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*The New England
Centenarian Study*



November 2017

New England Centenarian Study Updates

We hope this newsletter finds you and your family well. We've been quite busy since our last newsletter with conferences, new research publications, new participants, and new research partnerships as well as some staff changes to tell you about. We deeply value your help with our studies, and to our participants, obviously none of what we do would be possible without you!



Sisters Mildred MacIsaac & Agnes Buckley, ages of 100 years and 103 years, were kind enough to pose for a photo shoot for *Boston Magazine* which highlighted the Study's recent findings

Pennsylvania, who is also the second oldest person ever in the world! Of special note, we also enrolled Sarah's daughter Kitty at the age of 99 years and Kitty herself went on to become a centenarian.



Sarah Knauss, seated on the left, as the second oldest ever person in the world at age 119 years. Sarah is the oldest participant in the New England Centenarian study. There are six generations of the same family in this photo that includes Sarah's daughter Kitty, seated on the right, who herself became a centenarian!

Study Participant Recruitment

Since beginning our research in 1996, we have enrolled approximately 2,500 centenarians including 150 supercentenarians (people ages 110+ years old) and about 500 children of centenarians as well as our control subjects. The oldest participant so far has been 119 year old Sarah Knauss of Allendale,

A Quick Primer in the Demography of Exceptional Longevity

As you already know, centenarians, people 100+ years old, are quite rare. But how rare? Currently in the USA, they occur at a rate of about 1 centenarian per 5,000 people. Because we are such a big country though, there are a whopping 70,000 or so alive centenarians. The number of centenarians plummets with increasing age, with people at ages 105 years to 109 years, who are called “semi-supercentenarians”, occurring at a rate of about one per 250,000. This translates into about 1,400 “semi-supers” alive in the USA at any one time. Finally, supercentenarians, or people living to 110+ years, occur at the rate of about one per 5 million people, or a total of 70 supers alive at any one time in the USA.

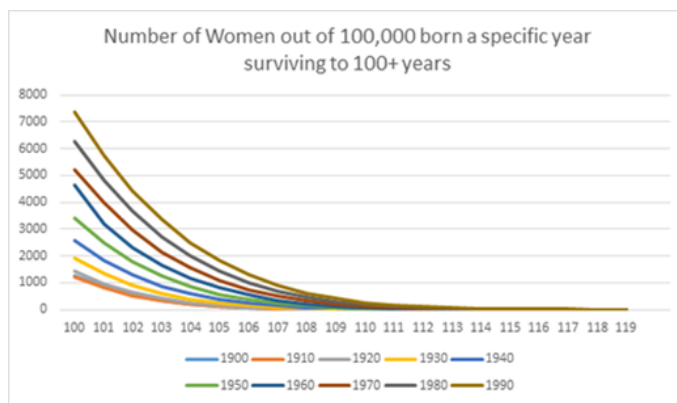
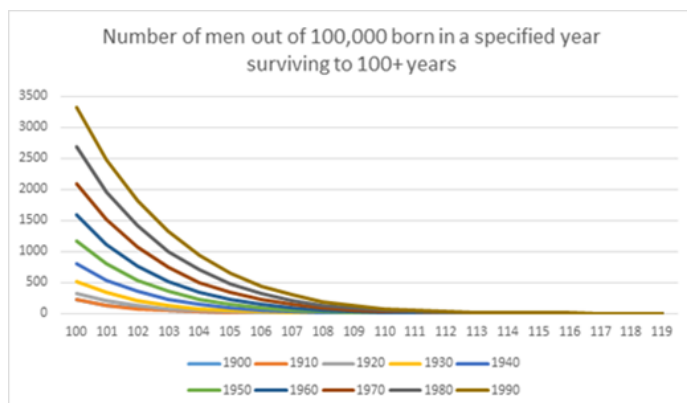
Because of social trends (such as average years of education, effectiveness of health care, popularity of smoking and many other factors), the number of people who go on to live to be a centenarian can be



Walter Breuning, at age 114 years, lived to be the 5th oldest man ever in the world (at 114 years and 205 days) and is the oldest male participant in the New England Centenarian study. Walter lived in Great Falls, Montana and when we interviewed him, his mind was amazingly sharp with no evidence of Alzheimer’s disease or other dementias. One of the study’s primary goals is to understand how people like Walter so markedly delay or escape a disease like Alzheimer’s. Evidence is suggesting that there are certain genes that dramatically slow the aging process and greatly decrease the risk for aging-related diseases such as Alzheimer’s.

very different depending on when they were born (see the below figures). For example, in 1915, the average years of education jumped from 8 years to 15 years. Years of education can tremendously impact upon life expectancy since more years of education means better socioeconomic conditions, better health care, better health-related choices etc.

Continued, next page ↗



The above two graphs show for people born in different decades, the actual, or in the case of later years, projected number of people out of 100,000 born, who lived to or will live to ages 100 through 119 years of age (derived from U.S. Social Security Administration data)

Demography lessons continued....

Up until around 1900, families lost about a quarter of their children to common infectious diseases like bacterial pneumonia, influenza, tuberculosis and diarrhea (30% of all deaths were among infants). At the time, average life expectancy was 47 years. By the teens to 1920s, cleaner water supplies were leading to much less diarrhea and enteritis and many more children survived. With nearly a fourth more of the population surviving into adulthood, many more people had the opportunity to much later, achieve old age.

By the mid-century, infectious diseases as a cause of infant death were much less common and heart disease in adults was (and continues to be) the number one killer. Now, improvements in prevention and treatments in many adult illnesses

are allowing many people in their 80s to approach centenarian status! When we began the New England Centenarian Study in 1995, the prevalence of centenarians was one per 10,000 in the population; that rate has doubled (!) since then, so that one person in 5,000 is currently a centenarian. As the 70 million-strong baby boomer generation ages, demographers predict anywhere between a million and 4 million centenarians in the U.S. by 2060.

The growth in and absolute number of supercentenarians is much slower and smaller, perhaps because rare combinations of many longevity-associated genes play a more influential role in living to ages 105+ years.

QUICK FACT #1

According to a 2014 U.S. Census Bureau report, centenarians pass away from pretty much the same things as younger old people, that is, heart disease, Alzheimer's disease, stroke, cancer, influenza and pneumonia. Their great advantage over the rest of the older population is that centenarians cope with these diseases much better, living independently up through at least their early to mid nineties. For those who live to 105+ years, they also either greatly delay the age of onset for these diseases or even escape them entirely.



Our Biostatistics colleagues from the B.U. School of Public Health. Left to right: Professor Paola Sebastiani, Benjamin Sweigart, Mandy Du and Anastasia Gurinovich



None of this would be possible without our Biostatistics colleagues...

Analysis of the data is not simple and actually requires highly trained experts who can figure out what is cause and what is effect, when is a finding an artifact of the way the data were collected, or even how to analyze the data in a way that patterns yield hypotheses and answers. These are just a few of many talents that our studies rely upon to generate the findings that move our efforts forward.

Highlights of Recent Published Findings

FOXO gene helps people live to their 90s but not to 100 and beyond

This research, published in the *Journals of Gerontology: Biological Sciences*, challenges previous findings indicating that some variants of the gene, FOXO3, played a role in exceptional longevity.

Centenarians experience slower aging throughout their lives, live independently well into their 90s, and spend only the last relatively few years of their exceptionally long lives with significant diseases or disabilities. Unlike average aging, centenarians appear to benefit from combinations of longevity-enabling genes that likely slow aging and decrease one's risk for age-related diseases and disability. Some of those variants are important to help people get to their 90s, and others, to 100. Other variants, in the right combination, are needed to get people to the rarest ages, such as 105+ years. Our research indicates that FOXO3, which previously had been touted by numerous studies to be a strong longevity gene, appears to be one of those genes that can help you get to your 90s but not older and rarer ages.

To conduct this research we analyzed genetic data from 2,072 participants from four studies: the New England Centenarian Study, the Southern Italian Centenarian Study, The Longevity Genes Project at Albert Einstein College of Medicine; and the National Institutes on Aging-funded Long Life Family Study. These studies are working together to discover the biological mechanisms that enable remarkable aging. We collectively attended presentations and read scientific papers claiming associations between FOXO3 variants and longevity, yet when we tested for these associations among centenarians, we were unable to reproduce the findings. We suspect that part of the reason may be because these earlier claims were coming from studies made up mostly of people in their 80s and 90s, and not those in their 100s.

There is still much more to learn about the FOXO gene. We know for sure that it influences aging, but what we show is that it may not be a key player in achieving truly exceptional age.

QUICK FACT #2

The top 10 causes of death in 1900, 1940, 2010 (from the CDC)

1900	1940	2010
1. Pneumonia & Influenza	1. Heart diseases	1. Heart diseases
2. Tuberculosis	2. Cancer	2. Cancer
3. Diarrhea, enteritis	3. Cerebrovascular disease	3. Chronic respiratory disease
4. Heart diseases	4. Kidney disease	4. Accidents
5. Cerebrovascular disease	5. Pneumonia & Influenza	5. Alzheimer's disease
6. Kidney disease	6. Accidents (not car)	6. Diabetes
7. Accidents	7. Tuberculosis	7. Kidney Failure
8. Cancer	8. Diabetes	8. Pneumonia & Influenza
9. Senility	9. Car accidents	9. Kidney disease
10. Diphtheria	10. Premature birth	10. Suicide

47 years

62 years
Average Life Expectancy

79 years

Highlights (continued)

Three centenarian studies and a family longevity study join forces to discover new extreme longevity-associated genetic variants

We have previously shown that centenarians markedly delay disability well into their nineties, even despite the presence of age-related diseases that they might have had for 10-20 years. Our study participants who live beyond 105 years of age generally also delay or escape age related diseases (like Alzheimer's, stroke, heart attack, restrictive lung disease, diabetes and cancer) beyond the age of 100 and even later. We have also published findings indicating that as people survive to older and older ages beyond 100, genes play a stronger and stronger role in this survival advantage. Thus, centenarians are an extremely promising group of people for the discovery of genetic variants that influence exceptional survival and healthy aging.

In this study, we combined the genetic data from the New England Centenarian Study, the Einstein College of Medicine's Longevity Study, the Southern Italian Centenarian Study and the Long Life Family Study resulting in the comparison of approximately 2,000 cases (men ages 98+ years and women ages 100+ years), and approximately 6,000 controls (average people). We found 10 genetic variants associated with exceptional longevity two of which were also associated with a decreased risk for heart disease (the number one killer in older people). The study was highlighted as the "Editor's Pick" in the most recent issue of the *Journal of Gerontology, Biological Sciences*.

We are now in the process of exploring how these genes can be further studied to discover drugs that can impart the same advantage to average people that occurs naturally in centenarians. The aim is not to facilitate a lot more people living to 100, which is very unlikely to happen, but rather, to help people delay or escape age-related diseases.

In July, the New England Centenarian Study and Long Life Family Study staff ventured to the University of California, Santa Cruz to participate in the 15th annual meeting of the International Centenarian Studies Consortium and to San Francisco for the combined Gerontological Society of America & International Association of Gerontology and Geriatrics World Congress in San Francisco. Along the way, we took a detour to visit the Monterey Aquarium.

From left to right: Marilyn Mostowy, Stacy Andersen, Julia Drury, Sara Sidlowski, Brittany Leonard, and Kelsey Whitaker.



The William M. Wood Foundation

We are forever grateful to the William M. Wood Foundation for its ongoing support of the New England Centenarian Study. This funding has enabled us to expand our research into five key priority areas: cardiovascular disease, cancer, eye health, and history.



Dr. Monti



Dr. Sebastiani

We are collaborating with other Boston University researchers to help us pursue these research priorities. Professor Paola Sebastiani and Associate Professor

Stefano Monti are helping us pinpoint genes strongly associated with cardiovascular health in centenarians.



Dr. Goldstein

In the realm of ocular health, we are working with Dr. Lee Goldstein in studying participants who amazingly have their natural eye lenses instead of having had them replaced long ago with artificial lenses due to cataracts. Using a special eye exam technique invented by Dr. Goldstein, we measure the accumulation of special proteins in the lens as a marker of rate of aging and risk for aging related diseases such as Alzheimer's and cardiovascular disease.



Dr. Johnson

In the area of cancer research, we are working with Geriatrician Michelle Rullan Johnson, MD and Oncologist Michael Voisine, MD to describe the cancers of 70 centenarians cared for at Boston Medical Center. Cancer appears to behave very differently in centenarians compared to younger patients; it is much less likely to spread and seems to be much less deadly. We of course want to know why. To discover why, we will work with Dr. Avi Spira, the director of Boston University School of Medicine's Cancer Center to analyze the genetics



Dr. Spira

and biology of these cancers using stored tissue samples from these amazing patients.

and biology of these cancers using stored tissue samples from these amazing patients.

Finally, our research assistants Sara Sidlowski and Julia Drury took a formal course in guided autobiography. They have started to conduct and voice record or videotape interviews with our study participants as a way to preserve the vast historical knowledge and personal wisdom of centenarians. Sara and Julia and the participants alike have been thoroughly enjoying this endeavor!



Regarding the William M. Wood Foundation, Mr. Wood was a Massachusetts native, born the grandson of William Madison Wood, who was the founder and longtime President of the American Woolen Company; at the time, the largest worsted woolen business in the United States. Mr. Wood was a graduate of Harvard College and Columbia University Law School. He served in the United States Navy during World War II. He practiced law in Massachusetts for many years, but he spent many years in Kentucky (as well as Florida in the later years of his life).

The William M. Wood Foundation is operated in accordance with the terms of a Declaration of Trust signed by William M. Wood in 2002. In accordance with the terms of the trust, the Trustees are directed to make grants to charitable organizations, with particular focus on the following endeavors:

- Medical research and treatment with respect to eye disorders, cancer and cardiovascular disorders;
- History, historical research and historical research repositories;
- The care and employment of blind persons;
- Charitable organizations in the geographical vicinity of Louisville, KY

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- History, historical research and historical research repositories;
- The care and employment of blind persons;
- Charitable organizations in the geographical vicinity of Louisville, KY

Recent Publications (2016-2017)



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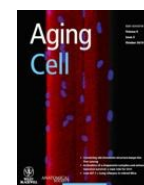
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Philanthropic Support

We are so very fortunate to benefit from the philanthropic generosity of **Paulette Samowitz** on behalf of her and her husband, Marty's, Foundation.

If you are interested in contributing to our research efforts, please do not hesitate to contact us. We can also be reached through the BU School of Medicine's Development Office, David Gillerman, 617-638-4566.

Recruitment

We are always looking for participants throughout North America for our studies. If you know of any centenarians age 103+ years who may be interested, please call our study toll-free at 1-888-333-NECS (6327) or email Stacy Andersen (stacy@bu.edu).

Send us your pictures!

We love getting your pictures! Please send us your photographs — email them or send them through the mail! We make regular submissions to various media and we love being able to include photographs of our amazing participants. If we decide to use your photo for any reason, we will contact you and your family first to obtain permission.

If you wish, we will be happy to return any mailed photographs to you. Our mailing address is on the front page. Email photos to stacy@bu.edu and make sure to include proper credit to the photographer.

Our study websites

www.bumc.bu.edu/centenarian

www.bumc.bu.edu/supercentenarian

www.longlifefamilystudy.org

A website about anti-aging quackery and growth hormone

www.hghwatch.com

The Life Expectancy Calculator

www.livingto100.com

