LLFS Newsletter

Greetings! We're excited to see you soon!

We love hearing from you, and we are ready to see you!

Over the past year, we have been keenly focused on finding the best way to conduct **Visit 3**, our third "in-person" visit of the LLFS study. We have worked in conjunction with safety boards, staff physicians and epidemiologists to design a visit with safety as the top priority. We are happy to now be able to schedule Visit 3 with you and your families, when all involved feel safe and comfortable. If you agree to participate in Visit 3, all in-person portions of the visit will be completed by vaccinated examiners wearing masks and gloves. According to your preference, we can also conduct certain components of the visit through video-conferencing. These options may differ from site to site due to varying restrictions. We are looking forward to seeing you all again!

If you wish to reach us, please contact our Columbia University site line at **212-342-1202** or email our study coordinator, Rebecca Abraham, at **rea2154@cumc.columbia.edu**

In the meantime, we wanted to take this time to share all of the exciting work happening behind the scenes in LLFS!

WHAT'S NEW?

For the first time, we want to enroll the next generation of LLFS families (Generation 3 or "Gen3"). Please start talking to your children/grandchildren **NOW** about this new opportunity, and we will discuss the specifics of how they can enroll when you are contacted for Visit 3.

FAQs

Why should I keep participating?

Each time you speak with our team or see us in person, you provide valuable information that allows us to **map the course of healthy aging** and identify the factors that are important for living long, healthy lives. Flip to the inside of this newsletter to see how your participation has directly impacted the science of aging! **PLUS**, all participants for Visit 3 will receive results of COVID antibody testing.

Resources

LLFS website:
www.longlifefamilystudy.wustl.edu

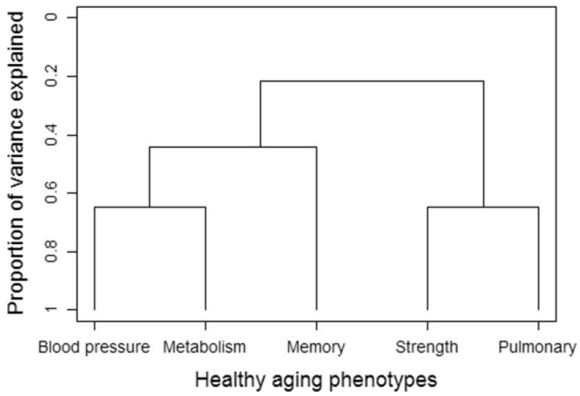
NIA website:
https://www.nia.nih.gov/health/

Recent Scientific Publications

We want to take this opportunity to tell you about some of our recent scientific findings made possible by your continued participation.

Heterogeneity of Healthy Aging: Comparing long-lived families across five healthy aging phenotypes of blood pressure, memory, pulmonary function, grip strength, and metabolism

Marron et al. published in Geroscience (2019)

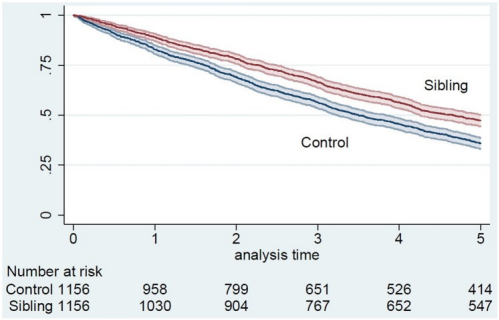


Through LLFS, we have learned that there are various ways in which families achieve exceptionally long lives, likely reflecting the different combinations of genetic, environmental, and behavioral factors that influence health over the lifetime. In this particular study by Marron and colleagues, we examined possible associations between five specific pathways toward longevity. We found that **healthy blood pressure and metabolic functioning were associated with each other,** possibly reflecting a common pathway of insulin sensitivity. We also found that strength and pulmonary functioning were most closely related, potentially reflecting underlying cardio-respiratory fitness. Understanding these overlapping pathways will enable more precise identification of the genes and behaviors that are critical to a long, healthy life.

Physical robustness and resilience among long-lived female siblings: a comparison

Galvin and Ukraintseva et al. published in Aging (2020)

Previous studies showed better health and survival in long-lived siblings compared to sporadic ("non-familial") long-livers. However, these studies did not examine the interplay between disease risk and survival. In the current study, we examined whether Danish long-lived female siblings have a better ability to avoid diseases at ages 65+ (proxy for "robustness") and/or survive to extreme ages (proxy for "resilience") compared to Danish sporadic long-livers. We found that long-lived female siblings had lower risks of some but not all health conditions, mostly depression and hypertensive and cerebrovascular diseases. They also had better survival to extreme ages compared to sporadic long-livers. These results suggested that familial longevity could be mainly related to a better resilience as the ability to overcome various life and health problems, rather than to a simply good health, and that being not depressed may be a key factor supporting robustness in advanced years of life.



APOE alleles and extreme human longevity

Sebastiani and Gurinovich et al. published in The Journals of Gerontology: Series A (2019)

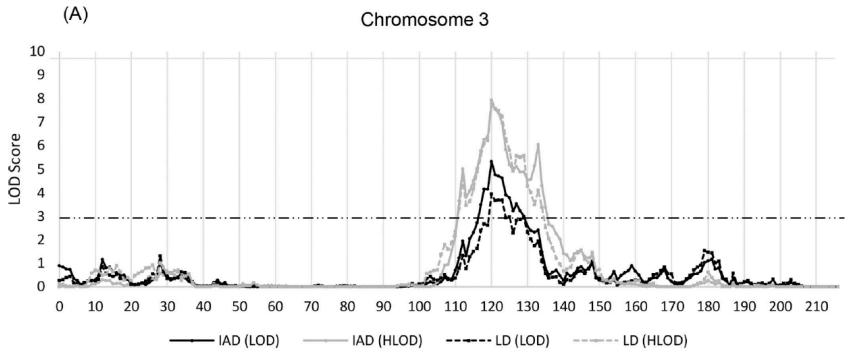
How do our genes contribute to long life? Our team examined the chance of becoming a centenarian in individuals with a variant of the APOE gene known as the E2 variant, using data from almost 29,000 people including people enrolled in the LLFS study. Our analyses showed that people with the E2 variant were **28% more likely to live to extreme old age** compared to individuals with the most common variant known as E3. This result was replicated in 3 different studies. The significance of this result is that by targeting the molecular product of the E2 variant, we may be able to develop treatments for healthy aging therapeutics.

Recent Scientific Publications

Genome-wide linkage analysis of carotid artery traits in exceptionally long-lived families

Kuipers et al. published in Atherosclerosis (2019)

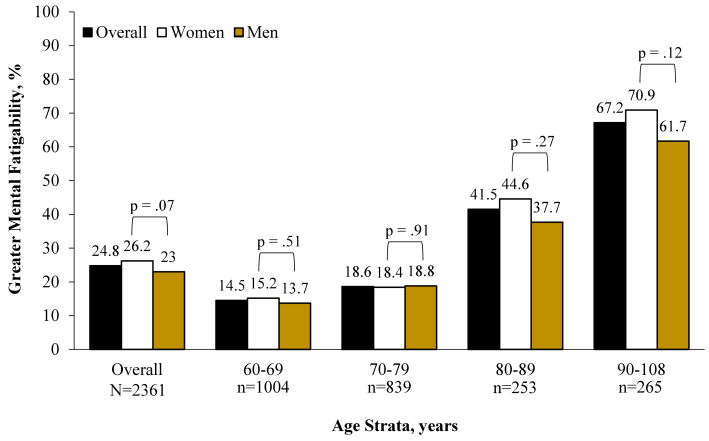
At the last LLFS visit, we added new neck ultrasound measures to study genes related to the health of your blood vessels. From your valuable participation we were able to determine that the health of your vessels is a part of what is inherited within your families. In fact, we found **specific gene regions on chromosomes 3 and 17,** indicated by the peaks on the figure to the left, that appear to be important for vessel health in long-lived families. These findings will help us learn more about the genes that are related to heart disease and stroke, and may lead to improved therapy options in the future!



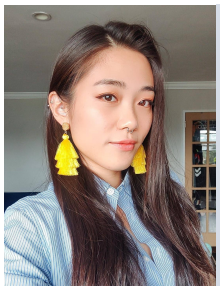
Prevalence and severity of perceived mental fatigability in older adults: The LLFS

Glynn Research Group published in the Journal of the American Geriatrics Society (2021)

LLFS co-investigator Nancy W. Glynn, PhD and colleagues developed the Pittsburgh Fatigability Scale in 2014, and included it as a novel measure in LLFS Visit 2 (2014-2017). Participants often wonder why we ask them to indicate the level of tiredness/exhaustion they would expect to feel after completing a range of activities, even if they have not done the activity in the past month. Measuring fatigue in relation to doing an activity is a more sensitive measure of how fatigue may limit someone physically and mentally. Our previous work showed that individuals actually do a very good job "imagining" how they would feel doing an activity even if they have not done it in a while. Our latest research focused specifically on how common it is to report higher perceived *mental* fatigability. We define perceived mental fatigability as a person's susceptibility to fatigue (i.e., tiredness, lack of energy) after performing mental activities that engage cognitive function. We found that nearly 25% of LLFS participants reported having a high mental fatigability score (13 or greater), but there were no differences in scores between women and men. Perceived mental fatigability was higher with age. Specifically, mental fatigability was lowest (14.5%) for those age 60-64 years and highest (67.2%) for those age 90-108 years (See figure). This is the first paper to report the burden of mental fatigability in older adults. Next steps will evaluate how higher mental fatigability may be related to physical and cognitive health.



Columbia University Research Assistant Spotlight



Kathleen Chan - Kathleen joined LLFS in August 2019 after graduating from Stony Brook University in NY with a degree in Biology. She hopes to pursue graduate work after gaining additional research experience through the LLFS. Kathleen has a particular interest in how various social (e.g., occupation) and biological (e.g., age of menopause) factors are associated with aging outcomes.

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Samantha Dargie - Samantha joined LLFS in August 2021 after graduating from Fordham University with a degree in Integrative Neuroscience. She hopes to attend graduate school to earn her PhD in neuroscience after gaining experience with LLFS. She is excited to join the team and learn more about patterns of cognitive aging in older adults.

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Stella Garriga - Stella joined LLFS in March 2021 as a research assistant while finishing her undergraduate degree in Cognitive Science at Lehigh University. She has a wide variety of research interests. She hopes to one day attain her PhD in Clinical Psychology and is looking forward to learning from all the families and researchers involved.

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Miji Suhr -

Esther Zheng - Esther joined LLFS as a part-time research assistant in February 2019 when she was a master's student at Teachers College at Columbia University. She graduated with a M.S. in Neuroscience and Education in May 2019 and started working full-time at LLFS. She hopes to earn a Ph.D. degree in psychology in the future. She is interested in using the LLFS data to investigate dementia assessment and diagnosis in older adults.

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