

Chapter 2 Recruitment

VISIT 3 PROCEDURES.

A. REORDERING FOLLOW-UP BY AGE AND HIGH LOD SCORE FAMILY APPROACH

Recognizing that mortality is high among the proband generation, preference for scheduling in person visits will follow the same approach as Visit 2. The schedule for the third in person visit will prioritize families based on the age of the oldest living individuals and contributing to the greatest number of LOD peaks. Those families with the oldest living members will attempt to be seen as a unit, or very close in time. To facilitate recruitment, the DMCC will send a suggested order of participant in-person visits to each field center. These lists are the preferred order; however, we realize that logistically it may not be possible to conform exactly to this order, and slight/moderate deviation from this preferred order is acceptable.

B. TIMING OF VISIT 3 IN RELATION TO VISIT 1 ANNIVERSARY DATE AND FOLLOW-UP

All participants have an anniversary date from their in-person or telephone Visit 1. This anniversary date is used for annual follow-up. Since the start date for Visit 3, as well as the order in which participants are seen is different from Visit 1, a strategy for incorporating Visit 3 and its follow-up is necessary to ensure that all participants have either an annual follow-up visit (Visit 3 follow-up) or a Visit 3 during each follow-up year in order to have complete data collection. Furthermore, if the new visit date for Visit 3 is less than ± 3 months from the participants' anniversary date, Visit 3 will replace the annual follow-up. **Figure A** lays out the three scenarios for Visit 3 and Visit 3 follow-up that may occur. In this table, the anniversary date is 6/1 (June 1). Each participant has a different estimated Visit 3 date. The acceptable date range (± 3 months) is based on the estimated Visit 3 date. If the anniversary date is before the visit range, participant A, this participant should have both a Visit 3 follow-up and then Visit 3 for that follow-up year. If the anniversary date is within the acceptable visit range (participant B), then they will only have an in-person Visit 3 that follow-up year. Lastly, if the anniversary date is after the acceptable visit range (participant C), the participant will have an in-person Visit 3 and then a V3 follow-up for that follow-up year. This will ensure that each participant is seen/followed annually and potentially will not be over burdened by participation in LLFS.

Visit 2 annual follow-up will continue for a participant up until the first day of Visit 3, expected June 1, 2020. Beginning on June 1, 2020, all participants will change to Visit 3 forms, both in-person and for annual follow-up. All Visit 3 follow-up visits will occur ± 1 month from the Visit 1 anniversary date.

Figure A. Examples of sliding window for Visit 3 based on Visit 1 anniversary date.

	Anniversary Date (Mon/Day)	Estimated Visit 3 Date (Mon/Day)	Acceptable Visit 3 Date Range (Mon/Day)	Resultant Visits During Year
Participant A	6/1	11/1	8/1-2/1	Visit 3 FU & Visit 3
Participant B	6/1	8/1	5/1 – 11/1	Visit 3
Participant C	6/1	2/1	11/1 – 5/1	Visit 3 & Visit 3 FU

C. RECRUITMENT OF THE GRANDCHILDREN GENERATION

At Visit 2, the Offspring generation was asked about their biological children using Panel 2a and its procedures outlined in the Visit 2 MOP Chapter 9. This allowed us to enumerate the number of potential US grandchildren of the proband generation available for possible recruitment during a Visit 3 funding cycle (Denmark has a more efficient way to enumerate their grandchildren). For US sites, Panel 2a should be retrieved from the Offspring participant files and can be used as an aid to help recruit the grandchildren generation. The DMCC will create and circulate by January 1, 2020 a Visit 3 preferred order recruitment list. This list will include all currently enrolled probands, offspring and enumerated grandchildren by family so we can take a family-based approach to the re-enrollment and new enrollment of grandchildren for Visit 3. Field Research staff will contact family members using a multi-pronged approach: 1) during the Visit 3 Annual Telephone Follow-up calls; 2) when contacting a proband or their proxy/study partner/LAR (who could be the grandparent or parent of an enumerated proband grandchild); 3) the parent(s) during another touch point. The methods for recruiting the proband grandchildren generation will be similar to the procedures from our original recruitment of other family members using a modified TS2 named the TS2-V3 and then TS1a-V3. See specific instructions below. Note: If spouses of the grandchildren express interest in participating, they should be screened with a TS1a-V3 using the procedures for recruiting spousal control participants using protocol described in Section D of this chapter.

Recruitment of a Proband Grandchild: Using the strategies outlined above, Research Staff will ask preferably the parent (but could contact other enrolled LLFS family members that seem to have a relationship with the enumerated proband grandchild) if they will contact the potentially interested proband grandchild to introduce the study. Full names and contact information will be obtained only for those proband grandchildren indicating a willingness to be contacted. These individuals will be contacted, and verbal consent will be obtained before the family members are screened as to their ability to participate. The contact and recruitment of proband grandchildren will be maintained on the TS2-V3.

INSTRUCTIONS FOR GRANDCHILDREN GENERATION CONTACT INFORMATION FORM (TS2-V3):

Instructions For Administration:

Recommended Resources: *Offspring's completed Panel 2a Interview from Visit 2.*

Enumerated proband grandchildren cannot be contacted without notification that they have agreed via another family member (likely the grandparent, parent, another sibling, etc). We use the TS2-V3 to track this effort. Thus, this form will be started with the proband grandchildren information that had been previously enumerated in Panel 2a that was collected from the offspring generation (the proband grandchild's parent).

The Panel TS2-V3 form should be completed for each enumerated proband grandchild.

Detailed Instructions:

Complete the name of the enrolled family member that you are speaking with regarding this form (also circle if the family member is from the proband or offspring generation). Note, if the parents and/or grandparents are deceased or withdrawn, ask the next of kin about ALL proband grandchildren (i.e. ask aunts/uncles). You should have a separate sheet (page 2) for each proband grandchild you are speaking with, and each grandchild generation participant should only be on one sheet (i.e. not a sheet from a grandparent and also a parent talking about the same proband grandchild, or a mother and a father talking with the same proband grandchild).

Question a. Complete the grandchild generation participant name (prefill from Panel 2a enumeration form).

Question b. Check the appropriate relationship of the grandchild generation participant to the offspring generation parent.

Question c. Check vital status of proband grandchild. If Deceased, go to Question h. If alive, go to Question d.

Question d. Ask enrolled family member speaking with if they have told the potential proband grandchild about LLFS. If yes, go to Question f, if no, please go to Question e.

Question e. For those proband grandchildren who have not been contacted, please indicate reason. This is important to track so you can follow-up, if applicable.

Question f. For those proband grandchildren who have been made aware about LLFS, you now need to document whether they are willing to be contacted. If yes, then proceed to Question i. If no, got to Question g.

Question g. Please ask enrolled family member speaking to for a reason why this proband grandchild is not interested in LLFS.

Question h. Fill in potential medical conditions for proband grandchildren that have passed away.

Question i. Please complete contact information and then proceed to contacting the proband grandchild for screening with the TS1a-gr.

TELEPHONE SCREENING INTERVIEW – Proband Grandchild (TS1a-V3):

Background and Purpose: At this time, you will be contacting those proband grandchildren who have provided verbal consent to be contacted. The purpose of this form is to document verbal consent from each proband grandchild and determine their eligibility to participate in LLFS Visit 3.

Detailed Instructions:

Confidentiality: Keep information obtained through these screening interviews separately from all other study data in a family file, as it contains identifiable information.

Interviewer Note: This interview entails calling a proband grandchild that has verbally consented to be contacted.

Interviewer Script: *Hi, my name is [insert your name here] and I am calling from [insert your institution here] about the LONG LIFE Family Study. We are attempting to learn why some families have more relatives living to a very old age than some other families. [Insert enrolled family member's name] told us that they spoke with you and that you are interested in learning more about participating in this family study. [Insert Proband's name] has lived a long life. That is why we are asking you to participate with [him/her] in an important international study of longevity. Your family has been involved in this study for over 10 years and now we have obtained new funding to enroll your generation. In addition to our university, this study is being conducted at two other American universities [insert names here], as well as at the University of Southern Denmark. Our goal is to find out what families with histories of long-lived individuals have in common. By participating in this study with your family members, you may have an opportunity to help improve the health of future generations.*

If it is okay with you, we have some questions we would like to ask you. Based on the telephone interview, some family members will be invited to participate in a more detailed part of this study. This would involve seeing you in person. You do not have to answer any questions that you do not want to. All information that I receive from you, including your name and any other identifying information, will be strictly confidential and kept in secure files. Your participation is voluntary; you do not have to answer these questions. This will take approximately 5-10 minutes. Is it okay to speak with you now?

Mark the "Yes" or "No" box. If no, determine a day and time when the proband grandchild can be called again to complete the screening interview

Question 1: Script: *"Do I have permission to ask you some questions about yourself"?* This interview should not_TRKOverview

The Long Life Family Study (LLFS), established in 2005 in response to an NIA RFA, enrolled families enriched for exceptional longevity (EL), to discover factors that contribute to healthy aging and survival. The “family longevity selection score” (FLoSS) was developed to select families with clustering of EL (Sebastiani et al. 2009). From 2006 to 2009, LLFS enrolled 539 sibships (G1, probands), their offspring (G2, offspring) and spouses (total 4,953). The probands were at least 78 years old in the US centers and 86 years old in Denmark. The families were selected to participate in the study based on The Family Longevity Selection Score (FLoSS), a score generated according to birth year cohort survival probabilities of the proband and their siblings. Probands and their families with FLoSS score of 7 or higher, at least one living sibling, and at least one living offspring (minimum family size of 3). Comparison with a referent cohort reveals that LLFS families have strong exceptional clustering of EL. The least exceptional LLFS G1 sibship shows more clustering of longevity than 99% of the Framingham Heart Study (FHS) sibships (Sebastiani et al. 2009). LLFS participants were comprehensively phenotyped by in-home visits (V1). The G2 offspring have a variety of Healthy Aging Phenotypes (HAPs), defined as an unusually low age-specific prevalence of one or more specific conditions or risk factors, compared to population-based cohorts suggesting enrichment of shared (possibly genetic) protective effects in LLFS families. There is considerable heterogeneity of HAPs in LLFS families: e.g. some show exceptional cognition (Barral et al. 2013); others show strong linkage to metabolic HAPs (An et al. 2013). Thus, LLFS is a unique resource for studying familial EL and its relationship to HAPs. In particular, G2 participants represent an unprecedented opportunity to prospectively study the progression of HAPs as related to survival in a cohort likely to show eventual higher EL prevalence.

The in-home visit consisted of demographic, anthropometric, cognitive, activities of daily living, ankle-brachial index, blood pressure, grip strength, pulmonary function measurements. Serum, plasma, lymphocytes, red cells, and DNA are stored for future studies. An array of biochemical assays were completed for Visit 1.

Establishment of the LLFS cohort

The original recruitment and examination for LLFS was conducted over a three-year period, April 2006 – May 2009. **LLFS successfully enrolled and extensively phenotyped 4,953 individuals from 539 two-generational families that demonstrated clustering for exception longevity in the upper generation from three US field sites (Boston University, Boston, MA; Columbia University, New York, NY; and University of Pittsburgh, Pittsburgh, PA) and one field site in Denmark (University of Southern Denmark, Odense, Denmark), Table 1.** These families included long-lived individuals (generally 90+), their siblings, spouses, offspring, and spouses of the offspring (a referent group). The LLFS has continued to recruit family members, growing to 5,097 participants (1,704 proband generation, ~1/3, and 3,393 offspring generation, ~2/3).

be administered until the prospective proband grandchild has agreed to answer the questions. If they do not agree, inquire as to an alternative time to contact them; if they still do not agree, then terminate the interview by thanking them for speaking with you.

Demographic Information:

Question 3: Age. Ask the proband grandchild if they are over age 18.

Assessment of Understanding of LLFS: This section asks the participant to provide a brief statement of their understanding of the purpose of the LLFS, in order to determine their ability to provide informed consent.

Interviewer Script for Those Continuing: *Before we continue, I want to ask you what is your understanding of the purpose of the LONG LIFE Family Study?*

Question 9a-9b: Write in the participant's response. Any references to family, living long or research is fine. Interviewer then marks the appropriate box in Question 9b as to their judgment whether the potential participant comprehends the study. If the potential participant clearly does not comprehend the study, end the interview using the **Script B**.

Script B – End Interview: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age." END OF INTERVIEW*

Question 9c: Interviewer does not ask the next question but assesses the potential participant's ability to communicate. If the participant is hard of hearing or cannot talk clearly or does not seem to understand the questions the interviewer should mark "YES" and terminate the interview using **Script B**.

Script B – End Interview: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age." END OF INTERVIEW*

Script for those who can continue: *Thank you for answering our questions. The information you provided is very helpful. At this point, we would like to invite you to participate in an in-person visit so that we can gather more information about your health and find out what common traits are present in families with long-lived individuals. This interview can be scheduled at your convenience either in your home or at our clinic. During the visit, trained clinical staff will obtain medical and personal information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, arm and leg blood pressures, carotid arteries, and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function, and a one-minute chair stand test for fitness. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed approximately 3-4 hours. We will use all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.*

Question 10a: *In-Person Visit.* If the Screenee answers "YES" to Question **10a**, then proceed to Question 10c. The option "No" should only be used if the Screenee clearly expresses that there is no way that they would be involved in this study. If so, then proceed to Question 10b. If "Don't know" is marked, the Recruiter should call back the potential participant at a later time after materials have been sent and/or the Screenee had the chance to think about the study.

Question 10b: *Refuses.* Check the answer that best fits their reason for refusing participation and then end the Interview using the End Interview Script provided. If the Recruiter feels that the Screenee's concerns can be addressed, they should try to do so. If the individual is refusing due to not willing to provide a blood draw, they should be asked if they are willing to provide a saliva sample. If the Recruiter deems that the Screenee is unsure after further discussion they can check "Don't know" and probe for the reason that the person is unsure. It is up to the Recruiter to do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website.

Question 10c: *Location of In-Person Examination.* Mark whether the Screenee prefers a home or clinic in-person examination. If Screenee chooses 'home' or 'clinic', proceed with scheduling the visit. Start a panel 14, participant contact information for the grandchild, verifying their name, address, and phone number for their upcoming visit. If they provide a response to the 'other' option, ask Q10d to provide the option of a Telephone Visit.

Suggested Script for Scheduling/Confirming Appointment: *"We are currently scheduling in-person visits for the week of _____. Are you available on _____? (Work with participant to schedule a convenient time.) The visit will take about 3-4 hours to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the visit. Do you have any questions at this time? We will call you the day before your visit to confirm the date and time. The visit will take under four hours to complete. Do you have any questions at this time?"*

*We are very excited about meeting you in-person on _____ [day/date] at _____ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

If the proband grandchild that you are screening lives out of town, and requests a long distant visit or will be visiting the area in the future, mark "Other" and specify the location of the long distant visit (City/State) or a projected date to follow-up with the individual as to when they will be in the area. Please end the interview for those desiring a long distant visit with the following script, "***We will follow up with you as soon as possible to update you when we will be in your area.***"

Question 10d: Telephone Visit. This is asked to provide the Screenee the option of a combination Telephone Interview(s), Mailed Questionnaires and a remote blood collection or provide a sample avoiding a clinic or in-person examination. If they answer "Yes", confirm that you will call them at the current number you reached them at (documenting it on Panel 14, participant contact information), confirm where to send the instructions sheet (record on Panel 14), and then proceed with the **Telephone Visit Script:**

Telephone Visit Script: *"We are currently scheduling telephone visits for the week of _____. Are you available on _____? (Work with participant to schedule a convenient time.) The call will take about _____ [minutes/hours] to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the call. Do you have any questions at this time?"*

*We are very excited to talk to you on _____ [day/date] at _____ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye. **END OF INTERVIEW***

Question 10e: If the Screenee answers "NO" to Q10d, then ask Q10e and proceed with the **End Interview Script:**

End Interview Script: *"Thank you so much for the information you have provided. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age. If you decide at a later date that you would like to participate in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

Spousal contact information. If, during the screening interview, a grandchild says their spouse would like to participate, record that information in this section of the TS2-V3. Then, proceed to screening the spouse control using the protocol detailed in Section D for completing a TS1a-V3.

D. RECRUITMENT OF NEW FAMILY MEMBERS AND SPOUSE CONTROLS (including grandchildren generation spouses)

We will not actively recruit additional family members and/or their spouses, including grandchildren spouses, unless additional family members express interest in joining the study. These individuals should be screened using the TS1a-V3 for new family members or for new spousal controls. Details on how to complete these forms can be found below and follows similarly to the instructions for completing the TS1a-V3. Their interest in the study should be documented on the TS2-V3 using the correct relationship.

LLFS TELEPHONE SCREENER – NEW FAMILY MEMBERS (TS1a-V3):

Background and Purpose: At this time, you will be contacting those family members who have provided verbal consent to be contacted. The purpose of this form is to document verbal consent from each family member and determine their eligibility to participate in LLFS Visit 3. Note: This Panel is only used if additional family members are enrolled – it is not used for the grandchild generation or spouse controls. This

form will likely be rarely used in Visit 3 as we are not actively enrolling other new family members unless they initiate the request to participate.

Detailed Instructions:

Confidentiality: Keep information obtained through these screening interviews separately from all other study data in a family file, as it contains identifiable information.

Interviewer Note: This interview entails calling a family member that has verbally consented to be contacted.

Interviewer Script: *Hi, my name is [insert your name here] and I am calling from [insert your institution here] about the LONG LIFE Family Study. We are attempting to learn why some families have more relatives living to a very old age than some other families. [Insert enrolled family member's name] told us that they spoke with you and that you are interested in learning more about participating in this family study. [Insert Proband's name] has lived a long life. That is why we are asking you to participate with [him/her] in an important international study of longevity. In addition to our university, this study is being conducted at two other American universities [insert names here], as well as at the University of Southern Denmark. Our goal is to find out what families with histories of long-lived individuals have in common. By participating in this study with your family members, you may have an opportunity to help improve the health of future generations.*

We have already spoken with [insert Proband's name] about your family, but if it is okay with you, we have some questions we would like to ask you. Based on the telephone interview, some family members will be invited to participate in a more detailed part of this study. This would involve seeing you in person. You do not have to answer any questions that you do not want to. All information that I receive from you, including your name and any other identifying information, will be strictly confidential and kept in secure files. Your participation is voluntary; you do not have to answer these questions. This will take approximately 5 minutes. Is it okay to speak with you now?

Mark the "Yes" or "No" box. If no, determine a day and time when the proband grandchild can be called again to complete the screening interview

Question 1: Script: *"Do I have permission to ask you some questions about yourself?"* This interview should not be administered until the prospective family member has agreed to answer the questions. If they do not agree, inquire as to an alternative time to contact them; if they still do not agree, then terminate the interview by thanking them for speaking with you.

Demographic Information:

Question 3: Age. Ask if participant is over 18 years old. **Assessment of Understanding of LLFS:** This section asks the participant to provide a brief statement of their understanding of the purpose of the LLFS, in order to determine their ability to provide informed consent.

Interviewer Script for Those Continuing: *Before we continue, I want to ask you what is your understanding of the purpose of the LONG LIFE Family Study?*

Question 9a-9b: Write in the participant's response. Any references to family, living long or research is fine. Interviewer then marks the appropriate box in Question 9b as to their judgment whether the potential participant comprehends the study. If the potential participant clearly does not comprehend the study, end the interview using the **Script B**.

Script B – End Interview: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age."* **END OF INTERVIEW**

Question 9c: Interviewer does not ask the next question but assesses the potential participant's ability to communicate. If the participant is hard of hearing or cannot talk clearly or does not seem to understand the questions the interviewer should mark "YES" and terminate the interview using **Script B**.

Script B – End Interview: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age."* **END OF INTERVIEW**

Script for those who can continue: *Thank you for answering our questions. The information you provided is very helpful. At this point, we would like to invite you to participate in an in-person visit so that we can gather more information about your health and find out what common traits are present in families with long-lived individuals. This interview can be scheduled at your convenience either in your home or at our clinic. During the visit, trained clinical staff will obtain medical and personal information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, arm and leg blood pressures, carotid arteries, and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function, and a one-minute chair stand test for fitness. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed approximately 3-4 hours. We will use all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.*

Question 10a: In-Person Visit. If the Screenee answers "YES" to Question 10a, then proceed to Question 10c. The option "No" should only be used if the Screenee clearly expresses that there is no way that they would be involved in this study. If so, then proceed to Question 10b. If "Don't know" is marked, the Recruiter should call back the potential participant at a later time after materials have been sent and/or the Screenee had the chance to think about the study.

Question 10b: Refuses. Check the answer that best fits their reason for refusing participation and then end the Interview using the End Interview Script provided. If the Recruiter feels that the Screenee's concerns can be addressed, they should try to do so. If the individual is refusing due to not willing to provide a blood draw, they should be asked if they are willing to provide a saliva sample. If the Recruiter deems that the Screenee is unsure after further discussion they can check "Don't know" and probe for the reason that the person is unsure. It is up to the Recruiter to do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website.

End Interview Script: *"Thank you so much for the information you have provided. We greatly appreciate the time and interest you have shown in our study. If you decide at a later date that you would like to participate*

*in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

Question 10c: Location of In-Person Examination. Mark whether the Screenee prefers a home or clinic in-person examination. If Screenee chooses 'home' or 'clinic', proceed with scheduling the visit. Begin a Panel 14, participant contact information using the information from their spouse and verify the address of the home visit and their telephone number. If they provide a response to the 'other' option, ask Q10d to provide the option of a Telephone Visit.

Suggested Script for Scheduling/Confirming Appointment: *"We are currently scheduling in-person visits for the week of _____. Are you available on _____? (Work with participant to schedule a convenient time.) The visit will take about 3-4 hours to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the visit. Do you have any questions at this time? We will call you the day before your visit to confirm the date and time. The visit will take under four hours to complete. Do you have any questions at this time?"*

*We are very excited about meeting you in-person on _____ [day/date] at _____ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

If the family member that you are screening lives out of town, and requests a long distant visit or will be visiting the area in the future, mark "Other" and specify the location of the long distant visit (City/State) or a projected date to follow-up with the individual as to when they will be in the area. Please end the interview for those desiring a long distant visit with the following script, **"We will follow up with you as soon as possible to update you when we will be in your area."**

Question 10d: Telephone Visit. This is asked to provide the Screenee the option of a combination Telephone Interview(s), Mailed Questionnaires and a remote blood collection or provide a sample avoiding a clinic or in-person examination. If they answer "Yes", start a panel 14 using information gathered from their spouse and confirm where to send the information packet and forms, and the correct contact telephone number for the interview; then proceed with the **Telephone Visit Script:**

Telephone Visit Script: *"We are currently scheduling telephone visits for the week of _____. Are you available on _____? (Work with participant to schedule a convenient time.) The call will take about _____ [minutes/hours] to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the call. Do you have any questions at this time?"*

*We are very excited to talk to you on _____ [day/date] at _____ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye. **END OF INTERVIEW***

Question 10e: If the Screenee answers "NO" to Q10d, then ask Q10e and proceed with the **End Interview Script:**

End Interview Script: *"Thank you so much for the information you have provided. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age. If you decide at a later date that you would like to participate in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW***

Spousal contact information. If, during the screening interview, the family member says their spouse would like to participate, record that information in the appropriate section of the TS2-V3. Then, proceed to screening the spouse control using the protocol detailed below.

SELECTION OF CONTROL INDIVIDUALS

The following protocol has been established for recruitment of controls:

- There are no selection criteria for interested spouses.
- Spouses will be administered the Telephone Screener to assess their willingness and feasibility of conducting the in-person visit (See detailed instructions for administering TS1a-V3 below).
- Spouses will undergo the complete protocol as the Proband and his/her enrolled family members.

LLFS TELEPHONE SCREENER – CONTROL SUBJECTS (TS1a-V3):

Background and Purpose: At this time, you will be contacting an interested spouse of an LLFS participant that was identified on the TS2-V3. The purpose of this form is to document verbal consent from this individual to participate in the Study, conduct a basic check of their health status to determine study eligibility, and confirm their willingness to participate. Once this has been accomplished, eligible spouses will be invited to participate in an in-person visit, and an enrollment visit should be scheduled, generally, at the same time as the family member to whom they are married.

Detailed Instructions:

Confidentiality: Information obtained through these screening interviews is to be kept separate from all other study data, as a participant’s written consent form has not yet been signed.

Interviewer Note: This interview entails calling a spouse of an enrolled family member, who has been identified and verbally consented to contact by the previously screened family member.

Interviewer Script: *Hi, my name is [insert your name here] and I am calling from [insert your institution here] about the Long Life Family Study. We are attempting to learn why some families have more relatives living to a very old age than some other families. Your [husband / wife] [Insert spouse’s name] told us that they spoke with you and that you are interested in learning more about participating in this study. Your [husband / wife] belongs to family we believe has had the good fortune have many members living long and health lives. Because your [husband / wife] is participating in this important international study of longevity, we would like to invite you to participate as well. In addition to our university, this study is being conducted at two other American universities [insert names here], as well as at the University of Southern Denmark. Our goal is to find out what families with histories of long-lived individuals have in common. By participating in this study with your family members, you may have an opportunity to help improve the health of future generations.*

If you choose to participate in our study, we would arrange to see you in person. For now, we have some questions we would like to ask you. You do not have to answer any questions that you do not want to. All information that I receive from you, including your name and any other identifying information, will be strictly confidential and kept under lock and key. Your participation is voluntary; you do not have to answer these questions. This will take approximately 15 minutes. Is it okay to speak with you now?

Mark the "Yes" or "No" box to indicate whether or not the screener agrees to proceed with the interview at this time. If no, determine a day and time when the family member can be called again to complete the screening interview

Question 1: *"Do I have permission to ask you some questions about yourself?"* This interview should not be administered until the prospective participant has agreed to answer the questions. If they do not agree, inquire as to an alternative time to contact them; if they still do not agree, then terminate the interview by thanking them for speaking with you.

Demographic Information:

Question 3: Age. Ask the participant if they are over age 18 years.

Key Elements/Assessment of Understanding of LLFS: This section asks the participant to provide a brief statement of their understanding of the purpose of the LLFS, in order to determine their ability to provide informed consent.

Interviewer Script for Those Continuing: *Before we continue, I want to ask you what is your understanding of the purpose of the LONG LIFE Family Study?*

Question 9a-9b: Write in the participant's response. Any references to family, living long or research is fine. Interviewer then marks the appropriate box in Question 9b as to their judgment whether the potential participant comprehends the study. If the potential participant clearly does not comprehend the study, end the interview using the **Script B**.

Question 9c: Interviewer does not ask the next question but assesses the potential participant's ability to communicate. If the participant is hard of hearing or cannot talk clearly or does not seem to understand the questions the interviewer should mark "YES" and terminate the interview using **Script B**.

Script B – End Interview: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age. Take care."* **END OF INTERVIEW**

Interviewer Script: *Thank you for answering our questions. The information you provided is very helpful. At this point, we would like to invite you to participate in an in-person visit so that we can gather more information about your health and find out what common traits are present in families with long-lived individuals. This interview can be scheduled at your convenience either in your home or at our clinic. During the visit, trained clinical staff will obtain medical and personal information about you. You will be asked to answer questions related to your current and past medical history, medication use, daily living activities, physical activity as well as your health habits. You will also be asked questions such as how many years of education you have had and where you were born and your occupation. Other questionnaires will include paper and pencil tests of your ability to process and recall information and a mood/personality assessment. With your permission, we will obtain measurements of your weight, height, waist circumference, heart rate, arm and leg blood pressures, carotid arteries, and lung function. You will also be asked to perform some simple physical tasks such as standing up from of a chair, gripping an object to measure hand strength and walking a short distance to assess your physical function, and a one-minute chair stand test for fitness. Additionally, you will be asked to perform a series of movements to test your balance. You will be asked if we can collect a small blood sample. This examination can be completed approximately 3-4 hours. We will use*

all this information to determine the different ways in which families can achieve long lives and successful aging. You may refuse to participate in any portion of the study.

Question 10a: *In-Person Visit.* If the Spouse answers "Yes" to **Q10a**, then proceed to **Q10c**. The option "No" should only be used if the Spouse clearly expresses that they are unwilling to participate in the study, including the blood draw. If so, then proceed to **Q9b**. If "Don't know" is marked, the Recruiter should call back the potential participant at a later time after materials have been sent and/or the Spouse had the chance to think about the study.

Question 10b: *Refuses.* Check the answer that best fits their reason for refusing participation and then end the Interview using the End Interview Script provided. If the Recruiter feels that the Spouse's concerns can be addressed, they should try to do so. If the Recruiter deems that the Spouse is unsure after further discussion they can check "Don't know" and probe for the reason that the person is unsure. It is up to the Recruiter to do his/her best to allay the fears/concerns of the potential participant by further explaining the study procedures and/or sending them more information (i.e., the Frequently Asked Questions) or directing them to the study website.

End Interview Script: *"Thank you so much for this information. We greatly appreciate the time and interest you have shown in our study. The information you provided is very important and will help us discover how some people and their families live to a very old age. If you decide at a later date that you would like to participate in this family study, please contact me at XXX-XXX-XXXX. Thank you and good-bye."* **END OF INTERVIEW**

Question 10c: *Location of In-Person Examination.* Mark whether the Spouse prefers a home or clinic in-person examination. If Spouse chooses 'home' or 'clinic', proceed with scheduling the visit. Begin a Panel 14, participant contact information using the information from their spouse and verify the address of the home visit and their telephone number. Be sure to try to coordinate with the preferences and scheduling of their spouse's assessment visit.

Suggested Script for Scheduling/Confirming Appointment: *"We would like to see you and your husband/wife together. He/she is scheduled for _____. Are you available that day? (Work with subject to schedule a convenient time.) The visit will take under 4 hours to complete. We will be mailing to your home a reminder letter and instruction sheet, prior to the visit. Do you have any questions at this time? We will call you the day before your visit to confirm the date and time. The visit will take under three hours to complete. Do you have any questions at this time?"*

We are very excited about meeting you and your husband/wife in-person on _____ [day/date] at _____ o'clock. If you have any questions or something comes up and you need to reschedule, please call me at XXX-XXX-XXXX. Thank you and good-bye." **END OF INTERVIEW**

E. CHANGE IN STATUS OF SPOUSAL CONTROLS

All spousal controls should be invited to participate in the in-person Visit 3. New spouses (multiple spouses due to change in marital status are allowed) in both the proband and offspring generations that express interest should be invited to participate using procedures described above. All spouse controls formerly assessed should be included, even if their status has been changed by separation, divorce, or death of their partner, since the primary outcome variables for analysis will be change scores in a wide variety of phenotypes. The interviewers should ascertain the status of the spousal control during the ongoing follow-up

phone interview or at the time of the phone call to initiate the 3rd in-person visit. If the spouses' status has changed, the interviewers should obtain contact information from the participant and call the spouse to ask if they are willing to continue in the study.

Study Documents Referred to in this Chapter:

- Panel 2A from Visit 2
- LLFS Relative Contact Information Form (TS2-V3)
- LLFS Telephone Screener (TS1a-V3)
- Panel 14, Participant Contact Information