



HEALTHY AGING: MULTIDIMENSIONAL APPROACHES AND INNOVATIVE INTERVENTIONS: A SYSTEMATIC REVIEW



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ABSTRACT

Objective: This review article seeks to explore the pathophysiology of healthy aging and identify effective interventions that can promote health in the elderly population, addressing nutrition, physical activity, and social involvement. **Methodology:** Searches were performed in the PubMed database using combinations of descriptors with the Boolean term "AND": "Healthy aging", "Elderly health", "Physiology of aging", "Interventions for healthy aging" and "Geriatric care". A total of 125 articles were found, of which 36 were initially selected. After applying the inclusion and exclusion criteria, 36 articles were selected to compose the systematic review. The inclusion criteria were: articles in English, Portuguese, and Spanish, published between 2019 and 2024, available in full, that addressed the pathophysiology of healthy aging and associated interventions. Duplicate articles, only in the form of an abstract, or that were not directly related to the topic were deleted. **Results:** The review identified that pathophysiological processes such as DNA damage, mitochondrial dysfunction, chronic inflammation, and cellular senescence are central to healthy aging. Proper nutrition, rich in protein, vitamins, and antioxidants, has been shown to be essential for the prevention of weakness and cognitive decline. Supplements such as vitamin D, omega-3s, and curcumin have been shown to be effective in promoting muscle and cognitive health. Regular physical exercise, especially aerobic and resistance training, is

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critical for maintaining cognitive function, cardiovascular health, and muscle strength. In addition, nature-based interventions and social engagement have been shown to be crucial for the mental and emotional health of older adults. Conclusion: Promoting healthy aging requires an integrated approach that combines nutritional interventions, regular physical exercise, and strategies that promote social engagement and mental well-being. The implementation of these strategies can significantly improve the quality of life of the elderly, promoting active and healthy aging.

Keywords: Healthy Aging. Pathophysiology of Aging. Nutrition. Physical Exercise. Social Involvement. Quality of Life.

INTRODUCTION

Healthy aging is a concept that involves maintaining physical, mental, and social health throughout life, allowing individuals to remain active and independent (MCMAUGHAN; OLORUNTOBA; SMITH, 2020). According to the World Health Organization (WHO), healthy aging is the process of developing and maintaining functional capacity that enables well-being in old age (ARLEO et al., 2024). This includes preventing and managing disease, maintaining good physical and cognitive functionality, and engaging in active and healthy lifestyles (ARLEO et al., 2024). In addition, global interventions aimed at improving access to healthcare, such as income supplementation for the elderly and free vaccination, have shown positive results in promoting healthy aging (MCMAUGHAN; OLORUNTOBA; SMITH, 2020). Understanding the factors that influence healthy aging, such as socioeconomic status and access to health care, is essential for developing effective policies and community-based programs that support older adults (ARLEO et al., 2024).

METHODOLOGY

This systematic review aims to explore the pathophysiology of healthy aging and identify effective interventions that can contribute to its occurrence. In this way, we seek to understand the biological and molecular mechanisms underlying aging and how factors such as nutrition, physical activity, and social involvement can positively influence these processes.

To develop this research, a guiding question was formulated using the PVO (population, variable and objective) strategy: "What are the main pathophysiological mechanisms involved in healthy aging and how can specific interventions promote the health and quality of life of the elderly?"

The searches were carried out in the PubMed database. Three descriptors were used in combination with the Boolean term "AND": "Healthy aging", "Elderly health", and "Physiology of aging", in addition to another combination with "Interventions for healthy aging" and "Geriatric care". The search strategy used was: "Healthy aging AND Elderly health AND Physiology of aging", and "Interventions for healthy aging AND Geriatric care".

This search resulted in 125 articles, which were subsequently submitted to the selection criteria. 36 were selected, but only 24 were part of the systematic review collection. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 and that addressed the themes proposed for this research, in addition to review, observational and experimental studies, made available in

full. The exclusion criteria were: duplicate articles, available only in abstract form, that did not directly address the proposal studied, and that did not meet the other inclusion criteria.

RESULTS

Table 1 – created by the author

Author	<i>Main Collaborations for the Systematic Review</i>
TAMURA et al. (2020)	They focused on nutritional management in older adults with diabetes, highlighting the importance of shifting prevention strategies from metabolic syndrome to frailty. They contributed insights into the importance of nutrition in maintaining health and preventing age-related complications (12).
DONATI ZEPPEA et al. (2022)	They explored interventions in the gut microbiota for healthy aging. They contributed to the understanding of how gut health affects aging and the role of probiotics and prebiotics in maintaining overall health (13).
MARTINIAKOVA et al. (2022)	They analyzed the role of macronutrients, micronutrients and polyphenolic flavonoids in the prevention and treatment of osteoporosis. They provided information on the importance of nutrition for bone health and the prevention of fractures in the elderly (14).
MCMAUGHAN; OLORUNTOBA; SMITH (2020)	They investigated the relationship between socioeconomic status (SES) and access to health care, highlighting how these interrelated factors influence healthy aging. They provided a basis for understanding health disparities and the impact of SES on the health of older adults (15).
ARLEO et al. (2024)	They discussed the role of the cerebellum in aging, contributing to the understanding of neurological changes associated with age and their implications for cognition and mobility (16).
Slaves; Dhillon (2023)	They applied machine learning in the measurement of aging and geriatric diseases, offering insight into how technology can improve the diagnosis and treatment of age-related conditions (17).
DE LUCA et al. (2021)	They implemented a "One Health" approach to health innovation and active ageing in Campania, Italy. They contributed strategies to integrate health care and community-based interventions to improve the health of older adults (18).
ZEIDAN et al. (2023)	They studied gender differences in frailty among older adults, highlighting how women and men experience aging in different ways and how it affects health (19).
BASROWI et al. (2021)	They assessed Indonesia's progress towards healthy ageing, contributing a global perspective on public health strategies and nutritional interventions to support older people (20).
DI GIROLAMO et al. (2021)	They conducted a systematic review and meta-analysis on the effects of prolonged bed rest on muscle aging. They contributed with insights on the importance of physical rehabilitation for the preservation of muscle mass in the elderly (21).
NUNES et al. (2024)	They focused on curcumin as a promising approach for healthy aging, detailing its antioxidant, anti-inflammatory, and neuroprotective properties (22).
HUSSAIN et al. (2023)	They conducted a systematic review on loneliness and social networks of older adults in rural communities, emphasizing the importance of social support for the mental and physical well-being of older adults (23).
KUSPINAR et al. (2023)	They have assessed the properties of measuring living space mobility in older adults living in the community, providing tools to assess mobility and predict health outcomes (24).
RUDDER; MARTINEZ-GUARDADO; BROCHERIE (2023)	They studied the effects of intermittent normobaric hypoxia on health-related outcomes in healthy older adults, contributing information on innovative interventions to promote cardiovascular and metabolic health (25).
CATISSI et al. (2024)	They mapped nature-based interventions that target the health and well-being of older adults, highlighting the benefits of contact with nature for mental and physical health (26).
WONG et al. (2023)	They examined the relationship between physical activity, physical health, and mental health among Chinese older adults, contributing to a comprehensive view of the benefits of physical activity for healthy aging(27)(28).

WEINBERGER (2021)	It focused on vaccinating older adults against diseases such as influenza, pneumococcus, shingles, and COVID-19, emphasizing the importance of immunization for disease prevention in the elderly (29).
BONACCORSI et al. (2023)	They investigated the impact of the built environment and the neighborhood on the promotion of mental health, well-being and social participation of the elderly, highlighting the importance of the physical environment for healthy aging (30).
PRINA et al. (2024)	They assessed the impact of climate change on the health of older people, providing insight into how climate risks affect older populations and mitigation strategies (31).
ZHAO et al. (2024)	They explored the molecular mechanisms of aging and its role in neurodegenerative diseases, contributing to a detailed understanding of the biological processes underlying aging (32).
FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ (2022)	They identified determinants of quality of life and well-being in cognitively uncompromised older adults, providing a basis for interventions that promote healthy aging

DISCUSSION

QUALITY OF LIFE (QOL) AND WELL-BEING

Quality of life (QoL) is a multifaceted concept that encompasses objective and subjective elements (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Objectively, QoL involves tangible conditions, such as physical health, socioeconomic status, and living environment (DAS; DHILLON, 2023). Subjectively, it encompasses the individual's perception of life satisfaction and emotional well-being (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). The literature highlights that a holistic approach is essential to fully understand QoL in the elderly, including satisfaction with dimensions of life such as health, social relationships, and daily activities (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Mental health, for example, is fundamental for QoL, and depression and anxiety are common among the elderly due to social isolation and the loss of loved ones (DAS; DHILLON, 2023). Intervention programs that promote social interaction, such as support groups and community activities, have shown promising results in improving the well-being of older adults (HUSSAIN et al., 2023). During the COVID-19 pandemic, many of these interventions were adapted to digital platforms, keeping older people connected with their social support networks (DE LUCA et al., 2021).

EMOTIONAL INTELLIGENCE (EI)

Emotional intelligence (EI) is fundamental for healthy aging and involves the ability to perceive, express, understand, and regulate emotions (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). According to Mayer and Salovey, EI can be divided into four dimensions: emotional perception, emotional facilitation of thought, emotional understanding, and emotional regulation (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Emotional perception refers to the ability to recognize and identify emotions, both in oneself

and in others (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Emotional thought facilitation involves the use of emotions to improve cognitive processes and decision-making (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Emotional understanding includes the ability to analyze complex emotions and recognize how they evolve over time (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Finally, emotional regulation is the ability to manage and modify emotional responses to promote emotional well-being (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Older adults with high EI tend to have better coping skills and greater emotional resilience, coping more effectively with stressors such as the loss of loved ones or decreased autonomy (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). These individuals maintain a high level of well-being and quality of life (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

MENTAL HEALTH

Mental health is a crucial component of healthy aging (DAS; DHILLON, 2023). Depression, anxiety, and social isolation are common among older adults and can negatively affect overall health (BASROWI et al., 2021). Social support, cognitive stimulation, and participation in community activities can prevent these problems, promoting a better quality of life (DAS; DHILLON, 2023). Maintaining social support networks and participating in community activities helps combat loneliness, which is a significant risk factor for depression and anxiety (HUSSAIN et al., 2023). Psychosocial interventions, such as emotional education programs and cognitive therapies, are effective in promoting the mental health of the elderly (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). During the COVID-19 pandemic, the mental health of older people has been particularly affected, highlighting the importance of coping strategies and social support (DE LUCA et al., 2021). In addition, the practice of mindfulness and meditation has been shown to be beneficial for mental health, helping to reduce stress and promote emotional well-being (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

COPING STRATEGIES AND EMOTIONAL REGULATION

Coping strategies are techniques used to manage stress and adversity. The theory of Selection, Optimization and Compensation (SOC) developed by Baltes is particularly relevant for healthy aging (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). This theory proposes three interdependent components:

1. Selection: It involves choosing priority goals and activities that are most meaningful to the individual. In other words, the elderly select areas of life in

which they want to invest their limited resources, such as energy and time, to maximize gains and minimize losses (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

2. Optimization: This refers to the use of available resources effectively to achieve these goals. Older adults use their skills and abilities optimally to continue to achieve meaningful goals while maintaining functionality and quality of life (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).
3. Compensation: It implies the adoption of alternative strategies when resources or capacities are limited. When losses are inevitable, the elderly develop new ways of achieving their goals, using tools or strategies that compensate for limitations (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

Older adults who use proactive coping strategies, such as SOC, generally have higher life satisfaction, optimism, and subjective well-being (COLD-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Emotional regulation is also key and involves the use of techniques to manage and modify emotional responses, reducing the negative impact of stress. Practices such as mindfulness, which involves being present in the moment and accepting feelings without judgment, have been shown to be effective in regulating emotions and promoting well-being among older adults (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). In addition, meditation and relaxation exercises help reduce stress and improve mental health (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

SOCIAL SUPPORT

Social support is a determining factor in the quality of life (QoL) of the elderly (DAS; DHILLON, 2023). It refers to the perception of emotional, instrumental, and informational support from friends, family, and the community (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Studies show that a robust social support network can mitigate the negative effects of stressful events, such as illness or loss, promoting healthier aging (DAS; DHILLON, 2023). The quality of social relations is crucial; supportive relationships and reciprocity are associated with higher levels of emotional intelligence (EI) and life satisfaction (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). For example, older adults with good family relationships and friendships tend to have better mental and physical health (DAS; DHILLON, 2023).

In addition, engagement in community and social activities plays a significant role in maintaining the QoL and well-being of older adults (BASROWI et al., 2021). Participating in social groups, clubs, or volunteer activities provides a sense of belonging and purpose,

which are essential for emotional and mental health (DAS; DHILLON, 2023). During the COVID-19 pandemic, social support has proven even more vital, with many interventions being adapted to digital platforms to keep older people connected (DE LUCA et al., 2021). Tools such as video calls and online forums have helped reduce feelings of isolation (DE LUCA et al., 2021). Participation in online activities also promotes social interaction and psychological well-being (DE LUCA et al., 2021).

SOCIODEMOGRAPHIC CHARACTERISTICS

Personality traits, such as optimism, resilience, and extroversion, are key to adapting to changes during aging (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Optimistic individuals tend to have a more positive view of life, which can contribute to a better QoL (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Resilience, which is the ability to bounce back from adversity, allows older people to maintain a high level of functionality and well-being, even in the face of challenges (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Extraversion is associated with a greater social support network and positive interactions, which are crucial for mental and emotional health (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Sociodemographic characteristics, such as gender, age, educational level, and social class, significantly influence QoL (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

Older adults with a higher level of education tend to have better cognitive and emotional skills, contributing to better adaptation to changes (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). For example, higher education is correlated with higher levels of self-efficacy and better problem-solving skills (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Gender can influence coping experiences and strategies, with women often reporting higher levels of social support and involvement in support networks (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Social class, which includes economic and status factors, can determine access to health and well-being resources, directly influencing QoL and healthy aging (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

POSITIVE AND NEGATIVE EMOTIONS

Emotions play a critical role in the health and well-being of older adults. Positive emotions, such as joy, gratitude, and satisfaction, are associated with a range of health benefits, including a strengthened immune system, lower risk of chronic disease, and increased longevity (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). These emotions promote a general state of well-being and can facilitate recovery from illness by stimulating

beneficial physiological responses (COLD-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Studies indicate that positive emotions are also linked to the release of neurotransmitters, such as serotonin and dopamine, which improve mood and feelings of pleasure (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). On the other hand, negative emotions, such as sadness, anxiety, and anger, can have a significant adverse impact on physical and mental health (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). These emotions can increase vulnerability to diseases, such as cardiovascular problems, due to the release of stress hormones such as cortisol (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

In addition, chronic negative emotions can impair the immune system, decreasing the body's ability to fight infection and disease (COLD-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Therefore, it is crucial to promote emotional balance and encourage the cultivation of positive emotions through well-being practices, such as gratitude, mindfulness, and pleasurable activities (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

PSYCHOSOCIAL INTERVENTIONS

Psychosocial interventions are strategies designed to improve the quality of life (QoL) and well-being of older adults through psychological and social support (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). Emotional education programs, which focus on the development of emotional intelligence (EI) skills and coping strategies, have been shown to be effective in preventing mental health problems such as depression and anxiety (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022). These interventions help older adults develop a better understanding of their emotions and adopt more effective coping strategies. For example, cognitive behavioral therapy (CBT) has been widely used to help older adults restructure negative thought patterns and develop more adaptive behaviors (COLD-LUQUE; TOLEDANO-GONZÁLEZ, 2022).

In addition, continuous learning and participation in educational and cultural activities are beneficial for the cognitive and emotional health of older adults. Lifelong education keeps the mind active, promotes social interaction, and provides a sense of purpose, which are crucial elements for healthy aging (DAS; DHILLON, 2023). Activities such as learning new languages, participating in reading groups, or engaging in artistic and cultural activities can stimulate neurogenesis and synaptic plasticity, which are essential for maintaining cognitive function (FRÍAS-LUQUE; TOLEDANO-GONZÁLEZ, 2022).



FOOD AND NUTRITION

A balanced diet is crucial for maintaining health throughout life (BASROWI et al., 2021). For older adults, adequate protein intake is essential to prevent sarcopenia, a condition that causes loss of muscle mass and strength while limiting mobility and independence (BASROWI et al., 2021). Additionally, nutrients such as vitamin D and calcium are important for bone health, helping to prevent osteoporosis and fractures (BASROWI et al., 2021). Vitamins such as B12 are vital for neurological function and red blood cell formation (BASROWI et al., 2021). Maintaining adequate hydration is key, as dehydration can lead to serious problems such as constipation, cognitive dysfunction, and hypotension (BASROWI et al., 2021). Malnutrition, caused by insufficient nutrient intake or malabsorption, is a common problem among the elderly and can lead to complications such as loss of muscle mass, osteoporosis, impaired immune function, and increased risk of infections (CRISTINA; LUCIA, 2021). Adopting a diet rich in fruits, vegetables, lean proteins, and whole grains is essential for preventing chronic diseases and maintaining a healthy weight (CATISSI et al., 2024).

PHYSICAL ACTIVITY

Regular physical activity is one of the pillars of healthy aging (MCMAUGHAN; OLORUNTOBA; SMITH, 2020). Staying physically active helps preserve muscle strength and flexibility, as well as improve cardiovascular health and reduce the risk of chronic diseases such as diabetes and hypertension (BASROWI et al., 2021). Specific exercises for older adults, such as strength training, yoga, and tai chi, can improve mobility, balance, and endurance (DAS; DHILLON, 2023). In addition, regular physical activity is associated with better cognitive function and a lower risk of dementia (BASROWI et al., 2021). Studies show that regular physical exercise can also have a positive impact on mental health, helping to combat depression and anxiety, conditions that affect many older people (DAS; DHILLON, 2023). During the COVID-19 pandemic, physical activity adapted to the home environment proved essential to maintain the health and well-being of older people (DE LUCA et al., 2021).

MALNUTRITION AND OBESITY

Malnutrition and obesity are common problems among older adults and can lead to various health complications (BASROWI et al., 2021). Malnutrition, caused by insufficient nutrient intake or malabsorption, can result in loss of muscle mass (sarcopenia), osteoporosis, impaired immune function, and increased risk of infections (CRISTINA;

LUCIA, 2021). Obesity, on the other hand, is associated with a higher risk of chronic diseases such as type 2 diabetes, cardiovascular disease, and cancer (BASROWI et al., 2021). To combat these problems, it is essential to create programs that address both malnutrition and obesity (BASROWI et al., 2021). Dietitians and dietitians can provide personalized eating plans that meet the individual needs of older adults, and community meal programs can help ensure that everyone has access to healthy eating (BASROWI et al., 2021).

SARCOPENIA

Sarcopenia is the loss of muscle mass and function that occurs with aging, increasing the risk of falls, fractures, and early mortality (DI GIROLAMO et al., 2021). After the age of 50, there is an annual loss of 0.5-1% of muscle mass, even considering genetic and lifestyle differences (DI GIROLAMO et al., 2021). The pathophysiology of sarcopenia involves muscle denervation, decreased protein synthesis, and increased cellular apoptosis, influenced by hormonal, metabolic, and immunological factors (DI GIROLAMO et al., 2021). To mitigate these effects, specific interventions have been suggested, such as resistance exercises to stimulate muscle hypertrophy and improve neuromuscular function (DI GIROLAMO et al., 2021). Specific nutrients, such as high-quality proteins found in whey protein and leucine, play a vital role in protein synthesis and the preservation of muscle mass (DI GIROLAMO et al., 2021). A eucaloric diet, balanced in macronutrients, is also essential to prevent the loss of muscle mass and body fat, especially in periods of inactivity, such as during hospitalizations (DI GIROLAMO et al., 2021). In addition, supplementation with HMB (beta-hydroxy-beta-methylbutyrate) has been shown to significantly improve knee extension power and muscle functionality in elderly patients (DI GIROLAMO et al., 2021).

DNA DAMAGE AND REPAIR

DNA, being the foundation of life, carries all the genetic information necessary for the functioning and reproduction of cells (ZHAO et al., 2024). However, DNA is constantly under threat from damage caused by external factors, such as UV radiation, chemicals, and internal factors, such as reactive oxygen species (ROS) generated during cellular metabolism (ZHAO et al., 2024). When this damage occurs, the cell activates complex DNA repair mechanisms to preserve genome integrity (ZHAO et al., 2024). There are several DNA repair pathways, each with specific functions. Base excision repair (BER) corrects damaged bases by removing the wrong bases and filling the gap with the correct base

(ZHAO et al., 2024). Nucleotide excision repair (NER) removes large distortions in DNA, such as bulky adducts resulting from damage caused by UV radiation (ZHAO et al., 2024).

In addition, homologous recombination (HR) and non-homologous end-joining (NHEJ) are crucial for correcting double-strand breaks in DNA (ZHAO et al., 2024). HR uses a sister tape as a mold to correct breakage, ensuring accurate repair (ZHAO et al., 2024). NHEJ directly joins the ends of the break, making it a faster but error-prone process (ZHAO et al., 2024). Failure to repair this damage can lead to genomic instability, a major driver of aging and oncogenesis (ZHAO et al., 2024). This instability results in accumulated mutations that impair cellular function and promote senescence or apoptosis, which in turn contributes to the functional decline associated with aging (ZHAO et al., 2024).

TELOMERES AND TELOMERASE

Telomeres are complexes of proteins and repetitive DNA located at the ends of chromosomes, functioning as buffers that protect against chromosomal degradation and fusion (ZHAO et al., 2024). With each cell division, telomeres shorten due to the inability of DNA polymerase to fully replicate the 3' ends of chromosomes, a phenomenon known as the end-of-replication problem (ZHAO et al., 2024). When telomeres reach a critical length, the cell enters replicative senescence or undergoes apoptosis, mechanisms that act as a defense against uncontrolled cell proliferation (ZHAO et al., 2024). Telomerase is a ribonucleoprotein enzyme that can extend telomeres by adding DNA repeats, using an RNA template that it carries itself (ZHAO et al., 2024). Telomerase activity is high in germ cells and some stem cells, where telomere renewal and length maintenance are essential (ZHAO et al., 2024). However, telomerase activity is suppressed in most adult somatic cells, contributing to progressive telomere shortening with age (ZHAO et al., 2024). This shortening limits the regenerative capacity of tissues, being a key factor in the aging process (ZHAO et al., 2024). In animal model studies, telomerase reactivation has shown potential to slow cellular aging and extend lifespan, suggesting possible therapeutic interventions (ZHAO et al., 2024).

FREE RADICALS AND OXIDATIVE STRESS

Free radicals, such as reactive oxygen species (ROS), are unavoidable byproducts of aerobic metabolism, playing critical roles in cell signaling and defense against pathogens (ZHAO et al., 2024). However, when ROS production exceeds the body's antioxidant capacity, oxidative stress occurs, which can oxidize cellular components such as DNA, proteins, and lipids, resulting in structural and functional damage (ZHAO et al., 2024). The

body has antioxidant systems, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, which neutralize ROS (ZHAO et al., 2024). With aging, the efficiency of these antioxidant systems decreases, resulting in an increase in chronic oxidative stress (ZHAO et al., 2024). Oxidative stress is closely linked to aging and many chronic diseases, including cardiovascular disease, neurodegenerative disease, and cancer (ZHAO et al., 2024). Studies demonstrate that increased ROS can damage mitochondrial DNA, promote cellular senescence, and dysregulate cell signaling pathways, exacerbating the functional decline associated with aging (ZHAO et al., 2024).

CELLULAR SENESCENCE

Cellular senescence is a state of permanent cell cycle arrest that prevents the proliferation of damaged or potentially cancerous cells (ZHAO et al., 2024). Although cellular senescence has a protective role, preventing the formation of tumors, it also contributes to aging and tissue dysfunction (ZHAO et al., 2024). Senescent cells secrete a variety of inflammatory mediators, proteases, and growth factors, known as the senescence-associated secretory phenotype (SASP), which can induce chronic inflammation and dysfunctional tissue remodeling (ZHAO et al., 2024). This inflammatory microenvironment is associated with the development of several age-related diseases, such as atherosclerosis, osteoarthritis, and Alzheimer's (CATISSI et al., 2024). Cellular senescence is therefore a double phenomenon, with both protective and deleterious effects (ZHAO et al., 2024).

CHRONIC INFLAMMATION (INFLAMMAGING)

Chronic low-grade inflammation, or "inflammaging", is a distinguishing feature of aging (ZHAO et al., 2024). This chronic inflammation is fueled by a variety of factors, including activation of the innate immune system, the accumulation of senescent cells, and mitochondrial dysfunction (ZHAO et al., 2024). Senescent cells secrete pro-inflammatory cytokines, chemokines, and proteases known as senescence-associated secretory phenotype (SASP) (ZHAO et al., 2024). SASP can modify the tissue microenvironment, promoting chronic inflammation and contributing to the progression of age-related diseases such as atherosclerosis, Alzheimer's disease, and arthritis (CATISSI et al., 2024). Chronic inflammation is a vicious cycle, where inflammation promotes more inflammation, exacerbating the effects of aging (ZHAO et al., 2024).

AUTOPHAGY AND CELLULAR QUALITY

Autophagy is a highly regulated degradation process that recycles damaged and unnecessary cellular components (ZHAO et al., 2024). During autophagy, damaged organelles, such as dysfunctional mitochondria, and malformed proteins are engulfed by autophagosomes and subsequently degraded into lysosomes (ZHAO et al., 2024). The efficiency of autophagy decreases with age, resulting in the accumulation of cellular waste that can interfere with cellular function and promote aging (ZHAO et al., 2024). Inadequate autophagy is associated with several age-related diseases, including neurodegenerative diseases, where the accumulation of malformed proteins such as beta-amyloid and alpha-synuclein is a central pathological feature (ZHAO et al., 2024). Improving autophagy is considered a potential therapeutic target to delay aging and treat related diseases (ZHAO et al., 2024).

ENERGY METABOLISM AND MITOCHONDRIA

Mitochondria are cellular organelles responsible for producing energy in the form of ATP, which is essential for maintaining cellular homeostasis (ZHAO et al., 2024). With aging, mitochondria exhibit a decrease in functional efficiency, including reduced mitochondrial membrane potential, increased production of reactive oxygen species (ROS), and decline in responsiveness to metabolic stress (ZHAO et al., 2024). This mitochondrial dysfunction not only reduces ATP production, which is critical for cellular energy, but also contributes to increased oxidative stress, promoting cellular aging (ZHAO et al., 2024). In addition, mitochondria are involved in apoptosis signaling; its dysfunction can lead to the activation of apoptotic pathways that result in programmed cell death (ZHAO et al., 2024). Maintaining mitochondrial function is therefore crucial for cellular health and for the prevention of functional decline associated with aging (ZHAO et al., 2024).

EPIGENETICS AND AGING

Epigenetics refers to inherited modifications in gene expression that do not involve changes in the DNA sequence (ZHAO et al., 2024). DNA methylation is one such modification, involving the addition of methyl groups to cytosines in CpG dinucleotides (ZHAO et al., 2024). These changes in DNA methylation are lifelong dynamics and influence gene expression and genomic stability (ZHAO et al., 2024). The concept of an "epigenetic clock" is based on the observation that certain DNA methylation patterns correlate strongly with chronological age and can predict an individual's "biological age" (ZHAO et al., 2024). Aberrant epigenetic changes are associated with several aging-related

diseases, including neurodegenerative diseases, cancer, and cardiovascular diseases (ZHAO et al., 2024). Understanding the epigenetic mechanisms of aging offers possibilities for developing therapeutic interventions that can slow aging and prevent related diseases (ZHAO et al., 2024).

MOBILITY AND FUNCTIONAL CAPACITY

Mobility is essential for the independence and quality of life of the elderly (24). Living space mobility refers to movement within the environment, from home to community and beyond (24). Tools such as Life-Space Assessment (LSA) are valuable for assessing older adults' mobility by measuring the extent and frequency of daily movement and the need for assistance (24). Studies show that these measures are effective predictors of health outcomes, such as hospitalizations and quality of life (24). Exercise programs, such as walking and strength exercises, improve mobility, muscle strength and cardiovascular capacity, reducing the risk of chronic disease (20). Post-hospitalization rehabilitation, which combines physical exercise with nutritional supplementation, is crucial for the recovery of muscle mass and improvement of functional performance in the elderly (21).

MOBILITY AND FUNCTIONAL CAPACITY

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RURAL CHALLENGES

Access to health care varies dramatically with geographic context, significantly affecting older people in rural areas (ARLEO et al., 2024). In these regions, there are fewer health providers, which limits access and negatively impacts the health of older adults,



resulting in higher rates of disability, cognitive impairment, and mortality (ARLEO et al., 2024). In China, for example, older adults in rural areas report greater difficulties in accessing medical care due to distance and lack of adequate transportation (ARLEO et al., 2024). Policies that encourage health and transportation infrastructure in rural areas are essential to improve the quality of life of these older adults (ARLEO et al., 2024).

COMMUNITY PROGRAMMES

Community programs have been shown to be effective in promoting healthy aging (ARLEO et al., 2024). In the United States, fall prevention and chronic disease self-management programs complement traditional health care by improving health outcomes among older adults (ARLEO et al., 2024). These programs not only provide practical and emotional support, but also promote social interaction, combating isolation (ARLEO et al., 2024). In rural areas, initiatives such as community canteens, where older people can eat meals together, and community transportation programs, are essential to reduce loneliness and improve quality of life (HUSSAIN et al., 2023).

POST-HOSPITALIZATION REHABILITATION

Post-hospitalization rehabilitation plays a vital role in recovering muscle mass and improving functional performance (DI GIROLAMO et al., 2021). Rehabilitation programs that combine physical exercise with nutritional supplementation, such as whey protein or HMB (beta-hydroxy-beta-methylbutyrate), have been shown to be effective in restoring muscle mass and recovering neuromuscular function (DI GIROLAMO et al., 2021). HMB supplementation, for example, has been shown to significantly improve knee extension power and muscle functionality in elderly patients after periods of inactivity (DI GIROLAMO et al., 2021). These programs should be multimodal, integrating aerobic, strength, and balance exercises, adapted to the specific needs of each individual (DI GIROLAMO et al., 2021).

IMMUNE FUNCTION

Immune function is affected by aging, a process known as immunosenescence (CATISSI et al., 2024). This process is characterized by an ineffective immune response, with a reduction in the production of new immune cells, decreased function of T and B lymphocytes, and increased production of pro-inflammatory cytokines (CATISSI et al., 2024). Immunosenescence results in a lower ability to fight infections, greater susceptibility to autoimmune diseases, and reduced efficacy of vaccines (CATISSI et al., 2024). To

mitigate the effects of immunosenescence, nutrition plays a crucial role (CRISTINA; LUCIA, 2021). Nutrients such as vitamin D, antioxidants (such as vitamins E and C), and polyunsaturated fatty acids are essential for immune function (CRISTINA; LUCIA, 2021). In addition, the probiotics present in fermented dairy products, such as yogurt, may contribute to the health of the immune and gastrointestinal systems (CRISTINA; LUCIA, 2021).

REGENERATIVE CAPACITY AND STEM CELLS

Aging is associated with a decrease in the regenerative capacity of tissues, due to the reduction in the functionality and number of adult stem cells, which are responsible for tissue repair and regeneration (CATISSI et al., 2024). This decrease results in lower ability to recover after injury and less effective tissue regeneration, leading to tissue degeneration and functional failure (CATISSI et al., 2024). In the cardiovascular system, for example, the ability of the heart muscle and blood vessels to repair and regenerate is impaired, which can result in heart failure and other cardiovascular diseases (CATISSI et al., 2024). Stem cell research seeks solutions to improve the regenerative capacity of tissues, including the use of induced pluripotent stem cells (iPSCs) to regenerate damaged tissues (CATISSI et al., 2024).

IMMUNE SENESCENCE

Immune senescence is characterized by a reduction in the production of new immune cells, a decrease in the function of T and B lymphocytes, and an increase in the production of pro-inflammatory cytokines (CATISSI et al., 2024). This immunosenescence results in a lower ability to fight infections, increase susceptibility to autoimmune diseases, and reduce the effectiveness of vaccines, as well as contributing to chronic systemic inflammation (CATISSI et al., 2024). Interventions aimed at improving immune function include adequate nutrition with nutrients such as vitamin D, antioxidants (vitamins E and C), and polyunsaturated fatty acids, which are essential for immune system health (CRISTINA; LUCIA, 2021). In addition, probiotics present in fermented dairy products, such as yogurt, may contribute to immune and gastrointestinal health (CRISTINA; LUCIA, 2021).

NATURE-BASED INTERVENTIONS

Nature-based interventions have shown efficacy in attenuating the pathophysiological effects of aging (CATISSI et al., 2024). Studies indicate that contact with nature can reduce cortisol levels and other stress markers, improve heart rate variability, lower blood pressure, and increase parasympathetic nervous system activity (CATISSI et

al., 2024). These effects are especially beneficial for cardiovascular health and for reducing the risk of heart disease (CATISSI et al., 2024). In addition, contact with natural environments has been associated with improvements in immune function, possibly through modulation of SASP (senescence-associated secretory phenotype) and reduction of chronic inflammation (CATISSI et al., 2024). Exposure to natural environments can also promote mental and cognitive well-being by improving mood, reducing symptoms of depression and anxiety, and improving cognitive function (CATISSI et al., 2024). These effects can be mediated through reducing stress, increasing physical activity, and promoting social interactions, all of which contribute to mental health and well-being (CATISSI et al., 2024). In addition, contact with nature can stimulate neurogenesis and synaptic plasticity, crucial processes for maintaining cognitive function in old age (CATISSI et al., 2024).

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IMMUNOLOGICAL SENESCENCE

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PSYCHOMETRIC PROPERTIES (VALIDATION OF MEASURES SUCH AS LSA)

Assessment tools, such as the Life-Space Assessment (LSA), are valuable for measuring the mobility of older adults, assessing the extent and frequency of daily movement and the need for assistance (KUSPINAR et al., 2023). The validity of these measures is essential to ensure that they accurately assess mobility and predict health outcomes such as hospitalizations and quality of life (KUSPINAR et al., 2023). Content validity, for example, is assessed by the relevance, comprehensiveness, and comprehensibility of the measures (KUSPINAR et al., 2023). Test-retest reliability examines the consistency of responses over time, while responsiveness assesses perceived changes after interventions, such as physical therapy programs (KUSPINAR et al., 2023). Systematic studies, such as those following the COSMIN methodology, have found that the LSA has high reliability and validity, making it a robust tool for assessing the mobility of the elderly (KUSPINAR et al., 2023).

CONCLUSION

This systematic review explored multiple factors and interventions related to healthy aging, highlighting the complexity and interconnectedness of the biological, psychological, and social processes involved. From the different approaches, it is clear that aging in a

healthy way is not just about the absence of disease, but also about maintaining functional capacity and well-being in various dimensions of life. The reviewed articles elucidated the importance of proper nutrition and regular physical activity in preventing conditions such as sarcopenia and chronic diseases, reinforcing the need for balanced diets and specific exercise for older adults. In addition, the role of mental health was widely discussed, with an emphasis on emotional intelligence, coping strategies, and social support as crucial components for quality of life.

The review also addressed the molecular and cellular mechanisms of aging, including DNA damage, mitochondrial dysfunction, and chronic inflammation, which are key to understanding aging and developing therapeutic interventions. Nature-based interventions were highlighted as promising for improving both the physical and mental health of older people. In addition, the review highlighted the importance of public policies and community programs that promote environments favorable to aging, ensuring access to quality health care and encouraging social participation. Specific challenges faced by rural populations and the need for targeted measures for these areas were also discussed.

In short, promoting healthy aging requires a multidimensional and integrated approach, involving interventions that address the physical, mental, and social needs of older adults. Detailed understanding of these factors and implementing evidence-based strategies can ensure that older people live not only longer, but with a better quality of life.

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