

Centenarians : the relative effects of genetics, diet and other lifestyle choices : a pilot study

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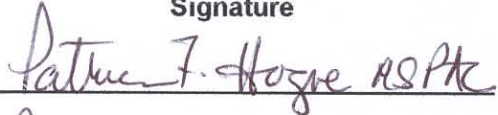
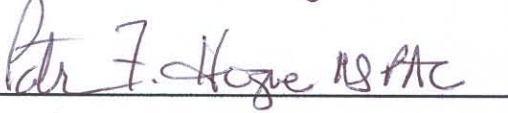

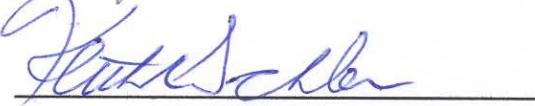
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A pilot study**

Jennifer Nichole Church

Medical College of Ohio

2004

Dedication

I would like to thank my wonderful parents for their continual support and love over the past two years.

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Patricia Hogue, thank you so much for your encouragement, continuous support and endless hours of work.

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Chapter 1

Introduction and Background

As of the year 2001 it has been documented that centenarians comprise the fastest growing age group in the entire population (Garry, 2001). Currently in the United States there are well over 70,000 centenarians (Lee, Wehrwein & Saunders, 2002). In the next fifty years this number is predicted to increase over eleven times! This means that by the year 2050 there will be around 800,000 Americans that are 100 years old, or older (Krach & Velkoff, 1999).

There are many different perspectives on the quality of life of centenarians. It is commonly believed that their health, cognitive functioning and social skills are deteriorating (Perls & Silver, 1999). It is frequently thought that as individuals age they become more helpless. Contrary to popular belief it is inaccurate to say that advanced age is accompanied by decreased health (Hitt, Young-Xu, Silver & Perls, 1999). Studies have revealed that centenarians remain extremely healthy until late in life (Lyell, 2002). Dr. Perls, director of the New England Centenarian Study (NECS) and author of *Living to 100*, stated, “The older you get, the healthier you’ve been” (Perls & Silver, 1999). The NECS, which was the first comprehensive study of centenarians, found that 95% of the centenarians were physically active, healthy, and cognitively independent well into their nineties, with low rates of mental illness or depression (Perls & Silver, 1999). The NECS also found that the centenarians had a lifetime of excellent health followed by a rapid decline before death. Of the 169 centenarians in the NECS, 25% were completely free of any cognitive disorder, only 50% were living in nursing homes or assisted living facilities and only three of the centenarians had a history of cancer (Perls & Silver, 1999). This statistic was similar to the entire 1990 United States centenarian population with 15% still living alone and around 48% living in nursing homes (Krach & Velfoff, 1999). Not only do

centenarians remain healthy, but also have a tendency to escape many life-threatening diseases such as cancer, myocardial infarction, and Alzheimer's disease (Hitt et al., 1999). Overall, centenarians are living healthier, happier and more productive lives than what is commonly thought.

The percent of Americans living to 100 or beyond has increased. In 1900 the ratio was 1 in 100,000, today it is 1 in 8,000 (Lyell, 2002). The fact that more Americans are living over a century has given rise to much discussion and debate regarding which factors contribute most significantly to longevity. Some studies suggest that the dramatic improvements in health care and technology are the most significant factors contributing to longevity, including screening tests, vaccinations, medications and public health measures (Lyell, 2002; Perls & Silver, 1999). However, other studies suggest that environmental and lifestyle factors are the essential aspects of longevity (Johnson, 1992; Perls & Terry, 2003; Bruunsgaard & Pedersen, 2000). Yet, other research suggests that genetic make-up is the sole factor for long life. Dr. Nir Barzilai, a Yeshiva University researcher of longevity genes states that, "We have 100-year-olds who have smoked all their lives; we have 100 year-olds who are fat" (Barzilai, Gabriely, Gabriely, Iankowitz, Sorkin, 2001). She also noted that research has found a few 100-year-olds that have had heart attacks, Alzheimer's and diabetes!

Studies and evaluation of the factors, which contribute to long life, are important to physician assistants in Ohio for several reasons. The immense increase of centenarians as well as the knowledge of potential changeable risk factors could directly influence the practice of physician assistants caring for these patients. Ohio, with 4.2% of the entire centenarian population, is the sixth highest in the United States (Krach & Velkoff, 1999). It is likely that physician assistants will be caring for this select population and will be in position to potentially

increase their longevity and enhance their quality of life. Centenarians comprise the fastest growing segment of the population in the United States, yet the reason for this phenomenal longevity and the relative contributions attributable to genetics, diet and other lifestyle choices are uncertain. I propose that genetics will be the major contributor of longevity with non-genetic factors such as lifestyle and diet only playing a minor role. Throughout this study it should become clearer what influence lifestyle, diet and genetic factors play in longevity.

Chapter 2

Literature Review

Multiple studies have been undertaken in an effort to discover which factors contribute most significantly to the phenomenal longevity of centenarians. The age-old quandary of ‘Genetics versus Environmental factors’ has been the topic of relatively heated debate among researchers for many years. Review of the literature tends to favor genetics as the primary factor associated with extreme longevity; however, there have been several reputable studies supporting the contribution of lifestyle and diet.

In 1990 the United States Census Bureau investigated the centenarian population to look at common characteristics within this group (Krach & Velkoff, 1999). Eighty-three percent of the 1990 United States centenarian population was born within the United States (Krach & Velkoff, 1999). The centenarian population is growing so fast it has doubled each decade since 1950 in the United States as well as in 11 other developing countries (Krach & Velkoff, 1999). In the United States the centenarian population is growing around nine percent per year which is a very high growth rate compared with other age groups (Krach & Velkoff, 1999). It was estimated that eighty-three percent of the centenarian population were between the ages of 100-

104, nine percent between ages 105-109 and seven percent age 110 and older (Krach & Velkoff, 1999).

The disparity between genders within the centenarian population is quite remarkable (Lee et al, 2002; Krach & Velkoff, 1999). Throughout most of the world, females, on average, live longer than males (Lee et al., 2002). This is no different with the 1990 centenarian population with four out of five being female (Krach & Velkoff, 1999). The reason females tend to outlive males is uncertain, however it has been suggested that it may be genes on the X chromosome, estrogen or possibly the tendency of women to be more social than men (Perls & Silver, 1999; Lee et al., 2002). Although women tend to outlive men, the men that reach their 100th birthday are found to be much healthier with a decreased risk of dementia or other serious conditions (Lee et al., 2002; Perls & Silver, 1999).

Not only is there a remarkable difference in gender, but also in race. Seventy-eight percent of the centenarian population in 1990 were non-Hispanic white and sixteen percent were African American (Krach & Velkoff, 1999). However, it is estimated that by 2050 non-Hispanic white centenarians will only account for fifty-five percent of this phenomenal population (Krach & Velkoff, 1999). The average of all races of the centenarian population completing some high school education was around fifty percent (Krach & Velkoff, 1999).

Genetics

In 1998 Schachter published a study that strongly supports the genetic basis for longevity in centenarians. The study proposed that centenarians are less likely to have genetic mutations that contribute to premature death and disease (Schacter, 1998). For example, the e4 allele of the apolipoprotein E gene (APOE), which is known to be associated with Alzheimer's disease and heart disease, is rarely found in centenarians (Schacter et al., 1994). On the other hand, the e2

allele of the apolipoprotein E gene, which codes for proteins less susceptible to oxidation, is rare among the general population but commonly found in centenarians (Schacter et al., 1994).

Researchers of the Longevity Genes Project at Albert Einstein College of Medicine performed a study on the lipid profiles of the offspring of centenarians and compared the results to controls of the same cohort (Barzilai, Gabriely, Gabriely, Iankowitz & Sorkin, 2001). This research proposed that to reach extreme longevity one must have a favorable lipid profile since there is a direct correlation between lipid profiles and atherosclerotic cardiovascular disease, which is a major cause of death (Barzilai et al., 2001). This research documented that both male and female offspring of centenarians had significantly higher HDL cholesterol levels and the male offspring also had significantly lower LDL cholesterol levels when compared with the control group (Barzilai et al., 2001). High HDL levels are considered to be protective against atherosclerotic cardiovascular disease (Gordon, Castelli & Hjortland, 1977). Due to the fact that the offspring have high HDL levels, it is presumed that their risk to get atherosclerosis is decreased and therefore they may live longer (Barzilai et al., 2001). The odds of the offspring having such a favorable lipid profile suggest that a specific gene or mutation may be inherited (Barzilai et al., 2001). Studies have been performed that support a specific gene or mutation that produce a favorable lipid profile (Inazu, Brown, & Hesler, 1990). For example, mutations in cholesteryl ester transfer protein are associated with production of large amounts of the beneficial high-density lipoprotein (HDL) that helps protect against atherosclerosis (Inazu et al, 1990). These mutations are thought to increase the HDL levels regardless of fatty diet, inactivity or smoking (Mercola, 2001). Another gene, APO A-1 Milano, has been shown to clear cholesterol from the bloodstream so rapidly that even those with elevated level of low-density lipoprotein (LDL) will not develop clogged arteries. It is believed by some researchers that

centenarians have had a consistent healthy level of cholesterol throughout their lives as a result of genetics or genetic mutations (Barzilai et al., 2001).

The European Group for the Study of Insulin Resistance (EGIR) conducted a study on healthy centenarians to look at the causes, relevance and development of insulin resistance with aging. Hyperinsulinemia is an indicator of metabolic syndrome, which has been found to be responsible for the increase in coronary heart disease in the adult population (Barbieri, Rizzo, Manzella & Paolisso, 2001). The EGIR study confirmed that insulin resistance increases with aging to a peak of 80 years. However, there was a significant reduction in insulin resistance in individuals living 90 years and an even greater reduction if they reached 100 years (Barbieri et al., 2001). In support of this fact it has been found that, in general, centenarians do not suffer from coronary heart disease (Barbieri et al., 2001). Insulin resistance is also a strong risk factor for diabetes mellitus; thus, it is no surprise, that very few centenarians have diabetes mellitus (Lillioja, Mott & Spraul, 1993). Another study that was published in 2002 agreed with the fact that insulin resistance decreased significantly after age eighty and suggested that this was strongly associated with a decrease in oxidative stress (Barbieri, Rizzo, Manzella, Rodolfo et al., 2002). Although aging, in general, has been associated with an increase in pro-oxidation factors and a decrease in anti-oxidation factors, centenarians commonly escape this association (Barbieri et al., 2002). However, there is still no evidence to prove whether insulin resistance precedes or follows oxidative stress or if this is due to genetics, environmental factors or both (Barbieri et al., 2002).

In support of the above research studies, Terry, Wilcox, McCormick, Lawler and Perls (2003) compared the health histories of 177 unrelated children of centenarians to birth cohort matched controls. After the multivariate adjusted analysis was performed significant health data

was found between the two groups. The offspring of the centenarians had a decreased prevalence of heart disease by 56%, hypertension by 66% and diabetes by 59% (Terry et al., 2003). These conditions that are typically associated with aging and cardiovascular disease were strikingly decreased in the centenarian offspring.

A study in 2002, published by Bonafe, Barbi, Storci, Salviolo & Capri et al. (2002) researched the genetics and immunology of centenarians to cancer. Demographics show the incidence and mortality due to cancer drop off between the ages on 85 to 90 (Bonafe et al., 2002). It has also been found on autopsy that centenarians had a lower than expected incidence, metastasis and mortality due to cancer (Miyaiishi, Ando, matsuzawa, Kanawa & Isobe, 2000). This study provided extensive research on anti-oncogene p53, oncogene HRSA1, CYP and GST which are involved with the metabolism of carcinogens, BRCA1 which is associated with an increased risk of breast cancer and SRD5A2 which is associated with an increased risk for prostate cancer. This study predicted that the frequency of these genes would decrease with age due to the increased risk of cancer and mortality in the carriers. However, no significant difference was found in any of these genes between the young and the old (Miyaiishi et al., 2000). Literature suggests that the carriers of these genes have an increased risk of developing cancer only if environmental stressors, such as viral infections or cigarette smoking occur (Miyaiishi et al., 2000). It was, however, found that centenarians have an increased number of T-cells and natural killer cells. An increase in the T-cell, CD4, increases the cytokines, interferon-gamma and interleukin-4 that have a potent anti-tumor activity. It has also been found that endocrine function and muscle mass tend to be preserved in centenarians with a high percentage of natural killer cells. Thus, it was proposed by Bonafe (2002) that the changing immune function in the oldest old creates an unfavorable environment for malignant growth.

Another study conducted in 2001 looked at the primary cause of death of individuals who died in their seventies, eighties, nineties compared to those individuals reaching one-hundred and older (Gessert, Elliot & Haller, 2001). After comparing the results between the groups it was found that many primary causes of death including diabetes, chronic obstructive pulmonary disease, Parkinson's Disease, myocardial infarction and most cancers decreased with advancing age (Gessert et al., 2001). However, it was found that congestive heart failure and degenerative neurological conditions occurred more frequently in centenarians (Gessert et al., 2001).

A number of pedigrees were studied to reveal if genetics are a significant component of exceptional longevity (Perls & Terry, 2003). Families of extreme old age from diverse backgrounds that lived between the 17th and early 20th century were identified with records and US Federal census entries validated their ages (Perls & Terry, 2003). The goal of this study was to determine if the clustering could be attributed to chance or if genetics must be playing a role. Cohort life tables were used to determine the probability of survival of each pedigree. The random chance of each pedigree occurring was between ten to the ninth and ten to the eighteenth power (Perls & Terry, 2003). Even taking into account the similar environments and lifestyle choices the probability of these pedigrees occurring by chance is still less than, "One per the number-of-families-in-the-world today" (Perls & Terry, 2003). To further investigate the genetics of centenarians, Perls & Terry (2003) analyzed death rates and survival probabilities of 444 centenarian pedigrees containing 2092 siblings. The results revealed a lifelong decrease in mortality risk by 50%! (Perls, Wilmoth, Levenson, Drinkwater, Cohen et al., 2002) The NECS found that siblings of centenarians were four times more likely than the population to live into their nineties and eight times more likely to reach one-hundred (Perls & Silver, 1999).

Diet

Two studies published in 1994 and 1995 showed that a high dose of Vitamin E (900mg/day) decreased the amount of free radicals in the plasma and improved insulin action (Paolisso, Maro, Galzerano, Cacciaputi, Varricchio et al., 1994 and Paolisso, Gambardella, Giugliano, Galzerano, Amato et al., 1995). Major sources of this antioxidant are found in vegetables containing Vitamin E. It was to no surprise to find that the New England Centenarian Study found that centenarians frequently consumed vegetables (Perls & Silver, 1999). Another study of plasma levels of healthy Italian centenarians found exceptionally high levels of vitamin A and E when compared to the non-centenarian participants (Mecocci, Polidori & Troiano, Cherubini & Cecchetti, 2000).

Another research study published by Johnston in 1992 compared the nutritional patterns of centenarians, octogenarians, and sexagenarians. It was found that centenarians consumed breakfast on a more regular basis, dieted less often and were less likely to have experienced fluctuations in body weight over their lifetime (Johnson, 1992). Centenarians were more likely to rely on their physicians rather than news media for nutrition information (Johnson, 1992). However, centenarians were less likely to consume low-fat diets and to comply with nutritional guidelines designed to reduce the risk of chronic disease (Johnson, 1992). The centenarians in this study met the recommended daily allowance for protein, vitamins A and C, and iron, but not for calcium (Johnson, 1992).

Lifestyle

The New England Centenarian Study was the first comprehensive study of centenarians that also looked at lifestyle choices. Diet, alcohol consumption and cigarette smoking were three of the many factors evaluated. The dietary patterns of the centenarians were extremely variable,

making it impossible to obtain significant information regarding dietary influence on longevity (Perls & Terry, 2003). It was noted, however, that ninety-nine percent of the centenarians were not obese based upon standard criteria (Perls & Terry, 2003). The study also revealed that eighty percent of the centenarians had no significant weight change throughout their lives (Perls & Terry, 2003). It was also documented that none of the centenarians had a history of alcohol abuse and only 2 of the 169 studied drank even a minimal amount of alcohol (Perls & Terry, 2003). Smoking cigarettes was extremely rare and those that had smoke did so for only a brief period of time (Perls & Terry, 2003).

Research suggests that physical activity is an essential part of longevity. According to the New England Centenarian Study, the majority of the centenarians were physically active and maintained a full schedule everyday (Perls & Silver, 1999). It has been found that highly conditioned elderly individuals have a better immune system than those who are less active, although, it has not been proven if this is due to their increased activity, lifestyle factors or genetics (Bruunsgaard & Pedersen, 2000). Being physically fit also promotes strength and balance making it less likely for the elderly to have disabling falls (Bruunsgaard & Pedersen, 2000). According to a study by Ferrucci, Izmirlian & Leveille (1999) exercise can add eleven to eighteen years to life for nonsmokers and reduces the amount of disability before death.

Many studies have been conducted to look at the personality of centenarians (Perls & Silver, 1999; Lyell, 2002). Throughout these studies it has been documented that centenarians are very good at handling stress (Perls & Silver, 1999). Other common characteristics found within the centenarian population were an optimistic attitude, good sense of humor, cheerful, tolerant, easy-going, adaptable, and less likely to complain when compared to other age groups (Buono, Uricioli & Leo, 1998; Perls & Silver, 1999). The NECS found a low tendency of

depression, sadness, fear, guilt, anger, anxiety, hostility and impulsiveness in centenarians (Perls & Silver, 1999). The Ohio Longitudinal Study of Aging and Retirement (OSLAR) conducted a study to compare longevity in individuals with a positive versus a negative self-perception of aging (Kasl, 2002). The results of this research indicated an increase lifespan of seven-and-a-half years for those individuals that were documented to have a positive self-perception of aging (Kasl, 2002).

Religion has been found to play a key role in the lives of the centenarians (Buono et al., 1998;Perls & Silver, 1999). A study of Notre Dame nuns by Snowdon in 2001 concluded that having a deep faith, just like having a positive outlook, buffers the tragedies and sorrows of life (Snowdon, 2001). Many longevity studies have researched religion and longevity and found that there is a strong relationship between religious belief, physical health and coping abilities (Buono et al., 1998;Perls & Silver, 1999; Snowdon, 2001).

Chapter 3

Methods

Instrument

Open-ended and closed-ended questions were developed to gather information based on genetics, diet and other lifestyle factors using basic one-on-one interview techniques. The questions for this study were derived from prior research of centenarians. The questionnaire was given to three faculty members at the Medical College of Ohio for review and assessment. Their recommendations were used to establish the comprehensiveness and validity to the questionnaire. The questionnaire consisted of four main components: demographics, lifestyle, genetics and diet.

Protocol

This study was reviewed by the IRB at the Medical College of Ohio and was approved as expedited research.

Subjects

The subjects of the study were male and female centenarians from Allen and Auglaize counties in Ohio. Nursing homes and assisted living facilities were found in the phonebook and over the Internet to locate the centenarians. A total of 17 subjects were located at 12 different facilities, 8 in Allen County and 9 in Auglaize County.

Procedure

A representative of each facility signed a form that requested permission to interview the centenarian residents (Appendix A). The research was explained to each centenarian and a witness from the respective facility. The centenarian and witness both signed the voluntary informed consent (Appendix B) prior to the interview questions (Appendix C). The goal of the interview was to better understand which factors, genetics, lifestyle or diet, contribute to the phenomenal longevity of centenarians.

Limitations

There were many limitations to this study including small sample size, death of participants before interview took place, limited area of study and participants from only nursing homes and assisted living facilities. Due to HIPPA regulations many organizations were unable to provide information on location of centenarians. The United States Census Bureau, National Center for Health Statistics, National Institute of Aging, American Association of Retired People, Ohio Department of Aging, Area Agency of Aging and the Department of Health and Human Services were unable to give information on location of centenarians. Under these

circumstances, this study had to be limited to those individuals living in nursing homes and assisted living facilities that agreed to participate. Another limitation of this study was the answer options to the interview questions. The choices may have been incomplete for some of the participants with only seven of thirty-five with the option of “other”. The limitations of this study make this research a very limited generalization of centenarians in Allen and Auglaize Counties in nursing homes and assisted living facilities.

Chapter 4

Results

Of the 17 subjects contacted at the beginning of the research, seven were remaining, willing and able to participate. Of the 10 subjects that could not complete the interview, two were unable to communicate effectively and did not have a reliable historian, two were unable to be interviewed due to administration objection and six passed away. The seven remaining centenarians acted as their own historian and answered every question during the interview.

Demographics

A total of four females and three males were interviewed with an average age of 102. Six of the participants were Caucasian and one was African American. One participant was born in England while all of the other centenarians were born within the United States, four in Ohio, one in Texas and one in Tennessee.

Lifestyle

One hundred percent of participants did not currently drink alcohol or smoke cigarettes, and only one participant had smoked cigarettes previously in their lifetime. Seventy-two percent felt that their current health was either average or above average. Five of the centenarians had between six and twelve years of schooling, two went to college but only one graduated. When

asked about their economic status, 100 percent felt they were within the middle class. Eighty-six percent of the centenarians had been previously employed with careers in areas of education, farming, factory work and work on the railroads. Seventy-two percent of the centenarians were physically active at least five days a week. Only one of the centenarians used a wheelchair, five used a walker and one centenarian used no assistance at all. All of the centenarians currently read with 72 percent reading on a daily basis. Social interaction was commonly found within the participants, with 43 percent keeping in contact with family and friends from one to three times per week and 57 percent keeping in contact on a daily basis. All of the centenarians had been married with only one divorce and six of them now being widowed. Religion played a key role in all of the centenarians' lives. They all stated that their religion was very important in their lives and all but one centenarian attended church on a regular basis. The current and past medical history of the centenarians consisted of two with high blood pressure, one with diabetes mellitus, one with cancer, four with heart disease, three with broken bones or fractures and zero with depression, stroke or heart attack (Graph 1). The mean age for their first health related problem was 78 years old with a minimum of 40 and a maximum of 100. One-hundred percent of the centenarians felt they had led a healthy life. Self-evaluation of each centenarian can be found on Graph 2.

Genetics

All of the children of the centenarians are still living with a mean age of 70, a minimum age of 61 and a maximum age of 85. The mothers mean age of death was 63 years with a minimum of 28 years and a maximum of 98 years. The fathers mean age of death was 59.5 years with a minimum of 30 years and a maximum of 89 years. Results of the questions asked regarding genetics are shown in Graph 3. The final question of the interview was for

centenarians to tell what factors he or she felt contributed to their longevity. Four felt their longevity was due to God, three felt their hard-work contributed to their longevity, one felt their longevity was due to their spouse being a nurse, another felt their longevity was due to frequently eating natural honey as a child and one centenarian felt genetics contributed to their longevity (Graph 2).

Diet

Body Mass Index (BMI) is a commonly used calculation to assess adults who are overweight and obese (CDC, National Center for Chronic Disease Prevention and Health Promotion, 2003). The calculation of BMI is defined as weight in kilograms divided by height in meters squared (kg/m^2) (CDC, National Center for Chronic Disease Prevention and Health Promotion, 2003). A score between 25-29.9 indicates an overweight adult and a BMI of greater than or equal to 30 indicates an obese adult (Table 1) (CDC, National Center for Chronic Disease Prevention and Health Promotion, 2003). The mean BMI of the centenarians was 21 with a minimum of 18 and a maximum of 23. Therefore, none of the participants fell into the overweight or obese category. All of the centenarians consumed fruits and vegetables on a daily basis. The centenarians did not purposely avoid fatty foods or diet throughout their lifetime. Three of the centenarians had a weight change of more than fifteen pounds at some point in their lifetime. Only two of the centenarians took vitamin supplements on a regular basis.

Chapter 5

Discussion

After an adequate literature review and very limited clinical study it has been found that many factors contribute to the phenomenal longevity of centenarians. Although genetics play a crucial role in preventing life threatening diseases, this role is not exclusive. Other non-genetic

factors, such as lifestyle choices and diet also contribute to long life. Throughout this discussion is should become more clear why there is not a sole component to longevity.

According to the National Vital Statistics Report the leading causes of death for all races and both genders older that 85 are heart disease, cancer, cerebrovascular disease, pneumonia, Alzheimer's disease, chronic lower respiratory diseases and diabetes mellitus (National Vital Statistic Report, 2002). Heart, cerebrovascular and hypertensive diseases are all components of cardiovascular disease. The heart disease component of cardiovascular disease is the leading cause of death among the elderly in the United States (Kinsella & Velkoff, 2002). According to statistics from 2002, heart disease accounts for 49% of death of individuals 75 years and older (Kinsella & Velkoff, 2002). It has been found through prior research as well as in this study that centenarians are spared from many of these fatal diseases (Hitt et al., 1999; Gessert et al., 2001; Schacter et al., 1994). Studies suggest that one possibility for the decreased incidence of cardiovascular disease in centenarians is due to their genetic composition that creates optimal cholesterol levels therefore protecting against atherosclerosis, which is the primary cause of cardiovascular disease (Brazilai et al., 2001; Inazu et al., 1990; Mercola, 2001). Centenarians also commonly lack the e4 allele of the APOE gene that is associated with Alzheimer's disease and heart disease (Schacter et al., 1994). In support of this, the centenarians in this study had very little if any cognitive impairment; however, four of the seven had some form of heart disease.

Other risk factors for cardiovascular disease include physical inactivity, smoking, hypertension, diabetes mellitus, and obesity. Throughout the literature and the results of this study it has been found that centenarians typically have very few, if any of these risk factors (Perls & Terry, 2003; Perls & Silver, 1999, Lilloja et al., 1993, Terry et al., 2003). The results of

this study were very similar with previous studies in the literature. Seventy-two percent of the centenarians in this study were physically active at least five days a week, one-hundred percent were currently non-smokers, only two of the seven had hypertension and all of the centenarians fell into the normal range for body mass index (Graph 1, Table 1).

Another primary cause of death in the elderly population is diabetes mellitus. Research has found that insulin resistance, a strong risk factor for diabetes mellitus, increases to the age of eighty and then continues to drop as the individual ages (Barbieri et al, 2001; Baribieri et al., 2002). It was no surprise to find that only one of the centenarians in this study had non-insulin dependent diabetes mellitus. Another study found that the decrease in insulin resistance was associated with a decrease in oxidative stress (Baribieri et al., 2002). However, the association of which precedes and which follows or if it is due to genetics or environmental factors is yet to be solved (Baribieri et al., 2002).

Cancer is another primary cause of mortality in the elderly population, but, once again, the centenarians are typically spared of this disease (Bonafe et al., 2002; Miyaishi et al., 2000). However, the risk of being a carrier of many of the genes associated with cancer is the same for all age groups, including centenarians (Miyaishi et al., 2000). Literature suggests that the carriers are only at an increased risk of developing cancer if environmental stressors, such as viral infections or cigarette smoking occur (Miyaishi et al., 2000). Once again this research study correlates with the literature with only one of the seven centenarians with a history of cancer and none of them being current smokers.

Other studies have shown the possibility of diet, specifically vitamin E, having an effect on aging (Paolisso et al., 1994; Paolisso et al., 1995). Vitamin E, which is found in many vegetables, has been found to decrease the amount of free radicals in the plasma and improve the

action of insulin (Paolisso et al., 1994; Paolisso et al., 1995). Studies have documented the high blood level of vitamin E and an increased consumption of vegetables, in centenarians, when compared to other age groups (Perls & Silver, 1999; Mecocci et al., 2000). One hundred percent of the centenarians in this study stated that they consumed vegetables on a daily basis.

The social interaction of the average centenarian also may have an impact on their decreased morbidity and mortality. It has been suggested that centenarians are happier and live longer because they are connected with family, friends and social groups (Perls & Silver, 1999). Their social connections give them a sense of purpose that in turn decreases their morbidity and mortality (Perls & Silver, 1999). Social interaction among the centenarians in this study found that 43% kept in contact with family and friends between one and three times per week, while 57% kept in contact on a daily basis. Within this study all of the centenarians were married with one divorce and six of the seven currently being widowed. Compared with the national average seventy-nine percent of the centenarians in 1990 were widowed; However, 1 of 4 males were currently married while only 1 in 25 females were married (Krach & Velkoff, 1999).

Strong dedication to religion was a common among this particular study as well as numerous prior centenarian studies (Perls & Silver, 1999; Buono et al., 1998; Snowdon, 2001). One-hundred percent of the centenarians in this study had a sense of spiritual gratitude and connectedness to their faith. Research studies have found a strong correlation with longevity, a strong religious faith, coping abilities and physical health (Perls & Silver, 1999; Buono et al., 1998; Snowdon, 2001).

Although there is no specific guideline to living a long life, many common themes have emerged from research on centenarians. Not only is longevity of a centenarian enhanced, but, the morbidity is also compressed. Centenarians do not typically experience prolonged periods of

disability or chronic disease (Perls & Silver, 1999). Research has found that they typically live an extremely healthy life, followed by a rapid decline before death (Perls & Silver, 1999).

Common characteristics found within this population include good nutrition, physical activity, normal weight, non-smokers, social activity, spirituality, positive attitudes, healthy immune systems and of course, genetics. Various combinations of these characteristics have led to the decreased morbidity and mortality of this phenomenal population.

Conclusions

Many factors contribute to the phenomenal longevity of centenarians. The debate of which factors, including genetics, diet and lifestyle, contribute most significantly to longevity continues. As of now, one specific longevity gene has not been discovered. However, certain genes that prevent life-threatening disease have been identified in the centenarian population. Research has discovered that a genetic predisposition for long life is not the only deciding factor. There is still room for non-genetic factors such as lifestyle choices including diet and exercise.

More research is needed to determine the modifiable and non-modifiable factors relating to longevity. Clearly, the more that successful aging is due to lifestyle factors, the more likely it is that we have the power to determine our health and vitality in old age. However, if genetics becomes the sole factor in longevity, the quantity of life is unchangeable; nevertheless, the quality of life may still be enhanced.

As the number of centenarians continues to increase it is important to continue researching this phenomenal population. With continual research, the significance of each component of longevity will become more clear and allow us to maximize the health, independence and productivity of the oldest old.

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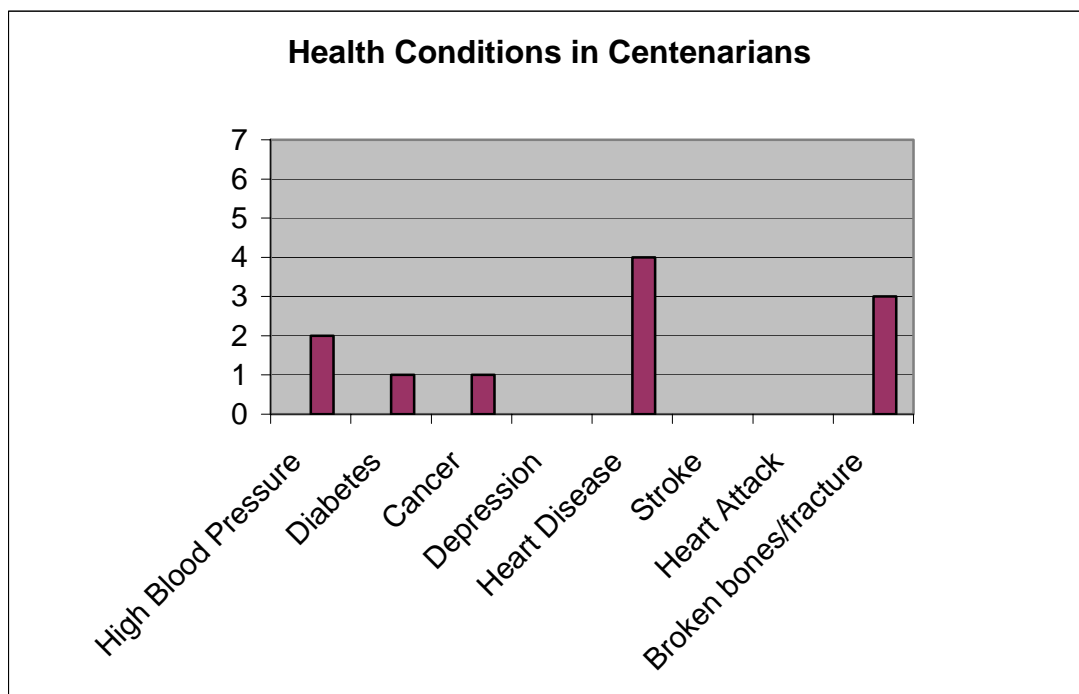
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Table 1: Current Guideline for Body Mass Index

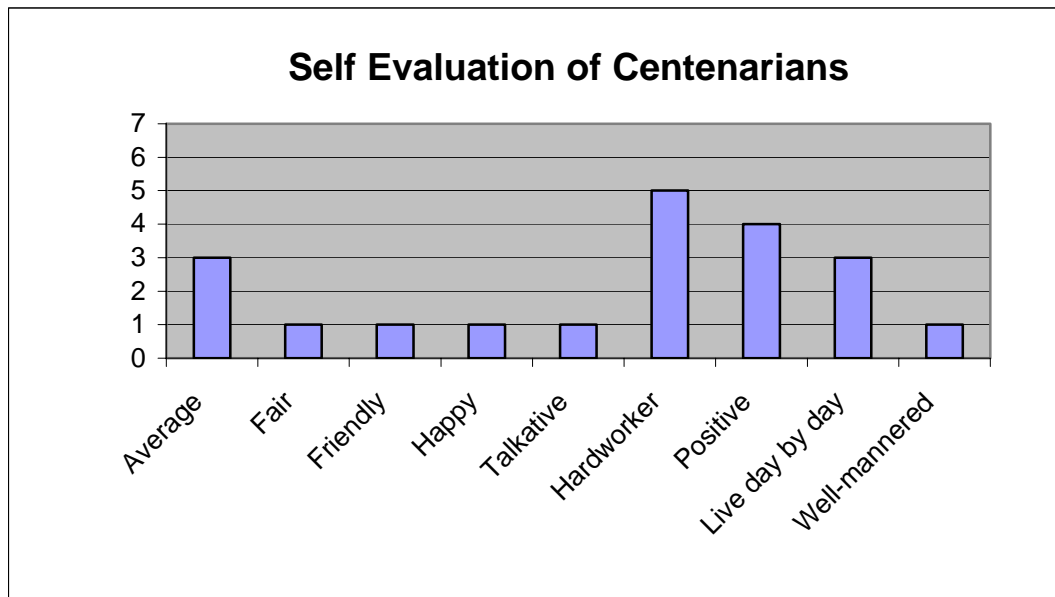
BMI*	Weight Status
Below 18.5	Underweight
18.5-24.9	Normal
25.0-29.9	Overweight
30.0 and Above	Obese

* (CDC, National Center for Chronic Disease Prevention and Health Promotion, 2003)

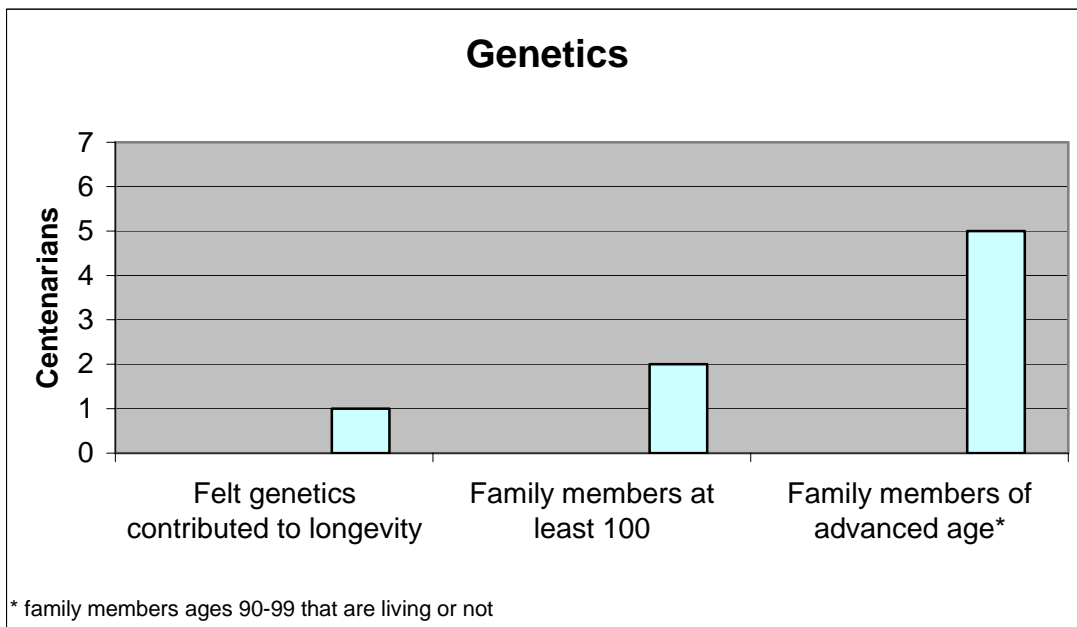
Graph 1: Health Conditions of Centenarians



Graph 2: Self Evaluation of Centenarians



Graph 3: Genetics of Centenarians



Appendix A: Sample Permission Form

Date

Name of Facility

Address

To Whom It May Concern:

I _____ give Jennifer Church the permission to come into our facility and interview any individual 100 years old and older, with their consent. This interview is research for a scholarly project based out of the Medical College of Ohio in Toledo. This interview will consist of asking questions about the lifestyle, attitudes and family history of centenarians. I understand that the interviewing process will be completed by May of 2004.

Signature: _____

Print name: _____

Date: _____

Appendix B: (MCO IRB:104587)

RESEARCH CONSENT FORM FOR ADULT SUBJECT INFORMED CONSENT

CENTENARIANS: THE RELATIVE EFFECTS OF GENETICS, DIET AND OTHER LIFESTYLE CHOICES: A PILOT STUDY

Principal Investigator: Patricia Hogue, MS, PA-C

Student Investigator: Jennifer Church, PAS-II

Phone number: 419-383-4807

PURPOSE

You are being asked to take part in a research study of individuals that are 100 years old and older. The purpose of the study is to look at diet, genetics and other lifestyle choices and see what they add to long life. You were selected as someone who may want to take part in this study because you are 100 years old or older. There may be up to 25 subjects in this research study.

PROCEDURES AND DURATION

If you decide to take part in this study, you will be asked to answer questions about your diet, genetics and other lifestyle choices. The interview should not take longer than 45 minutes.

RISKS AND DISCOMFORTS

There is a minimal risk of loss of confidentiality. Your name will not be given in any presentation or publication. If your name appears on any given information it will be blacked out immediately. All consent forms will be stored in a secure locked filing cabinet in the principal investigators office.

BENEFITS AND/OR COMPENSATION

The benefit of this study will be to learn what factors allow people to live a long life. We cannot and do not guarantee or promise that you will receive any benefits from this study.

CONFIDENTIALITY

By agreeing to take part in this research study, you give to the Medical College of Ohio, the Principal Investigator and all personnel associated with this research study your permission to use or disclose health information that can be identified with you that we obtain in connection with this study. We will use this information for the purpose of conducting the research study as described in the research consent form.

The information that we will use or disclose includes the information you give about your diet, genetics and other lifestyle choices. We may use this information ourselves, or we may disclose or provide access to the information that does not identify you as part of the research study. Under some circumstances, the Institutional Review Board and Research and Grants Administration of the Medical College of Ohio may review your information for compliance audits.

The Medical College of Ohio is required by law to protect the privacy of your health information, and to use or disclose the information we obtain about you in connection with this

research study only as authorized by you in this form. There is a possibility that the information we disclose may be re-disclosed by the persons we give it to, and no longer protected. However, we will encourage any person who receives your information from us to continue to protect and not re-disclose the information.

Your permission for us to use or disclose your personal health information as described in this section is voluntary. However, you will not be allowed to participate in the research study unless you give us your permission to use or disclose your personal health information by signing this document.

You have the right to revoke (cancel) the permission you have given to us to use or disclose your personal health information at any time by giving written notice to Patricia Hogue at 3065 Arlington Avenue, Toledo, Ohio, 43615. However, a cancellation will not apply if we have acted with your permission, for example, information that already has been used or disclosed prior to the cancellation. Also, a cancellation will not prevent us from continuing to use and disclose information that was obtained prior to the cancellation as necessary to maintain the integrity of the research study.

Except as noted in the above paragraph, your permission for us to use and disclose personal health information will stop at the end of the research study.

A more complete statement of Medical College of Ohio's Privacy Practices are set forth in its Joint Notice of Privacy Practice. If you have not already received this Notice, a member of the research team will provide this to you. If you have any further questions concerning privacy, you may contact the person identified in the Notice.

COST TO YOU FOR TAKING PART IN THIS STUDY

There is no cost to you, as a subject, in this study.

IN THE EVENT OF A RESEARCH-RELATED INJURY

In the event of injury resulting from your taking part in this study, treatment can be obtained at Medical College Hospital. You should understand that the costs of such treatment would be your responsibility. Financial compensation is not available through Medical College Hospital. By signing this form you are not giving up any of your legal rights as a research subject. In the event of an injury, contact Patricia Hogue at 419-383-4807.

VOLUNTARY PARTICIPATION

Taking part in this study is voluntary. If you decide not to take part in this study, your decision will not affect your future relations with the Medical College of Ohio, its personnel, associated hospitals and your living facility. If you do decide to take part in this research, you are free to withdraw your consent and to discontinue your participation at any time without a penalty.

OFFER TO ANSWER QUESTIONS

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

AUTHORIZATION

YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES THAT YOU HAVE READ AND UNDERSTOOD THE INFORMATION PROVIDED ABOVE, HAVE HAD ALL YOUR QUESTIONS ANSWERED, AND HAVE DECIDED TO PARTICIPATE.

BY SIGNING THIS DOCUMENT YOU AUTHORIZE US TO USE OR DISCLOSE YOUR PERSONAL HEALTH INFORMATION AS DESCRIBED IN THIS FORM.

The date you sign this document to enroll in this study, that is, today's date, MUST fall between the dates indicated on the approval stamp affixed to the bottom of each page. These dates indicate that this form is valid when you enroll in the study but do not reflect how long you may participate in the study. Each page of this Informed Consent Form is stamped to indicate the form's validity as approved by the MCO Institutional Review Board (IRB).

_____ Name of Subject (please print)	_____ Signature of Subject or Legally Authorized Representative	_____ Date
_____ Relationship to the Subject		_____ Time
		a.m. p.m.
_____ Name of Person Obtaining Informed Consent (please print)	_____ Signature of Person Obtaining Informed Consent (as required by ICH guidelines)	
_____ Signature of Witness to Consent Process (when required by ICH guidelines)		

YOU WILL BE GIVEN A SIGNED COPY OF THIS FORM TO KEEP.

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research subject or research-related injuries, please feel free to contact R. Douglas Wilkerson, Ph.D.; Associate Vice President for Research; Medical College of Ohio at (419) 383-4251.

Appendix C: (MCO IRB #: 104587)

Interview Questions and Demographics:

Sex:

Age:

Race:

Height:

Weight:

LIFESTYLE:

1. Prior to coming to this facility did you:

- Live alone
- Live with family
- Live with friends
- Other

2. Where were you born?

3. How much schooling have you had:

- 6-12 years
- Some college
- Graduate
- Other

4. What is your marital status:
- Never Married
 - Married
 - Divorced
 - Widowed
5. Which of the following do you consider yourself to be prior to coming to this facility?
- Poor
 - Middle class
 - Wealthy
6. Prior to coming to this facility were you employed?
- Yes
 - No
7. What was your occupation?
-
8. Do you use any on the following to get around or walk:
- None
 - Cane
 - Walker
 - Wheelchair
 - No mobility

9. Do you smoke cigarettes?

- Yes
- No

10. If you do not smoke, have you ever smoked? If so, for how long?

- Yes
- No

Period of time _____

11. Do you have or have you had any of the following: (if checked = yes)

- High Blood Pressure
- Diabetes
- Cancer
- Depression
- Heart Disease
- Stroke
- Heart Attack
- Broken bone(s)/fracture(s)
- Other

12. When was your first health related problem?

13. How would you rate your health today:

- Poor
- Fair
- Average
- Good
- Excellent

14. Do you feel you have had a good life?

- Yes
- No

15. How many days a week are you physically active:

- None
- 1-2
- 3-4
- 5-6
- Daily

16. What three words best describe you?

17. How often do you read?

- Never
- Rarely
- 1-3 times a week
- Daily
- Other

18. How often do you keep in contact with family or friends:

- Never
- Rarely
- 1-3 times a week
- Daily
- Other

19. Do you attend church?

- Yes
- No

20. How important is your religious faith to you?

- Not important
- Some what important
- Very important

21. How old do you feel in your mind?

GENETICS:

1. Has anyone related to you lived to be 100 years old? Who?

Yes

No

Relation: _____

2. Do you have children? If so, how many?

Yes

No

Number: _____

3. Are your children still living?

Yes

No

4. If answer to #3 is yes, how old are they?

5. If answer to #3 is no, what was the cause of their death?

6. Living or not living what is/was the age of your:

Mother: _____ Cause of Death: _____

Father: _____ Cause of Death: _____

Sibling: _____ Cause of Death: _____

Sibling: _____ Cause of Death: _____

DIET:

1. Have you ever had a significant weight change?

- Yes
- No

2. Do you eat fruits or vegetables:

- Never
- Rarely
- 1-3 times per week
- Daily
- Other

3. Do you purposely avoid fatty foods?

- Yes
- No

4. Do you drink alcoholic beverages:

- Never
- Rarely
- Socially
- Daily
- Other

5. How often did you drink alcoholic beverages:

- Never
- Rarely
- Socially
- Daily
- Other

6. Do you drink coffee:

- Never
- Rarely
- 1-3 times per week
- Daily
- Other

7. Do you take vitamin supplements?

- Yes
- No

FINAL QUESTION:

1. What factors do you believe have contributed to your long life?

Abstract

Centenarians: The relative effects of genetics, diet and lifestyle choices: A pilot study

Jennifer Church

Major Advisor: Patricia Hogue

Objective: Recognition and understanding of which factors, including genetics, diet and lifestyle contribute to the phenomenal longevity of centenarians. **Method:** Seven centenarians in Allen and Auglaize counties in Ohio were interviewed individually and asked open and close-ended questions relating to genetics, diet and lifestyle. **Results:** *Lifestyle:* 100% were non-smokers, 100% did not drink alcohol, 14% with DMII, 14% with history of cancer, 0% with depression, stroke or heart attack, 28% with HTN, 57% with heart disease. *Diet:* 100% fell within the normal range for BMI. *Genetics:* 71% with family members age 90 or older. **Conclusion:** Although genes have been discovered that prevent certain life-threatening diseases, non-genetic factors such as lifestyle choices including diet and exercise seem to play a significant contributory role. Further research is needed to determine the significance of each component.