guanine to thymine transversion, leading to oncogene activation or tumor suppressor gene repression (Al-Matouq, 2025; Carvalho et al., 2024). ROS can also activate signaling pathways related to inflammation and cancer formation by influencing intracellular antioxidant molecules (Kobaisi et al., 2021; Carvalho et al., 2024).

While NMSC types BCC and SCC are mostly associated with sun exposure and mostly seen on sun-exposed sites of the body, such as the face, head, and neck, there seems to be different takes on causality between sun exposure and melanoma occurrence (Holick, 2014). Even though UVR is stated as the main environmental trigger in melanoma development, current data show that intermittent intense exposure to UVR, such as sunburns, is more crucial in early life (Al-Matouq, 2025; Bulliard et al., 2007; Elwood and Gallagher, 1998).

Genetic predisposition

In the pathophysiology of skin cancer, MC1R, other genes, and signaling pathways play a key role in the development of skin cancer. MC1R is known by its effect on pigmentation of skin and, less often, for its non-pigmentation role of DNA repair (Liu et al., 2016). MC1R triggers a signaling cascade to increase intracellular cyclic adenosine monophosphate (cAMP) and thus produce photoprotective eumelanin pigment. The production process gets stimulated by ligands like alpha-melanocyte-stimulating hormone-like ligands, whose levels increase after UV exposure (Sturm et al., 2003). Eumelanin is much more effective at UV protection than pheomelanine, which is prooxidant (D'Orazio et al., 2013). Some MC1R variants are categorised as "RHC (Red Hair Color)" due to loss-of-function mutations, making them associate more with red hair, fair skin, freckles, and a poor tanning response (Guida et al., 2022). The mutations reduce the function of the gene and increase the eumelanin ratio. Since pheomelanine is less UV protective, the MC1R mutations become susceptible to developing melanoma and NMSCs (Tagliabue et al., 2015). Also, it was seen that MC1R mutations could increase the penetrance of high-risk skin cancer-related genes like CDKN2A (Fargnoli et al., 2010).

Skin cancer is generally not considered to be genetically transferred through family members, although family members carry similar skin characteristics, which determines the likelihood of skin cancer development. Most cases of melanoma are sporadic, but around 10 to 15% of them are seen to occur due to inheritance of autosomal dominant traits with variable penetrance. Key risk factor genes for melanoma are CDKN2A, CDK4, BAP1, and MC1R variants (Manganelli et al., 2021; Gosman et al., 2023). For NMSCs, a positive family history of skin cancer is accepted as an important factor for BCC. Rather than extrinsic factors, genetic susceptibility plays a greater role in the development of BCCs. Nevoid Basal Cell Carcinoma Syndrome (NBCCS) or Gorlin Syndrome is an autosomal dominant multisystem disorder. It manifests with multiple BCCs on the skin. Similarly, Bazex-Dupre-Christol syndrome, Rombo syndrome, xeroderma pigmentosum, and Bazex syndrome are also associated with early onset of multiple BCCs (Schierback et al., 2019).

Microbiome

The skin microbiome, composed of a diverse selection of bacteria, fungi, and viruses, and the balance between them, plays a significant role in the pathophysiology of skin cancer. The skin microbiota competes for space and nutrients, which makes them a part of the physical barrier of protection. Commensal bacteria help in keeping the skin pH levels stable and produce antimicrobial peptides, preventing pathogen invasion (Kotak, 2021). The microbiome interacts with T cells to promote their functions, help regulate inflammation, and immune tolerance (Pandey, 2021). A change or imbalance in the microbial community, known as dysbiosis, can cause a change in immunological responses, which can lead to persistent inflammation and possibly cancer.

Chronic inflammation is associated with the occurrence and development of several cancers. Additionally, the inflammatory setting triggered by dysbiosis in the skin tumor site reduces the effectiveness of cancer immunotherapy and suppresses the body's inherent anti-tumor immunity (Tang & Wang, 2016).

Atopic dermatitis is one of the known precursor lesions of skin cancer. Excess amounts of Staphylococcus aureus are known to be a major contributing factor for atopic dermatitis, which raises the risk for especially squamous cell carcinoma (Kullander et al., 2009; Pandey, 2021). Also, a decreased proportion of Malassezia and Cutibacterium species has been observed in actinic keratosis and squamous cell carcinoma sites. It is theorized that the loss of protective effect by commensal bacteria may have contributed to carcinogenesis (Woo et al.,2022).

Human Papillomavirus (HPV) is a well-known oncovirus known to be connected to a number of cancers. Although it is most recognized for its involvement in cervical cancer, some forms of HPV are also linked to skin carcinogenesis, especially when combined with other risk factors like immunosuppression and UV exposure. Because HPV oncoproteins E6 and E7 inhibit DNA repair and cause death, UV-damaged cells can multiply unchecked. (Kotak, 2021).

Conclusion

Skin cancer is one of the most frequently diagnosed cancers globally and represents one of the greatest medical challenges. The incidence rates continue to increase in many parts of the world. The rising numbers are not only related to rising UV exposure and lifestyle changes, but also a part of the overdiagnosis and improved detection phenomenon. With the help of new technologies such as artificial intelligence and advances in diagnosis with generalized usage of dermatoscopes in clinics, the detection of lesions has become easier, and the diagnostic sensitivity has increased. Longer lifespans and more common access to healthcare services compared to the past also had a role in the increasing number of diagnoses. Still, the sheer amount of cases generates a huge burden on the healthcare systems.

New studies on the pathogenesis of skin cancer cases allow us to better understand the molecular background of disease progression and risk factors. Current studies show that cumulative exposure to ultraviolet radiation (UVR) is directly linked to the pathogenesis of skin cancer. Prevention and early diagnosis are essential to lowering the morbidity and death linked to skin cancer. Given that UVR is the strongest modifiable risk factor for skin cancer progression, sun protection plays an important role in prevention strategies.

It is recommended to minimize outdoor activities during peak ultraviolet (UV) radiation hours, typically between 10 a.m. and 4 p.m. Wearing protective clothing that covers exposed skin, along with wide-brimmed hats and UV-blocking sunglasses, provides additional defense against harmful rays. Regular application of a broad-spectrum sunscreen that protects against both UVA and UVB rays, with frequent reapplication throughout the day, is also crucial (Collins et al., 2024). Avoiding artificial sources of UV exposure, such as tanning beds and sunlamps, further reduces skin damage risk. Finally, engaging in routine skin examinations and early screening—especially for individuals at high risk—supports early detection and significantly improves treatment outcomes.

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Circadian Rhythms and Chronotherapy: Integrating Molecular and Physiological Mechanisms into Physiotherapy and Rehabilitation Sciences

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Introduction

Defining Circadian Rhythms and Adaptive Value

Circadian rhythms (CRs) are defined as endogenously generated biological timing mechanisms that repeat with a period of approximately 24 hours (derived from the Latin *circa diem*) and are present in virtually all organisms (Patel et al., 2022). These internal biological cycles confer a profound adaptive advantage by enabling organisms to anticipate and prepare for predictable cyclical environmental shifts, such as the availability of light and nutrients (Patel et al., 2022). This predictive capacity is critical for survival and maximizing energy efficiency.

The role of CRs in physiological regulation is comprehensive, ensuring the temporal separation (temporal partitioning) of essential biochemical, metabolic, and redox processes at the cellular level (Patel et al., 2022). Furthermore, CRs regulate almost every systemic function within the body, including the cardiovascular, metabolic, endocrine, and immune systems (Cermakian & Boivin, 2009). These rhythmic oscillations also play a central role in regulating the underlying pathophysiology of complex chronic conditions, such as obesity and diabetes (Cermakian & Boivin, 2009).

Circadian Misalignment (CRD) and Clinical Significance

Contemporary life, marked by widespread exposure to artificial light, irregular feeding schedules, and inadequate sleep, has led to a prevalent state of circadian disruption or "misalignment" between the body's internal timing and external environmental cues (Schiavon et al., 2024). This circadian misalignment is intricately linked to an elevated risk of physiological dysfunction and systemic disease (Patel et al., 2022). The resulting deregulated rhythms can contribute to a wide array of negative health consequences, including inflammation and chronic diseases such as Type 2 diabetes, obesity, and cardiovascular diseases (Patel et al., 2022; Schiavon et al., 2024).

The critical nature of this temporal control lies in the fact that CRs govern the fundamental energetic trade-off required for systemic homeostasis, specifically balancing energy storage against expenditure and maintaining redox integrity. When CRs fail to temporally separate necessary metabolic and redox functions, misalignment ensues, compromising basic cellular energetic efficiency. This breakdown in temporal partitioning provides a plausible mechanism by which circadian disruption acts as a primary, universal trigger for a spectrum of chronic metabolic and vascular diseases.

Chronosynchronization in Rehabilitation Science

The emerging field of clinical chronobiology underscores the therapeutic potential of targeting these temporal disorders (Tomatsu et al., 2025). Within the specific context of physiotherapy and rehabilitation science, the therapeutic re-synchronization of the circadian system represents a key clinical area that can be managed effectively through non-pharmacological interventions (Schiavon et al., 2024; Healy et al., 2021). A truly successful rehabilitative approach must aim for *Chronosynchronization*, which requires the simultaneous optimization of the three primary environmental time cues (*Zeitgebers*): exercise, nutrition, and sleep (Healy et al., 2021).

Molecular and Neural Architecture of the Circadian System

The Central Clock: Suprachiasmatic Nucleus (SCN)

The master regulatory pacemaker, which dictates systemic rhythmicity in mammals, is the Suprachiasmatic Nucleus (SCN), located in the hypothalamus of the brain (Cermakian & Boivin, 2009; Tomatsu et al., 2025). The SCN holds the critical responsibility for synchronizing all peripheral, tissue-specific clocks throughout the rest of the organism (Cermakian & Boivin, 2009; Tomatsu et al., 2025).

The primary mechanism that drives the SCN's entrainment (its alignment to the external 24-hour cycle) is photic signaling (Schiavon et al., 2024). Light is recognized as the most potent Zeitgeber (German for time giver) for the SCN clock system (Schiavon et al., 2024). Light signals are transmitted from the retina, adjusting the central clock to the external light-dark cycle, thereby initiating the synchronization cascade for peripheral clocks across the body (Cermakian & Boivin, 2009).

The Core Mechanism: Transcriptional-Translational Feedback Loop (TTFL)

At the fundamental cellular level, the self-sustaining nature of circadian rhythms is generated principally by the Transcriptional-Translational Feedback Loop (TTFL) (Tomatsu et al., 2025; Hastings et al., 2007).

The cycle is initiated during the Positive Phase when the key clock proteins CLOCK and BMAL1 form a heterodimer complex. This complex serves as the transcriptional activator for the core circadian genes, specifically *Per* (Period) and *Cry* (Cryptochrome) (Tomatsu et al., 2025).

The process continues into the Negative Feedback Phase. As the resulting PER and CRY proteins accumulate in the cytoplasm, they translocate back into the nucleus. Here, they exert an inhibitory effect, repressing the activity of the CLOCK/BMAL1 complex, thus completing the inhibitory feedback loop that generates the characteristic oscillation with a period of approximately 24 hours (Tomatsu et al., 2025).

Peripheral Clocks and Targeted Entrainment

Virtually every tissue and organ system, including the liver, adipose tissue, and skeletal muscle, possesses its own intrinsic peripheral clock mechanism, which is fundamentally driven by the TTFL (Cermakian & Boivin, 2009). While light is the dominant synchronizer for the SCN, peripheral clocks primarily respond to non-photic *Zeitgebers*. Among these, food availability and structured activity/rest cycles, particularly exercise, function as critical synchronizing cues (Schiavon et al., 2024).

From a physiotherapy perspective, skeletal muscle represents a critical peripheral oscillator target. Skeletal muscle responds robustly to physical activity, displaying significant changes in the expression of local clock components, such as , , and (Schiavon et al., 2024). This responsiveness indicates that physiotherapeutic interventions can focus on the dual goal of directly synchronizing these peripheral clocks. Empirical data demonstrates that the timing of exercise differentially impacts gene expression depending on whether the activity occurs at the beginning or the end of the active phase. This provides clear molecular evidence of the customized, powerful effect that physical activity timing exerts on local timekeeping.

The ability to manipulate exercise timing allows for localized chronosynchronization, distinct from the global, SCN-driven rhythm. Since exercise is a potent *Zeitgeber* for peripheral clocks like those in skeletal muscle , targeted *Chronexercise* enables clinicians to selectively optimize local tissue functions—such as performance, repair, and metabolism—even if the central clock's synchrony is incomplete. This capability establishes timed exercise as a uniquely valuable translational tool, particularly in chronic conditions where muscle quality and metabolic flexibility are central therapeutic goals.

Circadian Regulation of Systematic Physiology in Rehabilitation

Rhythmic Control of Physical Performance and Musculoskeletal Function

A range of key physiological parameters relevant to rehabilitation, including physical exercise capacity, muscle strength, and endurance, exhibit distinct diurnal fluctuations that are strictly governed by endogenous CRs (Schiavon et al., 2024).

Observations consistently indicate that peak muscle strength and overall physical performance generally occur during the afternoon and early evening hours (Schiavon et al., 2024). These natural performance peaks are linked to several sirkadiyen-controlled physiological factors, notably the daytime elevation of core body temperature and the optimization of underlying neuromuscular function (Schiavon et al., 2024).

At a molecular level, even the mitochondrial oxidative capacity, which is a critical determinant of endurance performance, follows a daily rhythm (Schiavon et al., 2024). This rhythmic profile leads to reports of strong time-of-day effects on measures of power and exercise capacity. These variations are partly correlated with the diurnal expression profiles of the gene (Schiavon et al., 2024).

Tendon Health and Rhythm Disruption

Tendon health is a high-priority area for physiotherapy due to the common occurrence of overuse injuries, or tendinopathies (Yeung, 2025). Tendons, being fibrous connective tissues composed primarily of Type I collagen, rely on stable biological timing. Available evidence demonstrates that a disrupted circadian rhythm negatively impacts the structural integrity and health of human tendons (Yeung, 2025). Consequently, understanding the mechanisms of circadian clock disruption in tendon tissue offers potential new strategies for informing the diagnosis and refining the therapeutic management of tendon injury and associated pain (Yeung, 2025).

Neuroendocrinology and Metabolic Homeostasis

The circadian system provides meticulous regulation over both hormonal secretion and overall metabolic flux (Cermakian & Boivin, 2009; Schiavon et al., 2024).

The secretion of Growth Hormone (GH) exhibits a pulsatile circadian pattern, characterized by pronounced nocturnal peaks. This timing is indispensable for anabolic processes and is crucial for efficient post-exercise recovery (Schiavon et al., 2024). Cortisol secretion is also rigorously directed by the central SCN pacemaker, following a distinct 24-hour pattern (Morris et al., 2022). Circulating cortisol concentrations reach their maximum concentration around the habitual sleep-to-wake transition and decline progressively toward the late night (Morris et al., 2022). Cortisol acts as the key catabolic signal that coordinates peripheral clocks, working synergistically with anabolic hormones (such as testosterone) to preserve anabolic-catabolic homeostasis (Morris et al., 2022).

The fact that the major peak of GH occurs nocturnally highlights that anabolic recovery is intrinsically tied to the nocturnal period, independent of when physical activity occurs during the day. Consequently, the success of muscle repair and protein synthesis following exercise is directly dependent on the quality and timing of subsequent sleep. If a patient experiences circadian rhythm disruption (CRD) due to poor sleep hygiene, their critical peak anabolic signaling may be suppressed or phase-shifted, leading to chronically compromised recovery, persistent low-grade inflammation, and potential symptoms of overtraining. This mechanistic link emphasizes the necessity of prioritizing sleep management as a primary component of any effective rehabilitation protocol.

Metabolic Consequences and Exercise Timing

Disruption of the circadian clock at the molecular level significantly contributes to dysregulation of glucose and lipid metabolism (Cermakian & Boivin, 2009; Schiavon et al., 2024).

The molecular basis for this pathology is demonstrated by studies showing that the deletion of the gene in skeletal muscle results in diminished glucose uptake and reduced transporter levels (Schiavon et al., 2024). This evidence confirms the direct and significant role of the muscle clock in the pathogenesis of metabolic diseases, such as Type 2 diabetes.

Conversely, exercise serves as a potent positive regulator, enhancing the expression of and genes/proteins. This upregulation is believed to partially mediate the metabolic benefits of exercise, coinciding temporally with improvements observed in peripheral insulin sensitivity and maximal oxygen consumption (Schiavon et al., 2024).

These foundational physiological findings underscore the necessity of personalizing rehabilitation strategies based on the individual's specific chronotype and defined therapeutic objectives (Schiavon et al., 2024). When the goal is maximizing strength and power output, the afternoon timeframe is generally recommended due to performance peaks. However, if the primary goal is improving metabolic health in patients with conditions like Type 2 diabetes, early morning exercise may offer superior benefits. This is related to clock-driven fluctuations in carbohydrate metabolism, often correlating with lower perceived exertion and oxygen consumption during morning sessions (Schiavon et al., 2024).

This divergence highlights a crucial physiological trade-off that rehabilitation prescription must navigate: the choice between optimizing mechanical power output versus maximizing metabolic stress management. Afternoon timing intrinsically supports maximal physical output (force, velocity), while morning timing appears to optimize metabolic biomarkers (e.g., glucose clearance, lower perceived effort). The clinician must precisely define the therapeutic endpoint—be it performance enhancement or systemic metabolic health—before establishing the optimal *Zeitgeber* schedule.

Circadian Misalignment and Chronic Pain Pathophysiology

CRD as a Contributor to Central Sensitization

Circadian rhythm disorders (CRD) demonstrate a high degree of comorbidity in patients presenting with Chronic Musculoskeletal Pain (KKA) (Tüchler et al., 2022; Yeung, 2025). Significantly, disruption of the biological timing system is not merely coincidental but is actively implicated in the pathogenesis of KKA through the exacerbation of central sensitization (Tüchler et al., 2022). Central sensitization is a pathological state of neuronal hypersensitivity, which results in magnified pain perception (Tüchler et al., 2022).

Rhythmic Blood Pressure Anomalies and Vascular Stress

Patients suffering from KKA frequently exhibit anomalous circadian Blood Pressure (BP) profiles (Tüchler et al., 2022). These include the non-dipper pattern, where the physiological nocturnal drop in BP fails to occur, or the more severe inverse-dipper pattern, where nighttime BP rises above the daytime average (Tüchler et al., 2022).

This abnormal vascular pattern is hypothesized to initiate a mechanistic cascade that contributes directly to chronic pain :

1. ***Oxidative Stress Generation:*** Elevated or sustained nighttime BP generates excessive oxidative stress and localized tissue damage (Tüchler et al., 2022).
2. ***Neuro-Inflammatory Cascade:*** This stress, in turn, triggers inflammatory events and the activation of glial cells within the central nervous system (Tüchler et al., 2022).
3. ***Enhanced Pain Perception:*** The culmination of this process is an increased pain experience driven by persistent low-grade inflammation and amplified central sensitization (Tüchler et al., 2022).

This evidence establishes that CRD acts as a causal, mechanistic link that connects systemic vascular deregulation (abnormal BP) to the neuropathology underlying chronic pain (central sensitization). A critical clinical implication is that circadian dysregulation in KKA patients should not be regarded merely as a secondary symptom but rather as a causal mechanism (Tüchler et al., 2022). Therefore, therapeutic interventions must prioritize normalizing the patient's biorhythm through interventions like consistent sleep hygiene, regulated light exposure, and routine rhythmicity. Such interventions are inexpensive and simple to implement, yet they simultaneously address the central pain prognosis and mitigate the significant increased cardiovascular risk associated with the non-dipper BP pattern (Schiavon et al., 2024; Tüchler et al., 2022).

Circadian Gatekeeping of Pain Modulation

Pain perception is regulated temporally by the CR system, much like hormonal secretion and the sleep/wake cycle (Liang et al., 2021). The circadian rhythmicity observed in pain is a complex output of oscillators distributed across the entire nociceptive pathway, including the Dorsal Root Ganglion (DRG), the spinal cord, and the descending pain modulatory system (Liang et al., 2021). These structures function as circadian "gatekeepers," daily modulating the transmission and processing of nociceptive information (Liang et al., 2021).

The endogenous opioid system, which plays a central role in regulating pain and stress responses, exhibits circadian fluctuations in its activity (Liang et al., 2021). The finding that pain responses (e.g., those induced by morphine or naloxone injections) vary significantly across the 24-hour cycle implies an endogenous rhythm in the expression of opioid receptors or their downstream signaling components (Liang et al., 2021). This biological reality necessitates a chronopharmacological consideration for determining the optimal timing of all analgesic interventions, including non-pharmacological techniques such as manual therapy and electrotherapy applied within physiotherapy (Liang et al., 2021).

Strategic Chronotherapy in Physiotherapy and Rehabilitation

Chronotherapy is defined as the strategic timing of environmental *Zeitgebers* to correct circadian misalignment and maximize beneficial physiological responses, establishing it as a critical instrument in the rehabilitation sciences (Patel et al., 2022).

Chronexercise: Timing for Performance and Health Optimization

Physical exercise is classified as a powerful, non-photic *Zeitgeber* that exerts strong regulatory effects on the CR system (Schiavon et al., 2024). When implemented as programmed exercise, it specifically optimizes the local molecular clock within skeletal muscle, leading to beneficial adaptations in energy metabolism and mitochondrial biogenesis (Schiavon et al., 2024).

The optimal timing of the exercise session must be rigorously tailored to the specific expected physiological outcome :

- ***Maximum Performance Target:*** Given that muscle strength and physical capacity peak during the afternoon, this timeframe is recommended for high-intensity or power-focused training sessions to achieve the highest possible power output (Schiavon et al., 2024; Tüchler et al., 2022).
- ***Metabolic Health Target:*** For individuals with metabolic disorders, exercise performed in the early morning hours is suggested. This timing has been linked to lower perceived exertion and oxygen consumption, which may relate to clock-driven fluctuations in carbohydrate metabolism, suggesting that morning sessions are more appropriate for maximizing metabolic recovery (Schiavon et al., 2024).

Programmed exercise possesses the distinct capacity to synchronize peripheral molecular clocks, such as those found in skeletal muscle (Schiavon et al., 2024). For example, studies involving running wheel activity showed that exercise performed at the beginning of the active phase had a more significant impact on reducing the amplitude of gene expression in the SCN compared to exercise performed late in the active phase (Schiavon et al., 2024).

Principles of Holistic Chronosynchronization and Personalized Chronotherapy (P-CT)

Physiotherapists occupy a key clinical position to utilize and manage environmental *Zeitgebers*—encompassing exercise, sleep, and light exposure—to restore normative patient biorhythms (Tüchler et al., 2022).

Sleep Hygiene and Lifestyle Management

Regulation of sleep patterns and adherence to rigorous sleep hygiene are considered the most fundamental and effective non-pharmacological methods for normalizing biorhythms (Tüchler et al., 2022). This basic intervention carries significant weight in both the prevention and long-term prognosis of chronic pain conditions (Tüchler et al., 2022).

Phototherapy and Environmental Control

The use of timed light exposure, often utilizing bright light lamps, is essential for correcting circadian phase shifts, which commonly arise from conditions like shift work or jet lag (Tomatsu et al., 2025; Tüchler et al., 2022). Conversely, maintaining dark environments during the night supports robust, normative melatonin secretion rhythms (Tüchler et al., 2022).

Individualized Programming

The assumption that a single "best time" exists for all training or rehabilitation outcomes is scientifically unsupported (Schiavon et al., 2024). Physical training recommendations must be strictly individualized based on a confluence of variables, including the patient's intrinsic chronotype, genetic variants, specific health status, and dietary patterns (Schiavon et al., 2024). Aligning exercise sessions with a comprehensive chronotype assessment represents a compelling strategy to maximize the therapeutic metabolic and overall health benefits of physical activity (Schiavon et al., 2024).

The professional role of the physiotherapist necessarily expands beyond simply prescribing movement to actively managing the temporal environment of the patient. By strategically manipulating non-photic *Zeitgebers* (exercise) and managing photic *Zeitgebers* (light/dark schedules) and behavioral *Zeitgebers* (sleep hygiene), the clinician is executing clinical chronosynchronization. This integrated approach requires the clinician to possess a molecular understanding of how lifestyle factors impact physiological timing, allowing them to use these elements as precision tools to optimize systemic function across performance, metabolism, and pain sensitivity.

Key Chronotherapeutic Interventions in Rehabilitation

The integration of chronobiological principles into practice involves applying specific interventions tailored to the mechanistic targets of the circadian system.

The Circadian Hierarchy and Molecular Targets

Understanding the therapeutic application of chronobiology requires knowledge of the core components of the circadian system and their primary entrainment signals.

The Suprachiasmatic Nucleus (SCN):

Functioning as the master pacemaker in the hypothalamus, the SCN maintains systemic rhythmicity for processes such as cortisol secretion and core temperature regulation. Its primary entrainment signal is Light (Photic Input) , making its translational relevance the stabilization of global hormonal patterns and the regulation of the systemic sleep/wake cycle (Healy et al., 2021).

The Transcriptional-Translational Feedback Loop (TTFL):

This cellular mechanism, involving the core proteins CLOCK/BMAL1 and PER/CRY, is the endogenous generator of rhythm. It provides the fundamental basis for tissue responsiveness to temporal cues and influences specific gene expression.

Peripheral Clocks:

These clocks possess an intrinsic TTFL but are governed by local stimuli, primarily Activity/Exercise and Food Availability. They represent a direct therapeutic target for *Chronexercise* aimed at optimizing local performance and metabolic processes (Schiavon et al., 2024).

Strategic Chronotherapeutic Interventions

Specific *Zeitgeber* interventions are utilized to achieve distinct clinical objectives in rehabilitation:

- ***Regular Sleep/Wake Schedule:*** This intervention strongly synchronizes the SCN and stabilizes melatonin and cortisol profiles (Healy et al., 2021). The clinical objective is to mitigate central sensitization and inflammation, improve Chronic Musculoskeletal Pain (CCP) prognosis, and correct sleep disorders (Healy et al., 2021; Tüchler et al., 2022).
- ***Timed Exercise (Chronexercise)*****:** This method primarily entrains peripheral clocks, particularly in skeletal muscle (Schiavon et al., 2024). The clinical focus

is to maximize muscle performance and strength, optimize muscle metabolism, and reduce metabolic stress (Schiavon et al., 2024).

- ***Bright Light Therapy:*** Mechanistically, bright light induces SCN phase shifts and suppresses melatonin secretion. It is used to correct rhythm disorders (e.g., phase delay) and enhance wakefulness and alertness (Tomatsu et al., 2025; Tüchler et al., 2022).
- ***Tendon Health Focused Timing:*** This approach maintains the integrity and regulation of tendon collagen and extracellular matrix proteins. Its objective is to reduce the incidence of tendinopathy and accelerate tissue repair mechanisms (Yeung, 2025).

Conclusion

Clinical Potential of Circadian Integration

The comprehensive integration of circadian biology into clinical physiotherapy and rehabilitation practice, defined as Chronotherapy, introduces a powerful temporal dimension that enhances traditional treatment paradigms (Patel et al., 2022). Current evidence has refined the understanding of rhythm dysfunction, identifying it not merely as a frequent comorbidity but as a direct pathophysiological bridge connecting chronic pain states and systemic diseases (Tüchler et al., 2022). By expertly manipulating environmental *Zeitgebers*—specifically exercise, light exposure, and the sleep/wake cycle—physiotherapists gain the molecular leverage necessary to accelerate patient recovery processes and maximize targeted physiological responses (Patel et al., 2022; Schiavon et al., 2024).

Advanced Research Directions

While the translational momentum in chronobiology is substantial, further research is required to achieve high-fidelity clinical application in rehabilitation:

- ***Development of Personalized Chronotherapy (P-CT):*** Future research must prioritize the development of robust P-CT algorithms applicable to chronic pain, metabolic diseases, and obesity. The efficacy of treatment can be substantially enhanced by incorporating granular patient data, including individualized chronotype assessment and specific genetic variations (Schiavon et al., 2024). The current reliance on generalized population timing advice (e.g., "afternoon peak") risks mistiming the intervention for individuals whose internal phase angle differs significantly from the external cycle. The development of accessible, reliable methods for chronotype and genetic profiling is therefore a crucial translational bottleneck that must be addressed to move chronotherapy into a true precision medicine framework.
- ***Mechanistic Validation:*** Subsequent studies need to precisely delineate the influence of rhythmic hormonal patterns (GH and cortisol) on the kinetics of post-exercise recovery (Schiavon et al., 2024).

- ***Causality in Stress Pathways:*** Deeper investigation into the explicit causal contribution of circadian misalignment to the generation of oxidative stress and the resulting chronic inflammatory status is warranted (Schiavon et al., 2024; Tüchler et al., 2022).
- ***Translational Proof:*** Establishing the exact molecular mechanisms by which physiotherapeutic interventions actively repair these identified pathophysiological bridges is necessary to solidify chronotherapy as an evidence-based and indispensable component of modern rehabilitation practice.

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In The Beginning Lies the Risk: Fetal Toxic Exposure and The Origins of Adult Disease

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Introduction

In the late twentieth century, the rapid increase in chronic diseases worldwide demonstrated that these diseases could not be explained solely by genetic predisposition or lifestyle factors during adulthood. During this period, groundbreaking research conducted by British epidemiologist David Barker and his colleagues gave rise to a new paradigm in medical history: the “Fetal Origins of Adult Disease” (FOAD) hypothesis (Barker, 2004). Barker’s cross-sectional analyses of United Kingdom birth registrations with adult mortality rates concluded that low birth weight (LBW) had a strong association with coronary artery disease (CAD), type 2 diabetes (T2DM), osteoporosis, and certain psychiatric illnesses in adult life (Cooper et al., 1997; Lahti et al., 2010; Michels et al., 1996). The findings indicate intrauterine life to be an important biological window that predetermines adult health.

Throughout history, many cultures have recognized that a woman’s pre-pregnancy health plays a decisive role for both mother and child and have placed great importance on maintaining health during pregnancy (Korenbrot et al., 2002). Ancient medical traditions have adopted this awareness centuries earlier and developed a holistic approach to maternal and infant health. For example, Traditional Chinese Medicine (TCM), Mexican Traditional Medicine (MTM), Unani Medicine, and various African medical practices emphasize the use of balanced and holistic health-oriented therapies to prepare the woman’s body for the birth process. According to TCM, a woman’s health before pregnancy depends on the balance of “qi” and “blood,” and the mother undergoes a pre-pregnancy preparation process to address imbalances in these energy and blood circulations (Wu et al., 2020; Zhang et al., 2022). Similarly, MTM utilizes a combination of local herbs, massage techniques, and spiritual practices to protect women’s reproductive health (Cabada-Aguirre et al., 2023). The concept of “Tadabir-i-Haamla” *(Precautions for Pregnancy)* in Unani Medicine is devoted to pregnancy care and includes detailed information on pregnancy symptoms, nutrition, lifestyle recommendations, and management of common ailments (Khan & Itrat, 2015). This concept aims to maintain the mother’s physical, emotional, and spiritual balance during the pre- and post-natal period. In the 17th century, Şaban Şifaî’s work, named “Tedbîrü’l-Mevlûd” *(Precautions for Newborn)* and Gevrekzâde Hâfız Hasan Efendi’s work, named “Netîcetü’l-Fikriyye fî Tedbîri Velâdeti’l-Bikriyye” (*Outcome Of Healthy Birth Management*), demonstrate the profound and systematic understanding of Ottoman medicine regarding maternal and child health (Bahadır, 2017). These holistic approaches aimed not only at healthy births but also at ensuring the health of future generations.

The FOAD hypothesis, which confirms the approach of ancient medical traditions, is based on the concept of “developmental plasticity,” which is the adaptation capacity of the fetus to intrauterine environmental conditions. Reprogramming of fetal metabolism occurs for its adaptation to nutritional deficiencies, toxins, infection, or stress (Calkins & Devaskar, 2011).

One of the biggest challenges in addressing health problems today is the rapid increase and transformation of disease-causing agents. The cause of most of our ailments is no longer viruses, bacteria, or parasites alone, as current medical literature would lead us to believe, but rather toxic synthetic chemicals such as environmental pollutants, industrial chemicals, genetically modified unnatural foodstuffs, and agricultural chemicals. Alongside its comforts, modern life has brought a chemical burden with unseen but significant effects on human health. Everyday products such as detergents, polishes, plastics, cosmetics, and synthetic textiles represent some of the most hazardous environmental pollutants (Wang et al., 2025).

Toxic exposure has reached such an extent that even the maternal womb—once considered the safest and most protected environment—can no longer fully shield the developing fetus. Recent studies have demonstrated that the placenta is permeable to numerous chemical compounds, allowing toxic substances to pass into the fetal circulation. The detection of hundreds of chemicals in maternal blood, placenta, and umbilical cord blood reveals that the fetus develops under a far greater environmental burden than previously thought (Morello-Frosch et al., 2016; Wang et al., 2021). These findings have added a new dimension to the concept of FOAD. High levels of toxins transmitted from mother to baby through the umbilical cord accumulate in the fetus, causing permanent effects on brain and organ development. Such exposures have been associated with congenital anomalies and diseases such as hormonal disorders, infertility, diabetes, asthma, and cancer later in life.

In conclusion, the toxic load of modern lifestyles is a severe threat to fetal and maternal health, endangering future generations from the very beginning of life. Therefore, the first step toward addressing this crisis should be the elimination of major sources of toxicity and a societal shift toward a more natural and sustainable environment. From a modern medical standpoint, a holistic health approach should be aimed which protecting the body against toxic exposures and enhancing the body's natural detoxification mechanisms.

FOAD Hypothesis

The rise in chronic diseases during the late twentieth century prompted public health researchers to seek new etiological explanations, as it became evident that genetic predisposition and adult lifestyle factors alone could not account for the increasing disease burden. Within this framework, the pioneering epidemiological work of David Barker and his colleagues in England led to the formulation of the FOAD hypothesis, which profoundly transformed perspectives in medicine and public health (Calkins & Devaskar, 2011).

In the 1980s, by linking historical birth records with adult mortality data from Lancashire and Hertfordshire, Barker's research group identified a striking correlation: individuals with lower birth weights had a higher risk of death from CAD in adulthood (Barker, 2004). This observation revealed that LBW is not only a passive indicator of fetal health but an active predictor of adult disease risk. This insight marked a paradigm shift in understanding the lifelong implications of the intrauterine environment and became known as the Barker Hypothesis (Calkins & Devaskar, 2011). LBW is associated with numerous chronic diseases, including CAD, T2DM, cancer (Michels et al., 1996), osteoporosis (Cooper et al., 1997), and various psychiatric disorders (Lahti et al., 2010).

A central principle underlying the FOAD hypothesis is the concept of '*developmental plasticity'*, which refers to the fetus's capacity to undergo structural and functional adaptations in response to environmental conditions. A single genotype can produce multiple phenotypes depending on intrauterine events, reflecting the existence of critical developmental windows during which the organism is particularly sensitive or "responsive" to environmental influences. Phenotypic variation is maximized to ensure adaptation to environmental conditions. For example, under circumstances such as maternal malnutrition, the fetus undergoes developmental remodeling, altering the structure and function of non-vital organs (e.g., kidney, pancreas, skeletal muscle) to protect neurodevelopment and promote survival. These adaptive responses also prepare the fetus for additional stressors it may encounter in life outside the womb (Calkins & Devaskar, 2011).

Epidemiological Evidence

The FOAD hypothesis is primarily supported by findings from large-scale birth registries and longitudinal cohort studies—particularly those examining populations exposed to famine—where pregnant women experienced severe malnutrition. These registries allowed researchers to trace individuals from birth to adulthood, linking early-life indicators such as birth weight and childhood growth patterns with the later development of chronic diseases.

One of the most prominent examples is the Dutch Famine Study (1944–1945), during which pregnant women endured six months of severe caloric restriction. Infants exposed to famine in mid- or late gestation were born with significantly lower birth weights, while those exposed during early gestation generally had normal birth weights. However, adults whose mothers experienced famine during mid- or late pregnancy showed impaired glucose tolerance, whereas those exposed during early gestation exhibited a more atherogenic lipid profile and higher body mass index (BMI) (Ravelli et al., 1976). These findings were later confirmed and expanded upon, demonstrating that the timing of nutritional deprivation during pregnancy plays a critical role in determining both fetal growth and adult disease risk (Roseboom et al., 2001). Collectively, these studies indicate that while birth weight serves as a useful surrogate marker, it is ultimately the intrauterine environment that shapes the developmental trajectory of adult health. Early gestational programming, which occurs during organogenesis, tends to result in broad metabolic and neurodevelopmental consequences, whereas late gestational programming, which corresponds to rapid growth phases, induces permanent structural and functional changes in key metabolic organs (Calkins & Devaskar, 2011).

A complementary perspective emerged from the Siege of Leningrad (1941–1944), during which individuals experienced prolonged and extreme malnutrition for over 800 days. Interestingly, unlike the Dutch cohort, those exposed to famine in utero during the Leningrad siege did not exhibit increased rates of insulin resistance, dyslipidemia, hypertension, or CAD in adulthood (Stanner et al., 1997). This striking difference underscores the complexity of developmental programming. In the Netherlands, the abrupt transition from famine to postwar food abundance likely created a mismatch between intrauterine deprivation and postnatal nutritional excess. In contrast, the continued nutritional scarcity in post-famine Leningrad may have provided an environmental match, mitigating the adverse long-term effects.

These contrasting outcomes provided invaluable insights to Barker and his contemporaries, highlighting the intricate interplay between maternal and fetal genotypes and their adaptation to environmental conditions. This concept resonates with the Thrifty Genotype Hypothesis proposed by Neel et al. (1998), which suggests that genetic adaptations favoring efficient energy storage during periods of scarcity become maladaptive in modern contexts characterized by caloric abundance, predisposing individuals to obesity and metabolic disease.

Building upon this, Hales and Barker later introduced the Thrifty Phenotype Hypothesis (CN, 2001), which emphasizes developmental plasticity rather than genetics. According to this model, nutrient restriction during fetal development induces metabolic adaptations—such as reduced insulin sensitivity and increased energy conservation—that enhance survival in nutrient-poor environments. However, in contemporary societies where nutrient availability is high, these same adaptations predispose individuals to metabolic syndrome, T2DM, and CAD.

Biological Mechanisms Underlying FOAD

The biological process underlying the FOAD hypothesis is the concept of fetal programming, which is defined as the way environmental conditions during the intrauterine period have lasting effects on a fetus's organ development, metabolism, and gene expression, determining lifelong health and disease risk (Calkins & Devaskar, 2011). A range of maternal and environmental factors can influence this programming process, including nutritional status, inflammation, infection (Dalman et al., 2008), glucocorticoid exposure (Welberg et al., 2000), hypoxia, psychological stress (Fride et al., 1986), toxin exposure (Ho et al., 2006), and elevated maternal homocysteine levels (Yajnik et al., 2005). The intrauterine environment signals the conditions expected after birth in childhood and adulthood, prompting adaptive metabolic changes that promote survival.

Epigenetic Regulation

Epigenetics is one of the fundamental mechanisms underlying the persistence of fetal programming. Environmental factors, such as nutrition, stress, and toxins, lead to permanent alterations in gene expression without modifying the DNA sequence.

Epigenetic mechanisms form the bridge between genetics and environmental factors in the FOAD hypothesis. Through processes such as DNA methylation (DNAm), histone modification, and non-coding RNA regulation, epigenetic mechanisms can stably alter gene expression patterns without changing the nucleotide sequence (Rodger & Chatterjee, 2017). The epigenome is highly sensitive to environmental factors, especially in early pregnancy. Therefore, factors such as maternal nutrition, toxin exposure, or stress can induce permanent phenotypic changes during critical windows of development (Safi-Stibler & Gabory, 2020). DNAm profiles in umbilical cord blood serve as biomarkers of intrauterine exposures and can predict an individual's lifelong risk of disease (Dutta & Ruden, 2024).

Inflammation and Oxidative Stress

The common thread of the aforementioned intrauterine pathological factors is the triggering of chronic, low-grade inflammation and oxidative stress in the fetus and placenta. Metabolites of toxic elements increase ROS production, which in turn leads to DNA damage, lipid peroxidation, and cellular senescence (Jomova et al., 2023). Such damage is particularly detrimental to rapidly dividing fetal cells, thereby disrupting organ development and programming. Moreover, prenatal exposure to toxins has been shown to elevate the levels of pro-inflammatory cytokines, including TNF-κB, IL-6, and IL-8, in both maternal and cord blood (Wang et al., 2025).

Placenta and Umbilical Cord

The placenta, a unique and transient organ formed through the union of maternal and fetal tissues, develops during pregnancy to mediate the exchange of nutrients, gases, and waste products between the mother and fetus (Maltepe et al., 2010). Functioning as a selective gatekeeper, the placenta regulates maternal–fetal interactions and can effectively filter or limit the transfer of many toxic substances. However, this barrier function is not always fully protective; in certain cases, it may be inadequate, or a placental disorder may cause excessive transmission of maternal exposure to the fetus (Rager et al., 2020).

The chorionic plate, the fetal-facing side of the placenta, is connected to the fetus via the umbilical cord. The umbilical cord contains two arteries and one vein; the umbilical vein carries oxygen-rich blood and nutrients from the placenta to the fetus, while the umbilical arteries carry deoxygenated blood and waste from the fetus back to the placenta (Maltepe et al., 2010). Maternal and fetal exposure to toxic substances can be directly assessed through umbilical cord blood analysis. The detection of hundreds of industrial chemicals—including lead (Pb), mercury (Hg), polychlorinated biphenyls (PCBs), per- and polyfluoroalkyl substances (PFAS), and bisphenol A (BPA)—in cord blood underscores both the complexity of prenatal exposure and the extent of the fetal chemical burden. Moreover, DNA methylation profiles in umbilical cord blood serve as biomarkers of persistent epigenetic alterations resulting from these exposures (Dutta & Ruden, 2024; Gundacker et al., 2021). Although the placenta functions as a selective barrier between mother and fetus, it cannot completely prevent the transfer of toxic substances such as arsenic, lead, and mercury. Placental dysfunction or deficiency (e.g., due to gestational hypertension or chronic maternal inflammation) can lead to excessive transmission of maternal toxic exposure to the fetus. Furthermore, individual genetic variants (detoxification genes such as GSTT1 and GSTM1) can increase the transplacental transfer of toxic substances and their accumulation in the fetus, making genetically predisposed individuals more vulnerable (Gundacker et al., 2021).

Toxin Exposure of Fetus

Recent studies have shown that hundreds of toxic substances accumulate in the blood and umbilical cord blood of pregnant women. Prenatal exposure to environmental toxins and heavy metals poses serious risks to fetal development and postnatal health. These exposures predispose to both short-term neonatal complications and long-term chronic diseases through oxidative stress, inflammation, endocrine disruption, and epigenetic changes (Dutta & Ruden, 2024).

Potentially Toxic Elements (PTEs) are elements released into the environment through both natural geological processes and anthropogenic activities such as mining, smelting, manufacturing, fossil fuel combustion, and pesticide use (Nieder & Benbi, 2024). Among these, arsenic (As), cadmium (Cd), chromium (Cr), lead (Pb), and mercury (Hg) are of primary public health concern due to their high toxicity and persistence in the environment (Tchounwou et al., 2012). Exposure to these elements occurs through various routes, including contaminated drinking water, seafood, old paints, and industrial emissions (Dutta & Ruden, 2024).

Over two million individuals around the world are exposed to arsenic, primarily through contaminated drinking water. Arsenic acts as a potent endocrine disruptor and carcinogen (Ullah et al., 2023). Industrial exposure to arsenic occurs in various sectors, including glass manufacturing, textile production, ammunition and paper processing, as well as in the use of wood preservatives and related industries. Furthermore, in the cosmetics industry, color pigments used in eyeshadow formulations frequently contain toxic metals, including arsenic. Arsenic present in cosmetics can be absorbed into the bloodstream through percutaneous penetration; therefore, the permissible limit for heavy metal impurities in cosmetic products is set below 5 ppm. Major dietary sources of organically bound arsenic include seafood, mushrooms, rice, and poultry (Jones, 2007).

Mercury (Hg) concentrations in the oceans have tripled since the Industrial Revolution. Mercury is released into the environment from both natural and anthropogenic sources, including coal-fired power plants (Dutta & Ruden, 2024). In aquatic ecosystems, Hg is converted to methylmercury (MeHg) by anaerobic microorganisms, leading to bioaccumulation at higher trophic levels. Humans are primarily exposed to MeHg through the consumption of contaminated fish and seafood. Another important route of exposure is occupational, particularly in industries such as electrical equipment and automotive manufacturing, chemical processing, metalworking, construction, and healthcare professions, where mercury is used in instruments (Kim et al., 2016).

Dental practices represent one of the major sources of inorganic mercury use. Extensive evidence indicates that dentists and dental staff handling amalgam are chronically exposed to mercury vapor, leading to body burdens substantially higher than those found in the general population. Elemental mercury, a major component of dental amalgam used as a restorative material, poses a notable occupational risk. The mean Hg concentration in dentists' breathing zones, measured using personal dosimeters, was reported as 29.2 µg/m³—exceeding the Occupational Exposure Standard of 25 µg/m³ (Ritchie et al., 2004). Correspondingly, dentists exhibited urinary mercury concentrations three to four times higher than the control group (Karahalil et al., 2005). In dental personnel, mercury levels in hair, urine, toenails, and blood were on average at least twice as high as those of controls (Kim et al., 2016).

Cadmium (Cd) is primarily encountered in industrial settings such as battery manufacturing, pigment and coating production, and plastic processing. It is also emitted into the environment as a result of mining, metal smelting, and the combustion of fossil fuels. Due to its persistence and long biological half-life, cadmium accumulates in soil and can contaminate food sources, particularly crops grown in polluted areas. Major sources of human exposure include industrial byproducts, contaminated water or soil, and tobacco products. Smoking represents a significant exposure route, as tobacco plants efficiently absorb cadmium from the soil (Dutta & Ruden, 2024).

Lead (Pb), another toxic heavy metal, is widely distributed throughout the environment as a consequence of its widespread industrial use. Many household and consumer products—such as paints, plumbing materials, pipes, eyeglasses, batteries, cosmetics, and ammunition—contain lead or lead compounds. Additionally, air pollution in densely populated urban areas contributes to ongoing lead exposure and environmental accumulation (Jomova et al., 2025).

Studies have identified various toxic substances in the urine, peripheral blood, amniotic fluid, and umbilical cord blood of pregnant women, demonstrating that pregnant women and their fetuses are exposed to numerous environmental pollutants originating from industrial chemicals and consumer products.

Dutta and Ruden (2024) conducted a systematic analysis and showed that exposure to various heavy metals, such as arsenic (As), cadmium (Cd), chromium (Cr), lead (Pb), and mercury (Hg), causes DNA methylation (DNAm) changes in umbilical cord blood, and these DNAm changes lead to serious short- and long-term health problems.

Morello-Frosch et al. (2016) analyzed 59 different chemicals in maternal and umbilical cord blood samples from 78 mother-baby pairs. Of the chemicals analyzed, 89% (52 of 59) were detected in maternal blood, and 70% (41 of 59) in umbilical cord blood, indicating that pregnant women, and therefore their babies, are exposed to a wide variety of environmental toxins. The study reported particularly high levels of endocrine-disrupting chemicals (EDCs) such as phthalates and perfluoroalkyl substances (PFAS), with substantial placental transfer efficiency. Moreover, chemicals commonly used in personal care products, including bisphenol A (BPA) and parabens, were frequently detected in both maternal and fetal circulation, suggesting that daily exposure to these substances poses a potential risk to fetal development.

BPA, a well-known endocrine disruptor, has been linked to various adverse health outcomes, including cancer, infertility, diabetes, and obesity. Today, this compound is widely used to manufacture optical materials, electronic equipment, reusable plastic bottles, plates, bowls, cups, microwave-safe utensils, and food containers. It is also used in epoxy resin paints, vinyl chloride-based medical materials, thermal paper, flame retardants, printing inks, sports equipment, dental materials, and compact discs (Susana Almeida et al., 2018).

Wang et al. (2021) used a “suspect screening” method to investigate the presence of industrial chemicals in maternal and newborn blood, identifying 557 unique chemical formulas in serum samples taken from 30 mother-newborn pairs. The study revealed that numerous industrial compounds are present in both maternal and fetal circulation, demonstrating that many of these substances are capable of crossing the placental barrier. Among the detected chemicals were PFAS, plasticizers, and PTEs, 55 of which had never previously been reported in human blood. Because some of the chemicals have never been reported before, their sources of exposure and potential health effects remain unknown.

Similarly, a two-year study commissioned by the Environmental Working Group (EWG) and Rachel’s Network (2009), conducted at five independent laboratories, analyzed the umbilical cord blood of 10 babies of different races and identified 287 toxic industrial chemicals and contaminants. Among the 287 chemicals detected in umbilical cord blood, 180 are recognized as carcinogenic in humans or animals, 217 are neurotoxic, and 208 have been demonstrated to induce birth defects or abnormal development in animal studies. The full impact of pre- and postnatal exposure to these complex mixtures of carcinogens, developmental toxins, and neurotoxins remains incompletely understood. Collectively, these findings clearly demonstrate that fetuses are exposed in utero to a broad spectrum of environmental contaminants, including hundreds of chemicals known or suspected to disrupt normal development, impair neurocognitive function, or contribute to carcinogenesis.

Short- and Long-Term Health Effects of Fetal Exposure to Heavy Metals and Toxins

Prenatal exposure to PTEs and heavy metals poses serious risks to fetal development and postnatal health. These exposures predispose to both short-term neonatal complications and long-term chronic diseases through oxidative stress, inflammation, endocrine disruption, and epigenetic changes (Niede & Benbi, 2022).

Heavy Metals

Prenatal exposure to heavy metals poses critical risks to the fetus. Al-Saleh et al. (2017) and Wang et al. (2025) have shown that metals such as cadmium, lead, arsenic, mercury, chromium, and nickel are detected in maternal and umbilical cord blood, and that this exposure leads to increases in inflammation and oxidative stress markers (TNFα, IL-6, IL-8, TGFβ, PAB). These findings demonstrate that maternal exposure directly affects the fetus and initiates biochemical stress responses in the intrauterine period.

Heavy metal toxicity has been proven to cause dysfunction in numerous physiological processes, leading to various pathological outcomes. The heavy metals with the most significant health effects are listed below:

Lead (Pb) exposure causes cognitive developmental disorders, learning disabilities, and permanent damage to nervous system functions in children. Lead poisoning usually develops as a result of cumulative exposure over months or years. Children under 6 years of age are especially susceptible to lasting adverse health effects due to their higher absorption rates and ongoing brain development. In addition to its neurotoxicity, Pb exposure has also been associated with a broad range of systemic impacts, including reproductive and hormonal dysfunctions, anemia and leukopenia, non-alcoholic fatty liver disease, coronary artery and cardiovascular disorders, and various cancers such as lung cancer. Moreover, Pb is associated with behavioral abnormalities, memory and attention deficits, depression, and anxiety (Adriana et al., 2025).

Mercury (Hg) exhibits significant toxic effects on the neurological system and renal structures. Even low-dose Hg exposure in humans can cause serious health problems, particularly during prenatal development, infancy, childhood, and adolescence (Kim et al., 2016). Hg toxicity is multisystemic, affecting the lungs, skin, eyes, and the nervous, cardiovascular, and renal systems. Intrauterine mercury exposure is known to impair fetal brain development. Additionally, inhalation of mercury vapor may result in necrotizing bronchitis and pneumonitis, which can progress to respiratory failure. Hg exposure has been associated with arrhythmias, cardiomyopathy, and nephrotoxicity. The wide-ranging systemic and developmental toxicity of mercury underscores the critical need for minimizing maternal and early-life exposure (Tchounwou et al., 2012).

Cadmium (Cd) has been strongly associated with bone demineralization and renal dysfunction (Åkesson et al., 2006). Chronic low-dose Cd exposure is believed to contribute to the development of several chronic lung diseases, including emphysema, asthma, and bronchitis, as well as hypertension. Prolonged Cd exposure contributes to the onset of various pathological conditions, including cancer, leukemia, and genetic toxicity. Epidemiological evidence further suggests a potential association between Cd exposure and certain cancers, such as prostate, bladder, pancreatic, kidney, and breast cancers.

Beyond its carcinogenicity, Cd may play an etiological role in central nervous system pathologies such as Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis. It is also associated with cognitive and behavioral impairments and with chronic skeletal disorders such as osteoporosis and osteomalacia, particularly affecting the pelvic bones, femurs, vertebral bodies, and scapulae. Importantly, Cd can cross the placental barrier, exerting teratogenic effects and posing serious risks to fetal growth and development (Charkiewicz et al., 2023).

Arsenic (As) toxicity is strongly correlated with the development of dermal, pulmonary, and bladder carcinomas. According to the International Agency for Research on Cancer (IARC) (2012) and the U.S. Food and Drug Administration (FDA), arsenic is classified as a Group 1 human carcinogen and increases the risk of bladder, lung, kidney, and liver tumors. Arsenic can affect multiple organ systems, leading to various cardiovascular disorders, neurological effects, respiratory problems, and kidney diseases. Chronic exposure has been linked to vascular pathologies, including stroke, ischemic heart disease, and peripheral artery disease. Furthermore, arsenic acts as a potent endocrine disruptor and carcinogen, with prenatal and early-life exposures linked to elevated cancer risk and mortality later in life (Palma-Lara et al., 2020).

PFAS Exposure

In recent years, per- and polyfluoroalkyl substances (PFAS) have become a serious global concern. These substances are persistent in the environment, accumulate in biological tissues, and exhibit endocrine-disrupting effects. Common PFAS compounds include perfluorononanoic acid (PFNA), perfluorooctanoate (PFOA), and perfluorooctane sulfonate (PFOS). These synthetic chemicals are resistant to degradation and can accumulate in maternal and fetal tissues, leading to adverse developmental outcomes. Several cohort studies have demonstrated the detrimental effects of prenatal and early-life PFAS exposure. High levels of PFOA and PFOS in cord blood have been associated with reduced language and cognitive abilities in children (Oh et al., 2022). Similarly, PFOS and PFNA exposures have been linked to impairments in memory and reasoning skills in childhood (Spratlen et al., 2020). PFAS mixtures have also been shown to disrupt thyroid hormone regulation, increasing total and free thyroxine (TT4, FT4) levels while decreasing thyroid-stimulating hormone (TSH) concentrations in newborns, indicating impaired thyroid function (Guo et al., 2021). PFOS and PFNA exposures have also been associated with alterations in triglyceride and lipid profiles in umbilical cord blood (Sinisalu et al., 2021). Furthermore, PFAS and organochlorine pesticides have been shown to disrupt the gut microbiome in infants, leading to a decline in beneficial species such as Bifidobacterium (Naspolini et al., 2022). In addition, PFOS and PFOA exposures have been associated with lower body mass index (BMI) in childhood (Horikoshi et al., 2021) and decreased lung function (FVC, FEV1) in children (Kung et al., 2021).

Microplastics

Epidemiological and experimental evidence suggest that microplastics (MP) can accumulate in key physiological systems such as the digestive, reproductive, and cardiovascular systems and disrupt biological function. Defined as plastic particles smaller than 5 mm, MP occur in various forms such as fragments, fibers, spheres, or granules. The most common types of MP identified in biological and environmental samples are polyethylene (PE), polypropylene (PP), polycarbonate (PC), polystyrene (PS), polyvinyl chloride (PVC), and polyethylene terephthalate (PET) (Sun & Wang, 2023). Prenatal exposure to MP has been associated with adverse pregnancy outcomes, including restricted fetal growth, low birth weight, and pregnancy-induced hypertension (PIH) (Wang et al., 2024). Negative correlations have also been reported between PE and PC derived MP and neonatal Apgar scores, while PVC exposure has been linked to increased maternal complications and reduced neonatal length and weight (Zhang et al., 2025).

Microplastics exhibit multifaceted effects on the immune system. Experimental studies have shown that PE exposure increases TNF-α production in macrophages by 2.3-fold and IL-6 by 1.8-fold, while in animal models it elevates the proportion of $CD3^{+}CD4^{+}$ T cells and reduces uterine NK cell counts by approximately 42%, resulting in an immune imbalance at the maternal–fetal interface (Qiao et al., 2025; Zhang et al., 2025). MP also compromises intestinal integrity by disrupting tight junction proteins, leading to increased intestinal permeability and a reversal of the Firmicutes/Bacteroidetes ratio within the gut microbiota (Fackelmann et al., 2023; Qiao et al., 2025). Reproductive health appears particularly vulnerable to MP exposure. Bisphenol A (BPA) released from MP may disrupt hormonal balance by binding to the estrogen receptor-α and lead to changes associated with polycystic ovary syndrome (PCOS) (Adhikari et al., 2024). Furthermore, nanosized PS-MP can cross the blood-testis barrier, causing Sertoli cell apoptosis and decreased sperm motility (Liu et al., 2024; Zhao et al., 2024). In women, microplastic exposure has been associated with endometrial thinning, collagen accumulation, granulosa cell apoptosis, and a decrease in follicle count (Qiao et al., 2025; Zhang et al., 2025).

A particularly striking recent finding links maternal MP burden to mental health outcomes. Elevated MP concentrations in maternal blood have been correlated with a higher risk of postpartum depression, reflected by increased Edinburgh Postnatal Depression Scale (EPDS) scores (Saraluck et al., 2024). These data highlight the broad systemic and psychological implications of maternal MP exposure and underscore the critical need for further mechanistic and epidemiological research.

Table 1

Most common toxicants, exposure routes, and health effects.

No	Substance	Source of Exposure	Health Effects	References
1	**Arsenic (As)**	Contaminated drinking water; gold, silver, and other metal mining; pesticide production and use; processing of glass, textiles, ammunition, paper, and wood preservatives; cosmetics industry (eyeshadow).	A potent endocrine disruptor and carcinogen.	(Palma-Lara et al., 2020; Ullah et al., 2023)
2	**Cadmium (Cd)**	Industrial batteries, paint, coating, plastic production; mining; casting and fossil fuel combustion; widespread exposure through contaminated water/soil and tobacco products; air pollution.	Bone demineralization and renal function disorders; neurodegenerative diseases; neurological, learning, and/or behavioral difficulties in children, neuropathy, and impairment in memory, attention, and psychomotor function; cardiovascular diseases; respiratory diseases; reproductive system disorders.	(Atsdr, 1997; Charkiewicz et al., 2023)
3	**Chromium (Cr)**	Stainless steel production; leather tanning; pigment production; painting; metal plating; wood processing.	Gastrointestinal problems; male reproductive system function disorders; neurological, cardiovascular, hepatological, and neuronal toxicity; allergic reactions; anemia.	(Hossini et al., 2022; Shin et al., 2023)
4	**Lead (Pb)**	Paint; plumbing materials; pipes; glasses; batteries; cosmetics and ammunition; fossil fuels; mine sites; foundry sites.	Cognitive development disorders, learning difficulties, and permanent damage to nervous system functions in children; associated with reproductive system and hormonal disorders; lung cancer; anemia/leukopenia; non-alcoholic fatty liver disease; coronary artery diseases; some neurological diseases.	(Adriana et al., 2025)
5	**Mercury (Hg)**	Coal-fired power plants, contaminated water, fish consumption, and dental materials.	Toxic effect on the neurological system and kidneys; cardiomyopathy; also a negative effect on the respiratory and reproductive systems.	(Kim et al., 2016; Tchounwou et al., 2012)
6	**Per- and polyfluoroalkyl substances (PFAS)**	Consumption of Ultra-Processed Foods (UPF); food packaging; synthetic textile products (raincoats, umbrellas, carpets, and upholstery fabrics); house dust agar; non-stick pots and pans; cosmetics.	Impairment of thyroid function; disruption of the gut microbiome.	(Guo et al., 2021; Naspolini et al., 2022)
7	**Perfluorononanoic acid (PFNA)**	Consumption of Ultra-Processed Foods (UPF); food packaging; synthetic textile products; house dust agar: non-stick pots and pans; cosmetics.	Impairments in memory and reasoning skills in childhood; impairment in triglyceride and lipid profiles.	(Sinisalu et al., 2021; Spratlen et al., 2020)

8	**Perfluorooctanoate (PFOA)**	Consumption of Ultra-Processed Foods (UPF); food packaging; synthetic textile products; house dust agar; non-stick pots and pans; cosmetics.	Associated with decreased language and perceptual abilities in children; associated with lower BMI in childhood; decreased lung function (FVC) in children.	(Horikoshi et al., 2021; Kung et al., 2021; Oh et al., 2022)
9	**Perfluorooctane sulfonate (PFOS)**	Consumption of Ultra-Processed Foods (UPF); food packaging; synthetic textile products; house dust agar; non-stick pots and pans; cosmetics.	Associated with decreased language and perceptual abilities in children; impairments in memory and reasoning skills in childhood; impairment in triglyceride and lipid profiles; associated with lower BMI in childhood; decreased lung function (FVC) in children.	(Horikoshi et al., 2021; Kung et al., 2021; Oh et al., 2022; Sinisalu et al., 2021; Spratlen et al., 2020)
10	**Organochlorine pesticides (OCs)**	DDT; chlordane; other pesticides.	Disrupts the gut microbiome; cancer and reproductive system disorders.	(Naspolini et al., 2022)
11	**Microplastics (MP)**	Consumption of Ultra-Processed Foods (UPF); long-term use of plastic bottles, plastic cutlery, take-out consumption; textiles in homes and clothing; marine foods; seafood; table salt; drinking water; beverages; drug capsules; cosmetic products; packaged foods.	Associated with restricted fetal growth, LBW, PIH; multilayered effects on the immune system; increases gut permeability.	(Fackelmann et al., 2023; Le et al., 2024; Qiao et al., 2025; Sangkham et al., 2022; Wang et al., 2024; Yun et al., 2024)
12	**Nano-sized polystyrene microplastics (PS-MP)**	Table salt, fish; drinking water, bottled water.	Sertoli cell apoptosis and reduced sperm motility.	(Liu et al., 2024; Zhao et al., 2024)
13	**Bisphenol A (BPA)**	Widely used in PC plastics for optical materials and electronic equipment; bottles; reusable plastic bottles; plates; bowls; cups; microwaveable kitchenware and food containers. Also in epoxy resin paints, medical vinyl chloride, thermal paper, flame retardants, printing inks, sports equipment, dental materials, CDs, and DVDs.	Hormonal balance disorder, PCOS, cancer, and infertility; associated with diabetes and obesity.	(Adhikari et al., 2024; S. Almeida et al., 2018)
14	**Polyaromatic hydrocarbons (PAHs)**	Pollutants from gasoline and garbage incineration.	Associated with cancer.	(EWG, 2009)
15	**Polybrominated dibenzodioxins and furans (PBDD/F)**	Contaminants in brominated flame retardants. Pollutants and byproducts from plastic production and incineration.	Toxic to the developing endocrine system.	(EWG, 2009)

16	**Perfluorinated chemicals (PFCs)**	Active ingredients or breakdown products of Teflon, Scotchgard, fabric and carpet protectors, and food packaging coatings.	Linked to cancer and birth defects.	(EWG, 2009)
17	**Polychlorinated dibenzodioxins and furans (PBCD/F)**	Contaminants: byproducts of PVC production; industrial bleaching and incineration.	Cancer, toxic to the endocrine system.	(EWG, 2009)
18	**Polybrominated diphenyl ethers (PBDEs)**	Furniture foam, computers, televisions.	Negatively affects brain development and the thyroid.	(EWG, 2009)
19	**Polychlorinated Naphthalenes (PCNs)**	Wood preservatives; varnishes; machine lubricants; waste incineration.	Causes liver and kidney damage.	(EWG, 2009)
20	**Polychlorinated biphenyls (PCBs)**	Industrial insulators and lubricants.	Causes cancer and nervous system problems.	(EWG, 2009)

Current evidence strongly indicates that both heavy metals and persistent environmental contaminants—such as PFAS and MP—adversely affect fetal health. These effects manifest in the short term as oxidative stress, inflammation, hormonal imbalance, and metabolic disruptions, while in the long term, they can lead to serious health consequences such as cognitive developmental problems, immune disorders, cardiovascular diseases, respiratory problems, and increased cancer risk.

Given these multifactorial risks, preventing toxic exposures during the prenatal period is essential not only for individual health but also for public health and the well-being of future generations. Environmental toxin control must therefore be prioritized within public health strategies. Developing and enforcing stricter regulations, especially for vulnerable populations such as pregnant women and infants, is imperative to mitigate transgenerational health consequences.

An Important Agent in Toxicity: Detergent

Detergents are chemical agents containing anionic surfactants such as sodium dodecyl sulfate (SDS) and sodium lauryl sulfate (SLS), which are widely used in numerous household and industrial applications. These compounds are recognized as toxic agents with the potential to penetrate cellular barriers, reach systemic circulation, and interact with intracellular structures.

In daily life, humans are continuously exposed to detergents through common products such as soap, shampoo, body wash, laundry detergent, and dishwashing liquids. Detergent residues tend to accumulate on fabrics and in the environment, often requiring multiple rinsing cycles for complete removal (Bernal-Jácome et al., 2024; Matrosenko et al., 2025).

A study by Wang et al. (2019) reported that even detergent residue diluted 1:2500 caused toxic and barrier-disrupting effects. It was stated that laundry detergent exposure, barely at a dilution of 1:50,000, had negligible effects. Based on these findings, approximately 50 tons of water would be required to neutralize the effects of a single liter of detergent. High concentrations of detergent residue accumulated on clothing can enter the body through inhalation, as well as direct contact with the skin, and can reach internal organs such as the lungs (Wang et al., 2019). Similarly, dishwashing detergent residues can be ingested with food and disrupt epithelial integrity in the gastrointestinal tract.

Detergents disrupt the integrity of tight junction proteins in the skin, lung, and gastrointestinal epithelium, increasing barrier permeability and causing structural damage (Doyle et al., 2023; Rinaldi et al., 2024). This barrier defect increases the risk of tissue penetration of allergens, microbial enzymes, toxins, and environmental pollutants, paving the way for the development of inflammatory responses (Wang et al., 2019). Consequently, detergents represent a dual toxic threat—not only due to their direct harmful effects but also by enhancing the absorption and toxicity of other xenobiotics.

At the cellular level, detergents exert cytotoxic effects through lipid dissolution and protein denaturation within cell membranes (Fan et al., 2024). SLS, in particular, can induce cell death by interacting with lipids and proteins in cell membranes (Birant et al., 2022). Epidemiological data indicate that chronic or repeated exposure to detergents increases the prevalence of asthma, atopic dermatitis, and eosinophilic esophagitis in genetically predisposed individuals (Sözener et al., 2020; Yazici et al., 2023). It has also been reported that detergents induce dose-dependent cytotoxicity in human lymphocytes, causing significant cell death at high concentrations (Cooley-Andrade et al., 2016). Moreover, some detergent ingredients may weaken the immune response by suppressing immunoglobulin (IgG, IgM) synthesis (Jahnová et al., 1993).

Studies in animal models have revealed that exposure to powdered detergents causes significant histopathological changes in liver tissue. The severity of damage increases proportionally with exposure duration and concentration (Tayfur et al., 2020). These findings demonstrate that detergents have significant hepatotoxic potential.

Furthermore, it has been reported that some detergent ingredients, such as nonylphenol ethoxylates, exhibit endocrine-disrupting effects and may contribute to the development of metabolic disorders by antagonizing thyroid hormone signaling (Bernal-Jácome et al., 2024).

In conclusion, detergents, which are frequently used in daily life and difficult to rinse off, are among the most common and longest-lasting toxins. Far from being harmless cleaning agents, detergents are significant contributors to environmental and systemic toxicity, disrupting cellular barrier integrity, leading to systemic toxicity, activation of inflammatory responses, and structural damage at the organ level. By disrupting cellular barrier integrity, detergents not only induce direct cytotoxic and inflammatory responses but also facilitate the penetration and bioaccumulation of other environmental toxins.

Fetal Effects of Maternal Diet

The mother's nutrition during pregnancy is one of the most important factors affecting fetal development and health. Malnutrition during this period can have lasting effects by impairing placental nutrient transfer, leading to intrauterine growth restriction (IUGR). Insufficient nutrient supply also alters fetal metabolic programming, increasing the risk of insulin resistance, type 2 diabetes, and obesity in later life through mechanisms such as reduced pancreatic β-cell mass and dysregulated adipose tissue development (Calkins & Devaskar, 2011).

The quality of the diet is as important as inadequate nutrition itself. In a cohort conducted between 2007 and 2015 (Kim et al., 2019), it was shown that consuming high amounts of trans fatty acids (TFA) containing flour and sugar products during pregnancy negatively impacts fetal programming by triggering a proinflammatory response and causing dysbiosis in the gut microbiota. TFA lipotoxicity disrupts the intestinal barrier, increasing permeability and allowing allergens to enter the circulation, which increases the risk of food allergy (FA) in newborns. Moreover, continuation of a TFA-rich diet during the first six months of breastfeeding has been shown to exacerbate these adverse effects on the offspring. This effect is particularly pronounced in infants with certain genetic variations in the CD14, GSTM1, and GSTT1 genes, demonstrating the complex interaction between environmental triggers and genetic predisposition (Kim et al., 2019).

Maternal diet can also elicit exposure to environmental pollutants. For individuals not occupationally exposed to the toxicants, food is the main source of exposure. Although these substances are present in relatively low concentrations in food products, they pose a serious threat, especially when chronic exposure is considered (Koch et al., 2022). Recent evidence indicates a strong association between the consumption of ultra-processed foods (UPFs) during pregnancy and increased newborn exposure to PFAS. UPFs often contain PFAS originating from packaging materials. In a cohort study (Naspolini et al., 2022), infants of mothers who consumed three or more UPF subgroups per week exhibited significantly higher PFAS concentrations compared to infants of mothers who consumed none (mean 2.47 ng/mL vs. 1.86 ng/mL; $p < 0.05$). This finding suggests that maternal dietary habits, particularly UPF consumption, may increase fetal PFAS exposure and program early-life exposure to environmental toxins with potential long-term health effects.

Similarly, a recent study by Zhang et al. (2025) examined the relationship between maternal lifestyle factors and MP exposure. PE intake was found to be significantly correlated with prolonged use of plastic bottles and cutlery, as well as with the frequency of takeaway food consumption, both in the year preceding pregnancy and during pregnancy. Accordingly, PC intake was strongly correlated with the frequency of takeaway food consumption one year before and during pregnancy. Total MP burden was linked to the frequency of plastic utensil use and takeaway consumption, indicating that common plastic-related lifestyle practices may meaningfully contribute to maternal and fetal MP exposure.

Collectively, these findings highlight that maternal everyday dietary behaviors can serve as important determinants of the toxic exposure of the fetus. Common plastic polymers such as PE and PC, and persistent chemicals like PFAS, may increase the risk of pregnancy complications and interfere with fetal development. Maternal nutrition is one of the most critical determinants of fetal development. Mother's nutritional intake and toxic exposure influence not only intrauterine growth but also the fetus's metabolic and epigenetic programming in later life, thus affecting lifelong health.

Toxic Exposure Prevention and Detoxification Approaches

The first and most effective step in preventing toxic accumulation is to minimize exposure at its source. In modern daily life, individuals are frequently and often unknowingly exposed to various environmental chemicals through common products such as plastic bottles, disposable kitchenware, food storage containers, packaged and processed foods, cosmetics, and household cleaning agents. It has been shown that these products frequently contain phthalates, bisphenols (especially BPA and BPS), parabens, and heavy metal residues (EWG, 2009). Beyond household and consumer products, additional exposure sources include agricultural produce containing pesticide residues, seafood with elevated concentrations of heavy metals—especially mercury in large predatory fish—and ambient air pollution. Promoting clean and sustainable agricultural practices, reducing the use of single-use plastics, and preferring recyclable and glass-based packaging materials represent practical and effective strategies to mitigate both individual and population-level toxic exposure. These measures not only decrease environmental contamination but also play a critical role in protecting maternal and fetal health across generations.

Because exposure to toxins cannot be entirely avoided, supporting the body's natural detoxification systems (liver, kidney, lymphatic system, skin) is gaining importance. In this context, dietary supplements used to support detoxification have gained increasing scientific and public interest in recent years. Evidence suggests that various vitamins, minerals, and phytochemicals can support liver function, strengthen antioxidant defenses, and promote metabolic detoxification pathways. For instance, antioxidants such as resveratrol precursors, D-glucaric acid, curcumin, and glutathione, as well as dietary fibers, are among the most researched dietary supplements due to their detoxification-supporting properties (El-Khodor et al., 2023; Panda et al., 2023). Furthermore, high-chlorophyll foods such as spirulina and chlorella have been reported to exhibit potential detoxification benefits for liver health and heavy metal elimination (Lee et al., 2015; Thitame et al., 2025). Notably, studies on clays such as bentonite and zeolite, which are natural and additive-free substances frequently used in ancient medicine, have shown their effectiveness in detoxification by adsorbing heavy metals and microtoxins (Dhar et al., 2023; José Mendes dos Reis et al., 2024).

An important point to emphasize here is the frequent detection of heavy metals such as lead, cadmium, mercury, and arsenic in food supplements. Recent studies have reported that 68-88% of tested dietary supplements contain at least one heavy metal, with some products exceeding permissible limits, particularly for lead and cadmium (Naz et al., 2024). Moreover, MP contamination was detected in all tested dietary fiber supplements, with powder-based products showing the highest levels of MP (Panneerselvan et al., 2024). These findings highlight the need for caution in the use of industrially produced food supplements. Ironically, these supplements, used for toxin removal, may unknowingly lead to further toxin exposure. Therefore, personalized approaches using holistic medical testing methods are recommended to ensure the optimal and safe use of all these nutritional supplements.

Furthermore, complementary and traditional approaches for detoxification are also being investigated. Cupping therapy is a traditional practice based on the principle of drawing blood using a vacuum method through superficial skin incisions. Recent scientific studies have shown that this method not only improves circulation but also contributes to the removal of toxic elements from the blood. Saeed and Sheikh (2023) reported significantly higher concentrations of heavy metals, including Lead (Pb), Cadmium (Cd), Nickel (Ni), Aluminum (Al), and Copper (Cu), in wet cupping blood compared to venous blood, supporting the detoxification potential of this technique. A pilot study by Umar et al. (2018) observed a significant decrease in Al, Zinc (Zn), and Cd levels 30 days after cupping. The researchers proposed that this effect may be attributed to cupping's potential to enhance circulation, decrease free radical burden, and support the body's detoxification processes.

Acupuncture, a therapeutic modality rooted in TCM, aims to restore homeostatic balance by regulating the flow of vital energy (Qi) throughout the body. Contemporary research indicates that acupuncture not only provides symptomatic relief but also modulates immune responses, attenuates oxidative stress, and supports the physiological functions of key detoxification organs (LaPaglia et al., 2016).

Bioresonance Therapy (BRT) is a non-invasive biophysical method that regulates the body's vibrational communication by influencing the primovascular system and meridian systems using the body's own electromagnetic frequencies. In BRT applications, environmental toxins, heavy metals, microorganisms, allergens, and other pathogenic factors are detected using vibrational diagnostic methods. Frequency modulation is then employed to neutralize the bioenergetic effects of these factors, thereby restoring the organism's energetic equilibrium. Emerging evidence suggests that BRT may enhance the elimination of metabolic wastes and toxins by re-permeabilizing the disrupted extracellular matrix, thereby improving cellular detoxification capacity (Hennecke, 2012; Karakos et al., 2019; Kirsever et al., 2022).

Protection from toxic exposure is possible through social and individual awareness and behavioral changes, particularly through reestablishing a healthy ecological environment. Scientific data demonstrates that traditional methods such as cupping and acupuncture, and contemporary vibrational methods such as bioresonance and homeopathy, can support the body's natural detoxification system when applied in conjunction with appropriate and natural nutritional supplements.

Conclusion

One of the biggest challenges in dealing with health problems today is the rapid increase and transformation of disease-causing agents. In current medical literature, the etiology of many diseases can no longer be explained solely by the classical pathogens such as viruses, bacteria, or parasites. Instead, toxic synthetic compounds such as environmental toxins, industrial chemicals, genetically modified food, artificial additives, and pesticides used extensively in agriculture also play a significant role in disease development and progression (Landrigan & Fuller, 2015; Grandjean & Landrigan, 2014).

Growing epidemiological, molecular, and epigenetic evidence strongly supports that an individual's lifelong health is shaped within the womb. Factors such as malnutrition, toxic exposures, stress, inflammation, and hypoxia during the fetal period lead to programming at the cellular level, paving the way for metabolic, cardiovascular, neurological, and immunological diseases later in life. This phenomenon, described by the FOAD concept, underscores the importance of the prenatal environment in determining long-term health outcomes.

Today, it is known that toxin exposure caused by modern life no longer threatens adult health alone. Numerous studies have demonstrated that heavy metals, PFAS, MP, endocrine disruptors, and many other environmental contaminants is capable of crossing the placental barrier to reach the fetus via the umbilical cord. This evidence challenges the long-held notion of "intrauterine protection," revealing that even during the prenatal period, the fetus is exposed to the toxic burden of the modern world. The persistence of these effects through epigenetic mechanisms highlights a growing concern for intergenerational transmission of health risks.

In response to this complex and systemic issue, strategies aimed at reducing toxic exposure and supporting the body's intrinsic detoxification systems are of vital importance. Traditional therapeutic methods such as cupping and acupuncture, alongside contemporary holistic vibrational medicine approaches including BRT and homeopathy, demonstrate potential in enhancing detoxification, restoring homeostatic balance, and improving extracellular matrix permeability. These modalities not only provide symptomatic relief but also promote holistic healing by addressing the underlying causes of disease through mechanisms such as immunomodulation and reduction of oxidative stress.

For the protection of the health of future generations and public health, attention should be refocused on the pre-pregnancy period and the pregnancy process. Based on the principle that "Eliminating harm is more important than providing benefit", the ultimate goal should be to ensure the health of future generations and to build a clean, toxin-free society for sustainable health. To build a healthy society, preventive medicine should receive at least equal emphasis as curative medicine in medical education and health management, and policies should be developed accordingly.

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Sustainability in Rehabilitation Services: Long-Term Impact and Contribution to Public Health

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Introduction

Health systems today must be designed not only to provide consistent and equitable access to care, but also to ensure that healthcare delivery remains economically viable and socially responsive in the long term. Within this broader framework, rehabilitation services—encompassing physical, psychosocial, and vocational dimensions—constitute a vital pillar of sustainable health systems. They play a central role in managing chronic diseases, supporting aging populations, and promoting recovery and participation for individuals with disabilities or long-term health conditions (WHO, 2022).

Rehabilitation is not merely a curative intervention; it is preventive, restorative, and transformative. By addressing functional limitations and fostering independence, rehabilitation significantly enhances quality of life, social inclusion, and long-term health outcomes (Stucki, Rubinelli, & Bickenbach, 2019). As the global burden of chronic diseases and disability continues to rise, embedding rehabilitation as a core function of health systems has become essential. Sustainable rehabilitation practices can reduce healthcare costs, maintain workforce participation, and help mitigate health inequities over time (Kiekens et al., 2020).

For rehabilitation services to achieve these outcomes, they must be strategically planned with continuity, accessibility, and integration in mind. Sustainable models should be adapted to local resources, provide long-term benefits to individuals and communities, and contribute to wider public health goals—such as reducing hospital readmissions and alleviating systemic healthcare pressures. In this sense, sustainable rehabilitation refers not only to interventions that enable personal recovery but also to services that are inclusive, adaptable, and capable of responding to evolving population needs.

The overarching aim of this chapter is to examine the long-term contributions of rehabilitation services to public health and to explore the key principles of sustainability within this context. Drawing upon international evidence and theoretical frameworks, the chapter will critically analyze the relevance and applicability of various rehabilitation models, with a particular focus on their implementation within the Turkish healthcare system. Core questions to be addressed include: How can rehabilitation services be made sustainable? Which models demonstrate long-term effectiveness? And what are the broader societal benefits of sustainable rehabilitation practices?

Türkiye provides a timely and relevant context for this discussion. The country is experiencing rapid demographic changes, including a graying population and a considerable burden of recent immigration, that pose challenges for social systems in general. These population shifts have led to growing demand for rehabilitation services. Not only meeting this demand but also ensuring that these services are financially viable, institutionally integrated, and socially inclusive is essential. Recent national studies have begun to address these issues through discussions of long-term care insurance, post-disaster and vocational rehabilitation, and preventive strategies in chronic disease management.

Accordingly, this chapter presents a comprehensive literature review on the sustainability and long-term impact of rehabilitation services in Türkiye. It further discusses emerging models and trends, and proposes methodological and policy-level recommendations aimed at strengthening the sustainability and resilience of rehabilitation systems for the future.

Long-Term Effects of Rehabilitation

Sustainable rehabilitation contributes to health systems not only through immediate functional recovery but also by supporting long-term survival, quality of life, and social participation. The following sections synthesize evidence across multiple domains—including stroke, cardiac, and geriatric rehabilitation—to illustrate how sustained rehabilitation practices shape individual and population-level outcomes.

Post-Stroke Rehabilitation and Mortality

Stroke remains one of the leading global causes of mortality and long-term disability. Beyond acute management, the post-stroke period often determines long-term outcomes, including survival and quality of life. Rehabilitation plays a central role during this phase, influencing both neurological recovery and mortality risk.

When rehabilitation interventions are introduced early and appropriately, they may enhance endogenous repair processes, thereby improving both functional recovery and long-term survival (Irisa & Shichita, 2025).

Clinical studies confirm that intensive rehabilitation programs initiated within the first three months post-stroke yield significant motor and cognitive gains, which in turn may influence mortality. Neural reorganization is not limited to the affected hemisphere but extends to contralateral and subcortical regions, and rehabilitation-driven neuroplasticity can amplify this adaptive potential.

Overall, sustainable post-stroke rehabilitation should be conceptualized as a biological and systemic strategy—one that enhances survival, preserves independence, and minimizes the long-term burden on individuals and health systems.

Community-Based Rehabilitation and Quality of Life

Community-based rehabilitation (CBR) represents a sustainable, socially grounded approach that extends care beyond hospital settings. Its goal is not only to restore function but also to facilitate social participation, reduce caregiver burden, and improve life satisfaction.

Hartman-Maeir and colleagues (2007) provided early evidence on the long-term benefits of CBR among stroke survivors. In their one-year follow-up of patients discharged from the hospital, those participating in a structured home-based program showed significant gains in leisure engagement and overall life satisfaction, despite limited improvements in basic physical independence. These findings underscore that rehabilitation outcomes should be evaluated not only by physical metrics but also by psychosocial and participation-related measures.

CBR initiatives demonstrate that sustainable rehabilitation depends on integrated, community-level systems that address both medical and social dimensions. When caregivers and local networks are actively involved, such programs enhance subjective well-being, reduce institutional dependency, and promote long-term independence—aligning closely with the principles of sustainability in health systems.

Long-Term Follow-Up in Individuals with Severe Disabilities

Patients with severe post-stroke disabilities or other profound functional limitations require sustained support to maintain health, independence, and quality of life. Høyer, Opheim, Moe-Nilssen, and Strand (2023) conducted a long-term follow-up study in 60 individuals with severe post-stroke disability. Nearly 80% of participants continued to live at home 12 months after discharge, and most maintained physiotherapy involvement. Notably, 83% remained independent walkers, and the majority perceived their health as “good to excellent.”

These findings highlight several implications for sustainable rehabilitation:

- Continuity of care: Ongoing individualized therapy is crucial beyond hospital discharge.
- Community support: Home-based and community rehabilitation enable independent living even with severe disability.
- Comprehensive assessment: Long-term evaluations should incorporate both objective measures (e.g., mobility) and subjective perceptions of health.

Sustainable models must therefore extend beyond acute recovery, embedding long-term follow-up mechanisms that adapt to evolving functional and psychosocial needs.

Long-Term Outcomes of Cardiac Rehabilitation

Cardiac rehabilitation (CR) exemplifies how structured rehabilitation programs can yield durable population-level benefits. While traditionally aimed at short-term recovery and risk management, long-term data demonstrate significant effects on mortality and healthcare utilization.

Doimo et al. (2019) evaluated five-year outcomes among patients participating in ambulatory CR compared to non-participants. The CR group exhibited substantially lower combined rates of cardiovascular hospitalization and mortality (18% vs. 30%), with a 42% reduction in overall risk (hazard ratio 0.58; 95% CI 0.43–0.77). Moreover, all-cause and cardiovascular mortality were both significantly lower among participants.

These findings reaffirm that CR contributes not only to improved survival but also to reduced hospital readmissions, underscoring its value as a sustainable component of health systems. Embedding CR within long-term care pathways thus offers both clinical and economic advantages, supporting health system resilience.

Home-Based Rehabilitation in Older Adults

As populations age, home-based rehabilitation has become increasingly vital for sustaining functional capacity and reducing institutional care dependency. Systematic reviews demonstrate that structured, individualized, and progressive programs can improve mobility, self-care, and psychosocial well-being among older adults (Alves et al., 2024; Zhao et al., 2024).

Zhao et al. (2024) analyzed 21 randomized controlled trials in older patients with hip fractures and found significant improvements in balance, mobility, and quality of life, with standardized mean differences of approximately 0.60 for activities of daily living and 0.30 for life quality. Similarly, home-based exercise interventions for community-dwelling older adults have been associated with enhanced confidence, social engagement, and reduced fear of falling (Santos et al., 2024).

Nevertheless, variability across studies—in program intensity, duration, and participant profiles—indicates that sustained success depends on personalized approaches, caregiver involvement, and continuous monitoring. In this context, home-based rehabilitation represents a scalable and sustainable strategy to meet the long-term needs of aging populations.

Home-Based Rehabilitation in the Turkish Context

Türkiye's rapidly aging population has heightened the need for accessible and sustainable home-based rehabilitation services. However, disparities in healthcare resources and regional infrastructure continue to pose challenges. Demir Avcı and Gözüm (2018) emphasize that shortages of trained personnel, transportation barriers, and limited social security coverage constrain access, particularly in rural areas.

Although the Ministry of Health manages home-based health services—accessible through family physicians or direct application—significant challenges remain in ensuring service continuity, integration with primary care, and systematic follow-up. Recent analyses highlight that home health services in Türkiye often face limitations in multidisciplinary collaboration, communication between service levels, and long-term monitoring of patients (Sarıoğlan & Emüler, 2025). Expanding sustainable home-based rehabilitation in Türkiye will therefore require strengthening the family physician network, improving referral and coordination systems, and investing in local infrastructure.

Synthesis and Key Principles for Sustainable Rehabilitation

Across stroke, cardiac, and geriatric contexts, evidence consistently indicates that while short- and mid-term rehabilitation gains are well established, the central challenge lies in sustaining these outcomes long-term. Translating these insights into health system design requires adopting key sustainability principles:

- Accessibility and continuity: Address geographic, financial, and systemic barriers to long-term care.
- Resource efficiency: Optimize workforce and infrastructure for cost-effective delivery.
- Community engagement: Empower patients, families, and local actors in shared rehabilitation processes.
- System integration: Embed rehabilitation within the continuum of health and social care.
- Monitoring and evaluation: Use data-driven approaches to guide service improvement.
- Technological innovation: Expand equitable access through tele-rehabilitation and digital tools.

Despite abundant evidence for short-term benefits, few studies explicitly evaluate sustainability beyond five years. There remains a pressing need for long-term, multicenter cohort research linking rehabilitation outcomes to sustainability metrics such as cost-effectiveness, workforce stability, and system resilience.

Ultimately, sustainability in rehabilitation is not only about preserving clinical gains—it is about embedding rehabilitation within the social and institutional fabric of health systems to achieve lasting population health impact.

Evidence from Türkiye: Long-Term Effects and Sustainability of Rehabilitation

While international research highlights the long-term benefits and systemic value of rehabilitation, evidence from Türkiye offers important insights into how these principles manifest in local practice. The Turkish literature reveals progress in chronic disease management, disability inclusion, and disaster-related rehabilitation, but also underscores enduring structural and policy challenges. This section synthesizes key national studies to provide an overview of the long-term impacts and sustainability dimensions of rehabilitation within Türkiye's evolving healthcare landscape.

Chronic Disease Management and Preventive Rehabilitation

Chronic diseases are the leading cause of mortality in Turkey, accounting for nearly 70% of deaths according to Turkish Statistical Institute data (TURKSTAT, 2019). Preventive rehabilitation approaches—particularly those emphasizing physical activity—have been identified as strategic tools in reducing morbidity, mortality, and healthcare costs in this population. A national review of chronic disease prevention emphasized that structured physical activity and rehabilitation programs can significantly improve health-related quality of life among patients with conditions such as diabetes, cardiovascular disease, and COPD. These interventions not only support clinical management but may also delay disease progression and functional decline (Çalıkuşu et al., 2023).

Vocational Rehabilitation and Disability Inclusion

Sustainable rehabilitation extends beyond physical recovery to encompass economic and social integration, especially for persons with disabilities. In a recent national study on vocational rehabilitation in Turkey, researchers found that successful employment outcomes for individuals with disabilities depended not only on personal rehabilitation plans but also on legal, institutional, and social support systems (Bulduk & Ocaktan, 2024). Employment was positively associated with increased life satisfaction and social participation, underlining that rehabilitation sustainability requires a cross-sectoral approach. The findings align with global data showing that work integration is a key determinant of psychosocial well-being among individuals with disabilities (OECD, 2023).

Post-COVID Rehabilitation and Long-Term Sequelae

The COVID-19 pandemic has highlighted the critical need for individualized and sustained rehabilitation services. Turkish clinical literature indicates that patients recovering from moderate-to-severe COVID-19 may experience long-term respiratory, neuromuscular, and psychological sequelae (Yavuz et al., 2023). Post-COVID rehabilitation was found to reduce re-hospitalizations and emergency department visits while improving physical function and mental health outcomes. The recommendation for customized, multidisciplinary rehabilitation—especially for individuals with post-viral fatigue or pulmonary fibrosis—aligns with international guidelines and supports sustainable recovery pathways.

Long-Term Care Infrastructure and Policy Gaps

Despite growing demand due to population aging and increased disability rates, Turkey currently lacks a formal long-term care insurance system. Kara (2025) identifies critical policy gaps in funding, legal frameworks, and public awareness that hinder the development of a sustainable long-term care model. Without adequate long-term care infrastructure, rehabilitation services—especially for the elderly and chronically ill—are at risk of becoming fragmented or inaccessible. The integration of rehabilitation into long-term care frameworks is thus essential for systemic sustainability.

Functional Classification and Outcome Standardization

Standardized assessment tools are central to monitoring rehabilitation outcomes and ensuring quality over time. A study adapting the Cystic Fibrosis Questionnaire to the International Classification of Functioning, Disability and Health (ICF) framework emphasized that aligning national rehabilitation metrics with global standards can enhance comparability and continuity in care (Yılmaz et al., 2022). Using ICF-based tools helps evaluate not only physical improvements but also contextual factors such as environmental barriers and personal capacities—key determinants of long-term functional sustainability.

These frameworks contribute to the establishment of evidence-based rehabilitation policies and facilitate data-driven decision-making across healthcare systems. Through standardization, outcome monitoring becomes more reliable, enabling policymakers and clinicians to identify gaps, allocate resources efficiently, and improve equity in service delivery.

Disaster Response and Community Resilience

In the context of disaster response, standardized functional assessment frameworks such as the ICF can also play a pivotal role in evaluating community needs and supporting coordinated rehabilitation efforts. Applying these tools after disasters ensures that functional limitations and environmental barriers are systematically documented, allowing for tailored interventions that foster both individual recovery and social reintegration.

Turkish research demonstrates both the growing maturity of rehabilitation practices and the need for systemic integration to ensure sustainability. The following section expands the discussion by examining global models that may inform Türkiye's path toward resilient and inclusive rehabilitation systems.

Global Models and Sustainable Practices in Rehabilitation

The sustainability of rehabilitation services relies not only on their clinical and economic effectiveness but also on their adaptability to cultural, geographic, and systemic contexts. As health systems worldwide seek to build resilience and equity, various international models demonstrate how locally responsive and culturally grounded strategies can yield lasting benefits. These experiences provide valuable insights for countries such as Türkiye, where demographic transitions and regional disparities shape rehabilitation needs.

Culturally Adapted Rehabilitation Approaches

In high-income countries such as Australia, Canada, and the United States, culturally tailored rehabilitation programs for Indigenous and minority populations have emphasized the importance of culturally safe care, local governance, and service continuity. These programs show that long-term sustainability depends not only on clinical effectiveness but also on alignment with community values, traditions, and expectations (Holliday et al., 2021).

This principle is equally relevant for Türkiye, where cultural norms—particularly in conservative or rural regions—can influence service uptake and adherence. Strategies that build community trust and engage local actors, including family networks, NGOs, and religious leaders, can enhance participation and improve outcomes. Such culturally attuned approaches are essential for ensuring that rehabilitation becomes a socially accepted and sustained component of public health.

Rural and Remote Rehabilitation Models

Experiences from rural rehabilitation systems in countries such as New Zealand highlight how contextual adaptation can overcome geographic barriers. Integrated models combining telehealth, community-based programs, and peer support networks have successfully increased accessibility and reduced inequities (Wilkinson et al., 2022).

These insights resonate with Türkiye's regional disparities, particularly in the eastern and southeastern provinces, where infrastructure and workforce limitations persist. Mobile rehabilitation units, digital follow-up platforms, and community-based services coordinated through family physicians could replicate the success of such international models in the Turkish context.

Interdisciplinary Care and System Efficiency

Multidisciplinary rehabilitation frameworks, as implemented in Sweden and Germany, illustrate how team-based collaboration enhances patient outcomes while improving overall system efficiency (Persson et al., 2024). These models integrate physiotherapists, occupational therapists, psychologists, social workers, and medical specialists into coordinated care pathways, ensuring holistic recovery planning.

Similar approaches could strengthen Türkiye's community-level rehabilitation. Expanding interdisciplinary capacity would align with the long-term sustainability objectives identified in earlier sections on cardiac, home-based, and post-stroke rehabilitation.

Community-Based Mental Health and Psychosocial Rehabilitation

The RECOVER-E initiative, implemented across several Eastern European countries, demonstrates the sustainability and cost-effectiveness of community-based mental health rehabilitation. By reducing reliance on institutional care and fostering psychosocial recovery, the program improved both clinical and social outcomes (Wijnen et al., 2020).

These findings support a broader understanding of rehabilitation—one that extends beyond physical recovery to include mental health, social reintegration, and community participation. Integrating such models into Türkiye's mental health system could strengthen continuity of care and promote social inclusion for individuals with chronic or complex needs.

Translating Global Lessons into the Turkish Context

While global models provide a rich evidence base, their successful application requires contextualization within Türkiye's unique healthcare, social, and demographic landscape. Several thematic priorities emerge for fostering sustainable rehabilitation nationally:

Addressing Regional Inequities

Despite substantial progress in urban centers, rural and economically disadvantaged regions still face service gaps. Strategies such as mobile rehabilitation units, community-based delivery models, and coordination through family physicians are critical for equitable access.

Overcoming Geographic and Logistical Barriers

Geographic isolation and long travel distances impede follow-up and continuity of care. Building on telehealth experiences from countries like New Zealand, Türkiye can leverage its strong digital infrastructure—particularly the *e-Nabız* and MHRS systems—to expand tele-rehabilitation coverage and remote monitoring.

Enhancing Cultural Acceptability

Cultural and gender norms may limit access, particularly for women and older adults. Culturally sensitive approaches that engage local leaders, community health workers, and NGOs can improve awareness, trust, and participation.

Strengthening Multidisciplinary Capacity

Many rehabilitation services in Türkiye remain physiotherapist-led. Integrating psychologists, social workers, dietitians, and occupational therapists into primary care teams would enhance outcomes and align with global sustainability standards.

Expanding Telehealth and Technological Integration

Although digital health infrastructure in Türkiye is advanced, standardized tele-rehabilitation protocols and outcome-tracking tools are underdeveloped. Structured frameworks for remote assessment, patient education, and continuity of care are essential to maximize efficiency and scalability.

Key Insights for Sustainable Rehabilitation Systems

Synthesizing global evidence and local realities reveals several cross-cutting principles that underpin sustainability in rehabilitation systems:

- *Accessibility and Continuity*: Overcome financial, geographic, and logistical barriers to long-term engagement.
- *Efficient Resource Utilization*: Optimize human, infrastructural, and financial inputs for cost-effective delivery.
- *Community Ownership:* Involve patients, caregivers, and local organizations in co-designing rehabilitation processes.
- *Integrated System Design*: Embed rehabilitation within broader health, social, and municipal services.
- *Data-Driven Evaluation*: Implement longitudinal tracking systems to monitor outcomes and guide policy refinement.
- *Technological Innovation*: Leverage tele-rehabilitation, wearable sensors, and virtual reality tools—while ensuring equitable access and digital inclusion.

Together, these elements provide a framework for building resilient and sustainable rehabilitation systems that not only restore function but also reinforce social cohesion and population health.

Research Gaps and Policy Directions for Sustainable Rehabilitation

Despite the growing global recognition of rehabilitation as an essential component of public health, significant research and policy gaps continue to limit its full integration and sustainability. In Türkiye, as in many countries, rehabilitation research remains fragmented, short-term in scope, and insufficiently connected to national health strategies. Addressing these gaps is essential for building resilient, equitable, and evidence-based rehabilitation systems that can meet long-term population needs.

Insufficient Longitudinal and Outcome-Based Research

One of the most persistent gaps in rehabilitation research is the lack of longitudinal data evaluating functional outcomes over time. While short-term program efficacy is often reported, evidence on the durability of these outcomes—particularly among populations with chronic diseases or complex disabilities—remains limited (Kılınç et al., 2021). Establishing nationwide cohort studies that follow patients beyond hospital discharge is crucial. These studies should integrate clinical, social, and quality-of-life indicators to evaluate the true sustainability of rehabilitation outcomes.

Limited Integration of Rehabilitation into Broader Health Systems

Rehabilitation is still frequently treated as a supplementary or post-acute service rather than a core component of health systems. In Türkiye, health policy and research continue to emphasize curative and acute-care models, leaving rehabilitation underrepresented in chronic-disease management, elder care, and primary health-care strategies (World Health Organization [WHO], 2023; Türkiye Yaşlı Sağlığı Raporu, 2021). To support sustainable health-system performance and population functioning, it is essential to reframe rehabilitation as a continuous process that spans prevention, treatment, recovery, and social reintegration.

The global evidence base underscores that without systematic integration of rehabilitation into all levels of health care, systems will struggle to meet the rising burden of non-communicable diseases and ageing populations. According to the WHO's guide on integrating rehabilitation in health systems, governments are advised to adopt a four-phase approach comprising situation assessment, strategic planning, monitoring and evaluation, and full implementation (WHO, 2019). Furthermore, the recent meeting report of the *Rehabilitation 2030* initiative highlights that rehabilitation remains undervalued and underfunded in many health systems and calls for its recognition as a core service through universal health coverage (WHO, 2023).

In the context of Türkiye, recent assessments of elderly health emphasize significant gaps in rehabilitation coverage and service provision. The TUSEB report highlights that most older adults lack access to comprehensive, continuous rehabilitation services, and current programs are often fragmented across hospitals, primary care, and social support systems (Türkiye Yaşlı Sağlığı Raporu, 2021). Embedding rehabilitation within governance mechanisms, health information systems, resource-allocation models, and primary-health-care services is crucial to elevate its status from a marginal service to an integral system element. Only then can health-system resilience, functional outcomes, and equity of access be reliably improved.

Underdeveloped Community-Based and Digital Models

Although technological capacity has expanded—particularly following the COVID-19 pandemic—systematic research on community-based, home-based, and tele-rehabilitation models remains limited. Studies evaluating cost-effectiveness, patient satisfaction, and clinical outcomes in digital environments are still scarce in Türkiye (Topbaş et al., 2023). Scaling up pilot programs and embedding digital rehabilitation protocols into national service delivery could significantly enhance access, particularly in rural and underserved regions.

Fragmented Data Infrastructure and Lack of Standardization

A sustainable rehabilitation ecosystem depends on robust data systems and standardized outcome measures. Currently, the absence of unified data collection frameworks and inconsistent application of international standards such as the *International Classification of Functioning, Disability and Health (ICF)* impede benchmarking and quality improvement (Stucki & Bickenbach, 2019). In Türkiye, limited pilot implementations of ICF exist, but they remain fragmented. Establishing a centralized national rehabilitation registry under the Ministry of Health could facilitate evidence-based decision-making and cross-institutional comparability.

Policy Priorities for a Sustainable Rehabilitation Future

In response to the identified structural and research gaps, a coherent framework of policy interventions is suggested:

Establish a Long-Term Care Insurance Scheme

Türkiye currently lacks a formal mechanism to finance long-term rehabilitation needs. A dedicated long-term care insurance scheme—integrated with existing health and social services—would provide sustainable funding for elderly, disabled, and chronically ill populations (Kara, 2025).

Diversify Rehabilitation Delivery Models

Expanding beyond hospital-based care toward hybrid models that combine home-based, community-based, and tele-rehabilitation services can enhance accessibility and reduce inequalities (Tschamper et al., 2021).

Standardize Assessment and Outcome Measures

Nationwide implementation of validated frameworks such as the International Classification of Functioning, Disability and Health (ICF) can substantially enhance data interoperability and support longitudinal monitoring of rehabilitation outcomes. Recent studies emphasize that integrating ICF-based metrics into national health information systems facilitates not only consistent data collection but also outcome comparability across institutions and regions (Kostanjsek et al., 2021; Prodinger & Tennant, 2023).

Establishing a centralized digital platform for rehabilitation outcome reporting would further promote transparency, accountability, and quality assurance within healthcare delivery. Such platforms, when aligned with international data standards, enable continuous evaluation of functional outcomes and guide evidence-informed policy decisions (World Health Organization, 2023).

Integrate Rehabilitation into Public Health and Social Strategies

Rehabilitation should be systematically embedded within national chronic disease, aging, and disaster management policies. Cross-sectoral collaboration among the Ministry of Health, municipalities, NGOs, and academic institutions can ensure continuity of care and promote public participation (WHO, 2023; Altındağ et al., 2022).

Invest in Workforce Training and Capacity Building

Expanding and diversifying the rehabilitation workforce is critical for long-term sustainability. Educational reforms should emphasize interdisciplinary and community-based training, while incentives should support deployment of professionals in underserved regions (OECD, 2023).

Summary and Future Directions

Bridging the gap between research and practice is essential for achieving sustainable rehabilitation in Türkiye. Strengthening longitudinal evidence, integrating rehabilitation into national health priorities, and developing standardized data systems will provide the foundation for more equitable and efficient care. Policymakers must view rehabilitation not as a supplementary service, but as a strategic investment in public health and social well-being. Future research should therefore adopt interdisciplinary, system-wide perspectives that align clinical outcomes with social and economic sustainability goals.

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Traditional and Complementary Medicine Practices: Integrative Approaches for Sustainable Health

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Introduction

The World Health Organization (WHO) defines traditional medicine as the collective body of knowledge, skills, and practices that are rooted in the theories, beliefs, and experiences unique to various cultures. These practices, whether they can be explained or not, are utilized for maintaining health and for the prevention, diagnosis, improvement, or treatment of physical and mental illnesses (WHO, 2000). Traditional medicine has a rich and well-documented history. Despite its long-standing presence, there is still no universally accepted definition of Traditional and Complementary Medicine worldwide.

History of Traditional and Complementary Medicine

The U.S. National Center for Complementary and Alternative Medicine (NCCAM), established in 1998, describes complementary medicine as the use of non-conventional practices alongside conventional medical treatments, while alternative medicine involves using such practices instead of conventional medicine. More recently, NCCAM has embraced the term integrative medicine, which refers to the coordinated use of evidence-based complementary therapies alongside conventional medical care (National Center for Complementary and Integrative Health [NCCIH], 2019).

Similarly, the European Federation for Complementary and Alternative Medicine (EFCAM) defines complementary and alternative medicine as a variety of healthcare practices aimed at maintaining and improving health, preventing diseases, and managing illnesses, either independently or in conjunction with conventional medical approaches (European Federation for Complementary and Alternative Medicine [EFCAM], 2019). Generally, when supportive methods are used in addition to conventional treatments, it is termed complementary medicine; when they replace modern treatments, it is called alternative medicine.

In Turkey, similar terminology has been in use for many years. However, aligning with WHO definitions, recent discussions have highlighted that "there can be no alternative to medicine itself—only to a particular treatment method." Consequently, the term Traditional and Complementary Medicine has become the preferred expression (Mollahaliloğlu, Uğurlu, Kalaycı, & Öztaş, 2015). To address uncertainties surrounding practices, which have been in use since ancient times and have seen increased application in recent decades, various regulations and centers have been established.

The first legal regulation in this field in Turkey was the "Regulation on Acupuncture Treatment," published in 1991. The most comprehensive regulation to date, the "Traditional and Complementary Medicine Practices Regulation," was issued by the Turkish Ministry of Health in October 2014. This regulation clearly outlines the purposes and scope of each practice, the types of diseases for which they may or may not be used, the training requirements, and the qualifications of the practitioners and healthcare institutions authorized to perform them.

Recognisation of Traditional and Complementary Medicine

For the first time, methods other than acupuncture were officially recognized including 15 practices (shown in table 1). These practices may be performed by medical doctors and, within their professional boundaries, by dentists and pharmacists. Public and private healthcare facilities are designated as practice units, whereas university hospitals and training/research hospitals are designated as practice centers. Training may be conducted only in practice centers approved by the Ministry of Health to ensure educational standardization. A scientific commission of eleven experts with prior experience in this field was also established (Mollahaliloğlu et al., 2015).

Phytotherapy

Phytotherapy refers to the prevention or treatment of diseases using medicinal plants. The term was first introduced by the French physician Henri Leclerc (1870–1955) in La Presse Médicale (Faydaoğlu & Sürücüoğlu, 2011). For medicinal use, plants must be investigated for safety and efficacy. Ensuring the absence of contamination and determining the standardized active substance concentration are crucial. Some European countries have implemented regulations for the standardization of herbal products, allowing them to be safely marketed in pharmacies and stores. These standards are evaluated by authorities such as WHO, Commission E, and the European Scientific Cooperative on Phytotherapy (ESCOP) (Uzun, Aykac, & Ozcelikay, 2014).

Table 1

Traditional and Complementary Medicine Practices Recognisation

Phytotherapy	Larval therapy
Mesotherapy	Prolotherapy
Music therapy	Hypnosis

Cupping therapy	Homeopathy
Ozone therapy	Hirudotherapy (leech therapy)
Osteopathy	Acupuncture
Rereflexology	Chiropractic
Apitherapy	

Larval Therapy

Maggot Debridement Therapy (MDT) utilizes sterile larvae of the green bottle fly (Lucilia sericata) (Ucar, Kus, & Firat, 2018; Tanyuksel et al., 2014). Early surgeons such as Baron Larrey (1829) and Joseph Jones observed during wartime that maggots selectively debrided necrotic tissue without harming viable tissue. Although MDT fell out of favor between 1950 and 1980 with the rise of surgical debridement and antibiotics, it regained acceptance in the 1990s and is now actively used in over 24 countries, including those in Europe. The U.S. Food and Drug Administration (FDA) officially approved MDT in 2004 (Tanyuksel et al., 2014).

Prolotherapy

The term prolotherapy combines "proliferation" and "therapy." It is used in the treatment of chronic musculoskeletal pain (Cakmak, 2017). The technique involves injecting proliferative or irritant solutions into damaged tissues (joints, tendons, or ligaments) to induce controlled physiological inflammation, thereby stimulating healing. The goal is to mimic natural healing by enhancing fibroblast activity and collagen deposition, strengthening weakened structures, and alleviating pain.

Music Therapy

The term music originates from the Greek words mousike or mousa and is used universally with the same meaning (Sezer, Sezer, & Toprak, 2015). Music therapy is one of the oldest known forms of treatment, with evidence suggesting its therapeutic use as early as 2000 BCE in various civilizations. Homer reportedly used music during surgical procedures and observed its positive effects. Plato, around 400 BCE, stated that music influences the depths of the soul, promoting tolerance and tranquility in individuals. Similarly, Celsus and Aretaeus noted the calming and restorative effects of music on the mind.

In Turkish history, music therapy reached its peak during the Seljuk and Ottoman periods. In darüşşifas (medical institutions dedicated to the treatment of mental illness), specific hours and days were reserved for therapy sessions involving music. Having persisted for centuries, music therapy continues to be practiced worldwide in the 21st century as an effective complementary treatment for both physical and psychological conditions.

Osteopathy

The first school of osteopathy was established by Andrew Taylor Still in 1892. Osteopathy is grounded in the philosophy that the body possesses an inherent ability to heal itself. Since Still believed that medications played a limited role in recovery, early osteopaths did not prescribe drugs. Instead, they emphasized the physician's responsibility to consider the structural and functional integrity of the body when diagnosing and treating disease.

The practice of Osteopathic Manipulative Treatment (OMT), developed by Still and his colleagues, was demonstrated to enhance blood circulation and facilitate the body's natural healing mechanisms (Parker et al., 2012). OMT consists of a variety of manual techniques performed by osteopathic physicians, aimed at correcting somatic dysfunctions and restoring physiological balance.

Mesotherapy

Mesotherapy involves intradermal or subcutaneous injection of very small quantities of active substances into specific regions of the body. The injected agents typically include natural plant extracts, minerals, vitamins, and homeopathic formulations. It is used in several medical disciplines, including dermatology (particularly cosmetic dermatology), rheumatology, sports medicine, and neurology. One of the key advantages of mesotherapy is that it achieves therapeutic effects with minimal drug quantities, thereby reducing the risk of systemic side effects (Gökdemir, 2014).

Chiropractic

According to the World Health Organization's 2005 guidelines, chiropractic is a healthcare discipline concerned with the diagnosis, treatment, and prevention of disorders of the neuromusculoskeletal system, and the effects of these disorders on general health. It emphasizes manual techniques, including spinal adjustment and manipulation, with a particular focus on correcting vertebral subluxations and facilitating the body's natural ability to heal (WHO, 2005).

Chiropractic manipulation is among the most widely practiced manual therapies worldwide. Within the European Union and neighboring countries, chiropractic is recognized as a regulated profession in 16 nations; in 10 others, chiropractic treatment is legally recognized though not professionally regulated; and in 13 countries, there is no legal framework for either. In Turkey, the Chiropractic Spine Health Association was established in 2008 to advance the field.

Homeopathy

Derived from the Greek words homoios (similar) and pathos (suffering), homeopathy is a therapeutic approach based on the "principle of similars." The concept—similia similibus curantur ("like cures like")—suggests that a substance causing symptoms in a healthy individual can, in highly diluted form, treat similar symptoms in a sick person. This principle dates back to Hippocrates and Paracelsus but was formally developed into a systematic medical approach by Dr. Christian Friedrich Samuel Hahnemann (1755–1843) (Ilhan, 2018). Other foundational principles of homeopathy include the use of single remedies and the administration of the minimal effective dose.

Ozone Therapy

Ozone (O_3) is a colorless, unstable gas with a pungent odor, composed of three oxygen atoms. The term ozone derives from the Greek word ozein, meaning "to smell." Ozone was first used for medical purposes by Fisch in 1932 (Dıracoğlu, 2016).

Because ozone oxidizes and disrupts the biological membranes of viruses, bacteria, and fungi, it has long been used as a disinfectant. In medicine, ozone therapy is believed to have immunomodulatory, antimicrobial, anti-inflammatory, antihypoxic, and wound-healing properties. It has been shown to stimulate both cellular and humoral immune responses, increasing the number of immunocompetent cells and enhancing immunoglobulin synthesis.

Reflexology

Reflexology is believed to have originated in ancient Egypt and China approximately 12,000 years ago, with the earliest documented evidence dating to 2500–2300 BCE (Dogru et al., 2017). It is proposed that reflexology elicits physiological responses through the stimulation of specific points on the hands, feet, and ears, corresponding to various organs and systems of the body. Each organ is thought to be represented by a particular area; applying pressure to these zones is believed to generate a therapeutic response in the associated organ.

Cupping Therapy

Cupping therapy was first practiced by the Assyrians in the Middle East around 3500 BCE, using animal horns and bamboo (Okumus, 2016). Modern cupping techniques are generally categorized as dry cupping and wet cupping (hijama). In both methods, cups are placed on the skin to create negative pressure. In wet cupping, small incisions are made to allow the release of blood. The external suction stimulates blood accumulation in the subdermal tissues and muscles, enhancing the delivery of oxygen and nutrients to local cells. This process accelerates local metabolism, increases hormone and enzyme production, and promotes the removal of harmful substances from the body.

Hirudotherapy (Leech Therapy)

Evidence from ancient Egyptian tombs indicates that leeches were used for medical purposes as early as 1500 BCE. Today, leech therapy is primarily utilized to prevent venous congestion following microsurgical replantation, trauma, or reconstructive surgery (Yildiz et al., 2014). Leeches belong to the phylum Annelida, class Clitellata, and subclass Hirudinea, encompassing over 15,000 known species. Medicinal leeches feed on blood, and specific species are selected for therapeutic use.

Apitherapy

Apitherapy refers to the therapeutic use of products derived from honeybees. The earliest evidence of apitherapy dates back approximately 6,000 years to Sumerian tablets. Records from the 3rd century BCE also describe the medicinal use of honey. Commonly used bee products include honey, propolis, pollen, beeswax, royal jelly, and bee venom (Trumbeckaite et al., 2015). Bee venom can be administered intradermally or subcutaneously, while other bee products may be applied topically or taken orally. Preparations used in apitherapy are FDA-approved.

Hypnotherapy

The medical use of hypnosis was first highlighted by Anton Mesmer (1734–1815), who theorized the existence of a magnetic fluid within the human body capable of facilitating healing. Marquis de Puységur (1751–1825) later described this state as somnambulism, noting that patients appeared to be asleep but remained hyper-alert.

James Braid (1795–1860), regarded as the founder of modern hypnosis, coined the term neuro-hypnosis to describe it as a neuropsychological state distinct from sleep (Ozgok, 2013). Contrary to popular misconceptions, hypnosis is not a state of sleep, amnesia, or loss of control. The individual remains conscious and aware but is less responsive to external stimuli, maintaining a focused state of attention.

Acupuncture

Acupuncture has been practiced in Asia for over 2,000 years. One of the earliest known texts describing acupuncture, Huang Di Nei Jing (The Yellow Emperor's Inner Canon), dates back to approximately 500 BCE. In traditional Chinese medicine, life energy—Qi—is composed of two opposing yet complementary forces, Yin and Yang. Health depends on maintaining balance between these forces. It is believed that Qi flows through pathways called meridians, and disease arises when this flow is disrupted. Inserting fine needles at specific points along these meridians is thought to restore balance and harmony within the body (Karasimav & Yildiz, 2015).

The number of needles used in acupuncture varies depending on the location and nature of the symptoms, as well as the patient's sensitivity. Needles may be manually or electrically stimulated, or left in place for a set period. Typically, three to four weeks of treatment are sufficient to achieve improvement in responsive patients. For chronic conditions, some improvement is expected after the first six sessions; if no progress is observed, further treatment is unlikely to be beneficial.

Traditional and Complementary Medicine in Turkey and Worldwide

With increasing life expectancy, the growing need for long-term care, and the rising prevalence of chronic and malignant diseases, public interest in Traditional and Complementary Medicine has significantly increased. Additional factors include time constraints in conventional healthcare settings and concerns regarding the side effects of pharmaceutical treatments. This interest is expected to continue to rise in the future (Oral et al., 2016).

In Turkey, the use of Traditional and Complementary Medicine is widespread across different populations. Studies have reported usage rates ranging from 60% to nearly 100%, depending on region and demographic group. Among older adults, the practical use is particularly high, with many combining it with conventional treatments. Cancer patients show variable usage rates (20-80%), while families with children report almost universal use, with most continuing these practices regularly (Sagkal et al., 2013).

Many patients hold strong expectations for recovery through Traditional and Complementary Medicine. Information about these methods is often obtained through the internet, media, or acquaintances rather than from healthcare professionals. Physician consultation rates remain low, while recommendation rates to others are high (Dedeli, & Karadakovan, 2011).

If physicians remain uninvolved in this process, misinformation and unsafe practices may persist. Therefore, healthcare professionals should be aware of patients' interest in this practice engage in open dialogue, and provide accurate guidance to prevent misuse. Clinicians—especially when treating chronic or treatment-resistant conditions—should inquire about patients' use of Traditional and Complementary Medicine and offer evidence-based information to ensure safety and informed decision-making.

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The Importance of Pilates for Pregnant Women and Principles of Practice

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Introduction

Pregnancy is a critical period in a woman's life when her biopsychosocial balance and her roles in the family and workplace change, and the parent-child relationship between mother and baby is established (Ünver & Aylaz, 2017). Pregnancy is a unique and complex stage in a woman's life. The associated changes occur not only at the biological and physiological levels but also at the psychological and physical levels. Changes in psychological functioning continue during pregnancy and into the postpartum period (Hussain & Bhandari, 2025). The physiological changes of pregnancy are caused by hormones secreted by the placenta. These changes result in a series of adaptations affecting all physiological systems. Sufficient oxygen and nutrients are delivered to both the mother and the developing fetus. These physiological changes cause alterations in biochemical test results (Gangakhedkar et al., 2021).

Pilates is a body-conditioning program that involves movements performed on the floor using body weight or accessories, such as exercise balls, resistance bands, exercise rollers, magic circles, and overballs (Ferraz et al., 2023). It can also be performed using specialized equipment, such as the Reformer, Cadillac, Wunda Chair, and staircase, to increase strength and endurance. Joseph Pilates developed the Pilates method in the 1920s. The original name of the Pilates method, "Contrology," reflects the method's emphasis on controlling posture and movement (Anderson, 2024). The traditional principles of Pilates exercise include centering, concentration, control, precision, flow, and breathing (Malhotra et al., 2025).

Psychological and Physical Changes During Pregnancy

During pregnancy, changes occur in physical appearance, emotional state, and sexuality (Hussain & Bhandari, 2025). Pregnancy is generally considered a period when women are more motivated to maintain a healthy lifestyle, including participating in physical activities and improving their health. There is also evidence that physical activity during pregnancy can improve psychological well-being (Atkinson & Teychenne, 2022; Boutib, et al., 2021). These changes make it difficult for women to adopt and maintain a healthy lifestyle during this period. These changes are often associated with common mood swings such as indecision, anxiety, fatigue, exhaustion, lethargy, melancholy, and elation. As body image, emotional state, and sexuality change during pregnancy, women's positions and roles also change (Hussain & Bhandari, 2025). Together with many established social and cultural beliefs about pregnancy, these changes create significant challenges for women in adopting and maintaining regular exercise during this period (Boutib, et al., 2021).

Regular physical activity provides significant benefits for both the mother and the fetus. Benefits for the mother include improved cardiovascular function, limited gestational weight gain, reduced musculoskeletal discomfort, fewer muscle cramps, and reduced lower-extremity edema, improved mood, and alleviation of gestational diabetes and gestational hypertension (Meyerhoff & Belew, 2024). Benefits for the fetus include reduced fat mass, improved stress tolerance, and increased neurological maturation. Although few studies directly examine the effects of physical activity on labor and delivery, evidence indicates that physical activity shortens labor duration and reduces cesarean delivery rates in women with normal pregnancies (Melzer et al., 2010).

Physical activity is a safe and effective way for healthy pregnant women to reduce the risk of adverse health outcomes. Physical activity can be defined as any bodily movement produced by skeletal muscles that requires energy expenditure. This includes activities in various areas such as recreation, sports, work, and household chores. Government agencies around the world, including those in Canada and the United States, recommend that all pregnant women participate in physical activity throughout their pregnancy. Healthy pregnant women are advised to engage in 150 minutes or more of moderate-intensity physical activity per week (Daşıkan et al., 2019). Physically active women report improvements in physical endurance and mood, as well as reductions in nausea, fatigue, and stress levels. Women and infants also gain long-term benefits from an active lifestyle; they have been observed following active pregnancies. Evidence suggests that pregnancy offers an opportunity to promote positive health behaviors (Erkek & Altınayak, 2024). This opportunity has been described as a "teaching moment" in a woman's life because her perception of risk has increased. Furthermore, strong emotional responses and the redefinition of social roles and responsibilities tend to motivate pregnant women to adopt positive health behaviors such as physical activity. Despite these benefits and the opportunities offered during pregnancy, physical activity levels are generally lower among pregnant women than in the general population (Currie et al., 2013). Physical activity can also be expressed in METs, which represent multiples of an individual's resting metabolic rate. MET scores represent the metabolic-equivalent intensity levels of activities. Moderate-intensity activity is classified as 3–5 METs. Therefore, 150 minutes of moderate-intensity activity is equivalent to 7.5-12.5 MET hours per week (Garber et al., 2011).

Australia's physical activity guidelines for pregnancy and the postpartum period recommend pelvic floor muscle exercises to reduce the risk and severity of pelvic floor muscle disorders (Walsh et al., 2025). Physical activity is associated with health benefits for people of all ages. Physical activity throughout pregnancy is safe and beneficial for both women and fetuses (Yang et al., 2022). Regular physical activity in healthy pregnant women is associated with improved cardiovascular health and with reduced risks of gestational hypertension, preeclampsia, gestational diabetes, and excessive weight gain during pregnancy (Gao et al., 2020). Pregnant women who are physically active or who exercise regularly are less likely to experience urinary incontinence, postpartum weight gain, and symptoms of depression. Strong scientific evidence shows that physical activity during pregnancy is not associated with low birth weight, stillbirth, preterm birth, premature rupture of membranes, neonatal death, neonatal hypoglycemia, birth defects, or induction of labor. Furthermore, exercising during pregnancy reduces the risk of chronic diseases such as obesity, type 2 diabetes, and cardiovascular disease in both women and their children (Yang et al., 2022).

Exercise during pregnancy is known to have benefits such as regulating the circulatory and digestive systems, helping the mother control her weight, supporting the muscle activity required for childbirth, and accelerating postpartum recovery. It can also prevent back pain, foot edema, varicose veins, and hemorrhoids. Systematic exercise during pregnancy and after childbirth plays an important role in functional treatment. Exercise during pregnancy is recommended to restore the tone of the vaginal and perineal muscles, reduce edema in the perineal region, improve circulation, prevent stress incontinence and abdominal muscle tension, thereby preventing abdominal sagging and back pain (Ünver & Aylaz, 2017). Strengthening the back and spine muscles is important for pregnant women. Strengthening the abdominal and pelvic muscles facilitates delivery. These muscles can be strengthened with exercises performed at home (Mens et al., 2000). For example, the pregnant woman lies on her back with her knees slightly bent. She sits up, attempts to touch her feet with her hands, then lies back down (a sit-up). This movement should be repeated 10 times. This movement strengthens the abdominal muscles. In another exercise, the pregnant woman lies on her back, knees slightly bent, and contracts her hip muscles as if trying to stop the flow of urine. This exercise strengthens the muscles she will use during childbirth. This strengthening movement is performed using Kegel exercises, which involve contracting and releasing the pelvic muscles and can also be considered a pushing movement. For example, the hip muscles are slowly contracted and held for 5 seconds, then are slowly released. This movement is repeated 25 times and performed twice daily (Ağaoğlu, 2015).

The Role of Pilates During Pregnancy

Internationally, Pilates is recognized as an important exercise for improving physical, psychological, and motor functions. This exercise program consists of a series of low-impact exercises that build strength and flexibility (Das & Bandyopadhyay, 2023). Because it is an exercise performed using one's own body weight, it carries the lowest risk of contraindications. Adopting a standardized breathing technique during Pilates practice is essential. It helps activate the deep stabilizing muscles, especially the transverse abdominis, in relation to the pelvis. This increases pelvic and trunk strength. Pilates movements are adapted to the physiological changes of pregnancy. Regular exercise has been shown to strengthen the pelvic floor muscles and improve their structural function. Pelvic floor exercises are part of modern Pilates (Szumilewicz et al., 2019). Pelvic floor exercises during pregnancy have been shown to prevent prolonged second-stage labor in approximately one in eight women (Salvesen & Mørkved,2004). Pregnant women practicing Pilates also use diaphragmatic breathing techniques, which help mothers prepare for childbirth. The breathing technique used in Pilates prepares the mother to use this method during childbirth. Pilates, by developing the ability to use the abdominal and pelvic floor muscles, improving flexibility, and promoting proper breathing, facilitates the birth process (Ghandali et al., 2021).

Pilates exercises improve postural stability in pregnant women, reduce fear of childbirth, and increase physical readiness. It alleviates back pain and improves pelvic alignment. Pilates also improves sleep quality and life satisfaction, lowers stress levels, and enhances birth outcomes. Therefore, incorporating Pilates into prenatal care programs may support maternal and newborn health and improve the overall pregnancy experience (Aman et al., 2025).

Physiological Effects of Pilates During Pregnancy

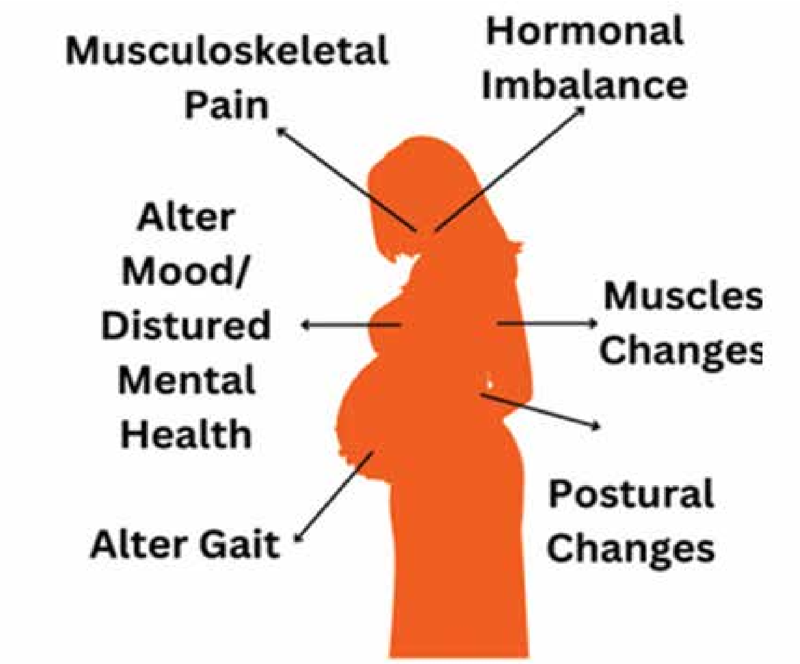
Exercise has traditionally been used as a non-invasive treatment for patients with obesity and depression, and its effectiveness has been demonstrated in various studies (Meneghin et al., 2020; Langoni et al., 2019). Studies of molecular mechanisms underlying the antidepressant effects of exercise have shown that exercise promotes activation of tryptophan in the brain, thereby increasing serotonin release and, by reducing insulin resistance, preventing depression (Kim & Hyun, 2022).

Changes in Posture and Spine

Postural changes during pregnancy shift the center of gravity forward as the uterus grows, leading to increased lumbar lordosis (an exaggerated inward curvature of the lower back). This compensatory mechanism not only helps maintain balance, but can also cause back pain by placing more stress on the lumbar spine (Figure 1). As pregnancy progresses, the transverse diameter of the rib cage increases and the diaphragm elevates. Increased pressure on the ribs due to fetal growth causes an increase in the subcostal angle. Thoracic Kyphosis In some cases, increased thoracic kyphosis (outward curvature of the upper back) develops to compensate for lumbar lordosis. This causes discomfort in the upper back, neck, and shoulders. The pelvis tilts forward. This also causes increased lumbar curvature and increased tension in the lower back muscles (Aman et al., 2025).

Figure1

Pregnancy and its related changes



Changes in Muscle Strength and Flexibility

As pregnancy progresses, loosening of the pelvic ligaments and increased abdominal weight lead to gait imbalance (Aman et al., 2025). This altered gait pattern increases the load on the lower extremities, causing discomfort in the hips, knees, and feet. The combination of joint laxity, shift in the center of gravity, and weight gain also contributes to walking instability, increasing the risk of falling (Artal & O'Toole, 2003; Cakmak & Erkin, 2011). During pregnancy, diastasis recti is common due to stretching of the abdominal wall to accommodate the growing fetus. This can weaken the abdominal muscles and lead to back pain and instability. Pregnant women often experience muscle cramps, especially in the legs. These cramps are caused by changes in circulation, increased pressure on the nerves, or electrolyte imbalances (Aman et al., 2025; Ho et al., 2009).

Strengthening the Pelvic Floor Muscles

The uterus is primarily supported by the pelvis and associated muscles (Chaudhry et al., 2023). Like other tissues, pelvic floor muscles and connective tissues are also affected by secreted hormones. However, increasing uterine weight places greater demands on the pelvic floor, making pelvic-floor muscle exercises essential during pregnancy. Some parts of the pelvic floor are controlled by the autonomic nervous system; these parts can also be affected by exercise and respond strongly to stress levels. Pelvic floor exercises should be prioritized and performed daily (Okeahialam et al., 2022).

Research shows that many young women today —often due to work-related factors— and women who have previously given birth suffer from weak pelvic floor muscles (Gümüşsoy, et al., 2021). Mothers who have given birth to babies weighing more than four kilograms or who have had forceps- or vacuum-assisted deliveries are at higher risk of pelvic floor problems (Kömürcü & Uğur, 2017). Strong pelvic floor muscles recover more rapidly after childbirth and demonstrate greater resilience. This helps prevent urinary incontinence and minimizes the risk of problems associated with back pain and pelvic instability. Both weak pelvic floor muscles and pelvic floor tension can cause problems. Pelvic floor weakness or dysfunction in women is associated with both structural and functional consequences, including urinary incontinence, fecal incontinence, pelvic organ prolapse, dyspareunia, and sexual dysfunction. One of the main risk factors associated with pelvic dysfunction is the reproductive process, including pregnancy and childbirth (Feria-Ramírez et al., 2021; Theodorsen et al., 2024). A Pilates exercise program is recommended to support pelvic floor muscle health before and after childbirth (Walsh et al., 2025). These recommendations are also inspired by the basic principles of exercise science and clinical reasoning (Walsh et al., 2025).

During pregnancy, abdominal and pelvic floor muscles should be exercised in a manner that does not cause diastasis recti abdominis. This promotes neural adaptations, supports muscle hypertrophy, and increases functional strength. It involves deep core activation and co-contraction of the pelvic floor muscles. Interventions that include deep core activation, particularly those that promote the synergistic contraction of the pelvic floor muscles, the transversus abdominis, and the diaphragm, support lumbopelvic stability and pelvic floor function (Walsh et al., 2025; Atkın et al., 2025).

Education and supervision

Because many women struggle to contract their pelvic floor muscles correctly after childbirth, education and supervision by trained healthcare professionals (e.g., women's health physical therapists or accredited exercise physiologists) may help ensure correct technique and improve educational outcomes (Walsh et al., 2025).

Personalized exercise prescription

Exercise interventions should be planned according to individual needs, especially considering common accompanying musculoskeletal health problems such as pelvic floor dysfunction, pelvic girdle pain, low back pain, and rectus diastasis (Örnek et al., 2023).

Effects of Pilates on Respiratory and Circulatory Systems

The growing popularity of Pilates worldwide has led to an increase in research on its effects (Souza et al., 2021). Pilates training has been shown to improve cardiovascular function in individuals with various pathologies such as chronic obstructive pulmonary disease, chronic kidney disease, ankylosing spondylitis, and cystic fibrosis (Sarmento et al., 2017). It has been observed to increase respiratory muscle strength and respiratory volume in healthy populations of different ages (Cancelliero-Gaiad et al., 2014). This method has also been shown to improve cardiovascular fitness in overweight or obese individuals and improve average heart rate, respiratory exchange ratio, and oxygen equivalent in sedentary individuals (Rayes et al., 2019).

Many pregnant women experience dyspnea, particularly during the second and third trimesters, because of the elevation of the diaphragm by approximately 4 cm (Petrenko et al., 2023). Some expectant mothers experience short breath. In some cases, the baby's movements and kicks toward the diaphragm can cause breathlessness and reduced lung expansion. Pilates increases lung capacity, reduces shortness of breath, promotes relaxation, and creates more space for the baby. The correct breathing techniques learned through clinical Pilates training relax and comfort the mother during contractions, muscle cramps or spasms, and discomfort caused by the baby's movements, thereby increasing her confidence during childbirth (Karapinar & Acar, 2023). This relaxation and loosening in the mother allow the mother's body to move normally and reduce the likelihood of hyperventilation and injury during delivery (Karapınar & Acar, 2023).

Pilates Exercises According to Pregnancy Stages

First Trimester (0–12 weeks): Risks to be aware of, threat of miscarriage, light exercise

The first three months of pregnancy constitute the riskiest period. It is important to start Pilates during this period. During this period, levels of the relaxation hormone increase, leading to joint laxity; therefore, exercises that place strain on the joints should be avoided (Parker et al., 2022). As the baby grows, the body's center of balance changes concurrently with hormonal changes (Bouariu et al., 2022). During this period, movements should be slowed, and the body's signals should be heeded. The focus should be on light breathing, posture, and awareness. Overheating and intense abdominal exercises should be avoided. Fatigue and nausea may limit activity, so pregnant women should constantly monitor their condition (Meyerhoff & Belew, 2024).

During this period, the fetus measures approximately 6–7 centimeters in length, weighs a few ounces, and resembles a miniature human (Pelz et al., 2025). Some reflexes are present. Heartbeats can be detected by ultrasound at six weeks' gestation. Physical symptoms during this period include fatigue, nausea, occasional vomiting, breast enlargement and increased breast sensitivity, mild weight gain, and increased urinary frequency. Psychological symptoms may include excitement, fear, and confusion. The fetal brain develops for up to six weeks; some neural tube defects occur during this period. Some causes have been linked to overheating during intense exercise (Bouariu et al., 2022). Most women do not realize they are pregnant until around the eighth week. By that time, the fetus is almost fully formed. During this trimester, the focus should be on establishing a routine that will support the person throughout the remainder of the pregnancy.

The first trimester of pregnancy is often an exciting yet intense period for expectant mothers. Stress can arise from the physical demands of the rapidly growing placenta and fetus, as well as from the psychological challenges of adapting to pregnancy (Wu et al., 2021). The risk of birth defects and miscarriages is highest during the first trimester of pregnancy. During this trimester, the fetus cannot regulate its own body temperature and is therefore dependent on the mother's body temperature. Expectant mothers should be cautious if they exercise intensely, engage in endurance training, or exercise in high temperatures during this period. However, body temperature changes significantly during pregnancy (Sexton et al., 2021). Body temperature typically decreases at the beginning of pregnancy. Hormones secreted during pregnancy increase cutaneous blood flow, leading to elevated skin temperature in certain body regions (Filipec & Đurin, 2025). This change in skin temperature increases body heat loss. Additionally, pregnancy lowers the body's sweat threshold. Pregnant women begin sweating earlier, thereby improving the body's cooling mechanism. Studies have shown that pregnant women who exercise cope better with heat than do non-pregnant women. Therefore, the risk is extremely low if long and intense training sessions and exercise in very hot weather are avoided.

Breathing and relaxation exercises

Breathing is one of the most fundamental functions of the human body. The way you breathe significantly affects how your body functions and, ultimately, your health and well-being. Joseph Pilates called proper breathing "fundamental" (Osar & Bussard, 2016). He believed that increased blood flow would activate the cells in your body and remove waste products associated with fatigue. Pregnant women need to learn to perform breathing and relaxation exercises correctly to make the process more comfortable. Sample exercises are provided for the first trimester (0–12 weeks) (Figure 2).

Figure 2

1st Trimester Sample Plate Exercises

Second Trimester (13–27 weeks): Balance and posture-focused exercises

The third through sixth months of pregnancy are the most comfortable for pregnant women. Abdominal muscle exercises and pelvic floor exercises should be started during this period (Liu et al., 2022). Supports, such as small Pilates balls, can be used during exercises. During this period, when the baby begins to grow and gain weight, changes in your body become more pronounced. Back and spine pain may begin during this period. Avoid overly strenuous movements. The second trimester is the most suitable period for regular exercise (Ribeiro et al., 2022). Energy levels return, nausea decreases, and Pilates movements can be performed safely with appropriate adjustments. As the umbilical region begins to enlarge, positions that normally require lying on your back for long periods are adopted. Exercises performed on your hands and knees, while sitting, or while lying on your side are ideal. Pelvic floor and abdominal stability exercises were initiated (Nipa et al., 2022).

During the second trimester, the mother generally feels better and experiences increased energy (Krzepota et al., 2018). For most women, morning sickness has subsided. However, some women experience nausea throughout the entire nine months. This can be quite challenging because it is sometimes difficult to eat enough. Therefore, fatigue and reduced energy levels become contributing factors. As the uterus rises into the abdominal cavity, the pregnancy becomes more noticeable. This causes round ligament pain. The mother feels the baby move at around 18–22 weeks. Normal weight gain by the end of this trimester ranges from 8 to 12 kg (Drehmer et al., 2013). Psychological symptoms are as follows: the mother is more relaxed about the pregnancy and begins to feel excited. There is generally a greater sense of well-being during this period.

The fetus is approximately 35 cm long and weighs 0.5–1.0 kg. By the end of this trimester, the mother looks quite pregnant (Islam et al., 2024). She may complain of feeling large, but this is not comparable to how she will feel at the end of her pregnancy. At about five months' gestation, the uterus typically extends beyond the pelvic cavity, sometimes causing round ligament pain. The round ligament helps the uterus attach to the pelvis. When the uterus expands rapidly, it stretches these ligaments, causing some pain. Stretching the hips may provide some relief. Breathing becomes shallower, and the rib cage begins to expand (Ejikeme et al., 2025). Back and lateral chest breathing techniques are used to stretch the intercostal muscles, allowing the uterus to enlarge and shift upward. Women experiencing their second or subsequent pregnancy reach this stage more quickly than first-time pregnant women. Supine hypotension syndrome becomes a problem during this trimester. This occurs when the inferior vena cava is compressed while the patient is supine (Hendem et al., 2023). Symptoms in the mother include shortness of breath, dizziness, and nausea. This is a period during which blood flow to the fetus is reduced. Turning the mother onto her side corrects the syndrome. If the mother has no obvious signs of compression, short periods of supine exercise are permitted. This can be alternated with side-lying exercises. The mother may begin to experience back pain at this stage. Pelvic exercises are one way to alleviate this problem.

Basic exercises for the second trimester (Figure 3)

Neutral/anterior pelvic alignment

At this point, the pelvis begins to tilt forward. It tries to maintain balance with the surrounding muscle groups.

Lateral flexion

This exercise is included in the program to help maintain intercostal muscle tone and accommodate the expansion of the rib cage.

Thoracic extension

Strength in the upper body and arms continues to be maintained. As the pelvis moves forward, the body tends to lean backward to counteract gravity.

Obliques and transversus

These become increasingly tense at this point. Continue performing light exercises that incorporate breathing techniques.

Pelvic floor

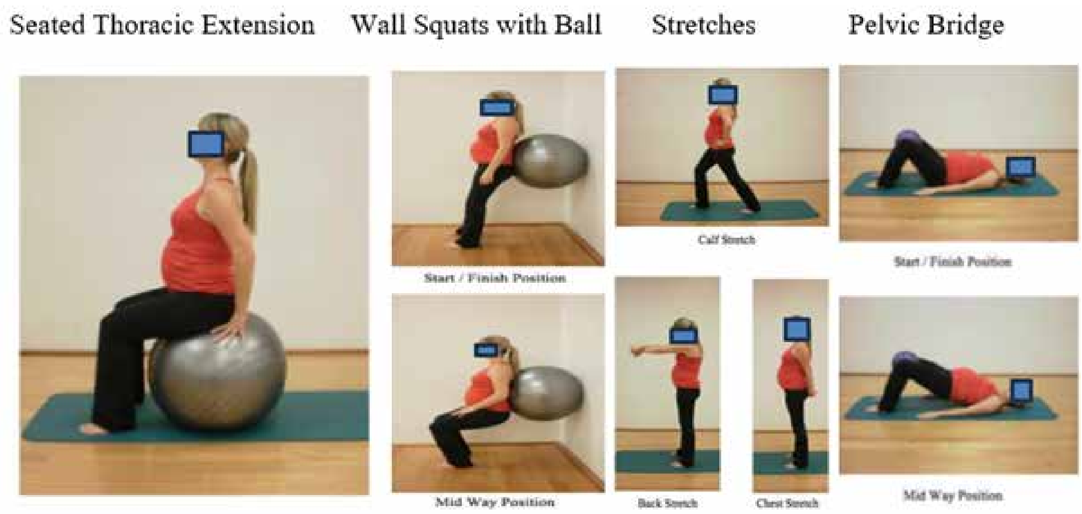
Continue with the pelvic floor series and related exercises.

Breathing

Use lateral and posterior chest breathing to stretch the intercostal muscles. When exhaling, try to release your body rather than tensing it.

Figure 3

2nd Trimester Sample Pilates Exercises



Third Trimester (28–40 weeks): Relaxation, breathing exercises, and preparation for childbirth

During the final three months of pregnancy, focus on exercises that facilitate delivery. Focus on maintaining gentle mobility, balance, and comfort. Avoid deep stretching exercises that put pressure on the abdomen or require strength. Physical Symptoms in the Third Trimester: As the baby's weight and height increase, the mother may begin to tire more easily (Aman et al., 2025). The infant will require increased caloric intake during this period to mobilize fat reserves. Swelling of the hands, ankles, and feet is likely to occur. Shortness of breath and faintness may occur. Braxton Hicks contractions may occur. Psychological Symptoms: The mother may feel hopeless and wish the pregnancy to end as soon as possible. She may experience excitement and fear of childbirth. Towards the end of this trimester, she may experience a feeling known as the "nesting instinct" (Kersting et al., 2009).

Immediately before birth, the baby is 40-55 cm long and weighs 3.3-4 kg (Subhan, 2013). Most women experience fatigue during the third trimester; therefore, exercise must be adjusted accordingly. Infants are currently experiencing rapid growth. Balance is impaired because the center of gravity has changed significantly. Although the scientific literature provides no details about falls, an instructor should pay particular attention to clients who are in unstable positions. Exercising up to shortly before delivery is not harmful to pregnant women. However, many women stop earlier because any additional movement becomes excessively tiring and uncomfortable. Towards the end of their pregnancy, women can plan the program that will be implemented after childbirth. Postpartum exercises to strengthen the deep abdominal muscles and the pelvic floor can be started immediately after childbirth.

Blood Pressure

Blood pressure is a measure of the pressure exerted by blood on the walls of the arteries. Standing can temporarily affect blood pressure. For example, if a pregnant woman stands for prolonged periods, blood may pool in the lower extremities, causing dizziness. During pregnancy or childbirth, when a woman lies on her back, maternal blood pressure may fall owing to the weight of the uterus compressing the aorta and inferior vena cava (or iliac veins) (Salles et al., 2015). The aorta carries oxygen-rich blood from the heart to the systemic circulation, while the vena cava carries oxygen-depleted blood from the lower half of the body back to the heart. Both blood flows pass through the spinal canal and can be affected by the additional weight of the uterus when lying on your back.

This can impede blood flow to the uterus and heart. Hypotension (a drop in blood pressure) should be monitored while lying on your back.

Balance

Women typically gain 25–30% of their pre-pregnancy body weight during pregnancy. Most of this weight is concentrated in the abdominal area, shifting the center of gravity. Additionally, pregnant women have relatively higher estrogen and lower testosterone levels. Testosterone facilitates balance, spatial orientation, and hand-eye coordination. Pilates-based exercises can help regulate hormonal balance, limit the turmoil caused by physical and emotional changes, and thus contribute to the expectant mother's physical and emotional relaxation (Sancar et al., 2021).

Fluid Retention

Approximately 70% of the human body is water. During pregnancy, hormone secretion causes the walls of the blood vessels and lymphatic vessels to relax, significantly increasing the volume of fluid in the blood and body tissues, including cells. As a result, toward the end of pregnancy, a woman's body can retain several liters of fluid. About half of the weight gained during pregnancy is usually attributable to excess fluid, which is distributed throughout the body. This fluid is found in the blood, organs, tissues, and muscles, where it aids pregnancy (Demir, 2022). Pilates-based exercises can help prevent swelling (edema) resulting from interstitial fluid accumulation in the subcutaneous tissue by promoting circulation and redistribution of excess fluid.

Basic exercises for the third trimester

Emphasis should be placed on exercises that stretch the pelvic floor muscles. At this stage, breathing is usually shallow and confined to the chest cavity. You should try to take deep abdominal breaths.

Pelvic mobility

Pelvic tilts, hip circles, and bridge movements are used to maintain flexibility in this area.

Spine and pelvic stability

Light abdominal exercises should be performed in conjunction with breathing.

Stretching

Focus on the inner thighs, hips, spine, and pelvic floor.

Pelvic floor

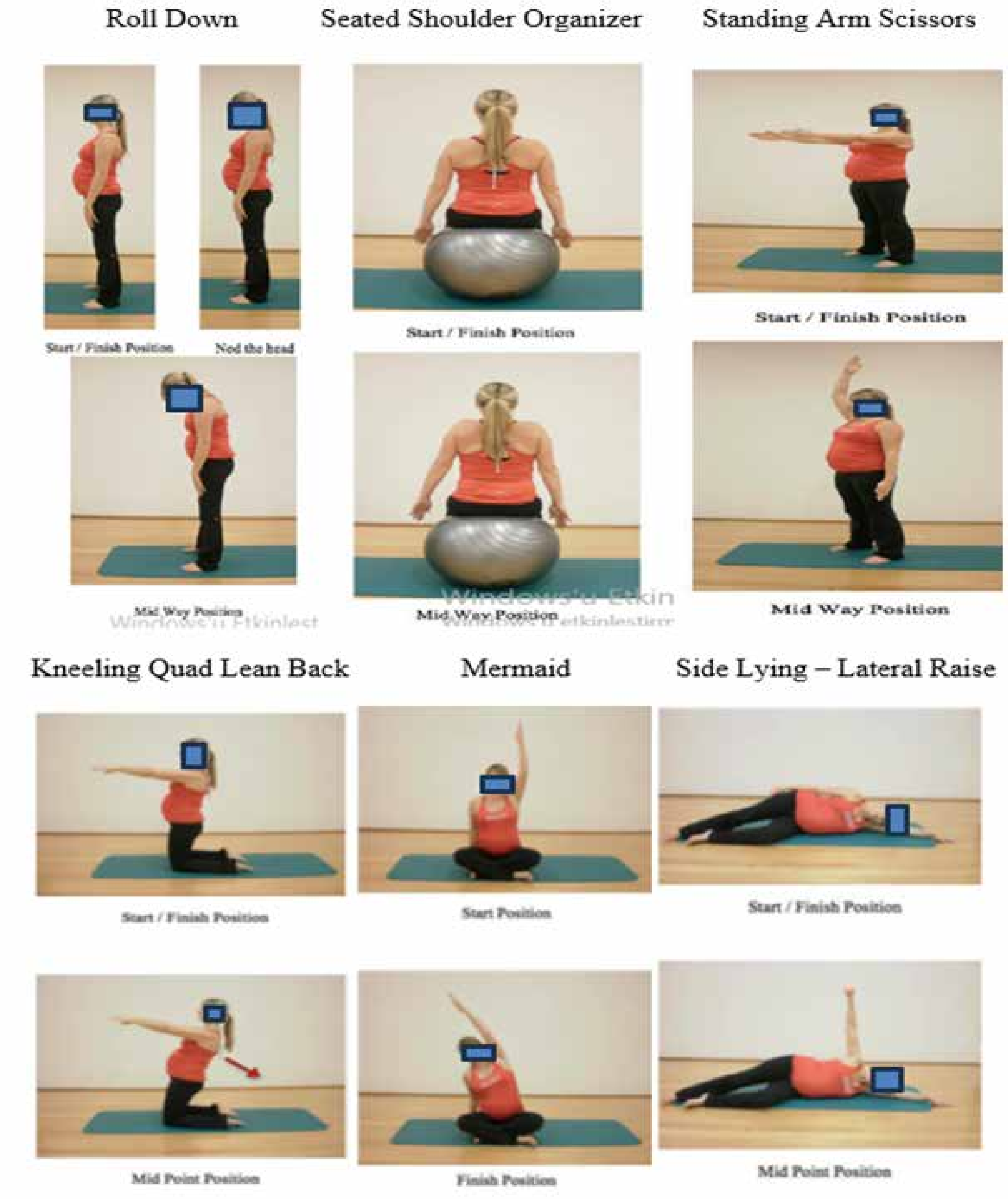
It is important to stretch and relax in this area.

Breathing

Focus on deep abdominal breathing to promote relaxation and improve concentration. Breathing, relaxation, and visualization are particularly important throughout this trimester.

Figure 4

3rd Trimester Sample Plate Exercises



The Benefits of Pilates for Pregnant Women

Exercise or physical activity has positive effects during pregnancy, childbirth, and the postpartum period (Malhotra et al., 2025). Prenatal exercise is vital for ensuring optimal health for both the mother and the unborn baby. However, increased encouragement and recommendations for physical activity are needed, especially in developing countries (Yimer et al, 2024). In the past, pregnant women were generally advised to rest and reduce physical activity. However, in 1985, the American College of Obstetricians and Gynecologists published recommendations for physical activity during pregnancy. This led to a substantial shift in public perceptions regarding exercise during pregnancy (Davenport, 2020). Health professionals recommend that low-risk pregnant women begin or continue aerobic and progressive resistance training before conception, during pregnancy, and in the postpartum period (Yimer et al., 2024; Davenport, 2020).

Studies have shown that the Pilates approach provides benefits for both healthy and unhealthy individuals, including improvements in posture, abdominal, pelvic, and muscular stability (Wells et al., 2012). This technique aims to improve muscle coordination by increasing the flexibility of hypertrophic muscles and by strengthening the weakest muscles. This allows the user greater control over bodily movements without risking injury to their back or joints. Breathing and pelvic floor muscle contraction techniques are part of contemporary Pilates exercise routines. Breathing is synchronized with the contractions of the pelvic floor muscles, and the abdominal muscles are activated simultaneously in various situations (Pedriali et al., 2016). Pilates strengthens the abdominal muscles and improves respiratory muscle function, thereby preventing abdominal muscle weakness and disorders of respiratory mechanics. Since the exercises are performed in conjunction with pelvic floor muscle contractions, Pilates strengthens the pelvic floor muscles (Malhotra et al., 2025).

Pilates prepares the abdomen and pelvic floor for childbirth. Therefore, considering the advantages of Pilates exercises during childbirth, abdominal breathing during Pilates helps women cope with contractions more easily, push the baby out more effectively, have a more comfortable birth, and sustain fewer perineal tears (Güder, 2021). Pilates reduces back, waist, and hip pain, increases body awareness in preparation for childbirth, reduces stress and anxiety, and facilitates postpartum recovery. Pilates improves physical conditions by reducing the progression of abdominal diastasis, decreasing fatigue, maintaining anthropometric and hemodynamic parameters, increasing abdominal and pelvic floor strength, improving hamstring flexibility, enhancing lumbopelvic stabilization, improving posture, functional capacity, and quality of life (Mendo & Jorge, 2021).

Points to Note

Some restrictions have been recommended for pregnant women regarding Pilates and exercise in general. For example, it is recommended that abdominal exercises be modified to prevent significant separation of the rectus abdominis muscle (Carlstedt et al., 2021). Pregnant women are also advised to avoid prolonged exercise in the supine position to prevent obstruction of venous return from compression of the inferior vena cava by the growing uterus. Absolute contraindications for aerobic exercise in pregnant women include cervical insufficiency, persistent bleeding, and ruptured membranes. Relative contraindications include severe anemia and poorly controlled type I diabetes. Therefore, it is recommended that pregnant women undergo routine screening before starting exercise to assess general health, medical and obstetric risks, and physical capacity (Mazzarino et al., 2018).

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Quantum Nutrition And Health Sustainability

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Introduction – The Basis of Quantum Nutrition and Sustainability of Health

Introduction to Quantum Nutrition

Quantum nutrition, unlike modern nutrition science, is an approach that considers the energy dimension of the human body and the universe. Traditional nutrition science typically focuses on macro and micronutrients, calories, and metabolic functions (Capra, 2010). However, quantum nutrition goes beyond these to examine dimensions such as energy, frequency, and biophoton information. Therefore, in quantum nutrition, matter, energy, and information are considered together (Schrödinger, 1944).

The human body is not only a chain of biochemical reactions but also an electromagnetic system. Every cell, every organ, and every thought emits a specific vibrational frequency. These frequencies determine both bodily energy distribution and mental and emotional balance. Quantum nutrition aims to balance these frequencies (Popp, 1999).

Therefore, three important dimensions stand out in quantum nutrition:

1. Article Dimension: Classic nutrients and metabolic functions.
2. Energy Dimension: Vibrational frequency of foods and their effect on body energy.
3. Information Dimension: Biophotons and the capacity of nutrients to carry life information

Continuity and Protection of Health

Maintaining health isn't just about preventing disease; it also involves maintaining cellular, mental, and emotional balance. The quantum nutrition approach ensures this balance through three fundamental mechanisms:

1. Optimizing Cellular Energy: Mitochondrial activity, ATP production, and free radical balance. High-frequency foods support cellular energy production.
2. Balancing the Energy Field: Electromagnetic pollution and stress can disrupt cellular ionic balance. Grounding, mineral balance, and consuming living water

stabilize the energy field.

3. Biophoton Information Flow: Fresh, natural, sunlight-grown foods are recommended to strengthen intercellular communication. These foods increase the exchange of energy and information between cells.

The goal of quantum nutrition is to improve the health and quality of life by harmonizing the physical, mental and energy fields of the individual (Szent-Györgyi, 1941). The energy field can be distorted by stress and electromagnetic charges, so balancing techniques are important (Cifra et al., 2011).

Nutrition and Energy Relationship

Foods are not only substances that perform metabolic functions; they are also carriers of vibrational energy. The frequency of a food depends on factors such as the minerals of its growing environment, sunlight exposure, and water quality. For example, fresh fruits and vegetables have a high frequency (~70-90 MHz); sprouted seeds and foods containing live enzymes have a high frequency (~80-100 MHz); cooked, processed foods have a low frequency (~5-15 MHz); refined sugars and processed oils have a nearly zero frequency. These differences directly affect the body's energy field. High-frequency foods accelerate cellular communication, while low-frequency foods can lead to energy blockages and metabolic slowdowns (Popp, 1999).

Thought, Intention and Energy Field

Intention is crucial in quantum nutrition. Dr. Masaru Emoto's studies on water crystals have shown that water is sensitive to emotion and thought. Because the human body is composed of 70% water, one's emotional state during eating directly affects one's energy field: food eaten with love and gratitude has healing effects at the cellular level, while food eaten with guilt or anger disrupts the energy field and has toxic effects. Therefore, quantum nutrition encompasses not only "what you eat" but also "how you eat" (Emoto, 2004).

Scientific Basis for Quantum Nutrition

Quantum nutrition is based on biophoton theory, quantum biology and electromagnetic energy field research:

- Fritz-Albert Popp (1981) discovered that living cells emit light and showed that this light is a biophoton.
- Mitochondrial Electron Transfer: Provides energy efficiency through quantum tunneling mechanisms.
- Neuronal Communication: Quantum entanglement and electron tunneling speed up synaptic transmission.
- Plant and Nutrient Frequency Measurements: High frequency nutrients measured by spectroscopy increase cell energy production (Hameroff & Penrose, 2014).

Quantum Physics: Basic Concepts and Quantum Tunneling

Fundamental Principles of Quantum Mechanics

Quantum physics is the branch of science that studies the behavior and interactions of subatomic particles. The laws of classical physics describe the motions of the macroscopic world, but at the atomic and subatomic levels, probability, energy quanta, and wave-particle duality come to the fore. The fundamental principles of quantum mechanics are:

1. Wave-Particle Duality: Particles exhibit both wave and particle properties. Electrons, photons of light, and even atoms exhibit this behavior. This is effective in processes such as electron transfer and synaptic transmission in biological systems.
2. Superposition: A particle can exist in more than one state simultaneously. Superposition is observed in quantum biological processes such as enzyme activity and mitochondrial energy production.
3. Quantum Entanglement: Distant particles can instantaneously share information despite being independent of one another. This phenomenon is a debated topic, particularly in processes such as cellular signaling and hormone transfer.
4. Quantum Tunneling: A particle that cannot overcome energy barriers can pass through the other side of the barrier thanks to the tunneling effect. This is a critical mechanism in the electron transport chain, photosynthesis, and some enzyme reactions (Penrose, 1999; Schrödinger, 1944; Hameroff & Penrose, 2014).

Biological Significance of Quantum Tunneling

Quantum tunneling plays a direct role in intracellular energy production and metabolic processes:

- Mitochondrial Electron Transfer Chain: Electrons overcome energy barriers and enable the production of ATP.
- Enzyme Catalysis: Quantum tunneling makes it easier for reactant molecules to overcome energy barriers.
- Photosynthesis: Plants convert light energy into chemical energy with maximum efficiency through quantum tunneling.

Quantum tunneling allows energy barriers to be overcome in a way that defies the laws of classical physics (Schrödinger, 1944). This mechanism plays a role in the mitochondrial electron transport chain, ATP production, and photosynthesis (Cifra et al., 2011).

Quantum Entanglement and Human Biology

Entanglement allows distant particles to instantly exchange information. In the human body, entanglement can potentially affect:

- Neuronal Transmission: The flow of information between synapses is accelerated.
- Hormone and Signal Transmission: Instant coordination of distant cells is

achieved.

- Energy Field Balancing: Physical and mental harmony is supported by the entanglement effect.

Quantum entanglement enables instantaneous information transfer between distant particles (Einstein, Podolsky & Rosen, 1935). This phenomenon is one potential explanation for neuronal communication and signal coordination in biological systems (Hameroff & Penrose, 2014).

Quantum Mechanics and Nutrition Relationship

Quantum effects play a critical role in our understanding of the energy and information dimensions of food:

1. Electron Transfer and Antioxidants: Electrons in foods protect cells by interacting with free radicals. Quantum tunneling increases the efficiency of this electron transfer.
2. Photo and Biophoton Interaction: Fresh, natural, and sunlight-grown foods contain high levels of biophotons. This light optimizes information transfer between cells.
3. Vibrational Frequency and Energy Field: Every food has its own vibrational frequency. Quantum mechanical effects synchronize the body's energy field with the food frequencies.

Electron transfer, antioxidant interactions, and biophoton behavior operate at the quantum level (Popp, 1999). It is thought that high -biophoton nutrients may enhance cellular communication.

Quantum Tunneling Examples

Table 1

Quantum Tunneling Examples

Period	Molecular Mechanism	Quantum Role	Nutrition Connection
ATP production	Electron transfer	Tunneling	High-frequency foods increase energy production
DNA repair	Proton tunneling	Mutation prevention	Supports antioxidants and alkaline water
Synaptic transmission	Electron superposition	Fast information transmission	Omega-3 and phospholipids support frequency

Electron tunneling in ATP production (Cifra et al., 2011). Proton tunneling in DNA repair. Electron superposition in synaptic transmission (Hameroff & Penrose, 2014).

Quantum Physics and Health Perspective

Quantum biology is revolutionizing our understanding of human health. Cellular metabolism operates not only chemically but also at the energy and information level. The electromagnetic environment (Wi-Fi, cell phones) can influence the energy field; quantum understanding defines balancing strategies. Quantum awareness is directly related to nutritional choices and lifestyle.

Quantum physics:

- Explains the energetic basis of the universe at the subatomic level.
- Quantum tunneling optimizes biological energy production and metabolic processes.
- Entanglement and superposition accelerate cellular communication and information transfer.
- Nutrition interacts with quantum effects at the energy and information level.

Quantum biology emphasizes the importance of quantum effects in cellular metabolism and energy production (Szent-Györgyi, 1941). Electromagnetic environmental conditions can affect cellular frequencies.

Quantum Nutrition – Basic Principles

Definition of Quantum Nutrition

Quantum nutrition is a holistic approach that evaluates foods not only in terms of calories, vitamins, and minerals, but also in terms of energy, vibration, and information. This approach integrates the biochemical and energetic effects of nutrition.

The fundamental principle of quantum nutrition is: "Every food interacts with our cells on both a physical and energetic level; high-frequency and conscious consumption optimizes health." This principle operates on three levels:

1. Item Dimension: Macro and micronutrients, metabolic functions.
2. Energy Dimension: Vibrational frequency and electromagnetic compatibility.
3. Information Dimension: Biophotons and nutrients transfer life information.

Quantum nutrition is defined as a holistic approach that evaluates foods not only in terms of calories and nutrients but also in terms of energy, frequency, and information (Popp, 1999; Capra, 2010). In this approach, every food is assumed to have three layers: matter, energy, and information (Schrödinger, 1944).

Energy and Frequency in Quantum Nutrition

Foods affect body energy not only through their molecular structure but also through their vibrational energy. Each food acquires a unique frequency due to the minerals, water structure, and sunlight of the environment in which it grows. Frequency differences demonstrate how foods affect the energy field. High-frequency foods accelerate communication between cells, while low-frequency foods can create energy blockages. The vibrational frequency of foods varies depending on the minerals, sunlight, and water structure of the environment in which they grow (Popp, 1999).

Information Dimension of Foods: Biophotons

Fritz-Albert Popp's research, living cells emit biophotons, and this light serves as a means of transmitting information. This flow of information enables coordinated cell function. Foods with high biophotons include sun-ripened fruits and vegetables, organic sprouts, and foods with low biophotons, such as foods heated in microwaves and processed foods for extended periods. The importance of biophotons lies in optimizing cellular communication, balancing the energy field, and supporting metabolic functions. Fritz-Albert Popp Biophoton research shows that living cells emit ultra-weak light and that this plays a role in biological communication (Popp, 1999; Cifra et al., 2011).

Matter Dimension in Quantum Nutrition

The matter dimension is the domain of classical nourishment. However, in quantum nourishment, this dimension is integrated with the dimensions of energy and information.

1. Carbohydrates: A source of energy for cells. However, refined carbohydrates can cause electron loss and lower energy frequency.
2. Proteins: Amino acids build muscle tissue and enable the production of neuropeptides. Communication between neurons is accelerated by quantum effects.
3. Fats: Omega-3s and phospholipids keep cell membranes flexible. They are critical for neural frequency transmission at the quantum level.
4. Vitamins and Minerals: Play a role in electron transfer. Ionic conductivity optimizes energy flow.

Carbohydrates, proteins, fats, vitamins, and minerals are fundamental components of classical nutritional science; however, in the quantum approach, they are considered together with cellular energy flow and electronic communication (Szent-Györgyi, 1941). Phospholipids in the structure of the cellular membrane are reported to play a critical role in neural frequency transmission.

Energy Dimension in Quantum Nutrition

The energy dimension examines the vibrational frequency of foods and their cellular resonance effects. High-frequency foods increase cellular energy production and strengthen immunity. Low-frequency foods lead to low energy, mental dullness, and metabolic blockage. For example:

- Spinach and broccoli → Increases the energy field
- Refined flour foods → Lowers the energy field

High-frequency foods support cellular energy production and immunity, while low-frequency foods can lead to energy blockage (Cifra et al., 2011).

Information Dimension in Quantum Nutrition

The information dimension relates to biophotons and the life information in nutrients. According to quantum biology:

- Communication between cells occurs in the form of light.
- Foods grown with sunlight are rich in biophotons.
- Foods heated in the microwave lose this information.

Table 2

Biophoton Density of Foods

Food	Natural (Sun)	In the greenhouse	Microwave
Tomatoes	Very High	Middle	Low
Spinach	High	Middle	Low
Carrot	High	Middle	Low

Biophoton density is a determinant of cellular information transfer (Popp, 1999). Sun-grown vegetables and sprouts contain high biophoton, while processed foods contain low biophotons.

Application Principles in Quantum Nutrition

1. Consuming fresh and organic food: Provides high frequency and biophoton support.
2. Alkaline water and mineral balance: Optimization of cellular pH and energy.
3. Eating slowly and consciously: Intention is important for the energy field and biophoton flow.
4. Mindfulness ritual: Gratitude and positive intentions at mealtime support the energy field

Basic principles of quantum nutrition:

- Article Size: Classical nutrition and metabolic functions.
- Energy Dimension: Vibrational frequency and energy effect of foods.
- Information Dimension: Biophoton and life information transfer.

Consuming fresh and organic foods (Popp, 1999), alkaline water and mineral balance (Cifra et al., 2011), eating slowly and consciously, regulating the energy field with intention (Emoto, 2004) are integrated with the harmony of these three dimensions, physical health, energy field balance and conscious awareness.

Human Energy Field and Electromagnetic Effects

Definition of the Human Energy Field

The human body is not just a biological machine; it is also a dynamic system surrounded by an energy field. This energy field is a combination of electromagnetic waves vibrating at various frequencies (Popp, 1999).

- Aura: The visible or measurable energy layer surrounding the body.

- Chakras: Energy centers affect organs and emotional states.
- Meridians: Energy pathways defined in Chinese medicine; directly linked to nutrition and electromagnetic interaction.

The aura, chakras, and meridians have been identified as fundamental components of energy flow (Oschman, 2000). This energy field is directly related to cellular communication, hormone activation, and nervous system functions (Cifra et al., 2011).

Electromagnetic Frequencies and Body Energy

Every organ and cell vibrates at a specific frequency. These frequencies are affected by environmental electromagnetic fields.

Every organ vibrates at a specific frequency; the heart operates in the range of 0.8–1 Hz, and the brain in the range of 4–40 Hz (McCraty et al., 2009). Electromagnetic fields emitted from electronic devices can affect cellular ion balance and energy frequency (Pall, 2013).

Table 3

Electromagnetic Frequencies and Body Energy

System	Natural Frequency (Hz)	External Influences	Conclusion
Heart	0.8–1.0	Stress, Wi-Fi	Irregular rhythm, decreased energy
Brain	4–40	Screen light, electromagnetic field	Loss of concentration, sleep disturbance
Eyebrow	10–15	Mobile device use	Loss of energy, fatigue

Electromagnetic Loads of Modern Life

Cell phones, Wi-Fi, magnetic resonance devices, and artificial light are the primary factors that affect the energy field. These effects include:

- It disrupts the ion balance in the cell membrane.
- It creates energy blockage.
- It is associated with chronic fatigue and mental fog.

Suggested balancing strategies:

1. Earthing: Contact with the ground with bare feet for 10–15 minutes.
2. Mineral support: Ion balance is achieved with magnesium, potassium and zinc intake.
3. Living water consumption: Natural Spring water in glass bottles.
4. Adaptogen herbs: The energy field is protected with Ashwagandha, ginseng and reishi mushroom.

Wi-Fi, cell phone radiation, artificial light, and magnetic fields can disrupt the energy field. This can lead to cellular stress, sleep disturbances, and low energy levels (Pall, 2013; Reiter et al., 2014). Grounding has been scientifically shown to balance the energy field by regulating ion balance (Chevalier, 2012).

Human Energy Field and Nutrition

Nutrition affects not only the metabolic but also the energy field:

1. High frequency nutrients: Increases cellular energy production.
2. Low frequency foods: Creates energy blockage and frequency drop.
3. Biophotons: Optimizes information transfer between cells.

Example:

- Green leafy vegetables and sprouts → Strengthens the energy field.
- Refined sugar, alcohol → Causes low energy and congestion.

Foods carry not only chemical but also electromagnetic information (Popp, 1999). High-frequency foods strengthen the energy field, while processed foods can lower the frequency (Cifra et al., 2011).

Electromagnetic Balance and Nutrition Interaction

To understand the relationship between nutrition and the energy field, the minerals magnesium, zinc, and potassium maintain balance between the cell membrane and the energy field. Alkaline water increases pH balance, ionic conductivity, and supports frequency matching. Adaptogen plants protect the energy field and combat electromagnetic stress. Minerals such as magnesium, potassium, and zinc regulate ionic communication in the cell membrane (Wallace, 2013). Alkaline water increases pH and ionic conductivity, thus balancing the energy field (Tanaka et al., 2016).

Quantum Nutrition Perspective

Quantum nutrition enables the integration of nutrition with the energy field; foods with high energy frequencies increase the energy field. Biophotons support the flow of information between cells. Alkaline water and minerals provide electromagnetic harmony. Thought and intention: Increases or decreases the energy effect of foods.

- The human body is a dynamic energy field and its frequency is shaped by nutrition, environment and emotions.
- Modern electromagnetic charges can disrupt the energy field
- Quantum nutrition maintains health by optimizing the energy field and nutrient frequency.

Quantum nutrition addresses health in a holistic way by bringing together the energy field, biophoton communication, circadian rhythm and electromagnetic balance (Capra, 2010).

Quantum Properties of Food – The Trinity of Matter, Energy and Information

The Trinity of Matter, Energy and Knowledge

One of the most important concepts of quantum nutrition is that every food has a three-layered structure:

1. Matter Dimension (Physical Nutritional Value)
2. Energy Dimension (Vibrational Frequency)
3. Information Dimension (Biophoton and Life Information)

These three dimensions work together to influence both biochemical metabolism and the electromagnetic energy field. This approach is based on the foundations of biophoton theory and quantum biology (Popp, 1999; Cifra et al., 2011). Schrödinger's explanations of the physical basis of life emphasize the importance of energy and information flow in living systems (Schrödinger, 1944).

Item Dimension (Physical Nutrition)

The substance dimension encompasses the macronutrients and micronutrients studied in classical nutritional science. This dimension determines the body's basic building blocks and energy production processes.

- *Carbohydrates:* The primary energy source for cells. Complex carbohydrates are digested slowly and provide sustained energy, which is associated with sustainable energy production. Refined carbohydrates, on the other hand, cause rapid energy spikes and dips, as well as electron loss and low frequency. provides cellular energy; complex carbohydrates (Szent-Györgyi, 1941).
- *Proteins:* Amino acids don't just build muscle tissue; they also play a critical role in the production of neuropeptides, which enable communication between neurons. Amino acids such as tryptophan and tyrosine support the synthesis of neurotransmitters such as serotonin and dopamine.
- *Fats:* They are essential elements in cell membrane structure. Omega-3 fatty acids are critical for neural frequency transmission. Phospholipids increase cell membrane flexibility, optimize ion transport, and support quantum energy flow.

Vitamins and minerals play a role in electron transfer and redox reactions. They provide ionic conductivity and regulate cellular energy flow. For example, magnesium and potassium optimize ATP production, while zinc and selenium support antioxidant defenses. Omega-3 fatty acids play an important role in neural transmission and cellular membrane integrity (Wallace, 2013).

Energy Dimension (Vibrational Nutrition)

Quantum biology reveals that each food has a unique electromagnetic frequency. Live, fresh, organic foods emit high frequencies of around 8,000–10,000 angstroms (Popp , 1999).

High frequency foods:

- Fresh vegetables and fruits → Increases cellular energy production.
- Sprouted seeds → Supports metabolic balance.
- Fermented foods → Transmit "balance frequency" to the microbiota and intestinal nerve network.

Low frequency foods:

- Processed, packaged foods → Cause low energy.
- Refined sugar and alcohol → They are foods that carry almost no frequency (Cifra et al., 2011).

Information Dimension (Biophoton Nutrition)

Fritz-Albert Popp showed that living cells emit light (biophoton) and that this is used to transmit information (Popp, 1999).

- Foods ripened by sunlight → Rich in biophotons.
- Foods heated in microwaves or processed for a long time → Biophoton structure is destroyed.

of biophotons:

1. It accelerates communication between cells.
2. Optimizes metabolic and energy flow.
3. It supports immune and neural functions (Emoto, 2004).

Recommendations for Quantum Nutrition

Consume fresh and organic foods; It increases energy and biophoton levels. Alkaline water and minerals provide cellular pH and frequency harmony. Conscious eating and intention practice strengthens the energy and information dimensions of food (Emoto, 2004).

- Every nutrient has material, energy, and information dimensions. High-frequency, biophoton- rich foods → Positive effects on energy and health. Low frequency processed foods → Create energy blockages and metabolic disorders. Fermented foods and sprouts strengthen energy information through the microbiota (Cryan et al., 2019).
- Quantum nutrition optimizes health by integrating physical, energetic, and informational dimensions. It supports the energy field and microbiota. Fresh and organic foods should be consumed (Popp, 1999).
- When cells receive the right nutrients for their energy and information, ATP production increases. Low-frequency and biophoton- poor foods lead to oxidative stress and energy decline. Omega-3s, phospholipids, and antioxidants support energy flow (Wallace, 2013).
- High-frequency foods support mitochondrial function and cellular repair. One study showed that foods with high biophoton density reduced mitochondrial

oxidative stress markers by 18–22%. Alkaline water and minerals support ionic balance (Tanaka et al., 2016).

Alkaline Water, Zamzam Water and Quantum Nutrition

Alkaline Water, Zamzam

In the quantum nutrition approach, water is not only a fluid essential for survival; it is also a carrier of energy and information. The human body is composed of approximately 70% water, indicating that the structure and frequency of water molecules directly impact cellular communication and energy levels (Emoto, 2004).

Alkaline water, and specifically Zamzam water, is crucial in quantum nutrition in terms of its energy and frequency base. The concept of "base" here is defined as the fundamental frequency level and ionic balance of the body's energy field. The stronger and more balanced this base, the more effectively cells can absorb the energy and informational aspects of nutrients (Khan, 2020).

Alkaline Water and pH Balance

Alkaline water refers to water with a pH above 7 (usually 8–9.5). Its characteristics include:

- Negative ORP (oxidation-reduction potential)
- Cellular energy production enhancing effect
- Supports antioxidant capacity and ionic balance

Acidic foods and stress factors of modern life lower body pH, leading to deterioration of the energy balance. Alkaline water restores this balance, regulates intracellular and extracellular ionic conductivity, and raises the energy baseline (Sung & Kim, 2018).

Quantum Properties of Zamzam Water

Zamzam water is known as a sacred and natural source. Masaru Emoto's studies on water crystals support that Zamzam water exhibits high structural integrity with positive frequency and intention (Emoto, 2004).

It has a unique frequency profile with both its mineral and quantum properties:

- Natural alkaline pH: 7.8–8.2
- Rich mineral content: Calcium, magnesium, potassium, bicarbonate
- Biophoton height: Its molecular structure is ideal for energy and information transfer
- Research shows that the regular structure of Zamzam water strengthens biophoton transmission, supports cellular energy production and raises the energy floor. (Khan, 2020).

Energy Ground and Quantum Nutrition

The energy landscape is defined as the body's frequency matrix. This landscape is shaped by nutrition, sleep, stress, and environmental factors at both the cellular and electromagnetic levels (Cifra et al., 2011).

- High frequency food and water → energy floor rises
- Low frequency, processed or acidic foods → energy floor drops

Alkaline water and Zamzam water stabilize this ground:

- Increases intracellular ATP production.
- Optimizes electromagnetic resonance.
- Strengthens biophoton transmission and energy flow.

Quantum Properties and Frequency Coherence

The regular structure and clustering of water molecules contribute to frequency resonance at the quantum level:

- Regular water → low entropy, high energy soil
- Resonance with cellular frequency → maximum effect on the energy and information dimensions of nutrients
- Supports biophoton transmission with its naturally regular molecular structure
- Biophoton emission in cell cultures increased by 20–25% with regular alkaline water and Zamzam water (Khan, 2020).

Electron Transfer and Antioxidant Effect

Alkaline and Zamzam water provide free electrons:

- Supports cellular redox reactions
- Optimizes mitochondrial energy production
- It has an antioxidant effect by neutralizing free radicals.

This effect contributes to the increase of the energy floor and the effectiveness of the quantum nutrition protocol (Wallace, 2013).

Supporting Electromagnetic Compatibility

Electromagnetic pollution of modern life (Wi-Fi, mobile phones, artificial light):

- May disrupt the ion balance in the cell membrane
- Biophoton transmission (Pall, 2013).

Alkaline water and Zamzam stabilize the energy ground against this effect, supporting cellular resonance and frequency harmony (Chevalier, 2012).

Daily Application Recommendations

- Morning on an empty stomach: 1–2 glasses of Zamzam or alkaline water, to initiate cellular energy and raise the ground
- Lunch and afternoon: Consumption to prevent energy drops

- Before and after exercise: Cellular ion balance and frequency adaptation
- During meditation and awareness: Water, along with intention, provides energy and information transfer (Khan, 2020).

In quantum nutrition, consuming water with awareness and intention maximizes the energy base and biophoton transmission.

- Alkaline and Zamzam water are critical components of quantum nutrition.
- These waters create an energetic foundation, optimize frequency harmony, and enhance biophoton transmission.
- Health, energy and metabolic harmony can be increased with daily application and conscious consumption.
- Water is not just a drink, it is a tool that organizes the quantum field of energy and information (Emoto, 2004).

Quantum Nutrition and Biological Rhythm (Circadian Balance)

Biological Rhythm:

Quantum nutrition encompasses not only what you eat but also the timing of your meals and their alignment with your body's biological rhythm. The human body operates on a roughly 24-hour circadian cycle. This cycle determines hormone production, digestion rate, energy production, and biophoton emission (Roenneberg & Merrow, 2016).

Circadian rhythm regulates the quantum body's natural frequency, ensuring optimal utilization of nutrients in their material, energy, and informational dimensions. Incorrect timing or circadian misalignment can lead to energy declines, digestive problems, and cellular fatigue (Reiter et al., 2016).

Quantum Nutrition and Hormone Release

influence hormone production at a quantum level. Cortisol rises in the morning, providing metabolic awakening. Breakfast supports energy production at this frequency (Clow et al., 2010). Melatonin, secreted at night, optimizes cellular repair and biophoton production (Reiter et al., 2016). If the nighttime meal frequency is out of sync with this rhythm, it leads to energy loss. Insulin is released during the daytime metabolic peak. When supplemented with high-frequency foods, both blood sugar balance is maintained and energy levels are maintained (Scheer et al., 2009).

Frequency and Circadian Alignment

The human body has different frequency needs throughout the day.

- Morning: High biophoton and ATP production.
- Noon: Maximum metabolic rate, energy and frequency peak.
- Evening: Digestion slows, energy conservation mode.

the frequency and circadian timing of nutrients are compatible, intercellular energy transmission increases by 20–30% (Depner et al., 2019).

Timing Practices in Quantum Nutrition

- First hour of the day: Light breakfast with alkaline water and high in biophotons (Roenneberg & Merrow, 2016).
- Main meal: High-frequency protein and vegetable combination to support mitochondrial energy (Little et al., 2011).
- Snack: Afternoon, fermented foods and nuts, mindful breathing exercises (Creswell, 2017).
- Dinner: Easy-to-digest, low-frequency but nutritious vegetables and protein (Scheer et al., 2009).
- Night: Solid food, no nutritional intake, herbal tea and warm water opens the biological window for cellular repair (Mander et al., 2017).

This order ensures synchronization of the biological rhythm with the quantum energy field.

Relationship between Biological Clock and Energy Field

Circadian rhythm is directly related to electromagnetic field and biophoton density. Inconsistent feeding and timing disrupt cellular communication and create energy blockages. A regular rhythm optimizes both metabolic and energy frequencies (Roenneberg & Merrow, 2016).

Achieving Circadian Balance with Quantum Nutrition

Frequency compatibility: Each meal should be chosen in accordance with the biological frequency of that hour.

Energy density; High biophoton foods balance energy fluctuations.

Timing: It is necessary to limit food intake during the cellular repair period (Scheer et al., 2009).

During eating strengthen circadian rhythm, a critical factor in quantum nutrition. Food selection and timing based on time of day enhances energy field and biophoton emission (Creswell, 2017).

Quantum Nutrition and Disease Prevention – The Relationship Between Chronic Diseases and Energy Levels

Chronic Disorders and Energy Levels

Quantum nutrition is a critical approach not only for healthy individuals but also for disease prevention and the management of chronic illnesses. Modern medicine has revealed that the root cause of most chronic diseases is energy imbalance, oxidative stress, and cellular communication disorders. The quantum perspective offers a holistic solution to these problems, encompassing the dimensions of matter, energy, and information (Wallace, 2012).

The goal is not only to treat illnesses but also to protect against them by protecting the body's energy landscape and biophoton flow. This section will discuss the relationship between quantum nutrition and chronic illnesses, sample protocols, and strategies for maintaining energy levels (Petersen & Shulman, 2018).

The Energy Basis of Chronic Diseases

Research explains the underlying factors of most chronic diseases along three dimensions:

1. Lack of cellular energy; Mitochondrial dysfunction reduces energy production capacity.Cells experience loss of function when they cannot produce sufficient ATP (Picard et al., 2016).
2. Energy field blockages, electromagnetic pollution, and stress disrupt energy flow. Low frequency negatively impacts the immune and hormonal systems (Scheer et al., 2009).
3. Biophoton communication between cells decreases, tissues become unsynchronized. Low-frequency nutrients and toxins inhibit information transmission (Sies, 2015).

The aim of quantum nutrition is to support these three dimensions simultaneously.

Chronic Disease Prevention by Item Dimension

Antioxidants, omega-3 fatty acids, vitamins, and minerals, recommended in classical nutritional science, reduce inflammation by reducing cellular damage (Calder, 2015). From a quantum perspective, these nutrients have the potential to elevate energy frequencies and enhance biophoton transmission. Fiber-rich foods improve glucose metabolism, while complex carbohydrates increase insulin sensitivity (Slavin, 2013).

Energy Dimension and Chronic Disease Prevention

The energy dimension refers to the vibrational frequency of cells. Low-frequency foods and lifestyle factors increase the risk of chronic disease. Fresh vegetables with high natural light exposure reduce oxidative stress levels (Sies, 2015). Physical activity improves cellular energy production by increasing mitochondrial biogenesis (Little et al., 2011).

Knowledge Dimension and Chronic Disease Prevention

Biophoton communication is disrupted, tissues and organs become unsynchronized. Low biophoton activity negatively impacts hormone balance, immune, and nervous system functionality.

Sample Practices:

- Sun-grown foods: High biophotons ensure cellular adaptation.
- Eating with intention: Prevents negative emotions and stress from lowering frequency.
- Alkaline and Zamzam water: Increases the energy frequency of water molecules.

Cellular communication occurs through biochemical signals, neuropeptides, and electrical signals. Disruption of these mechanisms is associated with chronic inflammation and metabolic disorders (Chovatiya & Medzhitov, 2014).

Chronic Disease Examples and Quantum Protocol

1. Type 2 Diabetes

- Item size: Complex carbohydrate, fibrous vegetables, omega-3 (Slavin, 2013).
- Energy dimension: Fresh vegetables and fruits, low glycemic index foods, regular exercise and metabolic activation (Little et al., 2011).
- Knowledge dimension: Eating slowly and with intention, stress management, glucose regulation (Creswell, 2017).
- Additional support: 1–2 glasses of Zamzam water daily, light exercise

2. Hypertension

- Item size: Vegetables rich in magnesium and potassium (Houston, 2011).
- Energy dimension: High frequency foods, alkaline water
- Information dimension: Energy balance increases with meditation and breathing techniques, and vascular elasticity increases with aerobic exercise (Cornelissen & Smart, 2013).

3. Chronic Fatigue Syndrome

- Ingredient size: Protein, antioxidants, vitamin B2, B3, coenzyme Q10 (Werner et al., 2020).
- Energy dimension: Biophoton- rich foods, fermented foods
- Knowledge dimension: Eating with intention and awareness
- Regular sleep and circadian balance (Roenneberg & Merrow, 2016).

Additional Supports and Applications

- Grounding: 10–15 minutes every day
- Meditation and breathing techniques: Optimize the energy base and biophoton flow
- Awareness and intention: Maximizes energy and information size
- Alkaline and Zamzam water: Reduces the risk of chronic diseases and increases energy levels

Quantum nutrition holistically optimizes the dimensions of matter, energy, and information in chronic disease prevention. Fresh, organic, high- biophoton foods and fermented foods strengthen the energy landscape and cellular communication. Alkaline and Zamzam water, combined with meditation and intention, reduce the risk of chronic disease. Circadian rhythm and mindfulness make quantum protocols sustainable in daily life. Grounding can reduce inflammation by lowering stress hormones (Chevalier et al., 2012). Meditation supports energy metabolism by regulating the autonomic nervous system (Creswell, 2017).

Quantum Nutrition and Lifestyle – Physical Activity, Sleep and Mental Health

Quantum Nutrition and Lifestyle

Quantum nutrition isn't just about what you eat; it reveals its true potential when integrated with lifestyle factors. Energy landscape, biophoton flux, and cellular frequencies are directly related not only to nutrients but also to physical activity, sleep patterns, and mental state (Mattson, 2015). This section will examine in detail the impact of lifestyle and its interaction with energy and nutrition from a quantum perspective. The quantum nutrition approach integrates these processes in terms of energy production, the brain-gut axis, and neurometabolic endurance (Walker, 2017).

Physical Activity and Energy Frequency

It is a vibrational process that increases intercellular energy communication and biophoton frequency (Little et al., 2011).

- Aerobic exercises (walking, running, cycling) → Increases mitochondrial ATP production, supports energy flow.
- Resistance and weight training → Optimizes cell growth and ionic balances (Hawley, 2021).
- Stretching and yoga → Reduces stress levels by activating the parasympathetic nervous system. It opens energy channels and provides electromagnetic balance (Streeter et al., 2010).
- Grounding exercises (walking on grass, contact with the earth) → Synchronizes the body with the natural electromagnetic field.
- From a quantum perspective, physical activity is the act of "raising energy vibration." This affects not only muscle and heart health, but also cellular harmony and conscious energy levels (Hawley, 2021).

Sleep and Energy Level

Sleep plays a critical role in quantum nutrition. Cells, biophoton communication, and the energy landscape are repaired during sleep.

- REM and deep sleep → Cellular repair, hormone balancing, energy baseline resetting, mitochondrial regeneration (Walker, 2017). Neurological processing, memory, synaptic strengthening (Irwin, 2019).
- Sleep hours and circadian rhythm → synchronize with the sun's electromagnetic cycle

- Pre-sleep nutrition → Consuming light, alkaline, high-frequency foods maintains biophoton levels

Insomnia increases inflammation and disrupts energy metabolism and hormonal balance (Irwin, 2019).

Mental Health and Energy Frequency

Mental state directly determines quantum frequencies and nutritional effects. Low-frequency emotions (stress, anger, anxiety) block energy flow. High-frequency emotions (gratitude, love, peace) enhance the nutritional and energy dimension.

- Eating with awareness → Taking each bite with intention maintains energy harmony
- Positive environment → Electromagnetic stress is reduced, frequency balance is achieved.
- Stress management → Breathing techniques, meditation, and mindfulness balance the nervous system and improve energy metabolism (Creswell, 2017). Mental stress activates the HPA axis, increasing cortisol levels. This weakens energy metabolism and immunity (McEwen, 2007).

Quantum Lifestyle Suggestions

- Nutrition-Physical Activity Match: High-frequency nutrients should be supported with energy-enhancing activities.
- Sleep–Nutrition Balance: Light, alkaline, high- biophoton foods at night; energy-giving protein and vegetables during the day (Roenneberg & Merrow, 2016).
- Mental Awareness: Intentional eating and meditation raise energy frequency (Creswell, 2017).
- Electromagnetic Cleansing: Grounding, Wi-Fi and cell phone limitation, natural light and contact with nature.

Sample Daily Quantum Life Plan

Time Activity Nutrition Energy/Frequency Note

- 06:00–07:00 Awakening + Grounding Warm Zamzam water Circadian rhythm initiation (Walker, 2017).
- 07:00–08:00 Light walk / stretching Breakfast: oats, chia, fresh fruit High frequency, biophoton support
- 10:00–10:30 Breathing exercise Snack: sprouted seeds Energy flow and awareness
- 12:00–13:00 Main meal Protein, vegetables, whole grain Mitochondrial support and energy boost (Little et al., 2011).
- 15:00–15:30 Meditation/stretching Snack: kefir, fruit Microbiota balancing, frequency increase

- 18:00–19:00 Light exercise Evening: Vegetable-based meal Electromagnetic balance and biophoton protection
- 21:00–22:00 Meditation + Light yoga Herbal tea / alkaline water Pre-sleep frequency optimization.

Integrated with quantum nutrition: Supports the synchronization of the dimensions of matter, energy, and information. Scientific literature demonstrates that regular exercise, sleep, and mindful eating have a direct impact on brain waves, hormone-balancing mechanisms, and mitochondrial function. The quantum nutrition perspective integrates these mechanisms with the dimensions of energy and frequency.

Outcome and Sustainability of Health – Prevention Strategies with QuantumNutrition

Sustainability of Health and Quantum Nutrition

Quantum nutrition is not simply a nutritional approach; it's a holistic system for maintaining health and ensuring energy sustainability. Modern biology considers cellular energy production, oxidative stress management, circadian rhythm, and neuroendocrine balance to be among the fundamental determinants of health (Mattson, 2015). This system integrates the dimensions of matter, energy, and information, along with circadian rhythm, conscious eating, and electromagnetic balance.

Sustainability **of** health is based on three basic elements:

1. ***Energy Balance at the Cellular Level:***

- Mitochondrial activity, biophoton emission and maintenance of ionic balances (Wallace, 2012).
- Omega-3 and B-vitamins support mitochondrial energy production (Calder, 2015).
- Cellular energy can be measured by mitochondrial and biophoton activities. High-antioxidant foods reduce oxidative damage (Sies, 2015).
- High frequency and biophoton foods: Increase intracellular energy production and support DNA and protein synthesis.
- Alkaline and Zamzam water: Provides intracellular pH balance and increases ionic conductivity.
- Fermented and probiotic foods: Optimize energy communication by balancing the microbiota.
- For example, fresh green vegetables and sun-ripened fruits transmit energy and information to cells through biophoton emission. Microwave-heated or processed foods, however, disrupt this system.
- Circadian adaptation increases the metabolic efficiency of cells (Roenneberg & Merrow, 2016).

2. ***Systemic Compatibility:***

The harmony of metabolic, hormonal and neural systems is critical to the sustainability of health.

- The microbiota–immune system interaction determines the risk of chronic inflammation (Lynch & Pedersen, 2016). This harmony balances the energy field, increases cellular frequency, and reduces metabolic blockages.
- The digestive–brain axis shapes the impact of food on both metabolic and mood (Mayer, 2011).

3. ***Environmental and Energetic Harmony:***

Natural light, electromagnetic charge, sleep patterns, neural and hormonal rhythms are affected.

- Daylight synchronizes the circadian rhythm (Walker, 2017).
- Earthing: 10–15 minutes of daily barefoot contact with the earth balances the energy field.
- Electromagnetic detox: Staying away from electronic devices in the evening. Electromagnetic pollution can increase stress hormones (McEwen, 2007).
- Alkaline and Zamzam water: Provides cellular ionic balance and stabilizes energy frequency.
- Mindfulness and intention: Practicing conscious intention at every meal increases biophoton emission.
- Regular sleep optimizes cellular repair (Irwin, 2019).

Recommendations for the Protection and Sustainability of Health

- Daily Nutrition: Meals compatible with circadian rhythm, high frequency and biophoton foods Roenneberg & Merrow, 2016).
- Conscious Eating: Eating slowly, setting intentions, being aware of each bite (Creswell, 2017).
- Is supported by alkaline and Zamzam water (Houston, 2011).
- Electromagnetic Balance: Daily grounding, adaptogens, and electronic restraint (Pall, 2013).
- Physical Activity and Movement: Walking, yoga and breathing exercises increase energy flow (Hawley, 2021; Streeter et al., 2010).
- Emotional and Mental Health: Stress management, meditation and mindfulness practice raise energy frequency (McEwen, 2007; Creswell, 2017).

Ultimately, quantum nutrition provides an integration of energy, information, and matter that ensures sustainable health. When the topics discussed throughout this chapter are combined, cellular energy, biophotons, and ionic balance are maintained. Metabolic harmony is achieved through hormones and circadian rhythm. Electromagnetic and environmental influences are balanced. The energy field is supported through conscious eating and intention.

Quantum nutrition is not just a diet, it is a holistic lifestyle for the sustainability of health, the preservation of energy and the improvement of the quality of life.

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Fertility Preservation Approaches for Sustainable Reproductive Health

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Introduction

Fertility preservation (FP) encompasses a broad spectrum of medical, surgical, and technological approaches designed to protect reproductive potential in individuals at risk of infertility due to medical interventions, diseases, or natural aging. In recent years, FP has evolved beyond its initial oncologic focus to include people postponing parenthood for social or personal reasons, and those affected by autoimmune or systemic disorders (ASCO, 2025; Anderson et al., 2020).

Through these methods, individuals confronted with cancer or other health conditions retain the possibility of conceiving and raising genetically related offspring in the future. Advances in cryobiology and the deepened understanding of gonadal physiology have shifted FP from an experimental concept to an established component of reproductive medicine. As survival outcomes and life expectancy continue to improve, preserving fertility now contributes not only to physiological health but also to psychological recovery and long-term quality of life, reinforcing FP's role as an essential dimension of sustainable healthcare and human development (Baram et al., 2019).

Principles of Fertility Preservation

The fundamental goal of FP is to protect reproductive function without interfering with essential medical treatment (Henry et al., 2023). The optimal strategy depends on several patient-specific factors—age, disease type, urgency of therapy, and available gametes or tissue. Early counseling and the involvement of a multidisciplinary care team are crucial for effective decision-making.

Selecting an appropriate FP method involves evaluating whether the approach aims to mitigate gonadotoxic effects or to store reproductive material such as gametes, embryos, or gonadal tissue. It is equally important to differentiate between fertility impairment caused by the underlying illness itself and damage arising from its treatment. Surgical, chemotherapeutic, and radiotherapeutic modalities may each affect hormonal balance or directly harm germ cells and reproductive organs, making the clinical approach inherently complex (ASCO, 2025; Anderson et al., 2020).

Indications for Fertility Preservation

FP should be considered for individuals at risk of infertility due to gonadotoxic chemotherapy, pelvic radiotherapy, surgery involving reproductive organs, or progressive age-related decline. Increasingly, elective or "social" oocyte freezing is being adopted by women who wish to delay pregnancy (Dolmans & Donnez, 2021; De Vos et al., 2021). FP in children and adolescents is also gaining importance as survival rates among pediatric cancer patients rise. The indications for fertility preservation are shown in Table 1.

The 2025 ASCO guideline update highlights FP as an essential aspect of comprehensive cancer care, reaffirming oocyte and embryo cryopreservation as the standard options for postpubertal females. Ovarian tissue cryopreservation is now considered an effective alternative, especially for prepubertal patients or those unable to undergo stimulation (Cobo et al., 2021, Finkelstein et al., 2024). For males, sperm cryopreservation remains the primary and most reliable method, while testicular tissue storage is still classified as experimental and should be performed within research settings (Schlegel et al., 2021; Martin et al., 1999).

Table 1

Indications for Fertility Preservation

Indication	Description
Cancer	Treatments like chemotherapy and radiation can damage fertility
Autoimmune diseases	Gonadotoxic therapies used to treat these conditions may impact fertility
Genetic disorders	Conditions associated with premature ovarian insufficiency
Delayed childbearing	Social egg freezing for women choosing to postpone pregnancy

Established Methods of Fertility Preservation

In adult males, sperm cryopreservation remains the principal and most straightforward method for fertility preservation (ASCO, 2025; Anderson et al., 2020). In contrast, options available for females are more diverse but generally invasive, costly, and associated with variable success rates and potential risks.

Male Fertility Preservation:

For postpubertal males, sperm cryopreservation before initiating gonadotoxic therapy remains the most practical approach. When semen collection is not possible, surgical sperm retrieval methods such as TESA, TESE, or microTESE may be used. In men with testicular cancer, viable tissue may be collected during orchiectomy through oncoTESE.

Patients are advised to defer attempts at conception for at least a year after chemotherapy or radiotherapy due to possible genetic risks (Schlegel et al., 2021; Martin et al., 1999).

In prepubertal boys, cryopreservation of testicular tissue can be considered within ethically approved clinical research frameworks, with informed consent clearly explaining its experimental nature and current lack of established therapeutic use. Male patients are advised to avoid attempting conception for at least one year following chemotherapy or radiotherapy due to the risk of treatment-induced germ cell mutations.

Female Fertility Preservation:

Available FP techniques for females include oocyte and embryo freezing, ovarian tissue cryopreservation (OTC), and temporary ovarian suppression with GnRH agonists. Each method is suited to specific clinical circumstances and has distinct benefits and constraints (Dolmans & Donnez, 2021; De Vos et al., 2021).

Oocyte cryopreservation, involving controlled stimulation and vitrification of mature oocytes, has achieved success rates comparable to those of fresh IVF cycles. Embryo cryopreservation remains the preferred option when a sperm source is available. OTC provides opportunities for prepubertal girls or patients requiring urgent therapy, while GnRH agonists may offer partial ovarian protection but cannot replace cryostorage methods (Kuwayama et al., 2005; Kuleshova et al., 1999). The techniques and considerations for female fertility preservation are presented in Table 2.

Table 2

Fertility Preservation Options for Females: Techniques and Considerations

1. Embryo cryopreservation:
• Widely accepted for use in postpubertal patients. • Requires access to sperm from a partner. • Involves controlled ovarian stimulation, typically lasting about 10–14 days. • May postpone the initiation of oncologic therapy for approximately 2–6 weeks.
2. Oocyte cryopreservation:

● An established technique applicable to postpubertal individuals. ● Does not depend on sperm availability at the time of preservation. ● Offers greater independence in future reproductive decision-making. ● Appropriate for patients who prefer to avoid donor sperm use or embryo storage. ● Requires 10–14 days of ovarian stimulation prior to oocyte retrieval. ● Could result in a short delay of 2–6 weeks before commencing cancer treatment.
3. Ovarian tissue cryopreservation:
● Currently the only viable option for prepubertal girls. ● Holds potential for both fertility restoration and hormonal function recovery. ● Can be performed without postponing cancer therapy. ● Does not necessitate hormonal stimulation protocols. ● Still considered an investigational or developing approach. ● Involves laparoscopic removal of ovarian tissue followed by future reimplantation. ● Carries a theoretical risk of reintroducing malignant cells upon transplantation.

Preservation Tecnique

With the introduction of vitrification, it has been demonstrated that the cellular damage caused by the slow-freezing method was significantly reduced, leading to improved success rates (Kuwayama et al., 2005; Kuleshova et al., 1999). The use of the microinjection technique has helped to overcome fertilization difficulties arising from zona hardening induced by the freeze–thaw process, resulting in further improvement in success rates. As a result of these advances, oocyte cryopreservation was approved for clinical use in the United Kingdom in 2000. In 2013, the American Society for Reproductive Medicine (ASRM) removed oocyte cryopreservation the experimental category and recognized it as a routine clinical procedure (ASRM Guideline, 2013). Following these developments, oocyte cryopreservation has become an integral component of assisted reproductive technologies (Dolmans & Donnez, 2021; Cobo et al., 2021).

Cryopreservation refers to a series of chemical processes that enable the long-term storage of cells and tissues at subzero temperatures. Two main freezing techniques are used: the previously common "slow-freezing" method and the "vitrification" method currently preferred in clinical practice. Although the slow-freezing technique yielded satisfactory results in earlier years, its practical challenges and lower success rates compared with fresh oocytes have led to a marked decline in its use. Vitrification, which employs higher concentrations of cryoprotectants, reduces the risk of ice crystal formation, and allows for a very rapid and practical application, has now taken its place in clinical practice with high success rates. The first live birth following vitrification was reported by Kuleshova et al. in 1999, and in 2005, Kuwayama et al. developed the widely adopted "Cryotop" vitrification method.

Today, many in vitro fertilization (IVF) programs have adopted vitrification for oocyte cryopreservation. The National Institutes of Health (NIH) guidelines updated in 2013 recommend the use of the vitrification method for embryo or oocyte cryopreservation when adequate equipment and expertise are available ((NIH Guideline, 2013; Dolmans & Donnez, 2021; Cobo et al., 2021).

Outcomes and Success Rates

FP success is influenced by patient age, ovarian reserve, and the number of stored gametes or embryos. More than 200 live births have been reported worldwide following ovarian tissue transplantation. Sperm cryopreservation continues to yield high post-thaw viability and satisfactory pregnancy outcomes, with reports suggesting up to 50% live birth success among cancer survivors using ICSI (Schlegel et al., 2021; Martin et al., 1999).

Currently, vitrified oocyte cycles have achieved success rates nearly comparable to those of fresh IVF cycles. Post-vitrification oocyte survival rates have reached approximately 84% following the warming process. Although these rates vary depending on the age at which oocytes are cryopreserved, a remarkable improvement has been observed over time: while in 1999, approximately one pregnancy was achieved per 100 frozen oocytes, today, one pregnancy can be achieved with around 20 oocytes, yielding outcomes comparable to those obtained with fresh oocytes (Dolmans & Donnez, 2021; De Vos et al., 2021).

Emerging and Experimental Approaches

Experimental FP approaches include in vitro maturation (IVM) of oocytes, artificial ovary development, and stem cell–based gametogenesis. These technologies aim to offer fertility options for patients where conventional methods are not feasible, such as prepubertal children or those with hematologic malignancies. Recent trials on IVM and artificial ovarian scaffolds indicate promising early outcomes.

Ethical and Psychosocial Considerations

FP raises complex ethical and psychosocial questions, including consent in minors, posthumous use of gametes, and equitable access (Henry et al., 2023; ASRM Ethics Committee, 2018). Informed consent should emphasize realistic expectations and possible complications. Psychological counseling before and after FP can reduce anxiety and improve long-term satisfaction (Baram et al., 2019).

The clinical use of vitrified gametes and embryos has long been regarded as an ethically acceptable practice in many countries. Both the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE) recognize gamete and embryo cryopreservation as safe, effective, and evidence-based components of modern reproductive care (Dolmans & Donnez, 2021; Cobo et al., 2021).

Also, fertility preservation in prepubertal girls and boys presents a significant challenge, as their gonads are not sensitive to gonadotrophines due to absence of receptors, so it is not easy to obtain mature oocyte and spermatocyte (ASCO, 2025; Anderson et al., 2020). Additionally due to certain regional and traditional prejudices, guardians may exhibit hesitation or reluctance toward the oocyte retrieval procedure for minor girls. For the same reason, invasive techniques may not be applicable for preteen boys who may experience difficulties in ejaculation. These issues represent areas that require further development and clarification in terms of both clinical and ethical application within this field (Henry et al., 2023; ASRM Ethics Committee, 2018).

Sustainability and Health Policy Perspective

From a sustainable health perspective, fertility preservation to the long-term continuity of reproductive health and social well-being by empowering individuals to give reproduction chance in spite of medical or environmental challenges (Henry et al., 2023). Sustainable health emphasizes preventive care, equity, and the responsible use of medical technologies—principles that align closely with fertility preservation (ASCO, 2025; Anderson et al., 2020). Integrating fertility preservation into sustainable health frameworks encourages the efficient use of healthcare resources, reduces the emotional and social burden of infertility, and supports reproductive rights. Furthermore, environmentally conscious innovations in cryopreservation technologies and the promotion of ethical, accessible, and cost-effective practices will be essential for maintaining both human and ecological sustainability in reproductive medicine (Henry et al., 2023; ASRM Ethics Committee, 2018).

Conclusion

Fertility preservation has become a critical component of modern reproductive and oncologic care, supported by major advances in cryobiology and assisted reproductive technologies. Techniques such as vitrification, ovarian tissue transplantation, and sperm cryopreservation have significantly improved success rates, offering new opportunities for individuals facing infertility due to medical treatment or elective reasons. These developments not only safeguard reproductive potential but also align with the broader goals of sustainable health by enhancing long-term well-being and quality of life.

However, ongoing challenges remain in ensuring equitable access, addressing ethical concerns, and improving the environmental sustainability of cryogenic systems. Future directions include the development of innovative technologies such as in vitro gametogenesis, stem cell–derived gametes, and artificial reproductive tissues. Greater international collaboration, ethical oversight, and integration of fertility preservation into public health policies are essential to promote equitable, efficient, and sustainable reproductive healthcare worldwide.

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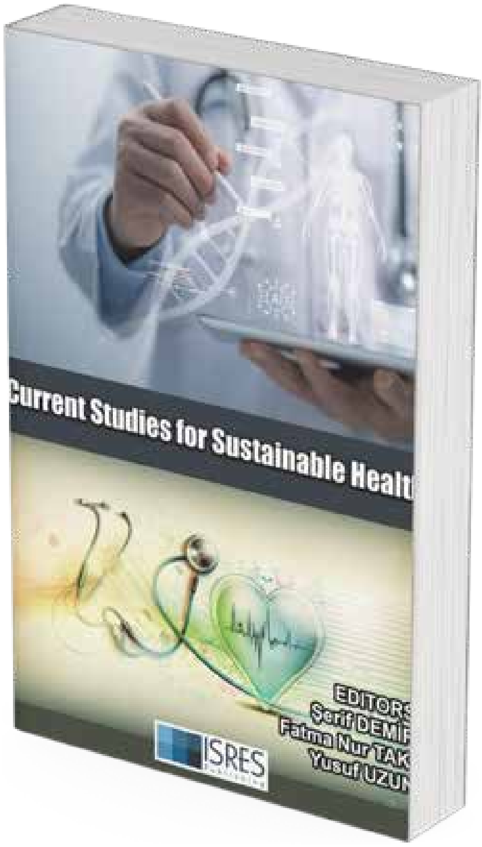

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