

Aging and Public Health: From Molecular Changes to Physiological Challenges

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Abstract

This review will discuss the aging from molecular, cellular and physiological perspective. Aging is the result of molecular processes such as DNA damage, telomere shortening and mitochondrial dysfunction leading to an overall wear and tear and function loss in the cells and system as such disorders. These aberrations result in critical organ dysfunction (heart, arteries, kidneys and brains) that predispose to cardiovascular disease, malignancies cognitive dysfunction and other age-associated diseases. Alterations in nutritional, lifestyle and exercise modifications reduce the ill effects of aging indicates promising strategies for increasing quality of life in the elderly

Keyword: again, gut microbiome, cognitive decline, aerobic training, sarcopenia

1. Introduction

Aging is a continuous process in which the molecular machinery of the body becomes disordered and disturbed. The disturbances at every level of molecules, ranging from DNA molecules and other cellular environments to tissue environments, occur (1). Over time, the disturbances accumulate in the body's communication systems so that coordination among components is reduced. This process, termed "mutual enslavement," is the interdependence of different bodily systems, in which disorder in one area negatively impacts the function of others (2). Therefore, these molecular abnormalities lead to cumulative alterations in the structure and function of the heart and arteries. With increasing age, these al-

terations lead to a reduction in cardiovascular performance and an increased risk of acquiring heart diseases (3). With improvements in health and nutrition, life expectancy has increased worldwide. According to research, by 2030, 1 in 6 people will be aged 60 years and above. Therefore, the 60+ age group is expected to grow from 1.4 billion in 2020 to 2.1 billion by 2050 (4).). Biologically, aging is a gradual process over time due to the accumulation of damage to various cellular and molecular structures. Due to these developments, people slowly lose their physical and mental strength and are more susceptible to many diseases (5). Aging is a gradual decline in physiological function and greater disease susceptibility, and reduced ability to maintain homeostasis.

Key features of aging are: Aging is associated with increased cellular accumulation of DNA damage, leading to dysfunctional cellular behavior and an increased tendency to mutations. Telomeres, the protective caps at the ends of chromosomes, progressively shorten at each cell cycle. Progressive loss eventually limits the cellular replication capability and leads to cellular senescence. The energy-producing cellular organelles, mitochondria, experience less function as life ages. Dysfunction results in low energy production and aberrant metabolic processes (6).

1-1 Methodology

The PRISMA guideline was followed in this review to synthesize molecular, cellular and physiological aspects of aging in relation to lifestyle interventions versus exercise on age-related decline. A literature search was performed in PubMed, Scopus, and Web of Science from (2015 to now) with specific keywords: aging cellular senescence cardiovascular aging osteoporosis cognitive decline gut microbiome depression Parkinson's disease. Additional studies were retrieved by hand searching the references. Both the included trials and biases were of high quality with respect to molecular mechanism of aging, clinical aspects including aging and language was English as well as full-text availability. This includes only studies with methodological major flaws, conference abstracts or non-peer-reviewed papers. Data on study characteristics (including participant demographics, key variables and outcomes) and intervention details were extracted using a pre-coded form. In view of the diversity of the studies, qualitative thematic synthesis was done and the outcome was groups according to affected organ systems and interventions. One limitation of our review is the exclusion of non-English studies, variations in study designs and outcomes and also possibly the delayed indexing of database that might lead to exclusion of recently published papers.

1-2 Physiological Changes

Prostate disease has a direct link with increasing age. The prevalence of the condition among men at the age of 40 is only between 5% and 10%, but among men in the 70- to 80-year-old age bracket, the occurrence is very high at 80%. This disease usually manifests because of benign prostatic hyperplasia (BPH) or prostate cancer (PCa) (7). Pros-

tate cancer (PCa) is the second most prevalent European cancer mortality in view of infrequent occurrence in individuals below the age of 45. Despite the fact that women do not possess a prostate gland, Skene's glands around the urethra are nearly equal and grow older along with them (8). Observe that due to aging and menopause onset, the body of women changes hormonal structure, which can affect such glands. Some of the normal conditions of Skene's glands in aged individuals are infection, inflammation, and even benign or malignant tumors (9). The other physiological change with age is nephrosclerosis or hardening of kidney tissue. It is a change that produces fewer functioning filters (glomeruli) to lead to reduced kidney function (10). Kidney function, quantified by the Glomerular Filtration Rate (GFR), declines with age because nephron compensation after age 50 is not as effective, making kidneys smaller. Despite this fact, the requirement of the body for optimal kidney function remains unchanged (11). To compensate for the changes that occur in kidney function with aging, researchers recommend performing aerobic and resistance exercises. Studies indicate that regular physical exercise can help reduce blood pressure and increase blood supply to the kidneys, particularly in older people, especially those with compromised kidney function (12). Large differences exist between women and men in the loss of kidney function with age. Men will have a more pronounced decline in glomerular filtration rate (GFR) than women (13). Men also have higher glomerular filtration rate (GFR) than women at younger ages; this trend is reversed after the age of 60, although differences are not always significant (14). Prevalence of kidney diseases among the elderly varies widely across different countries. Research indicates that in many low- and middle-income countries, the prevalence of chronic kidney disease (CKD) is higher due to a number of factors such as limited opportunities for access to healthcare services and adverse social and economic conditions (15).

Chronic kidney disease (CKD) is most prevalent in Saudi Arabia (45.66 cases per 100,000 people), Qatar, and the United Arab Emirates. In North Africa and the Middle East, the incidence of kidney disease is much greater than that of other regions at a rate of 36.55-39.58 per 100,000 individuals (16).

Menopause is a biological event in women's lives as a sign of the complete cessation of menstruation and the decline in estrogen and progesterone secretion. It usually happens at the age of 45 to 55 years, which is the termination of the reproductive age. Most commonly reported symptoms are hot flushes, night sweats, mood change, vaginal dryness, and low libido. Diagnosis of menopause occurs after 12 consecutive months of amenorrhea (17, 18). Physical exercise has been shown to have a positive effect on menopausal symptoms. Aerobic exercises are beneficial for reduction in frequency and severity of hot flushes as well as psychological symptoms. Resistance exercise and strength training maintain bone density and decrease risk for osteoporosis. Also, body-mind exercises like tai chi and yoga improve mental health and reduce stress (17, 19).

1-3 Muscle Tissue Changes

Sarcopenia is a condition referred to as 'muscle weakness, muscle function and muscle mass wasting' which occurs with age. Results: The reasons for this in fact is the decrease of muscle fibers numbers, motor neuron loss and protein synthesis derangement. This could all result in weakness and debility of physical function. The research has also shown that sarcopenia is related to inflammation (20), endocrine unbalance and malnutrition (21). Further, muscle power, also decreases among elderly who experience weight loss and hence falls easily. Other examples are the sarcopenic people exhaustion with less favorable exercise response once again reducing physical activity and muscle catabolic (20, 21). As age increases, the composi-

tion of fat changes with loss of subcutaneous fat and gain in visceral fat. As visceral fat surrounds the vital organs, this makes the environment predisposed for metabolic diseases such as insulin resistance and type 2 diabetes. People who are sarcopenic obese (loss of muscle mass with increased fat deposition) also mimic metabolic stress on the body (20). SASP pathway Inflammatory cytokines of the eponymous senescence-associated secretory phenotype (SASP) are etiologic contributors in sarcopenic muscle wasting (3). Although IL-6 is a cytokine where higher levels suggest a correlation between muscle damage and atrophy (22). IL-6 causes muscle catabolism by blocking the stimulation of muscle protein synthesis and in STAT3-IL-6 pathway. Improved muscle phenotype through the inhibition of IL-6 in animal models (23). IL-15 is also a cytokine implicated with sarcopenia and lies together IGF-1 to inhibit myotome differentiation into adipocytes as well support myosin synthesis (24).

1-4 The elderly and osteoporosis

As one ages, the body begins to stop being able to make and regenerate bone tissue at early life rates. Females are definitely affected more by the process, as bone erosion occurs much faster after menopause when estrogen levels start to drop. Excessive loss of bone occurs when this bone loss density results in diseases like osteopenia (density less in the bones) and osteoporosis thereby making a person prone to fractures (24).

Table 1: Molecular and Cellular Changes Associated with Aging

Molecular/Cellular Factor	Description	Physiological Impact
DNA Damage	Accumulated damage to DNA molecules due to oxidative stress	Impaired cellular function; increased mutation risk
Telomere Shortening	Progressive reduction of telomere length with each cell division	Limits cellular replication; leads to cellular senescence
Mitochondrial Dysfunction	Decline in mitochondrial energy production	Reduced energy output; impaired metabolic processes
Elevated Inflammatory Cytokines	Increased secretion of IL-6, IL-15 (SASP factors)	Promote muscle atrophy; disrupts tissue regeneration

The detrimental effect of physical inactivity on most diseases (such as osteoporosis which is a major public health problem all over the world) is shared by the increasing number of women affected by this disease (over 200 million) with almost 75 million cases in USA, Europe and Japan (25). Bone loss occurs generally in 35+, and speeds up after menopause. Among older women, hip fractures have a higher mortality rate of 10 to 20% over their same-aged counterparts and osteoporosis is more common than breast cancer or diabetes in women aged 45 and older (26). As a projected, hip fracture incidence in men is anticipated to increase by 310% and that in women by 240% by 2050 due to the ageing population. Thus, diagnosis, monitoring and treatment of osteoporosis becomes a matter of urgency (27).

We have evidence that osteoarthritis, osteoporosis are held tightly regulated by cellular senescence and ongoing inflammatory events as for the diseases like: Inflammatory arthritis. Lifestyle interventions, such as being active and eating appropriately are recommended as cost-effective approaches to counteract cellular aging (28), Weightlifting exercises, including resistance training (RT), are recognized as a method to prevent or reduce bone mineral density (BMD) loss. These exercises apply tensile stimuli to the bones, leading to an increase in bone mineral content (29). But low impact exercise and sports like cycling and swimming do not adversely affect bone density (30) Resistance training (RT) appears to be a narrow preventive intervention for dysosteogenesis by improving bone mineral density. Improved tissue metabolism is thought to be supported by small changes in the mass or density of bone. A Direct Positive Evidence: It is backed by many longitudinal studies, that resistance exercise is the single best to increase bone mass because it prevents BMD loss with age or can minimize increases. Large studies have noted minor declines in BMD (31, 32), and study results can differ by age, sex and ethnicity of subjects studied. Especially in women the bone mineral density undergoes a sharp decline with decrease in estrogen secretion typically starting from menopause. The result is subsequent fractures, mainly in the femur and hip bones and increase the mortality rate of patients with osteoporosis (33). It was noted that a few types such as Tai Chi Yoga, for example can stop bone-mineral density from decreasing

with the menopausal women. However, scientists say more research is needed in order for investigators to reach a level of confidence between the findings of this trial and its therapy protocols facility (34).

1-5 Breast and Liver Cancer

Breast cancer is an unregulated malignancy of breast tissue characterized by unregulated growth and accumulation of cells (36). Either invasive tumors or non-invasive and distant metastases may arise from without (35). In the year 2020, more than 23 million primary breast cancer cases were diagnosed leading to an estimated 685k deaths. These numbers represent the magnitude and global prevalence and impact of this disease. It is estimated that by 2040, more than 3 million will have cancer and over 1 million annually will die from its sequelae (36). Various factors can contribute to the development of breast cancer in women, the most significant of which include: If a family member (mother, sister, or daughter) has been diagnosed with breast cancer, the risk of developing this disease increases severalfold (37). Several genes, including BRCA1 and BRCA2 whereby breast cancer susceptibility could be exceptionally enhanced (38). Women with high levels of estrogen and progesterone have greater risk for breast cancer (39). Since exposure to chemical pollutants and X-rays has been identified as a risk factor, the overall likelihood of developing this cancer rises with age, particularly with higher levels of exposure (40). Other risk factors for breast cancer include over/underweight especially at menopause; irregular physical activity and alcohol consumption; and diet (41).

Adaptive or aerobic exercise (30-60 mins/day) walking including briskly cycling swimming for enhancing heart/lung/metabolic state. When body fat is lower, and hormones such as estrogen are either not produced, or not in as great reserve, these practices reduce the risk of breast cancer." (42) It releases adrenaline and noradrenaline as well as cortisol (43) to increase fat to be metabolized and energy metabolism. They improve insulin resistance at the same time, and reduce estrogen which lowers fat storage and improve blood sugar regulation. Along the way exercise boosts levels of IGF-1 and growth hormone but lowers myostatin (43).

Exercise is confirmed to be one of the significant factors in cancer prevention with changes on many biological markers by the means of aerobic movements. 44 This reduces pro-inflammatory cytokines, like TNF- α and IL-6; and enhances antioxidant enzymes such as superoxide dismutase (SOD) & glutathione peroxidase (GP, & thereby promotes p53; this is a tumor suppressor); (45, 46) Yoga, being a mind-body treatment has been shown by studies to have substantial and beneficial effects on breast cancer patients.(47) Benefits of yoga on breast cancer patients: reduction in stress, improvement of emotional well-being, and physical health.

Specific yoga practices, such as breathing exercises, meditation, and gentle postures, have been shown to lower levels of the stress hormone cortisol, which can lead to better immune function and a reduction in cancer-related fatigue (48, 49). Tai Chi is a non-competitive, mind and body exercise/meditation form that originated in China with roots from long-term Chinese martial art; it has long been used as a form therapy for physical and mental well being particularly good at what it does are those suffering from an incurable condition. It is a slow practice of movements, breath and consciousness which improves quality to live for the patients (50).

A study found that the exercises of Tai Chi influence the degree of hormone in breast cancer patients. It lowers cortisol, the fight-or-flight hormone (51) having slow movement and deep breathing due to this Tai Chi- reduces (50). Decreasing cortisol is associated with decreased inflammation and immunological function, especially for patients with cancer. (52) Tai Chi exercises can raise melatonin levels, some studies have found. Melatonin helps control sleep quality. By regulating the body's circadian rhythms (53). Tai Chi practice may be able to change the activeness of steroid hormones, such as estrogens. For example, high estrogen levels can add to an individual's chances of developing breast cancer. Tai Chi tends to calm hormone levels and lessens stress which in turn balances estrogen levels and decreases breast cancer recurrence (51). In addition to psychological and emotional aspects in patients as well Tai Chi exercises increase the concentration of stress related moderators (endorphins, dopamine.). These hormones help to reduce pain perception improve

mood and decrease feeling of relaxation all indirectly supporting the immune system (54). Being one of largest internal organ in the body and definitely the most important one within the upper right abdomen base under the rib cage is the liver. It carries out various useful functions to stay the health of the body. Metabolism and detoxification are among the liver's most important functions; it also stores numerous nutrients and produces chemicals needed for digestion right down to many other important body processes (55). Liver cancer (also known as hepatocellular carcinoma or HCC) is a type of malignant liver tumor arising from the epithelial cells. The most commonly diagnosed type of liver cancer starts in the main liver cells (hepatocytes) (56). The most common cause of liver cancer is chronic liver damage that is usually due to hepatitis B and C infections, long-term alcohol use and obesity, which leads to fatty liver disease as well as another condition known as cirrhosis (scarring), that slowly results from liver dysfunction (57). Liver cancer is more common in men than women (58).

Aerobic exercises such as running and cycling help improve the function of the heart and lungs and reduce the risk of cardiovascular diseases. These exercises increase blood flow and supply oxygen and nutrients to the cells, which improves liver function and reduces the risk of liver diseases (59) and decrease the chance of a liver disease. Fat burned and Weight Loss The exercises are also fat dissipating. Having too much body fat and obesity is one of the risk factors for liver disease. This is one of the most important points for an individual who have risk of diabetes and liver disease, because regular physical exercise can improve the insulin sensitivity and normalize successive glucose metabolism (60). The research also found that the same subjects have equivalent improvements in NAFLD by resistance training than aerobic exercise but without equivalence of frequency and intensity. In the presence of a NASH patient who has a low CV reserve, lacks the capacity for or intolerance to aerobic exercises, it may be more feasible as well beneficial to prescribe resistance training (61).

1-6 Cognitive decline

Dementia is a progressive mental health condition which affects the memory, thoughts and behaviors

Table 2: Physiological Changes in Different Organ Systems with Aging

Organ/System	Structural/Functional Changes	Risk Factors	Clinical Implications
Cardiovascular	Arterial stiffening; reduced heart performance	DNA damage; hypertension	Increased risk of heart diseases
Renal	Nephrosclerosis; decreased glomerular filtration rate	Aging; hypertension	Chronic kidney disease; reduced kidney function
Neurological		Aging; hormonal changes	Alzheimer's disease; dementia
Musculoskeletal	Sarcopenia; loss of bone mineral density	Physical inactivity; hormonal changes	Higher risk of fractures and osteoporosis
Digestive	Altered gut microbiota composition	Diet; decreased gut motility	Metabolic disorders; gastrointestinal diseases

and interferes with normal function of day-to-day life. It is a group of disorders characterized as dementia by Alzheimer's, vascular dementia and the Lewy body variant with a different biologic underpinning but localized impairments in reasoning, confusion and disorientation as well mood and personality change (62). The illness persistently causes expressive, impaired command and daily living problems. Dementia as the disease progresses becomes a great burden to patients and relatives, hence the need for comprehensive management strategies regarding quality of life and health (63). Alzheimer disease is the leading cause of dementia. These deposits consist of protein molecules called beta-amyloid and tau in the brain. These deposits injure nerve cells, as well cause an inflammatory response in the brain leading to cognitive deterioration and memory decline chronically (64). Beta-amyloid (A β) a well-known peptide involved in pathogenesis and disease progression in Alzheimer's disease, when beta-amyloid peptides accumulate in the brain, these plaques disrupt cellular communications. This disruption can lead to a chain of neuropathological events, including: Inflammation, Neuronal Damage and Disruption of Signaling: The accumulation of beta-amyloid can interfere with signaling pathways in the brain, contributing to a decrease in cognitive abilities and memory (65). Amyloid beta is also proposed to serve as a potential biomarker for predicting susceptibility to develop AD or dementia (66).

Women account for approximately two-thirds of Alzheimer's cases. This huge gender gap is caused by a multitude of biological and hormonal influ-

ences. The chief reason is that women live longer than men and through it the continual consequence is as followed weight of age associated condition for dense brain degeneration like Alzheimer's (67, 68). The second pivotal driver is the fast drop in estrogen levels following menopause. Estrogen protects the nerve from damage, and a lack may leave the female brain more vulnerable to developing Alzheimer-type changes. Moreover, women have two X chromosomes and this further confounds differential gene expression related to genes implicated in Alzheimer's disease including its pathological mechanisms (69). Recent evidence indicates that the differential incidence and severity of Alzheimer's disease between men and women can be partially explained by genetic and epigenetic modifications on the X-chromosome (70).

Genetically, the APOE ϵ 4 gene, a major risk factor for Alzheimer's, impacts women more. The gene is associated with greater accumulation of amyloid plaques and neuroinflammation in women compared to men (71). It has now been disclosed that the quantification of amyloid beta in the blood can provide useful insight into the risk of the development of Alzheimer's disease. (72). Research has shown that aerobic exercise, such as cycling and walking at a fast pace, when performed for at least 150 minutes a week, can increase blood flow to the brain. The increased blood flow leads to improved cognitive function by increasing the size of the hippocampus, part of the brain that is crucial for memory and which decreases in individuals with Alzheimer's disease. In addition, aerobic exercise can also help with memory and cognitive function

by reducing neuroinflammation and increasing vascular compliance (73).

1-7 Microbiome Components and Their Functions in the Gut

The guts of humans are populated by millions of microorganisms, that are much essential, especially bacteria (74) Four major types of bacteria are known to exist in a healthy person: Firmicutes; Bacteroidetes; Actinobacteria and Proteobacteria (75). The types of microorganisms in the gut can be altered by diseases. For example, the relative abundance of Firmicutes and Clostridia bacteria decreased significantly in type 2 diabetic patients. Conversely, however more Bacteroidetes and fewer Firmicutes are associated with an increased ratio between Bacteroidetes to Firmicutes, as well as both Bacteroidetes- Prevotella and (more positively) Betaproteobacteria (76). Recent research indicates that the fat composition in athletes differs from that in individuals with obesity. Notably, there is a decreased abundance of Bacteroidetes and certain subgroups of bacterial species in those who are obese. (70), while Firmicutes and their subgroups, in particular, increase (71) Conversely, these amounts are reversed for athletes. Also, muscle mass positively associated with Bacteroidetes decreases; that is, as a person has more muscle mass and lean body mass, there is a tendency for this type bacteria-to be reduced in the gut (77). Research conducted in Iran, China, and Ukraine indicates that the Firmicutes to Bacteroides (F/B) ratio is generally higher in obese individuals. This ratio is considered one of the indicators of microbial changes in obese individuals, and its increase may

reflect an imbalance in the composition of the gut microbiota associated with obesity (78–80).

1-8 The impact of gut microbiomes on the brain and cognitive function.

Gut microbiome is a diverse microbial ecosystem consisting of bacteria, fungi and viruses that live within your digestive system as a part of the human gastrointestinal tract. This metabolic ecosystem is not only key to the digestive process, but has a lot of importance on human health including but not limited to neurobiology, brain health, and cognitive functions. The gut-brain crosstalk is mediated through gut-brain axis that includes neural, hormonal, and immune pathways (81). Research and exploration of gut biomarkers are important as research has revealed meaningful relationships among changes in gut biomarkers toward diseases with numerous cancer types, cognitive abnormalities and neurodegenerative disorders, as well as cerebrovascular diseases [82]. Dysbiosis (Gut microbiota imbalance) caused major damage on the gut barrier function and also to autoimmune diseases, allergies. These alterations can be extremely dangerous, as it may interfere on the secretory action of immunoglobulin-A and number of lymphocytes (83). Blood-brain barrier is in CNS and is a semi-permeable barrier aimed to protect the brain from harmful substances and pathogens It mainly features established endothelial cells interconnected by tight junctions and allows them to modulate and selective confine the entry into the brain of multiple substances (84).

Table 3: Impact of Exercise and Lifestyle Interventions on Aging

Type of Activity	Effects on Specific Systems	Recommended Duration/Intensity	Scientific Evidence
Aerobics (e.g., walking, cycling)	Improves cardiovascular function; increases hippocampal volume	At least 150 minutes per week	Enhances heart health and cognitive function
Resistance Training (e.g., weightlifting)	Prevents bone density loss; enhances muscle strength	2–3 sessions per week with moderate to heavy loads	Increases bone mineral density
Mind-Body (Yoga/Tai Chi)	Reduce stress; improves balance and flexibility	2–3 sessions per week	Positive impact on mental health and symptom management

1-9 The impact of nutrition on gut microbiomes

Recent research has shown that diet is a crucial determinant of gut microbiota diversity and composition. On the other hand, researchers firmly believe that changes in gut microbiota have a direct impact on the brain (85). Through having knowledge about dietary principles and adhering to a healthy and well-balanced nutrition, unique to the physical and psychological characteristics of every person, e.g., dietary fiber, essential amino acids, and short-chain fatty acids, neurodegenerative disease and systemic inflammation can be well prevented, thereby maintaining brain health. Adhering to such principles may provide substantial improvement to cognitive functions as well as to prevention from associated mental illnesses (86).

1-10 depression

depression is an emotional condition that most commonly comes with sadness and can lead to loss of sleep, appetite, and even sex drive. Depression can lead to people losing interest and motivation to take part in activities of everyday life. Research has confirmed depression as one of the leading global emotional conditions (87). There is evidence to show that depression is not caused by one single factor; instead, it is the outcome of a combination of interrelated phenomena, viz., biological (including genetics and physical health), social, and psychological factors, which are intricately related and compounded to affect mental well-being, thus causing depression (88). The structure of the gut microbiome can impact depression significantly. Evidence suggests that the addition of probiotic bacteria such as *Lactobacillus* and

Bifidobacterium in the gut can help produce serotonin. Serotonin is also one of the most important neurotransmitters of the brain and is very prominent in mood, which makes individuals happy and satisfied. (89) In addition to this, serotonin and melatonin are also hormones and are very significant in sleeping. Furthermore, serotonin is involved in processes of learning and memory (90). Several antidepressant drugs, more specifically selective serotonin reuptake inhibitors (SSRIs), act by serving to increase the amount of serotonin in the brain. These medications combat depression by regulating the serotonin levels and alleviating the symptoms of such a condition (91). Swimming, cycling, running, yoga, which are all types of aerobic exercise, can have a beneficial impact on gut microbiota diversity, which is extremely significant for overall gut health as well as in the production of serotonin. Aerobic exercise was shown to increase bacteria diversity and balance in guts, e.g., by expanding protective types of bacteria like Firmicutes (92). Increased diversity is linked with improved gut-brain communication that is able to influence serotonin levels and, consequently, mood and mental health. Exercise has also been postulated to reduce inflammation of the gut and create a more hospitable intestinal milieu via microbiota alteration brought about by exercise, affecting neurotransmitter manufacture like serotonin (93, 94). Tai Chi exercises were found to greatly reduce anxiety and stress symptoms in depressed adults. They also suggest that Tai Chi practice results in lower salivary cortisol and, hence, lower activity of the hypothalamus-pituitary-adrenal (HPA) axis, which reduces stress and anxiety (95).

Table 4: Prevalence of Age-Related Diseases by Age and Gender

Disease	Age Group	Gender Differences	Prevalence Rates
Prostate Disease (BPH/PCa)	Men: 40 vs. 70–80 years	Significantly higher in older men	5–10% at age 40; up to 80% at age 70–80
Alzheimer's Disease	Primarily >65 years	Higher incidence in women	Two-thirds of cases occur in women
Chronic Kidney Disease	Older adults	Faster GFR decline in men	Example: 45.66 per 100,000 in Saudi Arabia
Osteoporosis	Postmenopausal women	Much higher in women	Over 200 million women affected globally
Breast Cancer	Middle-aged to elderly women	Predominantly affects women	Over 2.3 million new cases reported in 2020
Parkinson's Disease	Older adults (with young onset <65 cases)	Higher incidence in men	Approximately 25% of cases occur in individuals under 65

1-11 Conclusion

Finally, this review observes that aging is a multifactorial process activated by the concerted action of molecular damage, cellular malfunction, and systemic decline. The interaction of genetic, hormonal, and environmental determinants results in the onset of age-related chronic diseases cardiovascular disease, renal insufficiency, osteoporosis, cancer, and neurodegenerative disorders posing severe public health issues in the setting of an increasing elderly population. The data presented clearly demonstrate that some life style modifications, most significantly habitual aerobic and resistance training, are capable of countering several adverse consequences of senescence. Further studies will need to be aimed at further elucidating the specific cellular mechanisms of senescence, investigating the interacting processes of aging, and developing evidence-based interventions for not only lengthening life but also improving significantly the quality of life in elderly individuals.

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Reference

- 1.da Silva PF, Schumacher B. Principles of the molecular and cellular mechanisms of aging. *Journal of Investigative Dermatology*. 2021;141(4):951-60.
- 2.Guo J, Huang X, Dou L, Yan M, Shen T, Tang W, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. *Signal Transduction and Targeted Therapy*. 2022;7(1):391.
- 3.Lakatta EG. So! What's aging? Is cardiovascular aging a disease? *Journal of molecular and cellular cardiology*. 2015;83:1-13.
- 4.<https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>. 2024.
- 5.Li Y, Tian X, Luo J, Bao T, Wang S, Wu X. Molecular mechanisms of aging and anti-aging strategies. *Cell Communication and Signaling*. 2024;22(1):285.
- 6.López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: An expanding universe. *Cell*. 2023;186(2):243-78.
- 7.Lim KB. Epidemiology of clinical benign prostatic hyperplasia. *Asian journal of urology*. 2017;4(3):148-51.
- 8.Dagur G, Warren K, Imhof R, Gonka J, Suh Y, Khan SA. Clinical implications of the forgotten Skene's glands: A review of current literature. *Polish Annals of Medicine*. 2016;23(2):182-90.
- 9.Biancardi MF, Dos Santos FC, de Carvalho HF, Sanches BD, Taboga SR. Female prostate: historical, developmental, and morphological perspectives. *Cell Biology International*. 2017;41(11):1174-83.
- 10.Dybiec J, Szlagor M, Młynarska E, Rysz J, Franczyk B. Structural and functional changes in aging kidneys. *International Journal of Molecular Sciences*. 2022;23(23):15435.
- 11.Denic A, Glasscock RJ, Rule AD. Structural and functional changes with the aging kidney. *Advances in chronic kidney disease*. 2016;23(1):19-28.
- 12.Tidmas V, Brazier J, Hawkins J, Forbes SC, Bottoms L, Farrington K. Nutritional and non-nutritional strategies in bodybuilding: impact on kidney function. *International journal of environmental research and public health*. 2022;19(7):4288.
- 13.Melsom T, Norvik JV, Enoksen IT, Stefansson V, Mathisen UD, Fuskevåg OM, et al. Sex differences in age-related loss of kidney function. *Journal of the American Society of Nephrology*. 2022;33(10):1891-902.
- 14.Kalucki SA, Lardi C, Garessus J, Kfoury A, Grabherr S, Burnier M, et al. Reference values and sex differences in absolute and relative kidney size. A Swiss autopsy study. *BMC nephrology*. 2020;21:1-11.
15. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The lancet*. 2020;395(10225):709-33.
- 16.Liu Y, He Q, Li Q, Tian M, Li X, Yao X, et al. Global incidence and death estimates of chronic kidney disease due to hypertension from 1990 to 2019, an ecological analysis of the global burden of diseases 2019 study. *BMC nephrology*. 2023;24(1):352.
- 17.Crandall CJ, Mehta JM, Manson JE. Management of menopausal symptoms: a review. *Jama*. 2023;329(5):405-20.
- 18.Koysombat K, McGown P, Nyunt S, Abbara A, Dhillon WS. New advances in menopause symptom management. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2024;38(1):101774.

19. Zhang Z, Zhao M. Comparison of Physical Exercise and Psychological Intervention in the Healthcare of Menopausal Women. *International Journal of Healthcare Information Systems and Informatics (IJHISI)*. 2023;18(1):1-9.
20. Prado CM, Batsis JA, Donini LM, Gonzalez MC, Siervo M. Sarcopenic obesity in older adults: a clinical overview. *Nature Reviews Endocrinology*. 2024;20(5):261-77.
21. Schoene D, Kiesswetter E, Sieber CC, Freiberger E. Musculoskeletal factors, sarcopenia and falls in old age. *Zeitschrift für Gerontologie und Geriatrie*. 2019;52:37-44.
22. Wang J, Xiang Y, Wu L, Zhang C, Han B, Cheng Y, et al. The association between inflammatory cytokines and sarcopenia-related traits: a bi-directional Mendelian randomization study. *European Journal of Clinical Nutrition*. 2024:1-9.
23. Huang Z, Zhong L, Zhu J, Xu H, Ma W, Zhang L, et al. Inhibition of IL-6/JAK/STAT3 pathway rescues denervation-induced skeletal muscle atrophy. *Annals of translational medicine*. 2020;8(24).
24. Cai Y, Han Z, Cheng H, Li H, Wang K, Chen J, et al. The impact of ageing mechanisms on musculoskeletal system diseases in the elderly. *Frontiers in Immunology*. 2024;15:1405621.
25. Pinheiro MB, Oliveira J, Bauman A, Fairhall N, Kwok W, Sherrington C. Evidence on physical activity and osteoporosis prevention for people aged 65+ years: a systematic review to inform the WHO guidelines on physical activity and sedentary behaviour. *International Journal of Behavioral Nutrition and Physical Activity*. 2020;17:1-53.
26. Pouresmaeili F, Kamalidehghan B, Kamarehei M, Goh YM. A comprehensive overview on osteoporosis and its risk factors. *Therapeutics and clinical risk management*. 2018:2029-49.
27. Kim S-W, Seo M-W, Jung H-C, Song J-K. Effects of high-impact weight-bearing exercise on bone mineral density and bone metabolism in middle-aged premenopausal women: a randomized controlled trial. *Applied Sciences*. 2021;11(2):846.
28. Lawrence M, Goyal A, Pathak S, Ganguly P. Cellular Senescence and Inflammaging in the Bone: Pathways, Genetics, Anti-Aging Strategies and Interventions. *International Journal of Molecular Sciences*. 2024;25(13).
29. Wang Z, Zan X, Li Y, Lu Y, Xia Y, Pan X. Comparative efficacy different resistance training protocols on bone mineral density in postmenopausal women: A systematic review and network meta-analysis. *Frontiers in Physiology*. 2023;14:1105303.
30. Wenger D, Williamson D, Williamson K, Holderbaum C, McIntosh D, Fuentes D, et al. Cyclist and Weight Training for Bone Health: Necessary or not?
31. Bembien DA, Palmer JJ, Bembien MG, Knehans AW. Effects of combined whole-body vibration and resistance training on muscular strength and bone metabolism in postmenopausal women. *Bone*. 2010;47(3):650-6.
32. Massini DA, Nedog FH, de Oliveira TP, Almeida TA, Santana CA, Neiva CM, et al., editors. The effect of resistance training on bone mineral density in older adults: a systematic review and meta-analysis. *Healthcare*; 2022: MDPI.
33. Cauley JA. Estrogen and bone health in men and women. *Steroids*. 2015;99:11-5.
34. Liu X, Jiang C, Fan R, Liu T, Li Y, Zhong D, et al. The effect and safety of Tai Chi on bone health in postmenopausal women: A meta-analysis and trial sequential analysis. *Frontiers in Aging Neuroscience*. 2022;14:935326.
35. Horestani FJ, Schwarz G. Survival analysis of Young Triple-negative breast Cancer patients. *arXiv preprint arXiv:240108712*. 2024.
36. Burgers J, Azizi A, Singh V. Breast Cancer Screening in the Geriatric Population: Challenges and Future Considerations. *Current Breast Cancer Reports*. 2024;16(1):1-10.
37. Łukasiewicz S, Czezelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer—epidemiology, risk factors, classification, prognostic markers, and current treatment strategies—an updated review. *Cancers*. 2021;13(17):4287.
38. Couch FJ, Shimelis H, Hu C, Hart SN, Polley EC, Na J, et al. Associations between cancer predisposition testing panel genes and breast cancer. *JAMA oncology*. 2017;3(9):1190-6.
39. Zardavas D, Irrthum A, Swanton C, Piccart M. Clinical management of breast cancer heterogeneity. *Nature reviews Clinical oncology*. 2015;12(7):381-94.
40. Mertens E, Barrenechea-Pulache A, Sagastume D, Vasquez MS, Vandevijvere S, Peñalvo JL. Understanding the contribution of lifestyle in breast cancer risk prediction: a systematic review of models applicable to Europe. *BMC cancer*. 2023;23(1):687.
41. Sun Y-S, Zhao Z, Yang Z-N, Xu F, Lu H-J, Zhu Z-Y, et al. Risk factors and preventions of breast cancer. *International journal of biological sciences*. 2017;13(11):1387.
42. García-Chico C, López-Ortiz S, Peñín-Grandes S, Pinto-Fraga J, Valenzuela PL, Emanuele E, et al. Physical exercise and the hallmarks of breast cancer: a narrative review. *Cancers*. 2023;15(1):324.

43. Athanasiou N, Bogdanis GC, Mastorakos G. Endocrine responses of the stress system to different types of exercise. *Reviews in Endocrine and Metabolic Disorders*. 2023;24(2):251-66.
44. Naderifar H, Kazemi SS, Nezhad NH, Mehri F. The Effect of Resistance Training on P53 Gene Expression in Prostate Cancer Patients. 2023.
45. Voltarelli VA, Amano MT, Camargo AA, Brum PC. Role of aerobic exercise training on tumor-infiltrated immune cells. *The FASEB Journal*. 2022;36.
46. Bangsub L, Chung W. Effects of aerobic exercise on cytokine expression in a breast cancer mouse model. *Iranian Journal of Public Health*. 2020;49(1):14.
47. Hsueh E-J, Loh E-W, Lin JJ-A, Tam K-W. Effects of yoga on improving quality of life in patients with breast cancer: a meta-analysis of randomized controlled trials. *Breast Cancer*. 2021;28:264-76.
48. Heeter C, Lehto R. Benefits of Yoga and Meditation for Patients With Cancer. 2018.
49. Yi L-J, Tian X, Jin Y-F, Luo M-J, Jiménez-Herrera MF. Effects of yoga on health-related quality, physical health and psychological health in women with breast cancer receiving chemotherapy: a systematic review and meta-analysis. *Annals of palliative medicine*. 2021;10(2):1961975-.
50. Cai Q, Cai S-b, Chen J-k, Bai X-H, Jing C-X, Zhang X, et al. Tai Chi for anxiety and depression symptoms in cancer, stroke, heart failure, and chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Complementary therapies in clinical practice*. 2022;46:101510.
51. Li W, You F, Wang Q, Shen Y, Wang J, Guo J. Effects of Tai Chi Chuan training on the QoL and psychological well-being in female patients with breast cancer: a systematic review of randomized controlled trials. *Frontiers in Oncology*. 2023;13:1143674.
52. Irwin MR, Hoang D, Olmstead R, Sadeghi N, Breen EC, Bower JE, et al. Tai Chi compared with cognitive behavioral therapy and the reversal of systemic, cellular and genomic markers of inflammation in breast cancer survivors with insomnia: A randomized clinical trial. *Brain, Behavior, and Immunity*. 2024;120:159-66.
53. Zeng Y, Xie X, Cheng AS. Qigong or Tai Chi in cancer care: an updated systematic review and meta-analysis. *Current oncology reports*. 2019;21:1-6.
54. Wang CC, Geraghty S, Fox-Harding C, Wang C. Effects of a nurse-led Tai Chi programme on improving quality of life, mental wellbeing, and physical function of women with breast cancer: Protocol for a randomized controlled trial. *Women's Health*. 2022;18:17455057221127813.
55. Alamri ZZ. The role of liver in metabolism: an updated review with physiological emphasis. *Int J Basic Clin Pharmacol*. 2018;7(11):2271-6.
56. Feitelson M, Arzumanyan A. Liver Cancer-Genesis, Progression and Metastasis 2023.
57. Natarajan Y, El-Serag HB. Risk factors for hepatocellular carcinoma: A historical perspective. *Clinical Liver Disease*. 2021;18:1-13.
58. Chen J, Yang Z, Gao F, Zhou Z, Chen J, Lu D, et al. Influence of sex on outcomes of liver transplantation for hepatocellular carcinoma: a multicenter cohort study in China. *Cancer Biology & Medicine*. 2024;21(4):347.
59. DAYANANDA M. THE BENEFITS OF AEROBIC TRAINING EXERCISES FOR IMPROVING THE QUALITY OF LIFE. *Special Issue on*. 2024:90.
60. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-57.
61. Hashida R, Kawaguchi T, Bekki M, Omoto M, Matsuse H, Nago T, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: A systematic review. *Journal of hepatology*. 2017;66(1):142-52.
62. Werner P, Savva GM, Maidment I, Thyrian JR, Fox C. Dementia: introduction, epidemiology and economic impact. *Mental Health and Older People: A Guide for Primary Care Practitioners*. 2016:197-209.
63. Organization WH. Risk reduction of cognitive decline and dementia: WHO guidelines: World Health Organization; 2019.
64. Roda AR, Serra-Mir G, Montoliu-Gaya L, Tiessler L, Villegas S. Amyloid-beta peptide and tau protein crosstalk in Alzheimer's disease. *Neural regeneration research*. 2022;17(8):1666-74.
65. Health UDo, Services H. What happens to the brain in Alzheimer's disease. National Institute on Aging. 2017.
66. Hampel H, O'Bryant SE, Molinuevo JL, Zetterberg H, Masters CL, Lista S, et al. Blood-based biomarkers for Alzheimer disease: mapping the road to the clinic. *Nature Reviews Neurology*. 2018;14(11):639-52.
67. Burke SL, Hu T, Fava NM, Li T, Rodriguez MJ, Schuldiner KL, et al. Sex differences in the development of mild cognitive impairment and probable Alzheimer's disease as predicted by hippocampal volume or white matter hyperintensities. *Journal of women & aging*. 2019;31(2):140-64.

67. Burke SL, Hu T, Fava NM, Li T, Rodriguez MJ, Schuldiner KL, et al. Sex differences in the development of mild cognitive impairment and probable Alzheimer's disease as predicted by hippocampal volume or white matter hyperintensities. *Journal of women & aging*. 2019;31(2):140-64.
68. Zhu D, Montagne A, Zhao Z. Alzheimer's pathogenic mechanisms and underlying sex difference. *Cellular and Molecular Life Sciences*. 2021;78:4907-20.
69. Ferretti MT, Iulita MF, Cavedo E, Chiesa PA, Schumacher Dimech A, Santuccione Chadha A, et al. Sex differences in Alzheimer disease—the gateway to precision medicine. *Nature Reviews Neurology*. 2018;14(8):457-69.
70. Castro-Aldrete L, Moser MV, Putignano G, Ferretti MT, Schumacher Dimech A, Santuccione Chadha A. Sex and gender considerations in Alzheimer's disease: The Women's Brain Project contribution. *Frontiers in Aging Neuroscience*. 2023;15:1105620.
71. Mielke MM, Aggarwal NT, Vila-Castelar C, Agarwal P, Arenaza-Urquijo EM, Brett B, et al. Consideration of sex and gender in Alzheimer's disease and related disorders from a global perspective. *Alzheimer's & dementia*. 2022;18(12):2707-24.
72. Bun S, Ito D, Tezuka T, Kubota M, Ueda R, Takahata K, et al. Performance of plasma A β 42/40, measured using a fully automated immunoassay, across a broad patient population in identifying amyloid status. *Alzheimer's Research & Therapy*. 2023;15(1):149.
73. Stephens K. Exercise Boosts Blood Flow to the Brain, MRI Study Finds. *AXIS Imaging News*. 2021.
74. Banerjee S, Schlaeppli K, van der Heijden MG. Keystone taxa as drivers of microbiome structure and functioning. *Nature Reviews Microbiology*. 2018;16(9):567-76.
75. Bhabatosh Das BD, Ghosh T, Saurabh Kedia SK, Ritika Rampal RR, Shruti Saxena SS, Satyabrata Bag SB, et al. Analysis of the gut microbiome of rural and urban healthy Indians living in sea level and high altitude areas. 2018.
76. Walsh CJ, Guinane CM, O'Toole PW, Cotter PD. Beneficial modulation of the gut microbiota. *FEBS letters*. 2014;588(22):4120-30.
77. Komodromou I, Andreou E, Vlahoyiannis A, Christofidou M, Felekis K, Pieri M, et al. Exploring the Dynamic Relationship between the Gut Microbiome and Body Composition across the Human Lifespan: A Systematic Review. *Nutrients*. 2024;16(5):660.
78. Marvasti FE, Moshiri A, Taghavi MS, Riazi S, Taati M, Sadati SF, et al. The first report of differences in gut microbiota composition between obese and normal weight Iranian subjects. *Iranian biomedical journal*. 2020;24(3):148.
79. Koliada A, Syzenko G, Moseiko V, Budovska L, Puchkov K, Perederiy V, et al. Association between body mass index and Firmicutes/Bacteroidetes ratio in an adult Ukrainian population. *BMC microbiology*. 2017;17:1-6.
80. Hou Y-P, He Q-Q, Ouyang H-M, Peng H-S, Wang Q, Li J, et al. Human gut microbiota associated with obesity in Chinese children and adolescents. *BioMed research international*. 2017;2017(1):7585989.
81. Zheng Y, Bonfili L, Wei T, Eleuteri AM. Understanding the gut–brain axis and its therapeutic implications for neurodegenerative disorders. *Nutrients*. 2023;15(21):4631.
82. Zhu S, Jiang Y, Xu K, Cui M, Ye W, Zhao G, et al. The progress of gut microbiome research related to brain disorders. *Journal of neuroinflammation*. 2020;17:1-20.
83. Macura B, Kiecka A, Szczepanik M. Intestinal permeability disturbances: causes, diseases and therapy. *Clinical and Experimental Medicine*. 2024;24(1):232.
84. Zhao Y, Gan L, Ren L, Lin Y, Ma C, Lin X. Factors influencing the blood-brain barrier permeability. *Brain research*. 2022;1788:147937.
85. Ribeiro G, Ferri A, Clarke G, Cryan JF. Diet and the microbiota–gut–brain-axis: a primer for clinical nutrition. *Current Opinion in Clinical Nutrition & Metabolic Care*. 2022;25(6):443-50.
86. Frausto DM, Forsyth CB, Keshavarzian A, Voigt RM. Dietary regulation of gut-brain axis in Alzheimer's disease: Importance of microbiota metabolites. *Frontiers in neuroscience*. 2021;15:736814.
87. Remes O, Mendes JF, Templeton P. Biological, psychological, and social determinants of depression: a review of recent literature. *Brain sciences*. 2021;11(12):1633.
88. Ventriglio A, Castaldelli-Maia JM, Torales J, Chumakov E, De Berardis D. Social aspects of depression. *Oxford Textbook of Social Psychiatry*. 2022:361.
89. Schrodte C, Mahavni A, McNamara GP, Tallman MD, Bruger BT, Schwarz L, et al. The gut microbiome and depression: a review. *Nutritional Neuroscience*. 2023;26(10):953-9.
90. Dmitrzak-Weglaz M, Reszka E. Pathophysiology of depression: Molecular regulation of melatonin homeostasis—current status. *Neuropsychobiology*. 2018;76(3):117-29.
91. Clevenger SS, Malhotra D, Dang J, Vanle B, IsHak WW. The role of selective serotonin reuptake inhibitors in preventing relapse of major depressive disorder. Therapeutic advances in psychopharmacology. 2018;8(1):49-58.

92. Uchida M, Fujie S, Yano H, Iemitsu M. Aerobic exercise training-induced alteration of gut microbiota composition affects endurance capacity. *The Journal of Physiology*. 2023;601(12):2329-44.

93. Allen JM, Mailing LJ, Niemi GM, Moore R, Cook MD, White BA, et al. Exercise alters gut microbiota composition and function in lean and obese humans. *Medicine and science in sports and exercise*. 2018;50(4):747-57.

94. Souza PBD, de Araujo Borba L, Castro de Jesus L, Valverde AP, Gil-Mohapel J, Rodrigues ALS. Major Depressive Disorder and Gut Microbiota: Role of Physical Exercise. *International journal of molecular sciences*. 2023;24(23):16870.

95. Wu J, Song J, He Y, Li Z, Deng H, Huang Z, et al. Effect of Tai Chi on Young Adults with Subthreshold Depression via a Stress–Reward Complex: A Randomized Controlled Trial. *Sports Medicine-Open*. 2023;9(1):90.