



Change in physical and mental health due to aging: future perspective

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Abstract

Aims: By addressing these research issues and examining the findings of the pertinent studies, this systematic review aims to provide a thorough understanding of the changes in physical and mental health that are related with aging as well as the significant factors that contribute to these changes. This evaluation will also look into potential new treatments and technological advancements that could improve elderly people's health. The results of this work will offer crucial new perspectives on aging research and therapeutic practice in the future.

Methodology: "Aging", "physical health", "mental health", "wellbeing", "lifestyle interventions", "age-related health problems", "literature evaluation", "future perspectives", "key factors", "potential new interventions", and "health outcomes" were used to search Medline, pubmed, and Google Scholar. Successful search. Data analysis began with selecting relevant details. Second, the data was compiled into a table, followed by study conclusions. After reviewing each article, the overarching idea that best proves the study issue's relevance was chosen.

Results: The literature display includes several physiological and physical effects of aging and research and reference information. Aging affects skin, hair, nails, vision, digestion, bone density, muscle flexibility, and heart disease risk. Aging causes anxiety, memory loss, and executive dysfunction

Scientific Novelty: Potentially effective innovative measures to enhance senior citizens' health a study of the key elements influencing how physical and mental health vary as people age

Conclusion: The systematic review gave a thorough grasp of the alterations in physical and mental health brought on by aging, as well as the main causes of these alterations. The review also uncovered potential novel therapeutic approaches and scientific developments that might enhance the health of senior citizens. This work emphasizes the necessity of ongoing study and therapeutic application to improve older individuals' quality of life.

Keywords: Elder people; life style intervention; health problems; psychological issues.

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Introduction

The process of aging is characterized by slowness and continuity, and it begins in the early years of maturity. Many of the body's functions start to gradually decline when people are in their early to middle 40s. There is no one age at which a person automatically enters their senior years. Historically, the onset of old age has been considered to commence at the age of 65. However, the reason was not rooted in biology but rather in history. In Germany, the country that pioneered the concept of a national retirement system, the age of 65 was selected as the point at which one may officially retire [1]. In the year 1965, the United States government established the minimum age of eligibility for Medicare health insurance at 65 years old. This age is quite close to the real retirement age that the majority of individuals in economically developed cultures reach.

The question of how old a person is can be addressed in a few different ways: The only factor that affects one's chronological age is the passage of time. The number of years that a person has been alive. In terms of one's health, chronological age is of only little consequence. However, as people get older, their risk of developing a health condition rises. Contrary to popular belief, it is not the natural process of aging that leads to a decline in functional capacity in old age; rather, it is the health conditions that people experience. There are certain legal and financial applications for chronologic age due to the fact that it can forecast a variety of health concerns. The term "biologic age" refers to the

changes that take place in the body as a natural consequence of aging [2]. Some people are biologically old at the age of 65, while others will not be of that age until at least ten years later. This is because these changes impact some people quicker than others. However, the majority of noticeable disparities in apparent age between people of equivalent chronologic age are triggered by lifestyle, tradition, and the subtle effects of disease rather than differences in actual aging. This is the case even among people with the same chronological age. The way a person behaves and how they feel might help determine their psychological age [3]. For instance, a person who is 80 years old but continues to work, make plans, anticipate what the future holds, and take part in a variety of activities is regarded to be mentally younger. The majority of healthy and active individuals do not require the services of a geriatrician (a medical practitioner who specializes in the treatment of older people) until they reach the age of seventy, seventy-five, or even eighty years old. However, due to their medical conditions, some individuals require the services of a geriatrician at an earlier chronological age than is typical [4].

Age and health concerns are discussed in terms of chronological age, but other elements like heredity, way of life, and environment are not included. When determining how old a person is, these elements should be taken into account as they can also affect how they age. Frequent root causes of differences in perceived ages between individuals of equal chronological ages. It would be beneficial to give illustrations of these elements and how they could impact aging. the social and cultural aspects of aging, including ageism and age-related prejudices. As people age, these problems may have a big impact on how they see themselves and how others see them.

Literature Review

People frequently question whether or not the changes they're observing in their bodies as they become older are natural or aberrant. Despite the fact that people age in slightly unique ways, there are some changes that come about as a result of the process of aging itself. As a result, these shifts, despite the fact that they are undesirable, are seen as natural and are sometimes referred to as "pure aging." [5] These shifts take place in every person who lives a full life, and the fact that they are universal is a component of the notion of pure aging. Changes of this nature are to be anticipated and, in most cases, cannot be avoided. For instance, as individuals become older, the lens of the eye grows thicker, more rigid, and less able to concentrate on close objects, including reading material (this condition is known as presbyopia). Almost all elderly persons experience this transformation as they get older. Therefore, presbyopia is considered to be a natural part of aging. The words "normal aging" and "senescence" are also used interchangeably to refer to similar processes [6-9]. In addition to these differences, dementias such as Alzheimer's disease stand out from the natural process of aging in a number of other respects. For instance, brain tissue from persons who have Alzheimer disease (obtained during autopsies) appears differently from brain tissue from elderly people who do not have Alzheimer disease. Therefore, there is a clear distinction to be made between typical aging and dementia [10, 11].

These alterations are prevalent and, for the most part, inevitable. Presbyopia, which is seen as a natural component of aging, is caused by the lens of the eye thickening and losing flexibility. These organic processes are also referred to as "normal aging" and "senescence." Dementia, such as Alzheimer's disease, has been found to be unique from normal aging. Alzheimer's disease brain tissue differs from that of healthy older adults in appearance, demonstrating a substantial difference between normal aging and dementia.

Physical based aging effects

Bone and Muscle functionality: Bone and muscle are necessary for mobility, but in addition to this, they play an important role in the endocrine and metabolic systems. Both osteoporosis as well as sarcopenia can develop in conjunction with one another when bone loss and weakness of muscles happen at the same time, as can happen with aging and in many chronic conditions. This affects people of both sexes, but postmenopausal women appear to be more vulnerable to age-related bone and muscle loss, whilst males appeared to have greater safeguards against this [12]. Musculoskeletal gender dimorphism is largely caused by the presence of steroid hormones, particularly androgens such as testosterone and oestrogens such as estradiol. They promote mass in bones and muscles accretion between adolescence and midlife, and they minimize future loss in males as they age, but not in women who have gone through menopause. [13]. The existing evidence indicates that the clinical diagnose and therapeutic method for treating male osteoporosis is substantially comparable to that in postmenopausal women. This is the case despite the fact that randomized clinical research studies in male osteoporosis are fewer than those in postmenopausal women and, as a result, inadequate for some outcomes such as hip fractures [14].

Risk of cardiovascular disease: People who are getting older and are already elderly are at an increased risk of developing cardiovascular disease. Age is a risk factor in and of itself for cardiovascular disease, or CVD, in adults; however, the risks posed by age are increased by additional factors such as frailty, being obese, and diabetes [15]. It is well established that the presence of these factors both complicates and exacerbates the cardiac cardiovascular risk factors that are typically linked with the beginning of old age. Given that older women are said to be at a larger risk for cardiovascular disease than age-matched men, sexual orientation is an additional risk indicator in persons who are getting older. However, the risks associated with cardiovascular disease (CVD) increase with age in both men and women, and these link to a general decrease in sex hormones, primarily both testosterone and estrogen. This is applicable to both men and women [16].

Gut Health: From infancy into old age, the microbiome plays an essential part in the development, function, and control of the host immune system. This is true over the whole lifespan. In exchange, the body's immune system has co-evolved a symbiotic relationship with the trillions of helpful bacteria that reside within our bodies, allowing it to mount effective responses to the invasion of pathogens. Both the body's immune system and the microbiome of the gut go through major changes in constitution and function as we become older. These changes are directly related to an increased risk of contracting infectious diseases and a diminished response to vaccinations. Emerging research suggests that addressing age-related dysbiosis might extend both health and lifespan. This may be accomplished, in part, by reducing systemically moderate inflammation and immunosenescence, which are two characteristics that are associated with the aging process. However, a cause-and-effect relationship between age-related dysbiosis along with functional reductions in immune cell functioning has not yet been demonstrated in clinical settings. This is despite the fact that age-related dysbiosis is associated with aging [17].

Changes in skin, hair, and nails: The aging process affects many aspects of an individual's appearance, including their hair, nails, and skin. Alterations in the color, growth, and arrangement of the nails and hair are typical as a result of advancing age. In contrast to the process of aging that occurs in the layer of skin, the gerontobiological process of what happens to hair and nails through time has not been thoroughly researched [18-20]. Today's understanding of the processes that are involved in the graying of hair is improved by research on signaling pathways that are crucial for melanogenesis in the hair follicle. Variations in the lipid content of the nail plates that are age-dependent are the primary factor responsible for the differences in structure as well as overall performance of the nails that occur with advanced age. On the other hand, it is essential to acknowledge the age-dependent processes that occur in the shafts of hair and nails and to differentiate between the natural process of aging and alterations that are caused by disease [18].

Vision due to aging: At around forty years of age, structural changes in the eye cause an impairment of near vision. Later in life, these same changes cause an impairment in visual acuity due to changes in the lenticular and retinal structures. "Visual acuity, contrast sensitivity, scotopic vision, visual field, and visual processing speed" are some of the visual qualities that might alter with age. Alterations to any of these aspects of vision can have a substantial bearing on one's overall quality of life. The central vision is impacted by age-related macular degeneration (AMD), which also has a significant negative effect on quality of life as a result of vision impairment. Deficits in visual field caused by cerebral causes also have a negative impact on both the patient's quality of life and the outcomes of rehabilitation for neurological disorders in patients who have numerous deficits [21].

Physiological based aging effects

Decreased executive functioning: Executive functions, often known as EFs, are high-order cognitive abilities that encompass things like memory retention, inhibitory based control, flexibility in thinking, organizing, deductive thinking, and solving problems. Humans are able to accomplish goals, adjust to novel situations that arise in everyday life, and successfully navigate social relationships because to EFs. Traditionally speaking, EFs have been linked to the functioning of the frontal brain. More recent research has shown that the posterior and subcortical regions of the brain also play an important part in the processing of EF, particularly in the incorporation of sensory information as well as emotional experience [22]. The executive functions show a variable development and aging profile, with prolonged growth into early adolescence and reductions in later life. This pattern occurs in both children and adults. However, only a relatively small number of studies have chosen to include adults in the middle years of their lives when investigating age-related variations in executive functions [23, 24].

Memory changes: "The Spanish and English Neuropsychological Assessment Scales (SENAS) " were used to test executive function, spatial ability, episodic memory, semantic memory, and executive function. The amount of gray matter change and, more specifically, temporal lobe alteration, had a significant impact on cognitive deterioration. The significant relationship between the temporal lobe- gray matter changes and cognitive loss may be due to the contribution of temporal lobe structures, which are important for maintaining cognitive health in old age but are also susceptible to aging-related disorders [25].

Anxiety: It is believed that generalized anxiety disorder, also known as GAD, is the most frequent kind of anxiety illness found in older persons. This form of anxiety is characterized by racing thoughts, persistent worry, and a sense that there is no way out of the situation. It's not uncommon for older folks to struggle with anxiety, yet most of the time their issues go undiagnosed. Problems with anxiety can be brought on by either stressful or traumatic experiences. coffee, alcohol, and several drugs are all included. People who suffer from generalized anxiety disorder tend to worry incessantly about a variety of different things. They expect the worst from every circumstance, even when there is no basis for such expectations [26].

Although the study shows that working memory capacity keeps growing throughout adolescence and the first few years of adulthood, it also shows that functioning memory and inhibiting control start to decline as early as 30 to 40 years of age and continue into later life. The study also highlights a strong link between cognitive decline and alterations in the gray matter of the temporal lobe. The results indicate that although the temporal lobe structures are vulnerable to aging-related diseases, they are crucial for preserving cognitive health in old life. The book also emphasizes how common anxiety problems are in older persons, with generalized anxiety disorder being the most common type.

Research Problem

There is a dearth of full knowledge of the most effective ways for sustaining well-being and health in older persons, despite the fact that the process of aging is recognized to have an influence on both physical and mental health. The focus of this research should be on meeting the specific physical, mental, and social requirements of older persons in the future.

Research Focus

The purpose of this research is to conduct a thorough analysis of the previous research on the effects of aging on one's physical and mental health, with a particular emphasis on determining the most important elements that are responsible for these effects. This review will give significant insights into the potential future paths of research in aging and guide clinical practice in the treatment of both mental and physical wellness in older persons. This will be accomplished by synthesizing the present body of information on the subject at hand.

Research Aim and Research Questions

1. What are the primary variables that lead to changes in one's physical health that are associated with age, and what are the most typical alterations that accompany this aging process?
2. What are some of the most prevalent shifts in mental health that are associated with age, and what are some of the most important elements that contribute to these shifts?
3. In the future, what new therapies and technological improvements are being researched that have the potential to enhance the health of older adults?

This systematic review seeks to give a complete knowledge of the changes in physical and mental health that are associated with aging as well as the important variables that contribute to these changes by answering these research questions and analyzing the results of the relevant research.

Research Methodology

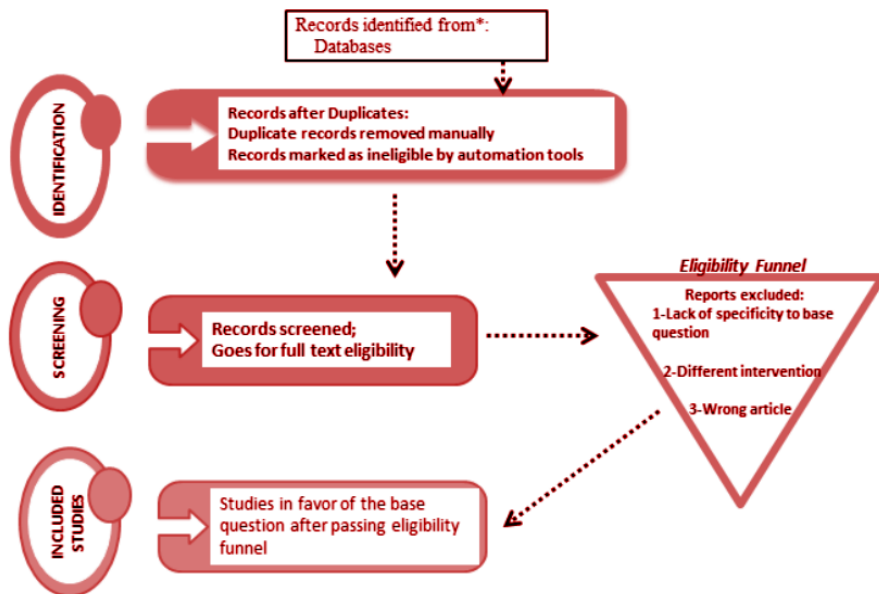


Figure 1. The graphical representation of literature search and studies selection

Source: Author's own development

General Background

The fundamental objectives of a narrative review are to firstly offer the author and the reader with a comprehensive overview of the subject matter at hand, and secondly, to call attention to key areas of research that have been carried out on the issue in question. Narrative reviews are effective tools for discovering errors in a study, as well as for refining and identifying new areas for further exploration. The literature search was conducted by utilizing a number of different database systems (for example, Medline, PubMed, and Google Scholar) with a combination of broad search terms, such as "aging", "physical health", "mental health", "wellbeing", "lifestyle interventions", "age-related health problems", "literature evaluation", "future perspectives", "key factors", "potential new interventions", and "health outcomes". The search was successful.

Data Analysis

The procedure for carrying out the analysis of the data started with the selection of the pertinent particulars as the initial step of the process. The information that was gathered was first organized into a table, which was the second step in the process, which was followed by the drawing of conclusions about the study. After the articles that had been selected for further examination were reviewed one at a time, the overarching notion that most effectively demonstrates the relevance of the study issue was then determined (see figure 1).

Research Results

Analysis

It was determined that a total of studies met the inclusion criteria after conducting the search. (Table 1). However, in the future, there will be a need for more research of this kind that is randomized and strictly monitored in order to determine how aging affects one's physical and mental health.

Table 1. The extracted information from screened studies

	Highlight of the review	Extracted information from Analysis	References
Physical based aging effects	Bone density loss	Aging leads to osteoporosis. Occur more in male and in menopause females	[13, 14]
	Decrease in muscle flexibility	Aging leads to sarcopenia	[12, 13]
	Increased risk of heart problems	Frailty, obesity, and diabetes increase adult cardiovascular disease (CVD) risk. These factors exacerbate advanced age-related cardiac risk factors. Since older women have a higher CVD risk than age-matched men, sex is another risk factor in aging adults.	[15, 16]
	Digestive changes	Leads to dysbiosis. Gut-microbial get low immunity.	[17, 27]
	Changes in skin, hair, and nails	Hair and nail gerontobiology has been less studied than skin aging. Signaling pathways involved in hair follicle melanogenesis help us comprehend greying. Nail plate lipid concentration determines nail structure and quality in older people.	[18-20]
	Vision	The central vision is impacted by age-related macular degeneration (AMD), which also has a significant negative effect on quality of life as a result of vision impairment.	[21]
Physiological based aging effects	Decreased executive functioning	Executive functions grow into early adolescence and decline in later life. Children and adults exhibit this trend.	[22-24]
	Memory changes	Temporal lobe structures, which are crucial for cognitive health in old age yet prone to aging-related disorders, may explain the substantial relationship between temporal	[25]

		lobe gray matter abnormalities and cognitive loss.	
	Anxiety	Suffered from generalized anxiety disorder.	[26]

Source: Author's own development

Interpretation

The table includes a collection of numerous physiological and physical impacts of aging as well as information gleaned from research and references. The physical side effects of aging include changes in skin, hair, and nails, vision, digestion, bone density, muscle flexibility, and heart disease risk. Anxiety, memory alterations, and impaired executive functioning are some physiologically grounded impacts of aging. There are additional references given for each consequence.

Discussion

The process of aging is an unavoidable part of the life cycle that occurs in all creatures that are still alive. As humans get older, their bodies go through a wide variety of physiological and structural changes, which results in a gradual loss of function and an increased susceptibility to illness [28]. In this article, we investigated the physiological and physical repercussions of aging, as well as the ways in which these effects manifest themselves in various parts of the body. The functionality of bones and muscles is significantly affected by aging, which is one of the most severe physical impacts of aging. Not only are bones and muscles necessary for movement, but they also have an important function in the endocrine and metabolic systems of the body. As people get older, their bones lose some of their density and their muscles lose strength, which can result in conditions such as osteoporosis and sarcopenia [29]. Because of their decreased estrogen production, which is a major factor in both bone and muscle mass, women who have gone through menopause and are now in their postmenopausal years are particularly susceptible to these problems [29, 30]. On the other hand, because males have more androgens in their bodies, such as testosterone, they are better protected against the age-related bone and muscle loss that affects females. However, both men and women can experience sarcopenia and osteoporosis as a natural part of the aging process. Diagnosis and treatment methods for osteoporosis in men are comparable to those used for postmenopausal women with the condition [31, 32]. Another one of aging's physical effects is an increased likelihood of developing cardiovascular disease (CVD). When it comes to cardiovascular disease in adults, age is a risk factor, and additional factors such as frailty, obesity, and diabetes can further enhance that risk [33, 34]. As people get older, their levels of sex hormones, especially testosterone and estrogen, decline, which is one factor that can contribute to the development of cardiovascular disease (CVD) in both men and women. It is commonly believed that women have a higher risk of cardiovascular disease (CVD) than males of the same age; nevertheless, the risks associated with CVD grow with age for both sexes [35, 36]. Along with the rest of the body, the microbiome in the gut goes through significant shifts as we get older, which can result in an increased likelihood of catching infectious diseases and a reduced immune response to vaccinations [37]. Because of the symbiotic interaction that exists between the immune system and the microbiome, treating age-related dysbiosis may result in an increase in both health and lifespan [38]. Both systemic inflammation and immunosenescence are hallmarks of the aging process, and age-related dysbiosis has been linked to both of these phenomena [39]. A variety of physical changes that occur as we age can have an impact on our overall health and happiness. Sarcopenia and osteoporosis are two examples of these alterations. Although they can affect both men and women, it is assumed that women are more likely to experience them due to their lower amounts of androgens like testosterone. For men and women, osteoporosis treatment and diagnosis approaches are comparable. As people get older, cardiovascular disease (CVD) can also become a problem. In addition to age being a risk factor for CVD, other variables like frailty, obesity, and diabetes can further raise the risk. Both men and women may acquire CVD as a result of hormonal changes brought on by aging, such as diminishing levels of estrogen and testosterone. The risk of CVD rises with age for both sexes, despite the belief that women have a larger risk than males of the same age. Age-related alterations in the gut microbiome also have a substantial impact on immune function and raise the danger of contracting infectious diseases. Age-related dysbiosis, systemic inflammation, and immunosenescence may all be associated with these alterations. Dysbiosis treatment may lead to increased longevity and health. Although typically true, other elements like nutrition, lifestyle, and environmental variables may also have a big impact on age-related health problems. When discussing health issues related to aging, it is crucial to approach the material cautiously and take a variety of elements into account.

Alterations in the way that the skin, hair, and nails appear are also common side effects of becoming older. The process of aging can alter several aspects of hair and nail growth, including color, arrangement, and growth rate [40]. The comprehension of the stages involved in the graying of hair has been significantly aided by studies of the signaling pathways that are active during melanogenesis in the hair follicle. The age-dependent changes in the lipid content of the nail plates are the principal factor responsible for the differences in structure and performance in general of the nails that occur with advanced age. These changes occur as a result of the natural process of aging [41]. Age-related macular degeneration has a major negative influence on quality of life due to vision impairment [42]. Structural alterations in the

eye lead to impairments in near and distant vision, and these impairments are caused by age-related macular degeneration [43]. Deficits in visual field induced by cerebral causes also have a detrimental influence not only on the patient's quality of life but also on the outcomes of rehabilitation for neurological illnesses in patients who have several deficits. Patients with multiple deficits are more likely to develop neurological disorders [44, 45]

Aging has a negative impact not just on a person's appearance but also on their physiological functioning. The decline in executive functioning that comes with becoming older is one of the most important physiological repercussions of getting older. The term "executive functions" refers to higher-order cognitive abilities such as memory retention, control based on inhibition, mental flexibility, organization, deductive reasoning, and the ability to solve problems [46, 47]. They are an essential component in achieving one's goals, adjusting successfully to the unexpected challenges that come in one's day-to-day life, and successfully navigating one's interpersonal interactions. Executive functioning requires contributions from multiple parts of the brain, including the frontal, posterior, and subcortical areas of the brain. It has been demonstrated through research that aging causes a loss in executive functioning, which can have an effect on the quality of life of an individual [48]. A decrease in sensory functioning is another one of the physiological effects of getting older. The process of aging can have an impact on a variety of sensory capabilities, including one's ability to hear, taste, and smell. Hearing loss, in particular, is a problem that is commonly associated with aging and can lead to social isolation and diminished quality of life [49, 50].

The field of anti-aging therapy is expanding, but there are numerous products and treatments that lack scientific backing for their claims. Slowing, stopping, or reversing the process of aging and its negative consequences, such as disease and weakness, are the goals of anti-aging medicine. Recently, aging in place has become more prevalent in healthcare services and policies. Technology has the ability to promote domestic independence. There is a dearth of literature on technology to support aging that is based on studies done in real homes and under controlled conditions. Therefore, a thorough investigation of the subject is required. Utilizing a biofeedback machine, an accessible computer, a pedometer wristband, a neurofeedback headband, and a platform for videoconferencing can add value. Both sexes are affected by the importance of bone and muscle function for mobility, the endocrine system, and the metabolic process, with postmenopausal women being more susceptible to age-related bone and muscle loss.

Conclusions

1. Age is a risk factor for cardiovascular disease (CVD), and other risk factors like frailty, obesity, and diabetes raise the risks for senior persons.
2. Changes in the structure and function of the gut are linked to an increased risk of developing infectious diseases and a decreased response to immunizations, and the gut plays a significant role in the development and management of the immune system.
3. In addition to changes in the lipid composition of nail plate structures and signaling pathways regulating hair color, aging has an impact on the look of hair, nails, and skin.
4. Age-related structural changes can impair near and far vision, whereas age-related macular degeneration (AMD) affects central vision. Vision impairment is an agreed-upon age-related alteration.
5. Executive functioning, which encompasses higher-order cognitive skills like memory recall and inhibitory control, declines with age.
6. Steroid hormonal substances, especially testosterone and estradiol, are to blame for gender dimorphism in musculoskeletal structure.
7. Age-related alterations in musculoskeletal structure are mostly caused by innate aging mechanisms such cellular senescence and oxidative stress.
8. The cause of osteosarcopenia, a disorder where muscle wasting and bone loss coexist, is unknown.
9. Despite the fact that there are fewer random clinical research studies in men, data suggests that detecting and treating osteoporosis in men is comparable to treating it in postmenopausal women.

References

1. Bookheimer SY, Salat DH, Terpstra M, Ances BM, Barch DM, Buckner RL, et al. The lifespan Human Connectome Project in aging: An overview. *Neuroimage* [Internet]. 2019;185:335–48. Available from: <http://dx.doi.org/10.1016/j.neuroimage.2018.10.009>
2. Rutledge J, Oh H, Wyss-Coray T. Measuring biological age using omics data. *Nat Rev Genet* [Internet]. 2022;23(12):715–27. Available from: <http://dx.doi.org/10.1038/s41576-022-00511-7>
3. Beadle JN, de la Vega CE. Impact of aging on empathy: Review of psychological and neural mechanisms. *Front Psychiatry* [Internet]. 2019;10:331. Available from: <http://dx.doi.org/10.3389/fpsy.2019.00331>

4. Rostoft S, O'Donovan A, Soubeyran P, Alibhai SMH, Hamaker ME. Geriatric assessment and management in cancer. *J Clin Oncol* [Internet]. 2021;39(19):2058–67. Available from: <http://dx.doi.org/10.1200/JCO.21.00089>
5. Rowe JW, Binstock RH. Aging reconsidered: Emerging research and policy issues. In: *Medicine and Society*. Routledge; 2019. p. 96–113.
6. McHugh D, Gil J. Senescence and aging: Causes, consequences, and therapeutic avenues. *J Cell Biol* [Internet]. 2018;217(1):65–77. Available from: <http://dx.doi.org/10.1083/jcb.201708092>
7. Howlett SE, Rutenberg AD, Rockwood K. The degree of frailty as a translational measure of health in aging. *Nat Aging* [Internet]. 2021;1(8):651–65. Available from: <http://dx.doi.org/10.1038/s43587-021-00099-3>
8. Greenwood N, Pound C, Brearley S, Smith R. A qualitative study of older informal carers' experiences and perceptions of their caring role. *Maturitas* [Internet]. 2019;124:1–7. Available from: <http://dx.doi.org/10.1016/j.maturitas.2019.03.006>
9. Chern A, Golub JS. Age-related hearing loss and dementia. *Alzheimer Dis Assoc Disord* [Internet]. 2019;33(3):285–90. Available from: <http://dx.doi.org/10.1097/WAD.0000000000000325>
10. Lisko I, Kulmala J, Annetorp M, Ngandu T, Mangialasche F, Kivipelto M. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med* [Internet]. 2021;289(6):807–30. Available from: <http://dx.doi.org/10.1111/joim.13227>
11. Yeo E-J. Hypoxia and aging. *Exp Mol Med* [Internet]. 2019;51(6):1–15. Available from: <http://dx.doi.org/10.1038/s12276-019-0233-3>
12. Laurent MR, Dedeyne L, Dupont J, Mellaerts B, Dejaeger M, Gielen E. Age-related bone loss and sarcopenia in men. *Maturitas* [Internet]. 2019;122:51–6. Available from: <http://dx.doi.org/10.1016/j.maturitas.2019.01.006>
13. Bonewald L. Use it or lose it to age: A review of bone and muscle communication. *Bone* [Internet]. 2019;120:212–8. Available from: <http://dx.doi.org/10.1016/j.bone.2018.11.002>
14. Sipilä S, Törmäkangas T, Sillanpää E, Aukee P, Kujala UM, Kovanen V, et al. Muscle and bone mass in middle-aged women: role of menopausal status and physical activity. *J Cachexia Sarcopenia Muscle* [Internet]. 2020;11(3):698–709. Available from: <http://dx.doi.org/10.1002/jcsm.12547>
15. Ji H, Kwan AC, Chen MT, Ouyang D, Ebinger JE, Bell SP, et al. Sex differences in myocardial and vascular aging. *Circ Res* [Internet]. 2022;130(4):566–77. Available from: <http://dx.doi.org/10.1161/CIRCRESAHA.121.319902>
16. Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, et al. Cardiovascular risks associated with gender and aging. *J Cardiovasc Dev Dis* [Internet]. 2019;6(2):19. Available from: <http://dx.doi.org/10.3390/jcdd6020019>
17. Bosco N, Noti M. The aging gut microbiome and its impact on host immunity. *Genes Immun* [Internet]. 2021;22(5–6):289–303. Available from: <http://dx.doi.org/10.1038/s41435-021-00126-8>
18. Eckhart L, Tschachler E, Gruber F. Autophagic control of skin aging. *Front Cell Dev Biol* [Internet]. 2019;7:143. Available from: <http://dx.doi.org/10.3389/fcell.2019.00143>
19. Park AM, Khan S, Rawnsley J. Hair biology: Growth and pigmentation. *Facial Plast Surg Clin North Am* [Internet]. 2018;26(4):415–24. Available from: <http://dx.doi.org/10.1016/j.fsc.2018.06.003>
20. Bonté F, Girard D, Archambault J-C, Desmoulière A. Skin changes during ageing. *Subcell Biochem* [Internet]. 2019;91:249–80. Available from: http://dx.doi.org/10.1007/978-981-13-3681-2_10
21. Owsley C, Gbate D, Kedar S. Vision and Aging. In: *The Wiley Handbook on the Aging Mind and Brain*. Chichester, UK: John Wiley & Sons, Ltd; 2018. p. 296–314.
22. Cristofori I, Cohen-Zimmerman S, Grafman J. Executive functions. *Handb Clin Neurol* [Internet]. 2019;163:197–219. Available from: <http://dx.doi.org/10.1016/B978-0-12-804281-6.00011-2>
23. Ferguson HJ, Brunsdon VEA, Bradford EEF. The developmental trajectories of executive function from adolescence to old age. *Sci Rep* [Internet]. 2021;11(1):1382. Available from: <http://dx.doi.org/10.1038/s41598-020-80866-1>
24. Cortés Pascual A, Moyano Muñoz N, Quílez Robres A. The relationship between executive functions and academic performance in primary education: Review and meta-analysis. *Front Psychol* [Internet]. 2019;10:1582. Available from: <http://dx.doi.org/10.3389/fpsyg.2019.01582>
25. Fletcher E, Gavett B, Harvey D, Farias ST, Olichney J, Beckett L, et al. Brain volume change and cognitive trajectories in aging. *Neuropsychology* [Internet]. 2018;32(4):436–49. Available from: <http://dx.doi.org/10.1037/neu0000447>
26. Beekman ATF. Anxiety disorders in old age: Psychiatric comorbidities, quality of life, and prevalence according to age, gender, and country. *Am J Geriatr Psychiatry* [Internet]. 2018;26(2):186–7. Available from: <http://dx.doi.org/10.1016/j.jagp.2017.10.004>
27. Fournet M, Bonté F, Desmoulière A. Glycation damage: A possible hub for major pathophysiological disorders and aging. *Aging Dis* [Internet]. 2018;9(5):880–900. Available from: <http://dx.doi.org/10.14336/AD.2017.1121>
28. Myerhoff B. Life history among the elderly: Performance, visibility and re-membering. In: *Life Course: Integrative Theories and Exemplary Populations*. Routledge; 2019. p. 133–53.
29. Laurent MR, Dedeyne L, Dupont J, Mellaerts B, Dejaeger M, Gielen E. Age-related bone loss and sarcopenia in men. *Maturitas* [Internet]. 2019;122:51–6. Available from: <http://dx.doi.org/10.1016/j.maturitas.2019.01.006>
30. Bonewald L. Use it or lose it to age: A review of bone and muscle communication. *Bone* [Internet]. 2019;120:212–8. Available from: <http://dx.doi.org/10.1016/j.bone.2018.11.002>
31. Aspray TJ, Hill TR. Osteoporosis and the ageing skeleton. *Subcell Biochem* [Internet]. 2019;91:453–76. Available from: http://dx.doi.org/10.1007/978-981-13-3681-2_16
32. Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment-facts and numbers: Editorial. *J Cachexia Sarcopenia Muscle* [Internet]. 2020;11(3):609–18. Available from: <http://dx.doi.org/10.1002/jcsm.12567>

33. Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, et al. Cardiovascular risks associated with gender and aging. *J Cardiovasc Dev Dis* [Internet]. 2019;6(2):19. Available from: <http://dx.doi.org/10.3390/jcdd6020019>
34. Izzo C, Vitillo P, Di Pietro P, Visco V, Strianese A, Virtuoso N, et al. The role of oxidative stress in cardiovascular aging and cardiovascular diseases. *Life (Basel)* [Internet]. 2021;11(1):60. Available from: <http://dx.doi.org/10.3390/life11010060>
35. Subramanya V, Zhao D, Ouyang P, Ying W, Vaidya D, Ndumele CE, et al. Association of endogenous sex hormone levels with coronary artery calcium progression among post-menopausal women in the Multi-Ethnic Study of Atherosclerosis (MESA). *J Cardiovasc Comput Tomogr* [Internet]. 2019;13(1):41–7. Available from: <http://dx.doi.org/10.1016/j.jcct.2018.09.010>
36. Yerly A, van der Vorst EPC, Baumgartner I, Bernhard SM, Schindewolf M, Döring Y. Sex-specific and hormone-related differences in vascular remodelling in atherosclerosis. *Eur J Clin Invest* [Internet]. 2023;53(1):e13885. Available from: <http://dx.doi.org/10.1111/eci.13885>
37. Calder PC, Ortega EF, Meydani SN, Adkins Y, Stephensen CB, Thompson B, et al. Nutrition, immunosenescence, and infectious disease: An overview of the scientific evidence on micronutrients and on modulation of the gut Microbiota. *Adv Nutr* [Internet]. 2022;13(5):S1–26. Available from: <http://dx.doi.org/10.1093/advances/nmac052>
38. Santoro A, Zhao J, Wu L, Carru C, Biagi E, Franceschi C. Microbiomes other than the gut: inflammaging and age-related diseases. *Semin Immunopathol* [Internet]. 2020;42(5):589–605. Available from: <http://dx.doi.org/10.1007/s00281-020-00814-z>
39. Santoro A, Bientinesi E, Monti D. Immunosenescence and inflammaging in the aging process: age-related diseases or longevity? *Ageing Res Rev* [Internet]. 2021;71(101422):101422. Available from: <http://dx.doi.org/10.1016/j.arr.2021.101422>
40. Fokias K, Dierckx L, Van de Voorde W, Bekaert B. Age determination through DNA methylation patterns in fingernails and toenails. *Forensic Sci Int Genet* [Internet]. 2023;64(102846):102846. Available from: <http://dx.doi.org/10.1016/j.fsigen.2023.102846>
41. Zhang J, Chen R, Wen L, Fan Z, Guo Y, Hu Z, et al. Recent progress in the understanding of the effect of sympathetic nerves on hair follicle growth. *Front Cell Dev Biol* [Internet]. 2021;9:736738. Available from: <http://dx.doi.org/10.3389/fcell.2021.736738>
42. Marakis TP, Koutsandrea C, Poulou MS. The impact of vision impairment on vision-related quality of life of patients with neovascular age-related macular degeneration. *Eur J Ophthalmol* [Internet]. 2022;32(1):481–90. Available from: <http://dx.doi.org/10.1177/1120672120972625>
43. Owsley C, Swain TA, McGwin G Jr, Clark ME, Kar D, Crosson JN, et al. How vision is impaired from aging to early and intermediate age-related Macular Degeneration: Insights from ALSTAR2 baseline. *Transl Vis Sci Technol* [Internet]. 2022;11(7):17. Available from: <http://dx.doi.org/10.1167/tvst.11.7.17>
44. Perini G, Cotta Ramusino M, Sinforiani E, Bernini S, Petrachi R, Costa A. Cognitive impairment in depression: recent advances and novel treatments. *Neuropsychiatr Dis Treat* [Internet]. 2019;15:1249–58. Available from: <http://dx.doi.org/10.2147/NDT.S199746>
45. Sasannejad C, Ely EW, Lahiri S. Long-term cognitive impairment after acute respiratory distress syndrome: a review of clinical impact and pathophysiological mechanisms. *Crit Care* [Internet]. 2019;23(1):352. Available from: <http://dx.doi.org/10.1186/s13054-019-2626-z>
46. Ballesio A, Aquino MRJV, Kyle SD, Ferlazzo F, Lombardo C. Executive functions in insomnia disorder: A systematic review and exploratory meta-analysis. *Front Psychol* [Internet]. 2019;10:101. Available from: <http://dx.doi.org/10.3389/fpsyg.2019.00101>
47. Elsevier. Evaluation and treatment of neuropsychologically compromised children. 1st ed. Nemeth DG, Glozman J, editors. San Diego, CA: Academic Press; 2020.
48. Perrotta G. Executive functions: Definition, contexts and neuropsychological profiles. *Neurosci Neurol Surg* [Internet]. 2019;4(3):01–4. Available from: <http://dx.doi.org/10.31579/2578-8868/058>
49. Grimmer M, Riener R, Walsh CJ, Seyfarth A. Mobility related physical and functional losses due to aging and disease - a motivation for lower limb exoskeletons. *J Neuroeng Rehabil* [Internet]. 2019;16(1):2. Available from: <http://dx.doi.org/10.1186/s12984-018-0458-8>
50. Rabbitt, P.M., An age-decrement in the ability to ignore irrelevant information, in *Cognitive Development and the Ageing Process*. 2019, Routledge. p. 5-18. <https://pubmed.ncbi.nlm.nih.gov/30332613/>