



The New England Centenarian Study

The New England
Centenarian Study
Boston University
Medical Campus

Our Toll-Free Number:
888-333-6327

Email: agewell@bu.edu

Websites:

bumc.bu.edu/centenarian
longevityomics.org

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For our research assistants,
please see page 8!

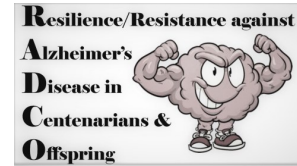
Recruitment

We are looking for participants throughout North America and Canada for our studies. If you know of any centenarians age 100+ years and/or their children who could be interested, please call our study toll-free number at 1-888-333-NECS(6327) or email agewell@bu.edu

Longevity Consortium's



Centenarian Project



Our National Institute on Aging-Funded Studies

2022

Greetings! We hope this newsletter finds you and your loved ones well and thriving. We have been very busy since our last newsletter adapting to COVID with Zoom calls and more data collection by mail and phone.

PLEASE be patient with us. We realize that in some cases, participants were enrolled months ago and have yet to be contacted for data and bio-sample collection. WE SINCERELY APOLOGIZE FOR OUR DELAY. OUR #1 PRIORITY IS YOUR HEALTH AND WELL-BEING.

As we get better and better adapting to our new COVID-reality, we are getting much faster at reaching out to our participants and carrying out our research with you. Our investigation of human exceptional longevity cannot happen without your participation and help. We are so very appreciative of your interest in our studies and your patience with us.

FOR ALL OF OUR PARTICIPANTS, FAMILY MEMBERS AND FRIENDS

Zoom Webinar, Thursday, March 3 2022, from 12-1 PM ET

Meeting ID: 925 9530 4502

Password: 524951

**LESSONS FROM CENTENARIANS AND THEIR KIDS:
MAXIMIZING YOUR POTENTIAL AT ANY AGE**

Tom Perls MD & Stacy Andersen PhD

If you want to reach us about anything, please call 888-333-6327 or email us at agewell@bu.edu

You can also contact the Director of our studies, Dr. Tom Perls, most any time via his cell phone: 617-733-7893 or by email: thperls@bu.edu

Participant shout outs and more..

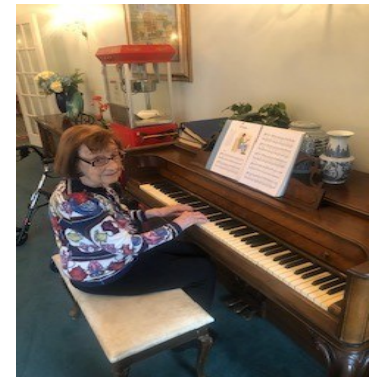


Hazel Nilson, age 110

From left to right: Project Manager Reena Karki, Hazel Nilson, 110 years old!, Principal Investigator Dr. Tom Perls and daughter-in-law Nancy Nilson.

Hazel's warm spirit and great sense of humor charmed many and we are very lucky to have had her as one of the oldest participants in our study.


Susan Jarrell, age 105, is one of our Longevity Omics Study participants. After retiring as a head start teacher, Susan dedicated her time as a pianist and became the first music teacher at the Nantucket Community School. Susan also founded the Nantucket Organ Crawl, which is an event where top organist from all over the world come and play on the Island's historic organs.



Susan Jarrell, age 105



Henry Naruszewicz, age 107, with his daughter and son-in-law Dottie and Bill Flanigan

Henry Naruszewicz, age 107, also one of our Longevity Omics Study participants is shown proudly holding a certificate of recognition. It states: Henry Naruszewicz, 276th Armored Field Artillery, served 1943-1945, Patton's 3rd Army. At the bottom, the recognition goes on to state: "I do not have to tell you who won the war. You know, the artillery did." 

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. One of their great advantages over other older people 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.

-Terry LA, Sebastiani P, Andersen S, Perls T. Disentangling the roles of disability and mortality in exceptional longevity. Archives Internal Medicine. 2008;168(3):277-83.

Our Studies

The New England Centenarian Study (the NECS) is our over-arching study and masthead. All of our funded studies fall within the NECS which was founded in 1995. The study is directed by Dr. Tom Perls and Dr. Stacy Andersen who have particular expertise in, respectively, clinical geriatrics and neuropsychology. *To-date, our studies, including the current ones noted below, have enrolled close to 3,000 study participants, making the NECS the largest study of centenarians and their family members in the world.* The NECS also includes 600 participants between the ages of 105 and 109, people that are called semi-supercentenarians and 200 supercentenarians, or people who are 110 years old or older. Data collected or generated from our participants are first deidentified, meaning that the data do not reveal the identity of a participant. Then, the deidentified data are ultimately shared with other interested investigators throughout the world, via the National Institute on Aging's database called the Exceptional Longevity Translational Resources (ELITE) webportal:

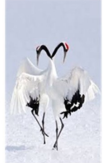


<https://adknowledgeportal.synapse.org/Explore/Programs/DetailsPage?Program=ELITE>



The Longevity Consortium's Centenarian Project (LCCP) is our research study funded by the Longevity Consortium, a group of National Institute on Aging-funded research projects and investigators based at Universities around the country. This project will enroll a total of 450 centenarians from whom we obtain detailed health history, physical and cognitive function, familial history of longevity and diet data as well as a blood sample for the generation of genetic, metabolic and proteins data. The LCCP also generates similar types of molecular data from other animal species such as bird and mammalian species that differ by lengths of life span. The main goal is to study and compare and contrast these data in order to discover biological mechanisms that facilitate longer life spans and health spans. The Longevity Consortium's website is: www.longevityconsortium.org.

Longevity
Consortium's



Centenarian
Project



The Integrative Longevity Omics Study (ILO) is another of our research studies funded by the National Institute on Aging which is an Institute of the National Institutes of Health (NIH). ILO is very similar to the LCCP, described immediately above. Partner study sites at Boston University and at Einstein College of Medicine recruit and enroll 700 participants each who are centenarians, their siblings, children and spouses of the children. These participants are different from those enrolled in the LCCP. Besides the inclusion of family members, ILO differs from the LCCP in terms of generating additional data from the blood samples, including gene expression and methylomic (this has to do with interaction between genes and the environment) data. We also ask for a stool sample from the participant to determine the role of different bacteria types in healthy aging and exceptional longevity. The ILO's website is: www.longevityomics.org



Our Studies and the New Kid on the Block



The Long Life Family Study (LLFS) is a multi-center study of families that demonstrate highly unusual clustering for exceptional longevity. Boston University School of Medicine is one of the LLFS Centers and we are responsible for studying about one fourth of the 5,300 participants in LLFS. Drs. Perls and Andersen are founding investigators of LLFS which began in 2004 and the study is now in its 5th round of funding from the National Institute of Aging.

Like our other studies, the study participants undergo detailed and careful cognitive function testing because we are so very interested in why centenarians and their family members delay or even escape Alzheimer's disease. We perform this testing and also obtain a blood sample every 5-8 years so that we can follow changes over time. The LLFS website is: longlifefamilystudy.wustl.edu.



**Resilience/Resistance against
Alzheimer's
Disease in
Centenarians &
Offspring**



And Announcing..

We are very excited to announce that our 5 year project, Resilience/Resistance against Alzheimer's Disease in Centenarians and Offspring (RADCO) was funded this last September by the National Institute on Aging. This project will enroll about 500 centenarian cognitive superagers. These are centenarians who

have cognitive function similar to cognitively intact people who are 30 years younger (70 year olds). We will also very carefully study the cognitive function of average centenarians, their offspring and the spouses of their offspring. In total, we plan on enrolling about 1,200 participants.

In this multi-site study with investigators from Boston University, Boston Medical Center, UCLA, Massachusetts General Hospital, Beth Israel Deaconess Medical Center, University of Utah, Albert Einstein College of Medicine, and Columbia University, we will gauge cognitive resilience, or the ability to avoid dementia, among these cognitive superagers, as well as our other participants by comparing cognitive testing results to neuroimaging (MRI) data, biomarkers in the blood, and brain autopsy results. The aims of the study include a concerted effort to enroll Hispanic and Black participants.

If you are a participant in one of our other studies you may hear from us because those studies are our primary source of participants for enrollment into RADCO. Our request to enroll a participant into RADCO will depend upon the results of their cognitive function testing in one of our other studies. Enrolling in RADCO will allow us to obtain more data from you about how and why you are resilient against Alzheimer's disease!



Highlights of Recently Published Findings

Reduced Prevalence and Incidence of Cognitive Impairment Among Centenarian Offspring

Familial longevity is a genetic and environmental based advantage that paves the way for a healthier and more resilient generation. This advantage has been most evident amongst centenarian offspring who, like their parents, have a lower risk of mortality and are generally able to delay the onset of age related diseases.

In this study, our objective was to see if centenarian offspring were less likely than controls (individuals whose parents died at average life expectancy), to be cognitively impaired during the initial time of enrollment and during a follow up period. Participants were cognitively tested yearly. Testing consisted of twelve items that assess orientation, general knowledge, working memory and an immediate recall of a word list. Results from these tasks helped determine cognitive impairment in the categories (also called cognitive domains) of episodic memory, working memory and executive function. Episodic memory helps us assess memory tied to a specific event, working memory looks at the ability to learn and work with new information and executive function helps an individual plan and execute tasks.

Based on the analysis of the test scores, we found that centenarian offspring were 46% less likely to have baseline cognitive impairment and 27% less likely to become cognitively impaired over a median follow-up period of 7.8 years. Additionally, we found that women were 51% less likely to have cognitive impairment in comparison to men, which is something we have also seen in our centenarians at least up to about age 101. At even older ages we believe men become more like women in terms of resilience and resistance to cognitive impairment.

The Apolipoprotein E (APOE) gene, Its Variants and European Ethnicities and Associations with Longevity

The APOE gene has been well-studied because one of its relatively rare variations, APOE e-4, is strongly associated with Alzheimer's disease, cerebrovascular disease and earlier mortality. The also rare APOE e-2 variant, on the other hand, is associated with healthy cognitive aging and it is more common among centenarians. However, some ethnicities demonstrate these associations more than others.

To conduct this research, we analyzed genetic data from 8,968 participants from a consortium of four studies including The New England Centenarian Study (NECS). The results showed that people born in and still living in Southern Italy had no adverse effect from the e4 variant, but Southern Italians living in the United States who had the e4 variant were 81% less likely to achieve extreme longevity. Our hypothesis, which needs to be further investigated, is that American versus Southern Italian diets could explain the difference. People living in Southern Italy tend to follow a Mediterranean diet, a diet that has been known to reduce the risk of Alzheimer's disease and which may counter the bad effects of the e4 variant.

Additionally, our analysis showed that Danish people living in Denmark had a stronger protective effect from the e2 allele than those living in the United States. Although the diets in Denmark and the United States are similar, one major difference is that Denmark was ranked the second happiest country in the *United Nations 2019 World Happiness Report*, whereas the United States was ranked nineteenth. This distinction points to a possibility that living in a "happier" country might play a role in the effect of the e2 protective allele. In the future, we hope to further analyze nutrition and environment as protective factors that enhance the benefits of the e2 variant and as negative factors that amplify the negative effects of the e4 variant.

2020-2021 Publications - A sampling...



Andersen, SL., *et al.*, **Digital Technology Differentiates Graphomotor and Information Processing Speed Patterns of Behavior.** *Journal of Alzheimer's Disease.* 2021; DOI: 10.3233/JAD-201119



Andersen, SL., *et al.*, **Slower Decline in Processing Speed is Associated with Familial Longevity.** *Gerontology.* 2021; DOI: 10.1159/000514950



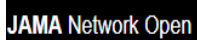
Fox-Fuller, JT., *et al.*, **Survey Findings About the Experiences, Challenges, and Practical Advice/Solutions Regarding Teleneuropsychological Assessment in Adults.** *Europe PMC.* 2021; DOI: 10.1093/arclin/acab076



Sweigart, B., *et al.*, **APOE E2/E2 Is Associated with Slower Rate of Cognitive Decline with Age.** *IOS Press.* 2021; DOI: 10.3233/JAD-201205



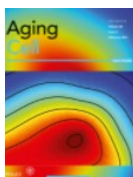
Xiang, Q., *et al.* **Studying the Interplay Between Apolipoprotein E and Education on Cognitive Decline in Centenarians Using Bayesian Beta Regression.** *Frontiers in genetics.* 2021; DOI: 10.3389/fgene.2020.606831



Perls, T., *et al.* **Cognitive Trajectories and Resilience in Centenarians-Findings From the 100-Plus Study.** *JAMA network open.* 2021; DOI:10.1001/jamanetworkopen.2020.32538



Gurinovich, A., *et al.* **Effect of longevity genetic variants on the molecular aging rate.** *GeroScience.* 2021; <https://doi.org/10.1007/s11357-021-00376-4>



Sebastiani, P., *et al.* **Protein signatures of centenarians and their offspring suggest centenarians age slower than other humans.** *Aging Cell.* 2021; <https://doi.org/10.1111/acel.13290>



Andersen, S., **Centenarians as Model of Resistance and Resilience to Alzheimer's Disease and Related Dementias.** *Hapres: Advances in Geriatric Medicine and Research.* 2020; DOI: <https://doi.org/10.20900/agmr20200018>



Sebastiani P., *et al.* **Patterns of multi-domain cognitive aging in participants of the Long Life Family Study.** *GeroScience.* 2020; DOI: <https://doi.org/10.1007/s11357-020-00202-3>



Monti, S., *et al.* **Contextualized Protein-Protein Interactions.** *Patterns.* (2020). <https://doi.org/10.1016/j.patter.2020.100153>



Lau-Ng R., *et al.* **COVID-19 Deaths in Long-Term Care Facilities: A Critical Piece of the Pandemic Puzzle.** *Journal of the American Geriatric Society.* 2020; DOI: <https://doi.org/10.1111/jgs.16669>



Feitosa MF., *et al.* **Gene discovery for high-density lipoprotein cholesterol level change over time in prospective family studies.** *Atherosclerosis.* 2020; DOI: 10.1016/j.atherosclerosis.2020.02.005



Marone, B. *et al.* **Purpose in Life Among Centenarian Offspring.** *The Journals of Gerontology, Series B: Psychological and Social Sciences.* 2020.

Spreading the Word!



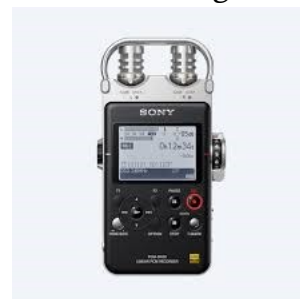
We've been busy sharing our results with the longevity and Alzheimer's disease research communities. Drs. Perls, Andersen, Milman and Sebastiani have recently presented at the Gerontological Society of America, the International Centenarian Consortium, the Alzheimer's Association International Conference and the International Neuropsychological Society.

Over the past 18 months, whole conferences, even with 5,000+ attendees, have had to be held by Zoom because of COVID. We hope that as the latest COVID variant dissipates by next Spring that scientific conferences will be once again be in-person!

Every Corner We Turn, Something New...

Preclinical Detection of Cognitive Impairment. The underlying causes of Alzheimer's disease begin years before someone starts experiencing significant changes in their memory and thinking and begins to perform poorly on cognitive tests. For example, someone with subtle brain changes may correctly answer a test question but at a much slower speed or with more hesitancy than someone without underlying brain pathology. Typical cognitive test scoring would classify the individual as unimpaired whereas taking into account how the person completed the task might detect subtle signs of cognitive impairment.

Dr. Stacy Andersen is particularly interested in this "preclinical" phase of Alzheimer's disease and in the development of new methods or markers for identifying these subtle changes in cognition. Therefore in our studies, we use digital technologies such as a digital pen and digital voice recorder during cognitive testing. Similar to the use of wearable sensors to track activity and sleep, these digital technologies allow us to capture high-precision, continuous data of the entire process of completing a cognitive test rather than just the final right or wrong answer. These devices also allow us to analyze subtle behavioral features such as pauses in responses and speed of writing which could not otherwise be reliably captured by an examiner. The hope is that we will identify earlier markers of change in brain function which will allow for earlier interventions to prevent cognitive decline.



Microbiomes Associated With Healthy Aging and Exceptional Longevity. Our lower gastrointestinal tract, called the colon, is teeming with thriving different species of bacteria (called the microbiome). Substances produced by these bacteria, like amino acids and certain proteins are absorbed by the bloodstream and have been found to be crucial for healthy aging. In a recent and scientifically exciting article from our Japanese Centenarian Study colleagues, there are certain bacteria found to be more common in centenarians that may be important for healthy aging and longevity. We are collecting stool samples from our Integrative Longevity Omics study participants to investigate this finding much more closely and in a much larger group of participants.

Meet our team!

Principal Investigators



Thomas Perls, MPH, MD



Sofiya Milman, MS, MD



Paola Sebastiani, PhD



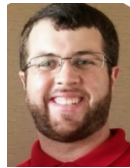
Stacy Andersen, PhD



Project Managers



Reena Karki, MPH, RN



Bradley Petrowitz, MPH



Lance San Souci, BA

Research Assistants



***Adriana Hernandez** - Adriana graduated from Lesley University with a degree in Biology and is pursuing a career in geriatric medicine and health equity for underrepresented populations.



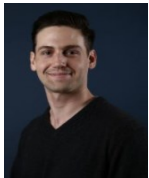
Christos Meimeteas- Christos graduated with a degree in Biology from the University of Vermont. He is particularly interested in population genetics, aging and neurobiology and is pursuing a career in medicine.



Harold Pang - Harold graduated from Wesleyan University with a bachelors degree in Molecular Biology and Neuroscience. He loves Neurology and is pursuing a career in Medicine.



***Habitou Diallo**– Habi graduated from the University of Massachusetts Boston with a major in Biology and almost has her MPH from BU. Habi is very interested in the genetics of longevity and maternal health and she’s aiming to be a physician.



***Stephen Gale** - With his degree in Biomedical Sciences, Stephen’s interests lie in risk factors for and prevention of strokes Stephen is aiming for a career as a Physician’s Assistant.



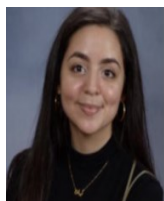
***Elise Tierney**– Elise earned her BA from Skidmore College and recently obtained her MPH from Boston University. Elise is looking forward to a clinical health sciences career.



Sabrina Blanchett-Anderson - With her experiences both within the study and as a hospice caregiver, Sabrina is especially interested in a career in geriatrics-palliative medicine.



Sara Topalovic– Sara earned her BA from Connecticut College. She is particularly interested in neurocognitive science and is pursuing a career in medicine. Sara is trilingual in English, Bosnian and English.



Leyla Remh - Just one day after graduating from Boston University with her Bachelors in Neuroscience, Leyla joined the NECS. Leyla is pursuing a career in neuroscience and cognitive behavior health.



Koinonia Wilson-Howard– Koinonia earned her BA degree from Lasell University. in Sports Medicine. She is especially interested in preventive medicine and healthy aging.

*** Senior Research Assistant**