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Longevity Recipe - Lifestyle Influences on the Quantity and Quality of Life

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ABSTRACT

Introduction and Purpose. For many years, people have been fascinated by the question of how to achieve a long and healthy life, seeking a recipe for longevity. Our lifestyle can play a significant role in this. The aim of this review is to enhance public awareness of longevity and to emphasise the consequences of our daily habits.

Materials and Methods. A literature review was carried out using the PubMed database, searching for the most recently published scientific sources.

State of Knowledge. The review details the impact of individual lifestyle elements on quantity and quality of life. The benefits of physical activity were discussed, including the amount of exercise necessary per week to reduce mortality risk, and the most efficacious sport disciplines for health promotion. It also emphasises the significance of dietary habits and the role of phytochemicals. Additionally, it addresses the following questions: Does consuming small amounts of alcohol prolong life? What is the extent of the damage caused by smoking? How can stress and sleep be managed? Why are social relationships an important protective element? Finally, it considers whether there is a cure for longevity.

Summary. A holistic approach that encompasses a sufficient level of physical activity, proper nutritional habits and the maintenance of a healthy body weight can contribute towards the attainment of longevity. Conversely, factors such as smoking, alcohol consumption, poor stress or sleep management and loneliness can have a negative effect on life expectancy. A search is underway for anti-aging pharmacological compounds that are both efficacious and safe.

Key words. Longevity; anti-aging strategies; lifestyle medicine; health promotion

INTRODUCTION

Aging is one of the most enigmatic experiences that humans undergo [1]. It represents a highly intricate and multifaceted process, with a number of molecular and cellular hallmarks. These include telomere shortening, epigenetic modifications, the depletion of stem cells, mitochondrial deterioration, and the loss of proteostasis [2]. Additionally, the development of chronic, sterile inflammation, known as inflammaging, is a characteristic feature. It may precipitate the acceleration of the aging process and lead to the occurrence of age-related diseases, including atherosclerosis, cardiovascular disease, metabolic syndrome, obesity, type 2 diabetes, cancer, neurodegeneration, sarcopenia, osteoporosis, osteoarthritis, and depression [3]. The process of aging is one that can be affected throughout the course of a lifetime [1]. Moreover, the influence of lifestyle on risk of premature mortality exceeds that of genetic predisposition [4]. It is therefore a significant objective to reduce the negative impact of advancing age and to extend healthspan [2]. A comprehensive approach and the modification

of lifestyle behaviours can prove pivotal in the achievement of healthy ageing and longevity. Figure 1 illustrates the key elements addressed in this review.

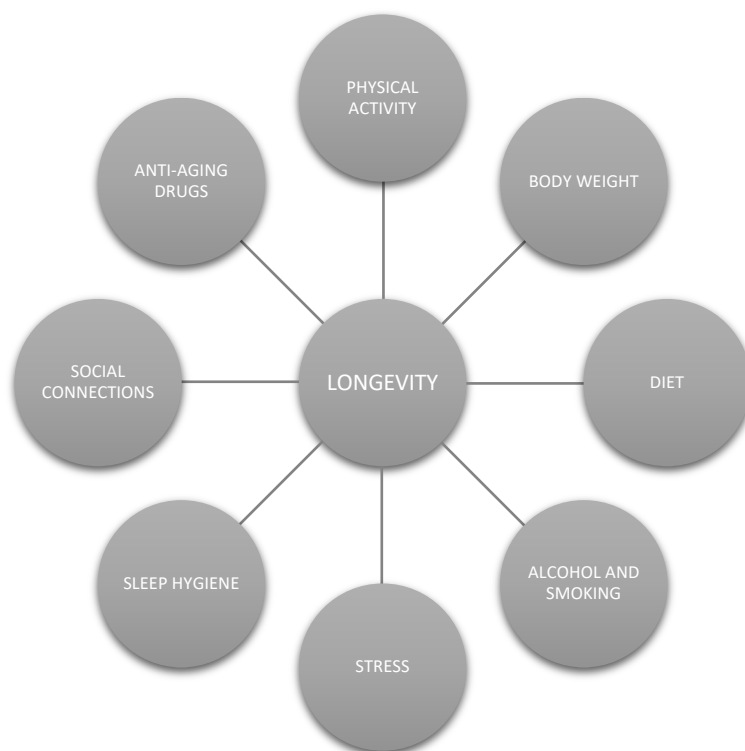


Figure 1 - Lifestyle elements with a positive/negative effect on longevity.

PURPOSE

The objective of this review is to raise public awareness of longevity and to highlight how our lifestyles affect the quantity and quality of life. It is crucial to emphasise the detrimental habits that diminish life expectancy and the health-promoting behaviours that enable people to achieve the longest possible healthy years. Furthermore, the aim is to consider the aspect of taking supplements and drugs with anti-ageing mechanisms. Is there an antidote to longevity?

MATERIALS AND METHODS

A review of the literature was carried out utilising the PubMed database. In order to ensure the inclusion of the most up-to-date scientific sources, the results were restricted to a period between 2018 and 2024. The following search terms were employed: “longevity”, “longevity physical activity”, “longevity diet”, “alcohol”, “smoking”, “sleep hygiene”, “stress management”, “loneliness”, and “anti-aging drugs”. All retrieved articles underwent an analysis.

STATE OF KNOWLEDGE:

The Power of Physical Activity

It is widely acknowledged that one of the most crucial factors contributing to a healthy and extended lifespan is physical activity. It is an efficacious method of preventing the development of a multitude of chronic diseases. These include dyslipidaemia, type 2 diabetes, metabolic syndrome, hypertension, coronary artery disease, stroke, cognitive impairment, depression, osteoporosis, sarcopenia, colon cancer, and breast cancer [5]. It has been demonstrated that middle-aged and older adults, including those who have experienced cardiovascular disease and cancer, can derive significant longevity benefits from increased physical activity. These advantages are regardless of previous levels of physical exertion and established risk factors, such as diet, body mass index, cholesterol, triglycerides and blood pressure [6].

Amount of Physical Activity - Mortality Risk

In individuals who are physically inactive, even minor increases in leisure-time activity may be associated with a reduction in the risk of mortality [7, 8]. The prevailing public health guidelines recommend that adults engage in a minimum of 150–300 minutes of moderate-intensity aerobic physical activity or 75–150 minutes of vigorous-intensity aerobic physical activity per week [9]. Adherence to and maintenance of these minimum recommendations at the population level has the potential to prevent 46% of deaths attributed to physical inactivity [6]. It is observed that additional benefits manifest when the level of physical activity is higher than the minimum recommendations. In terms of cardiovascular causes, the greatest reduction in mortality is observed when a weekly physical activity of 450-750 minutes is achieved, while > 1,200 minutes per week is needed to the maximum reduction in cancer-related mortality [10]. In addition, it is recommended that muscle-strengthening activities be performed on at least two days per week [9]. In individuals with low levels of physical activity, a significant reduction in muscle fibres can be observed as early as the age of 50 years. Exercise, particularly resistance training, represents the primary method for the prevention and treatment of sarcopenia, improving muscle mass and strength, and enhancing exercise capacity [11]. Resistance training also play a role in the prevention of osteoporosis by improving bone mineral density in the lumbar spine and femoral neck [12].

Sports Discipline - Does it Matter?

Any type of physical activity is associated with a reduction in mortality risk. However, the lowest risk of all-cause mortality is found in older adults who engage in racket sports and running. Both of these activities require the coordinated engagement of multiple muscle groups, with racket sports additionally necessitating intermittent bouts of intense exercise [7]. These types of activity are consistent with guidelines that recommend that older people engage in multicomponent physical activity that incorporates balance training in addition to aerobic and muscle-strengthening exercises [9]. The most prevalent form of physical activity is walking [7]. This is a simple and effective way to promote healthy lifestyle and prevent many chronic conditions. Although it is less intense than other types of exercise, its health benefits are considerable at any age. A minimum of four weeks of regular walking has been demonstrated to result in a statistically significant reduction in both systolic and diastolic blood pressure, with a mean decrease of 4–5 mmHg and 2 mmHg, respectively. This is associated with a reduced risk of stroke and myocardial infarction [8].

Metabolic Effects of Physical Exercise

It has been demonstrated that regular aerobic exercise training reduces the risk and severity of type 2 diabetes mellitus. It increases tissue sensitivity to insulin, thereby reducing insulin resistance. Furthermore, it exerts a beneficial influence on glycemic control with a reduction in the frequency of hyperglycemic excursions and a decrease in glycated hemoglobin A1C concentration [13]. The long-term regular physical activity has been observed to markedly enhance the overall configuration of lipoproteins, even in the absence of a change in weight [14]. It decreases a total cholesterol and low-density lipoprotein cholesterol (LDL-C). Additionally, it has also been shown to elevate levels of high-density lipoprotein cholesterol (HDL-C), which is associated with a reduced risk of developing cardiovascular disease [15]. The quantity of exercise is of greater consequence in modifying the lipid profile than its intensity [14].

Impact of Physical Activity on Cognitive Function and Mental Health

A sedentary lifestyle is a risk factor for the development of cognitive impairment and dementia. Physical exercise has been observed to regulate a number of biological processes

within the nervous system, including the amyloid β turnover, synthesis and secretion of neurotrophins, inflammation. Additionally, it has been linked to alterations in cerebral blood flow. The implementation of lifestyle modifications in the presymptomatic phase may have the potential to delay the onset of one-third of all dementia cases globally [16]. Physical activity also has a beneficial effect on mental health. Individuals who engage in high and moderate levels of physical activity have been found to exhibit significantly higher levels of life satisfaction and happiness in comparison to those with low levels of activity [17]. It can be estimated that adherence to the physical activity recommendations would have prevented 11.5% of cases of depression [18].

Maintaining a Healthy Weight - The Key to Longevity

It has been demonstrated that individuals who sustain a stable-lean body mass throughout their lifetimes enjoy enhanced longevity. Those whose Body Mass Index (BMI) is between 18.5 and 22.4, in conjunction with a high level of physical activity and a balanced diet, have the lowest mortality rates. A relatively modest increase in body weight (for instance, 5 kg) during the period of 18–55 years of age is associated with a markedly elevated risk of developing a number of serious health conditions. These include type 2 diabetes (by 30%), hypertension (by 14%), cardiovascular disease, obesity-related cancer, and premature death. Furthermore, the degree of weight gain is linked to a reduction in the probability of attaining healthy ageing, defined as the absence of major chronic illnesses and substantial limitations after the age of 55 [19]. A particularly dangerous condition is obesity ($\text{BMI} \geq 30$). This is accompanied by an increase in the size of adipocytes, which causes metabolic stress on the cells. This results in a rise in the secretion of pro-inflammatory cytokines and the development of chronic inflammation, which promotes a number of comorbidities. It is therefore of the utmost importance to maintain or return to a normal body weight [20].

The Role of Dietary Habits in Life Expectancy

Globally, dietary factors are the cause of 11 million premature deaths per year. These include excessive consumption of trans fat and sodium intake, and inadequate intake of omega-3 fatty acids, nuts, vegetables and fruit. Some dietary patterns, including the Mediterranean diet, the DASH diet (Dietary Approaches to Stop Hypertension), and the plant-based diet index (PDI), have been linked to reduced mortality and increased lifespan. The aforementioned diets

exhibit a number of common characteristics, notably an emphasis on unprocessed plant-based foods [19]. Their fundamental components including whole grains, vegetables, fruits, fish, and nuts, may exert a direct influence on the reduction of inflammatory processes by lowering C-reactive protein and tumour necrosis factor- α [3].

Importance of Macronutrient Quality

The particular food sources or types of fat, protein, and carbohydrates exert a greater influence on the risk of developing chronic conditions and mortality than their quantitative proportions [19]. For example, a greater intake of unsaturated fats, present in plant-based foods and marine fish, is linked to a reduced risk of mortality. Specific cardioprotective properties are ascribed to omega-3 polyunsaturated fatty acids, which reduce blood triglyceride levels and stabilise coronary plaques [21]. In contrast, an elevated consumption of trans fats and saturated fats is associated to a heightened risk of mortality. Moreover, trans fats, which are predominantly found in processed foods, are identified as a particularly detrimental ingredient. A heightened consumption has been linked to an elevated prevalence of cardiovascular incidents, cancer, and diabetes [21, 22]. A comparable situation exists with regard to protein intake. There is a positive correlation between elevated consumption of animal protein and cardiovascular mortality. The substitution of one serving of red meat per day with alternatives, including poultry, fish, nuts, legumes, whole grains, or low-fat dairy products is linked to a 7%–19% reduction in the likelihood of premature death. Furthermore, also in the case of carbohydrates, their quality plays a more important role in the prevention of diseases than the quantity consumed [19]. Diets with a high glycemic index (comprising starchy foods and a greater proportion of refined, low-quality grains) are associated with an elevated risk of obesity, metabolic syndrome, type 2 diabetes, cardiovascular incidents, and cancer. The ingestion of legumes, minimally processed grains, non-starchy vegetables, and fruits confer a degree of protection against the development of these diseases [23].

Exceptional Properties of Phytochemicals

The beneficial effects of fruit, vegetables and mushrooms are ascribed to phytochemicals, comprising such elements as alkaloids, polyphenols and terpenoids. These organic compounds may assist in prolonging lifespan by regulating metabolism. A high intake of polyphenols has been linked to a reduced risk of mortality, while flavonoid consumption has

an inverse correlation with the incidence of coronary heart disease and dementia [24]. One notable example is ellagitannins - the ingredients contained in pomegranate. These compounds have been demonstrated to function as a mitophagy activator, thereby preventing the accumulation of dysfunctional mitochondria. There is a possibility that mitophagy may prove to be a key factor in the treatment of age-related conditions and the prolongation of lifespan [25]. A comparable mechanism is exemplified by resveratrol, a polyphenol presents in grapes, which reduce the risk of Alzheimer's disease by inhibiting the accumulation of amyloid-beta protein in the brain [24]. Important are compounds with senolytic effects that induce apoptosis in senescent cells, reducing the release of pro-inflammatory cytokines and decreasing the levels of ageing markers. These include the flavonoid fisetin, found in strawberries, among others, as well as curcumin, luteolin, quercetin, piperlongumine [25].

Dangers: Alcohol and Smoking

Alcohol and smoking represent a significant global health issue. It is estimated that three million deaths per year are attributable to the consumption of alcohol, including those that extend beyond the immediate drinker, such as violence and road accidents. It is a proven carcinogen, contributing to the development of cancers of the oral cavity, throat, larynx, oesophagus, colon, liver and breast. Furthermore, it is linked to be associated with a heightened susceptibility to the development of liver disease, neurological disease, mental illness, and suicidal behaviour [26]. It is a commonly held belief in society that moderate drinking is beneficial to health, prolongs life, and reduces the risk of ischaemic heart disease, ischaemic stroke, and diabetes. However, the studies underlying these controversial conclusions involved carefully selected groups of people and are therefore currently considered unreliable and low quality [27]. Recent research have indicated that total abstinence from alcohol is the most optimal choice for health [26].

There is an association between smoking and an increased risk of premature death. In comparison to non-users, smokers have a reduced life expectancy. For women, this equates to approximately 12 fewer years of life, while for men it is approximately 13 less years of life. The cessation of smoking at any age has been linked with decreased rates of overall mortality, as well as a decline in the incidence of vascular, neoplastic and respiratory mortality. This is apparent as early as three years after quitting smoking, and cessation for at least ten years prevented about 10 years of life lost, resulting in survival rates comparable to those of never-smokers [28].

Stress - A Disrupter of Homeostasis

Stress plays a pivotal role in the development of numerous physical and mental health issues, including cancers, cardiovascular diseases, burnout, anxiety disorders, and depression. In response to the demands of the contemporary world, a considerable proportion of the population takes tranquilising medications, which are associated with a range of adverse effects and dependence. For these reasons, it is so essential to utilise non-pharmacological methods for the management of stress [29]. Relaxation techniques such as yoga and mindfulness-based stress reduction programmes decrease blood pressure by reducing the level of activity of the sympathetic nervous system, thereby reducing cardiovascular risk [30]. A further example is listening to music, which reduces anxiety and increases feelings of happiness by activating the amygdala and mesolimbic reward system in the brain. Additionally, it lowers cortisol levels, mean arterial pressure, and heart rate [29].

Recovery Time - Sleep Hygiene

Sleep is an integral component of maintaining physical and mental health, as it enables the body to recuperate and repair. Optimal sleep facilitates enhanced functionality of all systems, most notably the cardiovascular, neurological, immune, and endocrine systems. The practice of good hygiene entails obtaining 7-9 hours of sleep per night, for adults, and maintaining a regular sleep schedule [31]. Adequate restorative sleep is associated with a reduced incidence of cardiovascular disease, including conditions such as myocardial infarction, stroke, heart failure and atrial fibrillation [32]. The regularity of sleep is a more powerful predictor of certain health outcomes than is the total amount of sleep obtained. A higher degree of sleep regularity has been linked to a reduced risk of mortality from all causes by 20%-48%, cancer mortality by 16%-39%, and cardiometabolic mortality by 22%-57%. Sleep hygiene represents a straightforward way for enhancing overall health and survival [33].

Building Social Connections as a Foundation for Health

Social relationships are a significant determinant of health and longevity, yet this aspect is frequently underestimated. Meanwhile, it has been shown that they are just as critical for maintaining a healthy lifestyle as other well-established factors, such as physical activity, smoking cessation or restricting the intake of alcohol [34]. A deficiency in social connections

over an extended period is a contributing factor in the development of chronic disease, including type 2 diabetes, hypertension, cardiovascular disease, depression, addiction and Alzheimer's disease. This is associated with an elevated state of alertness within the central nervous system and the activation of the sympathetic nervous system, which results in the release of stress hormones, an inflammatory response, and an increase in blood pressure. Furthermore, loneliness has been linked to a heightened risk of premature mortality (26%), social isolation (29%), and living alone (32%) [35].

Hope for the Future: Development of the Pharmacological Approach

One of the most promising avenues for achieving longevity and healthy ageing may be pharmacological management. A significant number of chemical compounds have been described that possess anti-ageing properties [36]. This article focuses on those that currently seem to be the most known and effective, providing a characterisation of them.

The anti-diabetic drug metformin is currently being investigated as a potential anti-ageing strategy in healthy humans. It has been demonstrated to influence transcriptional activity by regulating DNA methylation and modifying histones. Additionally, it has impact on the process of inflammaging, possess senolytic activity, and extend telomeres [37]. The evidence suggests that diabetics who are taking metformin appear to may have a longer life expectancy than individuals without diabetes [24]. Furthermore, it confers protection against a range of age-related diseases. Nevertheless, this pharmaceutical agent is not employed for prophylactic purposes, such as promotion of healthy ageing, due to its adverse effect profile, which includes gastrointestinal complaints. Chronic administration results in alterations to motility and microbiota, which in 6% to 30% of patients leads to vitamin B12 deficiency as a consequence of malabsorption [38].

Resveratrol, a polyphenolic compound, exhibits multitargeted therapeutic properties and thus represents a promising avenue for support the management of diabetes, neurological and cardiovascular disorders. Additionally, it exerts an anti-obesity effect by strengthening the intestinal barrier function and enhancing microbial diversity within the intestinal tract [2]. The administration of resveratrol has the positive effect of reducing peripheral inflammation in adipose tissues. It also plays a role in maintaining pancreatic homeostasis. Resveratrol has been observed to induce the formation of certain types of cancerous cells and non-alcoholic fatty

liver disorder. Further research is required to ascertain the bioavailability and dosage effects [36].

Rapamycin (sirolimus) is a medication employed in the field of transplantology and anticancer therapies. Its mechanism of action involves the inhibition of the mechanistic target of rapamycin (mTOR), which may contribute to the prolongation of life [36]. The administration of this has been demonstrated to enhance a range of physiological attributes associated with the process of ageing in systems pertaining to the immune, integumentary and cardiovascular functions [39]. The use of rapamycin as a universal anti-aging drug is not currently recommended due to its immunosuppressive properties, which may be associated with serious adverse events [36]. In individuals afflicted with age-related conditions, there is a rise in the prevalence of infections and alterations to lipid profile, namely an elevation in triglycerides, LDL cholesterol, and total cholesterol. Nevertheless, there is not found no evidence of significant adverse effects of rapamycin in healthy subjects. This may be attributed to the paucity of long-term studies, as well as the dearth of data pertaining to the drug's impact on the gastrointestinal, respiratory, reproductive, and renal systems [39].

Senolytics are a class of drugs that eliminate senescent cells. Examples of these are navitoclax, and dasatinib. Preclinical studies have demonstrated that senolytics can impede, forestall, or mitigate the development of over 40 age-related disorders and their complications. These include cancers, frailty, and conditions affecting the cardiovascular, metabolic, neuropsychiatric, digestive, urinary, respiratory, musculoskeletal, and hematological systems. Clinical trials are ongoing for diabetes, Alzheimer's disease, osteoporosis, osteoarthritis, idiopathic pulmonary fibrosis, among others. This represents a promising avenue for the treatment of age-related diseases. Nevertheless, until the requisite clinical trials have been completed and demonstrated the requisite safety and efficacy, senolytics should not be widely used [40].

Polyamine spermidine is found in supplement form. Its endogenous concentration declines considerably with age, except in centenarians. It has been demonstrated to induce autophagy and enhance mitochondrial function. In model organisms, it reduces the risk of liver fibrosis, hepatocellular carcinoma, exhibits neuro- and cardioprotective effects and prolongs life. Further research is necessary to ascertain whether spermidine supplementation may be effectively and safely employed in humans [36, 41].

In order to introduce geroprotective treatments into widespread use, it is essential to confirm their safety and minimize adverse effects. Long-term studies would be crucial in this regard, as well as establishing a dosing regimens and optimal drugs concentrations in the blood [39].

SUMMARY

Human beings, through their lifestyle, have a significant impact on the length and quality of their lives. Behaviours such as physical activity, a low-processed plant-based diet and maintaining a healthy body weight are important anti-ageing strategies. On the other hand, habits such as alcohol consumption, tobacco use, irregular sleep patterns, stress management deficiencies, social isolation and loneliness accelerate the ageing process in the body, thereby reducing life expectancy and being triggers for the onset of many diseases. For this reason, the promotion of pro-health behaviors is so crucial among society. A number of substances have been identified as having potential anti-ageing effects. However, at this point in time, there is insufficient data on their profile of action and safety in humans to include them in widespread prevention strategies. With many studies underway, they may provide new insights into aspects of longevity in the future.

Author's Contribution

Conceptualization, Katarzyna Piotrowicz and Hubert Piotrowicz; Resources, Jacek Kurzeja, Agnieszka Bajkacz, Olga Jankowska and Wojciech Kraśnik; Writing – Original Draft Preparation, Katarzyna Piotrowicz and Hubert Piotrowicz; Writing - Review and Editing, Jacek Kurzeja, Anna Rogala, Joanna Osmólska, Wojciech Kraśnik, Olga Jankowska, Agnieszka Bajkacz, Katarzyna Piotrowicz and Hubert Piotrowicz; Visualization, Joanna Osmólska, Anna Rogala, Olga Jankowska and Wojciech Kraśnik; Supervision, Jacek Kurzeja.

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