



GREETINGS LONG LIFE Families!

WHAT HAVE WE BEEN DOING?

Welcome to our first issue of the LONG LIFE Family Study (LLFS) Newsletter.

LLFS is a collaborative research study, funded by the National Institute on Aging (NIA), and including several prestigious institutions from the U.S. and Denmark. Everyone involved – especially you, our valued participants - is dedicated to answering one important question:

Why do some people and their families live very long lives?

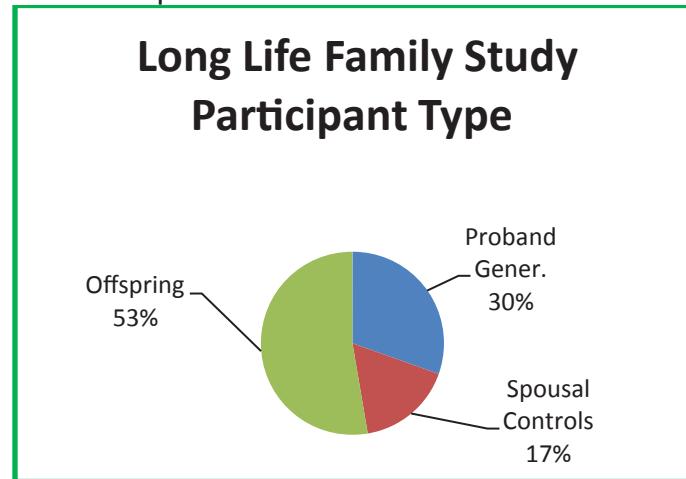
LLFS is a unique international project that is studying families with multiple members who have reached a very old age. Families from the U.S. and Denmark agreed to participate to help us learn why some live to a very old age, as well as why some families maintain their health far longer than others.

All of you agreed to share information about your life and family with us, which is going to help in improving the health of future generations. What we will learn from this study can also help older people in the future to maintain their health and well-being. Together we hope to discover the secrets to a long and healthy life!

The LLFS Project began in 2004, when all of the collaborating institutions came together and began formulating the Study Design.

In 2006, participant recruitment was launched and continued through June of 2009. The families of the LLFS Study had to meet very unique criteria, so this proved to be quite challenging. In 2009, all enrollment and participant visits were concluded.

A total of **4,923 visits** (4821 in-person and 102 telephone visits) were completed by the LLFS Field Centers. The number of families enrolled in the LLFS Study totaled **535**, consisting of **1,499** individuals in the Proband Generation, **2,594** individuals in the Offspring Generation and **830** Spouse Controls.





WHAT HAVE WE LEARNED?

Based on the information you shared with LLFS, some preliminary findings are very interesting. Anne B. Newman, M.D., MPH, principal investigator at the University of Pittsburgh field center has submitted a manuscript for publication. She prepared the following article showcasing the exceptional quality of our LLFS families.

LLFS Participants Show Better Health and Function Compared to Participants in Studies of the General Populations

Anne B. Newman, MD, MPH

The term “exceptional survival” refers to longevity, but also to having continued existence into late life without disease or disability. We wanted to determine whether LONG LIFE Family Study participants who were recruited on the basis of family longevity were more likely to show exceptional health across the spectrum of ages. The LLFS participants were compared with other cohorts, having similar data collection, including the *Cardiovascular Health Study*, the *Framingham Heart Study*, and the *New England Centenarian Study*.

Comparisons were adjusted for age, sex, race, educational attainment and smoking history, as well as family structure and medication use or body size where appropriate. Some initial findings include:

(Cont-pg. 3)



LLFS Family - Pittsburgh.

Siblings together for the first time in 40 years (2008); aged 94, 92, 88, 84 and 81.

Where Did Our Families Come From?

Families participating from within our Danish population were identified utilizing the Danish National Registry. However, unlike our Danish colleagues, identification and recruitment of families within the U.S. was a bit more challenging. Originally, families were identified based on geographic location of the Proband, in relation to our Study Centers. However, as recruitment efforts progressed, in order to identify as many and the most exceptional families, LLFS research teams from Boston University, Columbia University and the University of Pittsburgh, found it necessary to travel to 27 states, and at least two Canadian provinces, to enroll over 800 family members over a 2-year period. These visits took a great deal of careful planning and cooperation between the field centers, as well as the family members that we visited. Trips typically spanned between 2-8 days, seeing as many as 32 individuals in one trip!

We want to take this opportunity to express our gratitude to all of you for your willingness to accommodate our tight travel schedules. It was because of these long distance trips that we were able to see the maximum number of people within your respective families. Thank you again for opening up your home and/or coming to see us at our hotel.

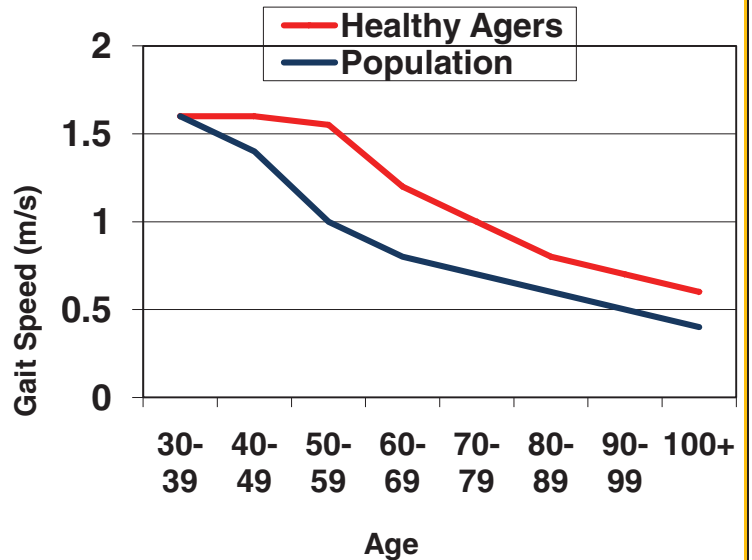


1. Diabetes, chronic pulmonary disease and peripheral artery disease tended to be less common in LLFS across the spectrum of ages, including both older generation and their offspring, when compared to similar aged persons in the other cohorts.
2. Cardiovascular risk factors were more optimal in LLFS. Pulse pressure (defined as systolic blood pressure – diastolic blood pressure) and triglycerides were lower, high density lipoprotein (HDL or “good cholesterol”) levels were higher, and a perceptual speed task (digit symbol substitution test) and gait speed were better in LLFS.

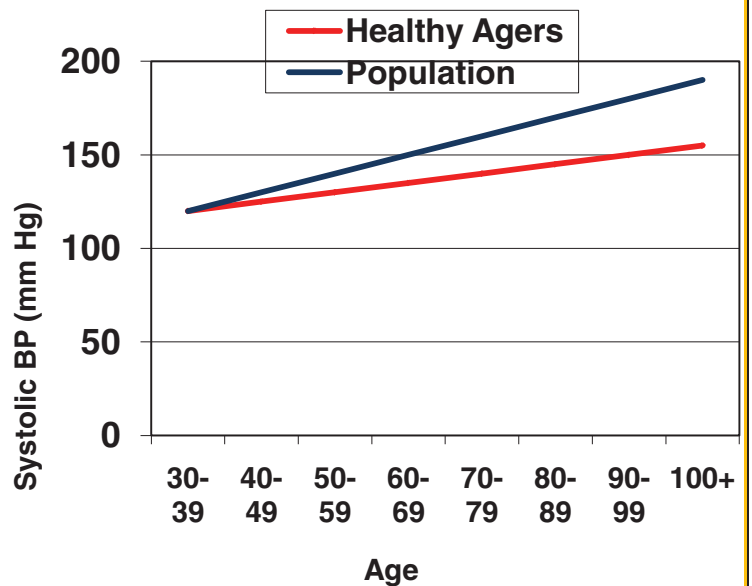
We also compared the older LLFS participants to participants in the New England Centenarian Study. In keeping with having exceptional health and survival, LLFS had similar excellent health history compared to the cohort of centenarians. Age-specific comparisons showed several patterns of differences that would be consistent with having a higher peak, a later onset of decline, or a slower rate of change across age in LLFS participants.

By selecting LLFS families who were characterized by having a strong history of longevity, we have identified individuals who are experiencing exceptional survival, including lower cardiovascular risk factors and higher levels of function. These findings point to these as priority characteristics for future analyses of genes that may be contributing to exceptional health and survival.

Example of Slower Rate of Decline in Gait Speed



Example of Slower Rate of Rise in Systolic Blood Pressure





WHAT DOES THE FUTURE HOLD?

Cleaning and quality control processing of the large amount of data that was collected during Phase I of LLFS was completed in July 2010. We were recently awarded a new grant to follow all of you for another 3 years via telephone! As we move forward into Phase II of this project, investigators will now be focusing on data analyses of the baseline information as well as preparing the genetic material (DNA) for analysis. It is during this important phase of the project that we will be searching for, and hope to discover, some genes which are key in longevity and healthy aging . . . to answer the question:

Why do some people and their families live very long lives?

leads a large group of analysts who will be working with the data that results from all of information collected. During the initial phase of this project, we were responsible for HIPAA compliance of data collection and storage, as well as coordinating all of the efforts among the various institutions in the LLFS Study and serving as a liaison with the Project Officer(s) at the National Institute on Aging. It is amazing how much work goes into a study besides that which you see on your end!

We are so pleased to be bringing you this Newsletter to try to keep you informed and up-to-date on what we are doing and where and how your valuable participation is being utilized. Below, please find a very "personal" update from each of our participating institutions written especially for this Newsletter . . . to you!

NOTES FROM OUR RESEARCH CENTERS . . .



Greetings from the Midwest!

Happy Holidays to all of our LLFS families. **Washington University School of Medicine**, in St. Louis, MO has been honored to serve as the Data Management Coordinating Center for the LLFS Study since its inception.

Like our colleagues from Minnesota (as you will see below), we also operate in large part, from behind the scenes. Our team at Wash-U is led by Michael A. Province, Ph.D., Professor of Genetics and Biostatistics and Chair of the Division of Statistical Genomics. Dr. Province



News from the Central Laboratory

We would like to introduce ourselves to you. We are the **University of Minnesota Advanced Research and Diagnostic Laboratory**. Since we work behind the scenes, we are not fortunate to have met any of you. In fact, we have no idea who you are, since your samples arrive in our laboratory with only a number on them. Nonetheless, we know that each sample is a highly valuable donation from each of you.

Here at the Central Lab, we put together the kits of tubes that were used to collect and ship your blood. In the U.S., your blood samples were shipped to us overnight by Federal Express and, upon arrival in our lab, we



divided your samples into many smaller samples. One was used for immediate testing, while the rest are stored in freezers at a very cold temperature. In Denmark, your blood samples were sent to the University of Southern Denmark where they were divided, stored, and shipped frozen to our laboratory in large batches.

You received the results from the tests that we performed shortly after your visit. The remaining samples that are stored will be used to perform additional tests in the future. To date, we have received samples from 4,883 participants from the four Centers. Each participant's samples were divided into 35 smaller samples and are stored in four freezers.

to perform paper and pencil tests, ask questions about lifestyle habits, and collect blood pressure measurements. This in-person assessment will last about 2.5 hours. We will then compare the results of participants from long-lived families to participants who do not come from long-lived families. This will help us to examine how much of preserved brain function in long-lived individuals is because of genes that run in families and how much is due to other factors, such as healthy lifestyle habits. This additional study of memory and brain aging is completely voluntary. We look forward to explaining this study in more detail with you!

Since 2006, we have had the opportunity to be welcomed into your homes to gather information about you and your families. In addition to enrolling participants within 3 hours of Boston, we traveled to several states across the United States from Vermont to California to enroll exceptionally long-lived families. We also visited the Canadian provinces of Ontario, New Brunswick, and Prince Edward Island.



It is our pleasure at **Boston University** to wish all of our LLFS participants and their families Happy Holidays and a wonderful New Year! We would like to share with you some exciting news about the Boston field site as we continue to move forward and learn more about healthy aging and family longevity.

As you know, we are still keeping in touch with you by conducting telephone follow-ups to find out how you have been doing since we met with you. We call every year and have a tremendous appreciation for your continued participation. Thank you!

Soon we will be asking participants of the Boston field site of the LLFS to participate in a study on memory and thinking in long-lived families. We will travel to participants' homes



Family seen by **Boston University**. This family was recruited and enrolled in 2008.



Here are some fun facts about some of our outstanding participants at the Boston site: the oldest participant was 110 at the time of our visit, the youngest participant was 32 at the time of our visit, the largest number of enrolled siblings in one family is 9 and the largest number of enrolled family members in one family is 49.

We have a number of participants who are keeping busy well into their 90s and beyond! In addition to being able to live independently or with little assistance, many of these folks participate in activities including going into the office every day, woodworking sculptures and Styrofoam sculptures, bowling every week, painting, Pilates (muscle strengthening exercises), playing cards (some with their siblings!), quilting and sewing, cooking and baking, writing poetry and still doing household repairs, gardening and general upkeep of their homes. Keep it up and let us know what you've been up to!

And in the news...our very own Dr. Thomas Perls was interviewed for the cover story by TIME Magazine for an issue devoted entirely to aging on February 11, 2010 ("How to Live 100 Years" by Alice Park). An LLFS family was profiled as well! The Hurlburts have eight siblings participating in our study – 6 live in New England and 2 live in California and they now range in age from 82 to 97. The article looked at the research being done to determine how much of longevity can be attributed to genes and how much to environmental factors and lifestyle.

Time doesn't stand still for your family or for the staff at BU! We have had the pleasure of working with some wonderful research

assistants since 2006 and have said some fond farewells. Dorothy, Cherrell and Timea have moved on to nursing schools, Craig got married and moved back to North Carolina but is still working in research, Kirsten is finishing up a program for Occupational Therapy, Ilana got her Master's in Social Work and also got married, Amy just started a Master's in Public Health program and Nikki, Maureen and Ashlin are in medical school. Our current staff is also keeping busy in addition to following up with LLFS families. Stacy is working on her dissertation for her Ph.D.in Behavioral Neuroscience at BU, Lori is applying to a Master's in Social Work program, Jaimie and Alex are working towards going to medical school and Nick is taking classes towards becoming a Physician's Assistant.

We look forward to your continued participation as we learn more about healthy aging from your extraordinary families.



Columbia Participant.
92-y/o retired NY Police Officer. Self-employed and enjoys dancing



Greetings, LLFS participants from **Columbia**

University! We would like to send our best



wishes for the New Year to you and your family members, and to thank you for your continued participation in our LONG LIFE Family Study.

After meeting with each of you and, now, beginning to analyze the study data, we are very excited about developing a better understanding of the ways to, not only increase our life span, but to live healthier lives well into our 90s and 100s. We thought this would be a great time to update you on the progress of our Long Life Family Study.

In May 2009, we proudly reached our participation goal of 1,086 study participants across 167 families and, by that time, had also visited all of you to obtain details on the ways your family has maintained a long and healthy life! Thanks to all of you for the warm welcome into your home, advice and stories, and cookies and tea! We enjoyed meeting everyone and feel each of you have helped us to gather important information to better understand the secrets to longevity!

Now for some details about you and your family members! Although the majority of our participants are located in the New York Tri-State area, many of you reside in states as far as California, Wisconsin, Florida and Minnesota. Our team traveled through heat waves, snowstorms and rain to be warmly welcomed into your home. We saw beautiful scenery on the way and made lasting memories while meeting each of you. The largest long-lived family in our study hails from the Northeast and has a total of 22 participating family members. As you can imagine, our participants vary widely in age since we have visited siblings, offspring and spouses. Our oldest participant is turning 109

this winter and our youngest participant is only aged 27. As diverse as our participants are in age, there is certainly one commonality among all of our families and it is longevity!

Now for your secrets on how to live a long and healthy life! Along with our collaborators, Columbia University researchers are currently analyzing the data from the LONG LIFE Family Study and we hope to have some answers soon. Just quickly we can tell you that remaining active, one way or another, is a trend we've seen among nearly all of you despite your age. For example, we've met a participant in his 90s who runs the NYC marathon every year. Additionally, many of you regularly engage in hobbies (i.e. take dance lessons, knit and crochet, play musical instruments, etc.), go out on dates and have active social lives with a full weekly calendar of scheduled events. While several of our participants are retired, a number of you have chosen to continue your careers well into your 90s and travel into an office daily! Additionally, several long-lived participants have attributed their exceptional longevity to their strong faith and religion.

We continue to keep in touch with our participants by phone each year to obtain health status updates. Several participants, who we visited in 2006, have already completed their fourth year of annual follow-up surveys. We've discovered that our participants look forward to our annual correspondence and enjoy sharing new updates about their families, such as the birth of new grandchildren, great-grandchildren, and weddings.



The same new announcements and milestones have also occurred for the familiar faces of our research staff who visited with you and have communicated with you by phone. As of last year, Karen is the proud mom of a beautiful baby girl named Joanie. Sylwia held a beautiful wedding ceremony in September 2009, while Beth, Jeff, Jen, Jennifer, Julia, Mike, Nikki, Sana, Stephanie and Yilliam have each been pursuing professional or doctoral degrees in a medical/health-related field. One of our current research staff members, Katey, is planning to attend graduate school to become a physician assistant, while Evelyn, our newest hire, is looking forward to obtaining additional research experience by working on the LLFS study before applying to graduate school. In many cases, meeting you and your family members has further inspired them to continue working toward a health-related degree, and they have many fond memories of the home visits.

Our participants continue to be excited about their participation in the Long Life Family Study because they take great pride in their family's longevity and know that they are exceptional. It has been our pleasure to become acquainted with you and your family, and we look forward to maintaining our continued relationship, all with the hope of identifying ways to maintain a healthier, longer life for future generations! Many thanks to all of you and we will speak with each of you in the near future.

May 2011 be filled with peace and good health.

We want to take this opportunity to share some information about the LONG LIFE Family Study. We were very fortunate to enroll 1,310 people from 158 families through our field center in western Pennsylvania. Our oldest enrolled participants were 104 years at the time of their study visit and the youngest offspring was 36 years. One family had 36 family members participate, including 9 siblings ranging in age from 79 to 100. It is also interesting to note that we mailed almost 82,000 brochures to identify all of you!

Since this study began in 2006, our dedicated research team has spent countless hours on our highways and country roads conducting home visits in 24 counties in Pennsylvania, 39 counties in Ohio, 8 counties in West Virginia, and one county in both New York and Maryland. We were even invited to a family reunion and conducted study visits at the host hotel. What an enjoyable day for us. Further, 234 participants were seen on long distance trips! We traveled to Arizona (twice), California, Delaware, Florida (3 times), Georgia, Iowa, Kansas, Kentucky, Michigan, Minnesota, Nevada, New Mexico, South Carolina, Texas, Virginia, Washington, DC and Wisconsin. Participants from our Pittsburgh families were also visited by our colleagues. In fact, 192 people were seen in either the Boston or in the New York City local area or while they conducted long distance trips. We even did telephone visits with family members living in Australia and Japan (too bad we couldn't see them in person ☺)! Thank you everyone for opening up your homes to us, answering our questions over the phone and then getting your blood drawn/saliva samples mailed, or coming to see us at our health studies research center.



Happy holiday greetings from the research team at the **University of Pittsburgh!**



We were successful because of your efforts in encouraging your family members from near and far to participate.

All of the Long Life Family Study field centers have received new grant funding from the National Institute on Aging to continue telephone visits for 3 more years! So, expect to keep hearing from us through at least 2013! If you are in the older generation, we will continue to ask you a number of questionnaires every year. We know it gets frustrating answering the same questions over and over, but please bear with us, it is important to track this key information. If you are in the offspring generation, we only conduct the longer version of the telephone visit around the 3rd anniversary of your enrollment visit. So, some of you may have already reached that milestone and for others it will be coming up over the next few years. We truly appreciate the time that you give us to answer these questions, they are very important to the continued success of your Long Life Family Study.

LLFS investigators are currently examining the baseline data and we plan to share our findings with you on a regular basis via future newsletters. Please see Dr. Anne Newman's (the Pittsburgh Field Center Principal Investigator) article in this newsletter which shows that LLFS is exceptional.

We wish you a very happy and healthy new year and look forward to talking to each one of you in the coming year. In the meantime, feel free to call us just to say hello or to share any family news. We'd love to hear from you! We can be reached at 1-800-552-8140.

Together, we will understand the factors that protect against disease and disability and lead

to exceptional survival. Stay well and stay tuned!



And . . . from our Friends Across the "Pond" . . .

We at the **University of Southern Denmark** are very pleased that we are able to contribute to the LONG LIFE Family Study (LLFS), in collaboration with our US colleagues.

Over the past 20 years, our research unit, led by Kaare Christensen, Ph.D., DMsc., has studied human aging and longevity, and we are pleased to be able to provide our experience and expertise to the LLFS Project. We have, for instance, provided data on the life expectancy of twins, which has contributed to developing the basis of the criteria for selecting families for participation in the LLFS.

The Danish participants have been following the same protocol as those participants from the US, and in Spring 2009 we completed the in-home visit phase of the study. From Denmark, a total of 1268 persons and 76 different families participated in the study.

Denmark offers particularly good opportunities for carrying out research projects like the LLFS. The University of Southern Denmark is geographically situated in the middle of the country, namely in Odense, perhaps best known as the birth place of fairy tale writer Hans Christian Andersen. Denmark is considered a small country with a limited number of inhabitants (5.3 million), but our population does provide us with some unique advantages:



- (a) From the Danish national registers we have information about the place of residence and the age of all citizens of Denmark.
- (b) If a citizen moves to another residence, the new residence will immediately be recorded in the registers.
- (c) Regardless of where a participant is residing in Denmark, it seldom takes more than 3 hours by car from the University in Odense to get there.
- (d) Denmark has established national registers from which other information can be obtained, for instance, information about the participants' health.



One of the 76 Danish participating LLFS families. From this family 8 out of 9 siblings participate. At the time of participation in 2007, the siblings were between 75 to 98 years of age. On the photo the family is united during one of their annual joint picnics - © SDU.

Thus, we have been able to include families from every single part of Denmark in the LLFS. Furthermore, our intimate knowledge of the population demography ensures that it has been possible to enroll participants with a high average family selection score. It also means that relatively fewer Danish families were enrolled than families from each of the US Centers, because the Danish families are typically large. From several families over 25 individuals are participating, and from a single family as many as 79. This may prove important to the genetic studies that are carried out, among others, in the LLFS. It's also worth mentioning that during our study, we were introduced to a family with members at both sides of the Atlantic Ocean, thus participating both in Denmark and in Boston.



Your Feedback is Important!

As we conclude our first edition of the LONG LIFE Family Study Newsletter, we hope that you, our valued family members, enjoyed reading this information. It is our goal, as a Study Team, to provide a newsletter to you on a semi-annual basis. Therefore, we are very happy to receive any ideas, feedback or comments which you might want to provide. Since the newsletter is compiled at Washington University School of Medicine in St. Louis, with contributions from each of our Centers, please feel free to contact our Project Manager, Ms. Amy Sleeter, at longlifefamilystudy@gmail.com or by telephone at 1-877-362-2074.

Best Wishes for a Happy and Healthy 2011!