Factors that affect human longevity

by

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Abstract

Longevity, and factors that may increase the human lifespan, have been the topic of many research studies attempting to pinpoint direct positive influences. Research demonstrates that among those who live beyond an average life expectancy, approximately 25% of the increased lifespan is related to genetics. The remaining 75% is largely due to environmental factors, mainly diet and lifestyle factors, that have the ability to influence genetic effects for increased longevity. The following types of studies on diet and lifestyle factors for increasing longevity and decreasing the incidence of chronic conditions were reviewed: Prospective cohorts, longitudinal, in vitro, randomized controlled trials, and prospective case-controlled studies. Results related to the Mediterranean Diet were consistent in the conclusion that adherence to this diet increased the lifespan and delayed the development of chronic conditions although calorie restriction demonstrated an increase in longevity, the studies examined failed to correlate this diet to the reduced incidence of disease development. Red meat and alcohol consumption, though both are considered carcinogenic, demonstrated some benefits to the elderly. However, both need to be consumed with caution as they may negatively impact health when consumed outside of moderation. Physical activity demonstrated a consistent benefit to the elderly by increasing longevity and decreasing age-related conditions. Epigenetic research consistently concluded that a diet high in antioxidants and healthy fats both increase telomere length and decrease DNA damage though the exact mechanism remains unknown. Studies on the impact of regular social interactions and time spent on leisure activities in advanced age are consistent in the conclusion that both contribute to health and well-being in this demographic group, but failed to connect to an increase in longevity.

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Chapter 1 - Introduction

According to the Centers for Disease Control and Prevention the human lifespan for all races and both sexes in the United States in 1900 was an average of 47.3 years. In 2015, the lifespan had increased by 31.5 years to an average of 78.8 years. The 2016 Census report shows that in 2015 approximately 617.1 million, or 8.5% of the global population is aged 65 years or older. This number is expected to increase by more than 60% over the next 15 years totaling one billion, or 12% of the share of total global population. This demographic will continue to rapidly increase and by the year 2050, the number of those 65 and older is projected to total 1.6 billion, or 16.7% of the worldwide population (He, Goodkind, & Kowal, 2016). The population of "oldest old", or those who are aged 80 and older, is projected to increase from 126.5 million to 446.6 million between 2015 and 2050, more than triple the current population, with many of these growths occurring in developing countries such as Asia, Latin America, and Africa (National Center for Health Statistics, 2017). In the United States, centenarians, or people age 100 or older, have increased in number from around 32,000 in 1980 to more than 53,000 in 2010. If life expectancy continues to increase at the current trajectory, it is possible that the number of centenarians could increase to more than 600,000 by 2060 (Mather, 2016). To put these numbers into perspective, by the year 2020, the population of those aged 65 and older will outnumber those aged 5 and younger. By the year 2050, the 65 and older demographic will outnumber the 5 and younger demographic by more than twice their population. These numbers are, to date, unprecedented (He, Goodkind, & Kowal, 2016).

The aging process and longevity itself are affected by several events. Environmental factors, diet, lifestyle and epigenetics play a crucial role in how long we live. Better health care including preventative testing, the ability to manage and treat diseases once they manifest, and

pharmacological agents, are some of what has largely influenced increases in the lifespan. Much research in human nutrition has been and continues to be conducted on the dietary components that contribute to lasting good health along the lifespan. Two eating patterns, the Mediterranean diet and calorie restriction have emerged as having a positive impact on the lifespan by contributing to the decrease in common diseases of advanced age (Chrysohoou & Stefanadis, 2013). This report will evaluate the latest research on these diets and why they are believed to increase longevity, as well as the contributions of other positive lifestyle factors including social interactions, the contribution of regular physical activity, and advances in epigenetic research that may be able to pinpoint how diet and lifestyle can manipulate telomere length and genetic influences on longevity. Current diet and lifestyle practices that negatively impact optimal health and longevity and what research has discovered will also be addressed, including the impact of red meat, protein, alcohol intake, sedentary influences, obesity, and the dietary connection to increases in life shortening diseases such as cardiovascular disease, diabetes and cognitive dysfunction.

Chapter 2 - Dietary Influences

The Mediterranean Diet and its relationship to longevity

The Mediterranean Diet has been widely studied and proven through numerous epidemiological studies to contribute to exceptional health and longevity (Chrysohoou & Stefanadis, 2013). The main components of this diet are mostly plant-based with the bulk of meals consisting of whole grains, vegetables, fruits, legumes, and moderate amounts of dairy, mainly low-fat yogurt and cheese. Nuts and seeds are regularly consumed and olive oil is the main source of fat. Less often consumed are chicken, fish and eggs, with red meat and sweets rarely eaten. Wine is consumed in moderation and water in copious amounts, typically 1-2 liters each day (Ross, 2015).

Vasto and coworkers researched the dietary habits of the people in an area of western Sicily called Monti Sicani, home to a large number of centenarians. These people, notably men, have longer than average lifespans and are reaching old age with low incidences of cardiovascular disease and cancer. Compared to the national ratio of centenarians, this area contains a four-fold greater ratio. The diets of these centenarians were studied and were typical of the Mediterranean Diet: High amounts of plant based foods and low amounts of meat consumption were common. Moderate amounts of dairy and fruit were consumed, and most of the protein came from legumes. Smaller meals were eaten with greater frequency. Meals were high in complex carbohydrates and contained little or no sweets and processed foods. Snacks consisting of local prickly pears, pistachios and oranges were often consumed often (Vasto, Buscemi, Carlo, Accardi, & Caruso, 2014).

Researchers also studied the dietary habits of the larger Sicilian city of Palermo where there is less adherence to the Mediterranean Diet. They obtained diet information from 1,297

adult residents in Palermo. Twenty two percent of the cohort consumed a diet considered

unhealthy as it consisted of high amounts of soda pop, fried foods, cured meats, seed oil, butter,

sweets and red meat. Thirty four percent of the cohort consumed what was considered adherence

to the Mediterranean diet and the individuals in this group were on average 10 years older than

the other members. The remaining 45% consumed foods somewhere in between. The study

concluded that although those who closely followed the Mediterranean Diet were 10 years older

than the other subjects, they did not have an increased prevalence of cardiovascular disease.

Instead, they demonstrated a higher HDL concentration and a more efficient insulin sensitivity.

The researchers noted that living in the Mediterranean did not translate into adherence to the

Mediterranean Diet. Those living in the larger cities such as Palermo consume large amounts of

street food, which is often fried in cheap animal fat. This type of diet is associated with increases

in body mass index, hypertension, and lower HDL concentrations. The study demonstrated an

increase in mortality rates related to cardiovascular disease and no increases in longevity were

observed like those seen in the small coastal towns (Vasto et al., 2014).

Zbeida and coworkers aimed to research a possible association between the

Mediterranean Diet and better physical function among older adults in the United States and

Israel. Data was obtained from the 1999-2002 National Health and Nutrition Survey as well as

from the 2005-2006 Israeli National Health and Nutrition Survey which contained both

nutritional and physical functions data of a sample of people aged 60 and older. Using

multivariate logistic regressions, it was determined that those who closely adhered to the

Mediterranean Diet had better physical function. The United States NHANES measured walking

speed to assess physical performance while the Israeli NHANES utilized a questionnaire related

to activities of daily living to assess physical functioning. Participants with the closest adherence

to the Mediterranean Diet had an 11% lower risk of declining physical functioning (Zbeida, et al., 2013). Interestingly, the diets of the U.S. and Israeli participants varied slightly. The Israeli participants consumed more fruits and vegetables and less non-recommended meat, while the U.S. participants tended to consume lower amounts of fruits and vegetables and higher amounts of meat, though still staying within the parameters of the Mediterranean Diet.

This study concluded that further research is needed to obtain dietary recommendations for the elderly age group, and whether benefits can be achieved if adoption of this diet begins in old age or if the benefits are achieved only with lifetime consumption (Zbeida et al., 2013).

Olive oil and other polyphenols. Hippocrates, the "father of medicine," often used olive oil to treat the ailments of his patients. Although olive oil is no longer used to treat physical ailments, the health benefits achieved through regular consumption have been confirmed through research. The phenolic compounds of olive oil possess a high bioavailability that positively affect plasma lipoproteins, inflammatory markers, oxidative stress, antimicrobial activity and cellular function, which contributes to the reduction in cardiovascular disease, Alzheimer's Disease and other common ailments of advanced age (Ross, 2015).

Letois and coworkers conducted a prospective cohort study involving 8,937 French participants determined that olive oil use was inversely associated with all-cause mortality risk, but only in women. According to their summary a possible explanation could be related to an already longer life expectancy among women. A major limitation of this study is the wide variables related to data collection, differences in consumption standards, and the availability of food resources which are all common issues with food frequency questionnaires (Letois, et al. 2016).

A study by Gimeno and coworkers found a significant drop in the LDL cholesterol of participants after one week of olive oil consumption (Gimeno, Fito, & Lamuela-Raventos, 2001). A randomized trial found an increase in HDL cholesterol after regular olive oil consumption (Covas, Nyyssonen, & Poulson, 2006). Researchers believe the benefits lie in olive oil's high concentration of polyphenols and monounsaturated fatty acids, which reduces oxidative stress and improves endothelium function (Letois et al., 2016).

The combined results of these studies suggest a positive relationship between regular olive oil consumption and a reduced risk of cardiovascular disease development, and the difference noted between men and women may lie in an already existing greater longevity for women.

Alcohol consumption. Alcohol consumption as it relates to longevity has been extensively studied. Many epidemiological studies have concluded that moderate alcohol consumption, one drink per day for women and up to two drinks per day for men, reduces the risk of cardiovascular disease, cognitive deficits, and results in a lower risk of all-cause mortality within the middle aged and older population. The effects of alcohol on cancer risk have been widely studied and shown to be a direct cause of several cancers and is considered a carcinogen. However, a systematic review of red wine and its effect on organs and systems concluded that the harmful effects of wine consumption are still up for debate. Several clinical trials have resulted in identical findings that red wine consumption is beneficial to human health. What is unclear is whether the polyphenols or the alcohol in red wine are providing benefits (Artero, Artero, Tarin, & Cano, 2014).

Most studies conducted on the effect of alcohol consumption on cognition have been based upon on the amount of alcohol consumption only. A 2017 study by Richard and

coworkers assessed alcohol amount and frequency and its connection to cognitive health and longevity. They used a standardized questionnaire and a sample size of 1,344 community-dwelling adults aged 85 years and older. Cognitive function was assessed every four years from 1988-2009. Researchers concluded that those who reported a moderate to heavy amount of alcohol consumption per day (up to 3 drinks per day for both sexes over 65 years and up to 4 drinks per day for men under 65 years), had a more than three-fold chance of living to age 85 without cognitive impairment than those who were non-drinkers or who passed prior to age 85. Those who reported daily or near daily alcohol consumption or moderate to heavy intake had a significantly greater protective effect on cognition compared to light or non-drinkers. Moderate and heavy drinkers had twice the odds of living to age 85 compared to non-drinkers without cognitive impairment. These results remained after researchers adjusted for other health and lifestyle characteristics. Researchers discuss their results as being consistent with previous studies that provide a positive connection between moderate alcohol consumption and cognitive health (Richard, et al., 2017).

Researchers are unsure of the exact mechanism with which alcohol provides protective cognitive effects. One theory connects alcohol and its ability to increase HDL concentration while decreasing LDL, fibrinogen and platelets, as well as stimulating an increase in antioxidant activity. These effects combine to reduce the formation of arterial plaques and preserve the brains vascular health. A limitation of this study is it is the first study known to examine both amount and frequency of alcohol intake and the impact within a cognitively healthy sample of elderly participants compared to those who were cognitively impaired or who passed prior to age 85. More research is needed within these same parameters before cause and effect can be firmly established (Richard et al., 2017).

Moderate alcohol consumption within the Mediterranean Diet has been extensively researched and has consistently been shown to contribute to a reduction in cardiovascular disease risk in those who adhere to this diet. A study by Carloccio and coworkers concluded that the resveratrol in wine inhibits the adhesion of monocytes to the vascular endothelium within the arterial walls, thus contributing cardioprotective benefits (Carloccio, et al., 2003).

These studies have demonstrated that the regular consumption of moderate amounts of alcohol, notably wine, contribute to the decreased incidence of cardiovascular disease and declining cognition in those who regularly imbibe, thus contributing to the odds of greater longevity, though further studies conducted on amount and frequency are needed to assess the accuracy of the results. However, the role of alcohol on cancer risk is clearly defined and even small amounts of alcohol contribute to an increased risk.

Calorie restriction's relationship to the lifespan

The "Blue Zones" are five areas of the globe that contain an unusually high number of centenarians. These areas haves been the subject of much research on the diet and lifestyle practices of these centenarians that may contribute to their longevity. The "Blue Zones" are Loma Linda, California, with their Seventh Day Adventist population of vegetarians, Okinawa, Japan, Sardinia, Italy, the Nicoya Peninsula, Costa Rica, and Ikaria, Greece. Though some variations exist within each area's dietary components, the common denominator is a largely plant-based, nutrient dense diet, which is naturally lower in calories. It is this reduction in total daily caloric intake that is an area of research believed to contribute to the longevity of many in the elderly population, though no scientific evidence to date supports this theory (Chrysohoou & Christodouloss, 2013; Davinelli, Wilcox, & Scapagnini, 2012).

Few studies have been conducted on humans and how calorie restriction impacts health and longevity, though a large number of research studies exist that have resulted in determining that oxidative stress is the primary cause of ageing, and that calorie restriction reduces the oxidative stress in the body by reducing the number of reactive oxygen species, or ROS produced (Davinelli et al., 2012). A 2-year, randomized controlled trial nicknamed CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy), was designed to determine if calorie restriction increases the human lifespan. The participants decreased their usual daily caloric intake by 25%. The results of this study found that calorie restriction was a viable option for reducing age-related cardiovascular disease risk factors and metabolic conditions without a reduction in quality of life for the participants. These results paralleled some, but not all results, from rodent studies associated with calorie restriction and longevity. More research is needed on the exact mechanism with which lifespan is increased in relation to calorie restriction (Ravussin et al. 2015).

A 2015 in vitro study conducted by Richardson and coworkers concluded that similar life extending results could be achieved with both a 10% and a 40% dietary restriction from ad libitum. Dietary restriction has been widely researched and has been shown to increase the lifespan as well as reducing the incidence of age related conditions and slowing age related declines in yeast, spiders, rats, mice and dogs with a 40% dietary restriction. This study sought to determine if the same results could be achieved with a more modest dietary restriction of 10%. The researchers divided the rats into three groups: The first group was fed an ad libitum diet throughout the lifespan, group two was fed 60% of the same ad libitum diet, and group three was fed 90% of the ad libitum diet. Body weight was closely monitored throughout the study. After 20 months of age the body weight of all three groups peaked, and at this point the rats on the ad

libitum diet began to decrease in weight and die. Groups one and two had similar life extending benefits, with increases of 15% for the 10% group and 19% for the 40% group compared to the ad libitum group. The 40% group had a significantly decreased incidence of cancer, whereas the 10% group did not show a decrease in cancer. This study has important implications for humans as it concluded that even a modest dietary restriction may increase human longevity though more research is needed to determine if 10% dietary restriction has the potential to decrease the incidence of age related conditions and chronic diseases in humans (Richardson, Austad, Ikeno, Unnikrishnan, & McCarter, 2015).

Fasting mimicking practices. According to a review by Handshcin, it is difficult to determine a baseline percentage for total daily calorie reduction and achieve total long-term compliance from the subjects in order to obtain outcomes. He reviewed existing research related to "mimicking" calorie restriction and exercise using in vitro subjects and human clinical trials given pharmaceuticals, notably Metformin and resveratrol, that were designed to illicit similar alterations to skeletal muscle and mitochondria that occurs with physical activity and reduced calorie intake. Several pathways were researched in both in vitro and human clinical trials, primarily the inhibition of anabolic pathways, which affected both metabolic activity and nutrient metabolism, and not surprising, were somewhat intertwined. Results of multiple studies were mixed. The effects of anabolic pathway disruption as an exercise and nutrient metabolism showed some improvement in subjects with existing health conditions but little to no improvement was observed in healthy subjects. Metformin created negative side effects with in vitro subjects that cancelled out any positive results. Variations in dose response were noted, as well as the inability to accurately mimic actual exercise benefits and those of calorie restrictions. Researchers noted that the possibility of a more positive outcome may be achieved using partial

diet restriction and some exercise in combination with pharmaceuticals, which would potentially alleviate some of the negative side effects that were observed. Limitations of these results include the lack of clinical trials on healthy individuals. In subjects with existing conditions, small sample sizes and variants in doses and methods hamper collective interpretations. Other questions remain related to mechanisms, toxicity and bioavailability. Therefore, further studies on this topic are needed (Handschin, 2016).

Protein consumption. Weight loss among the 70 and older population is a common occurrence and contributes to increased mortality, limited mobility, frailty, and institutionalization. The current recommendation for optimal protein intake for this population is .8g/kg/day but some research has concluded that protein intake prevents the loss of lean body mass in the elderly when consumed in amounts closer to 1.2 g/kg/day. However, studies have also concluded that protein consumption in excess of .8g/kg/day prior to age 70 can have negative health effects (Gray-Donald et al. 2013).

A review by Dongyeop and coworkers discussed the results of a large scale, long term study conducted on European subjects that noted a 75% increase in overall mortality when consuming a diet high in animal protein. This level of consumption was also associated with a four-fold increase in cancer related death in the 50-65 age group. The harmful effects of animal protein consumption did not translate to plant derived protein consumption. In addition, the plant based protein was associated with decreases in serum cholesterol levels and body fat in obese individuals (Dongyeop, Wooseon, Murat, Dae-Eun, & Seung-Jae, 2015).

A prospective case-controlled study conducted by Gray-Donald and coworkers sought to determine a link between functional decline in the elderly and decreased protein intake below the current recommended daily allowance of .8 g/kg/day. The study consisted of 422 healthy

participants who provided three non-consecutive 24-hour diet recalls at baseline. Body weight

and fat free mass was measured in order to more accurately assess the origin of weight changes

during the study. The control group consisted of those who had experienced weight loss of <2%

over the previous year. After two years the weight and body mass of the participants was re-

measured. During this time, the average lean body mass lost in the control group was $1050 \pm$

1200g, while the case group experienced a 1610 ± 1680g, which was determined by a *t* test to be

significant losses among the case group. 51.9% of participants in the case group consumed <1.0

g/kg/day compared with 39.6% of the control group. When the data was analyzed a direct

association between reduced protein intake and weight loss was observed. When compared to

the participants who consumed 1.2g/kg/day of protein, those who consumed .8g/kg/day had

twice the amount of weight loss, and those who consumed .8-1.0 g/kg/day had a 70% incidence

of weight loss. These results contribute to the debate that while those under 70 years of age may

have negative health effects with excessive protein consumption, the optimal protein needs in the

elderly population may be insufficient at the current recommended amount (Gray-Donald et al.,

2014). Despite these results, no studies to date have been successful in making a direct link to

protein intake and human longevity (Dongyeop et al., 2015).

Dietary factors that negatively affect longevity

  Red meat consumption. As previously discussed, the older population is vulnerable to

malnutrition and decreased muscle mass as well as a reduction in the ability to synthesize B

vitamins. A fine line exists between obtaining the benefits of high quality red meat

consumption, which provides protein, vitamins A and B, and heme iron, and the possible

increased risk of non-communicable diseases such as cardiovascular disease and cancer in this

demographic. Red meat consumption as it relates to human mortality has been extensively

studied. Large numbers of meta-analysis reviews have shown a clear association with red meat consumption and increases in cardiovascular disease, stroke, and cancer. However, when studying the effects of red, unprocessed meat on CVD and cancer risk, the link is much less clear (Chrysohoou et al. 2013).

A 10-year cohort study which consisted of Swedish men aged 45-79 years aimed to determine whether or not a link to red meat consumption and stroke risk existed. A significant link was demonstrated between stroke risk and processed meat only (Larsson, Virtamo, & Wolk, 2011). Another 5-year cohort study of Italian men aged 65 and older, a significant link between all-cause mortality and total red meat consumption was observed (Fortes, Forastiere, Farchi, Ropiti, & Pastori, 1999).

A randomized case-control study named Cardio2000 was conducted which consisted of both male and female subjects with a mean age range of 59-65 years. Each subject had already experienced a cardiovascular event. This study found that a 60g increase in unprocessed meat consumption per month was associated with double the likelihood of a heart attack or unstable angina (Kontogianni, Panagiotakos, Pitsavos, Chrysohoouc, & Stefanedes, 2007).

The carcinogenic effects of red meat consumption are believed to originate from the formation of heterocyclic amines, substances that are formed when meat is cooked at high heat. Processed meats and the sodium and nitrous preservatives are believed to be what contributes to the development of cancer. A recent meta-analysis of prospective studies reviewed the possible connection between all meat consumption and cancer mortality risk, mainly colorectal and stomach cancer in individuals aged 60-90 years old. The results indicated that for every 100g/d of total meat consumption, a 14%, 23%, and 31% increase in colorectal, colon, and rectal cancer was observed (Chrysohoou et al., 2013).

Stomach cancer is a common disease of advanced age, with 6 out of every 10 individuals diagnosed over the age of 65. A clear link has been established between processed meat consumption as a result of the preservatives and high sodium content. A recent meta-analysis of observational studies concluded that an average of 45% increase in stomach cancer related to red meat consumption of all types, though a high level of mixed results demonstrates the need for further research (Chrysohoou et al., 2013).

The World Health Organization has classified red meat in the following categories: Processed meats are in Group 1 which is considered a carcinogen. Unprocessed meats are in Group 2 which is considered potentially carcinogenic. To date the role of red meat consumption in the elder population and its impact on longevity cannot be clearly established until further research has been conducted individually on the subtypes (Chrysohoou et al., 2013).

Chapter 3 - Genetics and the Nutrition Connection

Studies conducted on the aging process have concluded that 20-30% of an individual's longevity is determined by genetics, and the remaining percent is affected by environmental factors that have a direct effect on gene expression (Herskind et al.,1996).

Epigenetic research

A recent avenue of research related to longevity is the study of epigenetics and the dietary components that have the ability to promote or inhibit the stability of cellular DNA strands and telomere length, thus slowing down or speeding up the aging process. DNA is continuously modifying itself based upon outside environmental factors. Therefore, it is vital to protect DNA in order to prevent or delay a myriad of adverse health conditions by allowing the continuous process of DNA damage and repair to be kept at a minimum, reducing the chances of early cell death and premature aging. Epigenetics is important as it controls the genetic expression by transferring information from the environment to the DNA strand.

Numerous in vitro studies have been conducted on calorie restriction and have resulted in identifying a link between calorie restriction and a reduction in DNA damage and a more efficient DNA repair process by inducing the cellular clean-up which repairs and restores macromolecules. A study by Barger and coworkers found that resveratrol mimics the process of calorie restriction which slows the aging process (Barger et al., 2008). A study conducted by Sarker and coworkers on curcumin, which is a derivative of turmeric, demonstrated a pathway of DNA repair similar to calorie restriction (Sarker et al., 2015).

Three studies conducted on the epigenetic effect of isoflavones, anthocyanins concluded that both substances decrease DNA damage. DHA and polyunsaturated fatty acids induced apoptosis in cancer cells. Researchers discovered that DHA has the ability to break DNA strands

for an efficient DNA repair process. However, because the exact mechanism of this process, and

the mechanics of other dietary epigenetics as a whole is not well understood, more research is

needed (Kropat et al. 2012; Lukiw & Bazan, 2008; Davis, Kucuk, Djuric, & Sarkar, 2001).

Nutritional effects on telomere length

Telomeres are located at the ends of each chromosome and are made up of nucleotides

and specific proteins (Boccardi, Paolisso, & Mecocci, 2016). During the aging process, as cells

divide and replicate, the telomeres shorten. When the telomere becomes too short, cell death and

disease risk occur. Telomere length has been studied extensively and it is possible to shorten or

lengthen telomeres through lifestyle practices.

One study by Boccardi and coworkers determined that people who lived in the

Mediterranean countries had longer telomeres than those of other industrialized countries, though

it is the lifestyle as a whole rather than one specific nutrient that contributes to telomere length

(Boccardi, Paolisso, & Mecocci, 2013). The Nurses' Health Study, a prospective cohort study

involving 121,700 female nurses aged 30-55 years, examined whether or not a greater adherence

to the Mediterranean Diet would result in longer telomere length. Participants submitted a 61

item semi-quantitative food frequency questionnaire on their dietary intake over the past year.

Follow-up dietary information was provided regularly for the next 10 years. At the 10-year

mark, blood was drawn from all participants. Results showed that greater adherence to the

Mediterranean Diet resulted in longer telomere length which remained significant after

researchers controlled for variables in lifestyle, weight and age (Crous-Bou et al. 2014).

Evidence suggests that a diet high in antioxidants, fruits and vegetables, and healthy fats may

influence telomere length but the exact mechanism remains unclear and is an area for further

research. Other Lifestyle Factors Connected to Longevity

Physical activity versus sedentary behavior

Studies conducted on physical activity among middle-aged participants commonly demonstrate an increase in survival rates through some inconsistencies exist when examining physical activity and the "young old", or those under 75 years of age. Gregg and coworkers found that current physical activity among elderly white women was more relevant to longevity than past physical activity though the benefits did not continue after age 75 (Gregg, Cauley, & Stone, 2003). In both the British Heart Study and the Zutphen Elderly Study, positive benefits on survival were noted for those in their early 70's (Bijnen et al., 1999). Other studies conducted on physical activity vs sedentary among the elderly, though unable to connect longevity to regular physical activity, nevertheless were able to show an increase in mortality rates with sedentary behavior. One study, the Copenhagen Male Study, determined that an increase in ischemic heart disease was related to increased recent physical activity (Suadicanl, Hein, & Gyntelberg, 1996). It must be noted that no other study has succeeded in replicating these results (Stessman, Hammermand-Rosenberg, Cohen, Ein-Mor & Jacobs, 2009; Lissner, Bengtsson, Jorkelund, & Wedel, 1995; Wannamethee, Shaper, & Walker, 1998).

Stessman and coworkers studied data from a longitudinal cohort study which spanned the years 1990-2008 and examined various levels of physical activity and the effects on function, health status, and survival of those aged 70-88 years. They found that the participants who were regularly physically active reported good health, took fewer medications, and remained independent with ADL's longer than sedentary individuals. Physically active elderly also reported a decreased incidence of falls and fewer reports of chronic and painful joints. Researchers evaluated death certificates of all participants and among the physically active versus sedentary, decreases in mortality ranging between 12% decrease for those aged 70, a 15%

decrease for those aged 78, and a 17% decrease for those aged 85. Researchers also discovered that a decrease in mortality was observed when physical activity was initiated between ages 70-85. This study confirms that both continuing physical activity into old age and initiating physical activity at old age provides benefits related to function and improved survival, and increased in magnitude with advanced age. The greatest increases were observed among the oldest old. The primary distinction observed with this study were the differences in function and survival among the sedentary vs physically active participants and no clear dose-dependent effect. Limitations of this study include participants self-reporting levels of physical activity, including the variables of what constitutes intensity, the lack of documented physical activity reported, and the diminished sample size at follow-up due to death, which is a common drawback in longitudinal studies of this range (Stessman, Hammerman-Rosenberg, Cohen, Ein-Mor, & Jacobs, 2009).

Carter and coworkers studied the mitochondrial changes associated with aging that affect muscular function and decline. Age-related loss of muscle mass, or sarcopenia, is dependent upon regular physical activity though to date the exact connection between sarcopenia and mitochondrial function is unclear. Many studies have determined that a decline in organelle content is contributory, as well as an overall impairment in mitochondrial function resulting from aging. Researchers found that regular physical activity can delay sarcopenia in the elderly but not completely prevent some muscle mass loss, as a part of this decline is age-related regardless of activity. The author suggests more areas of research include genetic changes that contribute to decreases in mitochondrial function in muscle tissue, the variations in genetic transcription related to the types of physical activity, and the sex-specific differences in mitochondrial changes (Carter, Chen, & Hood, 2015).

Comorbidities and the impact on longevity

Obesity is a major cause of comorbidities among the current population of adults aged 20 and older. Data from the Centers for Disease Control list the latest statistical rates of grade I obesity (BMI of 30.0-34.9) currently affecting 20.7% of adults, grade II obesity (BMI of 35.0-39.9) affecting 9.5% and grade III obesity (BMI of 40.0 and up) affecting 7.6% of adults. One third of the remaining population is categorized as overweight (BMI of 25.0-29.9). As increases in longevity are noted, rises in chronic disease and disabilities are common, adversely affecting the quality of life during advanced age. Many of these diseases are the direct result of the obesity epidemic (National Center for Health and Statistics, 2016).

A 2012 longitudinal study, which spanned 1986-2005, examined the effects of modifiable risk factors on function and mortality later in life. Data were categorized into three sections: Low, medium, and high-risk groups, and were based upon the number of risk factors of each participant at baseline. Risk factors included smoking status, lack physical activity, and overweight. Researchers concluded that those in the low-risk group had a delay of 8.3 years of disability on set or mortality compared with the medium and high-risk group (Chakravarty et al. 2013).

Aarts and coworkers collected data for a prospective study to examine the influence of comorbidities on cognition within a healthy population aged 24-81 years. Researchers accessed medical records at baseline, six and twelve years and analyzed cognition based upon verbal memory and psychomotor speed. Their results demonstrated a significant increase in impaired cognition related to cerebrovascular disease, heart disease, cancers and movement disorders when clustered together, as are often seen in today's elder population, though researchers discussed the need for further research related to a possible dominant condition and the uneven

contribution provided compared to other conditions in the cluster, a clear limitation of this study (Aarts et al. 2011).

Though research continues to be ongoing related to the assessment of comorbidities and how they relate to longevity, these studies concluded that obesity, cardiovascular disease and cancers increase the risk of disabilities and cognitive dysfunction in advanced age.

Social connections

It has been postulated that an active social life in later years increases the quality of life, extends life, and assists in the decreased risk of mental decline. A lack of social engagement among the elderly that contributes to feelings of loneliness has been shown to increase the incidence of health problems and may negatively impact mortality (Stessman, Rottenberg, Shimshilashvili, Ein-Mor, & Jacobs, 2014).

A study conducted by James and coworkers examined the relationship between a high level of social engagement in advanced age and a reduced risk of cognitive impairment. They utilized data from 1,100 participants aged 65 and older, who did not have cognitive decline at baseline, and followed them for an average of five years. They determined that those who experienced more regular social activity had about one fourth the rate of cognitive decline compared with the group who were the least socially active, though researchers are clear that the exact mechanism of these results is unclear. A limitation of this study is the self-reporting social activity of the participants which may involve recall bias (James, Wilson, Barnes, & Bennett, 2011).

Stessman and coworkers examined data obtained from the Jerusalem Longitudinal Cohort study to determine if loneliness among elderly individuals negatively impacts health and mortality. The researchers discuss differences between past studies on loneliness in this

demographic compared to their research and point out that a wide range of age and the inclusion of depressed individuals introduces bias into the results. This study involved the examination of 407, 661, and 1,113 participants aged 70, 78, and 85 years respectively, and excluded all individuals who were depressed. Participants were provided a questionnaire performed in their homes by a study nurse or occupational therapist trained in collecting data for the use of research. The length of the study was 20 years and the primary outcome was death. After researchers adjusted for marital status, education, gender, physical activity levels, comorbidities and chronic pain, results did not indicate an increase in morbidity or mortality related to loneliness at any level. Researchers acknowledge that these results contradict the majority of previous studies that have connected loneliness to an increase in morbidity and mortality among the elderly. They relate the differences in methodology as the reason for the conflicting results and acknowledge that the existence of significant research to the contrary warrants interventions from health care practitioners. Limitations of this study include the use of only one global measure, though researchers defend their methodology based upon the accuracy of previous studies using single-item tools. A second limitation involves the lack of diversity among participants. The cohort demonstrated similar data as primarily Western countries and results may be affected by the inclusion of different races and cultures. More research using this methodology among a more accurate global representation is needed. Researchers of this study stand by their conclusion that loneliness does not significantly increase morbidity and mortality among the elderly (Stessman, Rottenberg, Shimshilashvill, Ein-Mor, & Jacobs, 2014).

A study by Fastame and coworkers involved 83 participants aged 70 years and older from one of the "Blue Zone" regions of Sardinia, Italy. Participants were questioned on lifestyle, socio-demographics self-perceived well-being, and symptoms of depression. Researchers

concluded that a high level of participation in leisurely activities such as time spent volunteering, time with family members, crafts and hobbies, and time outdoors in particular increased a sense of well-being with or without others. Limitations of this study involve the use of simple examples of leisure activity, as well as a lack of the use of individual measures to each activity. More research is needed on whether applying non-linear measurements for individual activities would yield different measures of satisfaction (Fastame, Hitchcott, & Penna, 2017).

Based upon the conclusions of these studies that a robust social life and time spent on leisure activities positively impacts the health and well-being of those aged 65 and over and is an important component of healthy aging, none of the studies in this report connected social and leisure activity with an increase in longevity.

Chapter 4 - Conclusion

The purpose of this report was to evaluate the research related to human longevity and the various topics of research that are believed to directly affect the lifespan. As the 65 and over population increases it is of great importance to identify not only what dietary and lifestyle practices increase the lifespan, but also factors that maintain health and well-being for the purpose of decreasing the burden on health care systems that manage and treat chronic health conditions that are commonly seen in this demographic. Although the Mediterranean Diet and specifically certain components of this diet, as well as the lifestyle practices of those living in coastal Mediterranean countries and other "Blue Zones" clearly offer the benefit of increased longevity and/or decreased comorbidities, other areas of research evaluated that seek to identify factors that increase longevity need further investigation. These areas include the impact of the Mediterranean Diet when adopted over the age of 70, the optimal amount and frequency of alcohol consumption on longevity, and the relationship between extended human longevity and calorie restriction. Researchers consistently acknowledge that data obtained through questionnaires limits the accuracy of results due to recall bias, at this time the ability to more accurately evaluate information on dietary and lifestyle, most notably in longitudinal studies, has not been identified. A particular area of interest for future research is epigenetics, a fairly new area of research which offers many opportunities for discovering how genetic manipulation may increase health and longevity. Though research has already been conducted in some areas on this topic, further studies are needed to determine the exact mechanisms of how diet and lifestyle have the ability to impact DNA.

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