

Why Study Centenarians? An Overview

THE NEW ENGLAND CENTENARIAN STUDY

A Model of Aging Well. Centenarians (age 100+ years) markedly delay disability towards the end of their very long lives, at an average age of ~93 years (that's 33 years beyond the age of 60!).¹ We regard these individuals as wonderful models of aging well. Some of our subjects, ~15% have no clinically demonstrable disease at age 100 years and we call them "escapers". About 43% are "delayers", or subjects who did not exhibit an age related disease until age 80 years or later. Finally, there are about 42% of our subjects who are "survivors", or those with clinically demonstrable disease(s) prior to the age of 80 years.² Supporting the compression of morbidity hypothesis, that as one approaches the limits of lifespan, diseases (morbidity) must be delayed (or escaped) towards the end of these longest lived, we have observed amongst supercentenarians (age 110+ years), that health span equals lifespan. Thus we believe that instead of the aging myth "the older you get the sicker you get", it is much more the case of "the older you get, the healthier you've been".



History The study began in 1995 as a population-based study of all centenarians living within 8 towns in the Boston area. The prevalence of Alzheimer's Disease and other dementias in centenarians was the focus. At the time, the prevalence of centenarians in industrialized countries was approximately one centenarian per 10,000 people in the population. Thus, at any one time, we were studying approximately 46 centenarians within a total population of 460,000 people (2). The NECS has gone on to enroll centenarians from throughout the United States and other countries and has grown to be the largest comprehensive study of centenarians in the world. There are currently ~1,600 centenarians, 500 children (in their 70s and 80s) and 300 younger controls. Amongst this group is the largest sample in the world, by far, of supercentenarians (age 110+ years) - there are about 107 of these oldest of the old subjects in our study.

Current and Previous Funders: We are tremendously thankful and beholden to the following foundations for supporting our enrollment and data collection efforts: the Alzheimer's Association, the Ellison Medical Foundation, the Institute for the Study of Aging (now the Alzheimer's Drug Discovery Foundation), the American Federation Aging Research, and the Glenn Foundation for Medical Research. Currently we receive our funding from the National Institute of Aging (NIA), an institute of the National Institutes of Health (NIH), the William Wood Foundation and the Martin Samowitz Foundation. Our studies are supervised and approved by the Boston University Medical Campus Institutional Review Board.

Demographics: In the U.S. and other industrialized nations, centenarians occur at a prevalence rate of about 1 per 6,000. When the centenarian study began in 1994, the prevalence rate was one per 10,000, making centenarians one of, if not the fastest growing segments of the population. In 2010, there are about 70,000 centenarians in the U.S.

Eighty-five percent of centenarians are women and 15% are men. Among supercentenarians, the female prevalence may increase to about 90%. Though women by far and away win the longevity marathon, paradoxically the fewer men are generally functionally better off and healthier. This may be because women handle age related diseases better (how they do this is not clear) whereas at these ages, the men more readily die from them. Thus, the men who survive have to be relatively healthy and functionally fit.

Supercentenarians, people who are 110+ years old occur at a rate of about 1 per 5 million. In 2010, there were about 60 to 70 supercentenarians in the US. In 2017, the New England Centenarian Study enrolled its 150th supercentenarian, thus constituting by far and away the largest sample of such subjects in the world.

Geography: There are several geographical areas that have claimed inhabitants with extreme longevity, but after closer examination, these claims have been found to be false. Vilacamba, Ecuador almost became a tourist attraction because natives claimed their water was a fountain of youth leading to the many super-centenarians (age >110 years) in that region. What about the reports of people in the Russian Caucasus living to 150 years and beyond? Remember the Dannon yogurt commercials? In fact, those purported supercentenarians were taking on the identities of their parents, aunts and uncles. The oldest person from whom we have multiple forms of proof-of-age is Madame Calment who died at the age of 122 years in 1997.

These regions of purported exceptional longevity still merit careful study however. Though claims of extreme age are untrue, there still may be an unusually high prevalence of very old fit people in these regions. In the Tibetan mountains for instance, octogenarian and

nonagenarian elders, impressively many of them men, still herd live stock and still lead physically strenuous lives.

Predictors of Reaching 100: Once it truly became apparent that living to 100 was a terrific advantage, not just in years of survival but importantly in many more years of quality life, we set out to understand what factors the centenarians had in common that might explain such an advantage. Not all centenarians are alike. They vary widely in years of education (no years to post-graduate), socioeconomic status (very poor to very rich), religion, ethnicity and patterns of diet (strictly vegetarian to extremely rich in saturated fats). However, the centenarians we have studied do have a number of characteristics in common:

- Few centenarians are obese. In the case of men, they are nearly always lean.
- Substantial smoking history is rare.
- A preliminary study suggests that centenarians are better able to handle stress than the majority of people.
- Our finding that some centenarians (~15%) had no significant changes in their thinking abilities disproved the expectation by many that all centenarians would be demented.⁴ We also discovered that Alzheimer's Disease was not inevitable. Some centenarians had very healthy appearing brains with neuropathological study (we call these gold standards of disease-free aging).⁵
- Many centenarian women have a history of bearing children after the age of 35 years and even 40 years. From our studies, a woman who naturally has a child after the age of 40 has a 4 times greater chance of living to 100 compared to women who do not.⁶ It is probably not the act of bearing a child in one's forties that promotes long life, but rather, doing so may be an indicator that the woman's reproductive system is aging slowly and that the rest of her body is as well. Such slow aging and the avoidance or delay of diseases that adversely impact reproduction would bode well for the woman's subsequent ability to achieve very old age.
- At least 50% of centenarians have first-degree relatives and/or grandparents who also achieve very old age, and many have exceptionally old siblings. Male siblings of centenarians have an 17 times greater chance than other men born around the same time of reaching age 100 years and female siblings have an 8½ greater chance than other females also born around the same time of achieving age 100.⁷
- Many of the children of centenarians (age range of 65 to 82 years) appear to be following in their parents' footsteps with marked delays in cardiovascular disease, diabetes and overall mortality.⁸
- Some families demonstrate incredible clustering for exceptional longevity that cannot be due to chance and must be due to familial factors that members of these families have in common.⁹
- Based upon standardized personality testing, the offspring of centenarians, compared to population norms, score low in neuroticism and high in extraversion.¹⁰

- Genetic variation plays a very strong role in exceptional longevity (see below)

Nature Versus Nurture: The Role of Genes Versus Environment in Aging and Exceptional Longevity. Gerontologists often cite studies of lifespans amongst identical twins reared apart to describe the genetic and environmental components of aging. Based upon these studies, the common answer is 70-80% environment and 30-20% genes. This makes sense in the context of results from the study of Seventh Day Adventists at Loma Linda University who as a group have perhaps the longest average life expectancy in the United States, 88 years or 88 years for men and 89 years for women. The main attributes that these individuals have in common is that their religion for the most part asks that they have very good lifestyle choices. That is, they tend to be vegetarian, they don't smoke, they regularly exercise and they spend a lot of time with their families and with their religion. Many Americans do the opposite (e.g. excessive meat consumption, lack of exercise, smoking, etc) and thus it is not surprising that on average, Americans die 8-10 years sooner. What the 7th Day Adventist results also show us is that the average American has the genes to reach their mid-late 80s, they just need to take very good care of themselves with proper lifestyle choices. Also note that the oldest subjects in the twin studies lived to their early to mid-eighties. Therefore, again, these findings indicate what it takes to live to what should be average life expectancy for most of us, age 86 years for men and 89 years for women.

However, we have learned from our studies of the siblings of centenarians and of supercentenarians that exceptional longevity runs very strongly in families. Also, a Danish study of nonagenarians and centenarians has noted that the power of an exceptional longevity (EL) study to discover genetic factors associated with EL increases with the age of the subjects. These and other study results strongly suggest that the genetic component of exceptional longevity gets larger and larger with increasing age and is especially high for those age 106 years and older. The week of July 1, 2010, we will have a paper come out in Science that delineates the roles of genes in exceptional longevity much more clearly (media embargoed until July 1, 2 pm).



Neuropsychological and Neuropathological Studies. We are particularly interested in how centenarians are able to markedly delay or in some cases escape Alzheimer's disease. We perform detailed and annual neuropsychological examinations on centenarians living within 3-4 hours of Boston. A number of these subjects have indicated their willingness to donate their brains for neuropathological studies once they pass away, thus allowing our scientific collaborators to better characterize the health of the centenarians' exceptionally old brains.

We also expend significant resources to disseminate our findings and to advocate for older people, providing an optimistic and enabling view of aging. Most people have the genetic makeup to live into their mid to late eighties in very good health, and like centenarians, compress the time they are sick towards the end of their lives. Much of their ability to do so depends upon healthy behaviors including a diet conducive to being lean, not smoking, and strength training exercise. Promoting this philosophy will have a much greater impact now on many more people than our genetic research. We will be forever beholden to Dr. Robert Butler and the International Longevity Center for their guidance and collaborations.¹¹⁻¹³

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