Chapter 18

Participant Follow-Up (Phase 6 and 7)

Phase 6 of the LLFS will begin September 1, 2014. An Exam 2 in-person visit may be substituted for one annual telephone follow-up. Visits will be prioritized with a preference to see the oldest participants first along with other relatives in the same area who can be tested at the same time. In the follow-up year in which Exam 2 is completed Panels 1-15 will be administered via telephone or in-person during the exam. If this visit is within ±3 months of the participants' anniversary date from the first in person visit, then this second in person visit will replace Panel 16, Annual Follow-Up. If the second in person visit is not within the ±3 month anniversary window, the participant will complete both the second in person visit and will also complete Panel 16 when they enter their usual follow-up window. For all other follow-up years the participant will complete Panel 16 Annual Follow-Up as described in Participant Follow-Up (Phase 4, Visit 1 MOP Chapter 18). Offspring over the age of 70 will convert to the extended follow-up on a yearly basis instead of every three years.

Continued follow-up by telephone is important for tracking changes in functional status, onset of disease, and monitoring vital status of study participants. Administration of the extended follow-up including the medical history update is intended to add new diagnoses to the health record rather than to repeatedly capture previously reported medical conditions.

If a participant misses a telephone follow-up or the telephone follow-up is replaced by the second in person visit, the annual follow-up panel (panel 16) in REDCap should be completed using the date and the reason for non-completion (K for missing or H for in person visit replaces follow-up). The DMCC will then use this information and fill out the non-completion reason for all other forms that should be included in that follow-up telephone call.

Additions to Panel 16-Follow-Up Questionnaire

Additions to Panel 16 were made to collect information on indicators of changes in functional status as well as to harmonize with Framingham Heart Study data collection. The following fields were added:

- Q2a-f, Panel 16. Modified to obtain disease specific information about hospitalizations. This is to assist in recall and allowing LLFS to request the appropriate medical record documentation for each condition.
- Q3d, Panel 5-II. Have you fainted or lost consciousness in the past year?
- Q3e, Panel 5-II. How many times have you fainted or lost consciousness in the past year?
- Q3c, Panel 16. We now collect more detailed information about additional hospitalizations.
- Q10d, Panel 16. Have you been admitted to a nursing home (or skilled facility) in the past year?
- Q10e, Panel 16. What is your current housing situation?
- Panel 5-II. Discomfort in the calf while walking (claudication) was added to the list of medical conditions.

Changes to procedure in Phase 6:

- Hospitalizations should only refer to overnight hospital stays as indicated by the revised wording of Q3a: "Have you been hospitalized overnight in the past year?"

Some medical conditions were amended as follows:

- High Blood Pressure ➔ High Blood Pressure or Hypertension
- Chest Surgery ➔ Chest Surgery or Abdominal Surgery

Some medical conditions that were previously listed as "Condition X or Condition Y" have now been separated as individual incidents for reporting. The following medical conditions were separated:

- Atrial Fibrillation/Pacemaker ➔ Atrial Fibrillation
  Pacemaker
- Deep Vein Thrombosis (or blood clots in legs) or Pulmonary Embolism (blood clot in lung) ➔ Deep Vein Thrombosis (blood clots in legs)
  Pulmonary Embolism (blood clot in lung)
- Rheumatic Fever or Heart Valve Problems ➔ Rheumatic Fever
  Heart Valve Problems
- Depression or Anxiety ➔ Depression
  Anxiety
- Blood Cancer, Leukemia, or Lymphoma ➔ Blood Cancer or Leukemia
  Lymphoma

*New medical conditions (claudication) and newly itemized medical conditions will need to be assessed for lifetime onset at the first administration of Panel 5 or Panel 5-II either at the in-home visit or the first extended telephone follow-up after September 1, 2014. These conditions are indicated by a * on Panel 5 and Panel 5-II.

The hospitalization coding table has been updated to reflect the division of the above medical conditions.

HOSPITALIZATION CODING

a. Heart Disease	
Myocardial Infarction or Heart Attack	A1
Coronary Angioplasty or Coronary Artery Bypass Grafting (CABG)	A2
Heart Failure or Congestive Heart Failure	A3
Atrial Fibrillation	A4a
Pacemaker	A4b
Deep Vein Thrombosis (blood clots in legs)	A5a
Pulmonary Embolism (blood clot in lung)	A5b
Rheumatic Fever	A6a
Heart Valve Problems	A6b
High Blood Pressure or Hypertension	A7
Other	A8
b. Stroke	
Stroke or Cerebrovascular Accident	B1
Transient Ischemic Attack (TIA) or Mini-Stroke	B2
Other	B3

c. Lung Disease	
Asthma	C1
Chronic Bronchitis	C2
Emphysema or Chronic Obstructive Pulmonary Disease (COPD)	C3

Pneumonia	C4
Pulmonary Fibrosis	C5
Chest Surgery or Abdominal Surgery	C6
Other	C7
d. Arthritis	
Arthritis of the Knees, Hips or Spine	D1
Other	D2
e. Endocrine/GI/Kidney	
Diabetes	E1
Thyroid Disease	E2
Osteoporosis	E3
Chronic Liver Disease, Cirrhosis, or Hepatitis	E4
Kidney (Renal) Disease or Failure	E5
Other	E6
f. Neurological	
Alzheimer's Disease or Dementia	F1
Parkinson's Disease	F2
Depression	F3a
Anxiety	F3b
Other	F4
g. Cancer	
Breast Cancer	G1
Blood Cancer or Leukemia	G2a
Lymphoma	G2b
Colon (Bowel) or Rectal Cancer	G3
Lung Cancer	G4
Malignant Melanoma	G5
Other Skin Cancer	G6
Esophageal Cancer	G7
Pancreatic Cancer	G8
Other Cancer	G9
Prostate Cancer	G10
Enlarged Prostate, not cancer	G11

j. Fractures	
Hip	J1
Wrist or Forearm	J2
Spine	J3
Other	J4
k. Other Illnesses not listed above	K1

Clarifications about administration of the annual follow-up questionnaire:

- Diagnoses of medical conditions refer only to those conditions that have been diagnosed FOR THE FIRST TIME since the previous administration of the Medical History. Recurrences of medical conditions such as depression should not be recorded if they have been previously noted. Subsequent episodes of medical conditions should not be reported (e.g., a second heart attack).

- Cataracts – If the participant has already reported cataract surgery in one eye and now reports cataract surgery in the second eye, then mark as Cataract Surgery in Both Eyes.

- Discrepancies in participant reported age of diagnosis should not be corrected in subsequent years. Age of diagnosis is considered to be most valid at the earliest reported time point (i.e., the first year reported).

DEMENTIA QUESTIONNAIRE (DQ) AMENDMENTS

- Administration of the DQ during extended follow-ups will provide information for analyzing the onset and course of cognitive impairment in our study cohort. Information collected during an extended follow-up should refer to changes since the most recent administration of the DQ. Starting September 1, 2014 the CDR Panel will be filled out by the research assistant following administration of the DQ. Please see Chapter 11 for CDR administration guidelines.
- The DQ should be given to an informant that is identified by the participant. As of January 2019, the DQ will be administered on a limited basis as follows:

  - 1) The DQ will be NOT be administered to individuals considered to be cognitively normal. It will only be administered when participants score **< 27 on the MMSE (or TICS Total Score (not including Q12) < 31 for annual phone follow-ups)** OR when the examiner is concerned about the participant's level of cognitive functioning.
    See Figure at end of Chapter for detailed instructions on when to administer the DQ.

    2) The DQ will NOT be collected in individuals who have previously endorsed "Yes" to at least 3 of the first 6 DQ items o*n two consecutive* DQ assessments.

    3) The DQ should not be administered more than once every 6 months.

Due to variations in administration of the DQ identified during data cleaning, modifications to the DQ have been made.

Note: Prior to March 2014 each site was administering the DQ according to different rules as stated below:

Boston: Research assistants at Boston were indicating "Yes" for any symptom positively endorsed on the DQ regardless of the underlying etiology. For Daily Functioning questions, items that were positively endorsed but due only to sensory or physical impairments rather than cognitive impairments were marked as "Yes" and a notation was made in the Notes and Examples box under Q22. If no Memory/Cognition or Expression items were endorsed and Daily Functioning items were endorsed only due to sensory or physical impairments, then the Recognition of Problem questions were not administered as the participant was not determined to have a cognitive problem.

Columbia: Research assistants at Columbia were indicating "Yes" for any symptoms positively endorsed on the DQ regardless of the underlying etiology. Recognition of Problem questions were administered whenever a symptom was positively endorsed on all preceding questions regardless of etiology.

Pittsburgh: Research assistants at Pittsburgh were indicating "No" for symptoms that were present in the participant but due only to sensory or physical impairment rather than cognitive impairment. Recognition of Problem questions were not administered as the lack of an endorsed symptom would have triggered the skip pattern.

Clarification of administration procedures at this point:

- Follow-up DQ administrations should refer to changes in cognitive function since the previous administration of the DQ. A second note to interviewer had been added to the instructions to clarify this.

  Change to DQ Panel: Added "Note to Interviewer: If this is a repeat follow-up, then add: 'We are interested in your perspective on [participant's name] changes since we last interviewed you on [insert date of last interview].'"

- The date/age of onset for memory/cognition questions (Q1-7) and expression questions (Q10-12) should not be recorded if it has already been indicated on a previous DQ. Q8 "Did the trouble begin suddenly" should not be administered if it has already been recorded on a previous DQ.

- ADL questions (Q13-20) refer to problems caused by sensory/physical impairments as well as cognitive impairments and should be coded as "Yes". The cause of the daily functioning problem (e.g., participant is blind but knows how to dress him/herself), if known by the informant, should be noted in the "Notes and Examples" section after Item 20.

Change to DQ Panel: Added note to interviewer under Daily Functioning section of the DQ form. "Note to Interviewer: Indicate 'Yes' for problems due to physical, sensory, and/or cognitive impairments." An option was added for the interviewer to indicate the cause of deficits in daily functioning. Interviewers can choose from "sensorimotor", "cognitive", "both", "other", or "unknown".

- Q16b (retired) and Q30 (drives) may be omitted if it has already been recorded that the participant has retired and stopped driving, respectively. If retirement has been previously recorded, the interviewer skips to Q17. If driving cessation has been previously recorded, the interviewer skips to Q36.

- Recognition of Problem section (Q21-25b) should not be asked for participants who have a problem on Items 13-15 or 16c-20 that is due only to sensory or physical impairments (i.e. no cognitive impairment), as the Recognition of Problem questions are not typically relevant to sensory- or physically-based impairments.

Change to DQ: Change note to interviewer from "Interviewer Note: If the participant has answered "YES" to any of Q1-7 or Q10-20 above, ask Q21-25b; if all responses above are "NO", skip to Q26a." to "Interviewer Note: If the informant has answered "YES" to any of Q1-12 above, ask Q21-25b below. If the informant has answered "NO" to Q1-12 and answered "YES" to Q13-15 or 16c-20 above not due solely to sensory or physical impairment, ask Q21-25b; otherwise, skip to Q26a." If Recognition of Problem questions have been previously recorded, the interviewer skips to Q26a.

- Items 26k and 26l should not be asked for participants who do not have memory loss. If Q1-12 are answered as "No" and Q13-15 or 16c-20 are answered "Yes" only due to sensory or physical impairment then these items are not relevant as there is no memory loss.

Changes to DQ: Change note to interviewer from "Interviewer Note: If there is both stroke (Q26a=Yes) and memory loss (Any of Q1-7 or Q10-20=Yes), explain that they are..." to "Interviewer Note: If there is both stroke (Q26a=Yes) and memory loss (Any of Q1-12=Yes or any of Q15 or 16c-20=Yes and is not due only to sensory or physical impairment), explain that they are..." If Q26k and Q26l have been previously recorded, the interviewer skips to Q27a.

- In a repeat administration of the DQ, Q27a "Since [date of last interview] does [participant name] have a drinking problem or a history of alcoholism?" refers only to changes since the previous administration of the DQ. Therefore, the phrase "history of alcoholism" should be replaced with "alcoholism".

- A skip pattern to omit Q37 "most frequent type of contact" was added for responses of "Live together for Q36 as it can be assumed that the most frequent type of contact is "Mostly In-Person for Q37.

Administration of the DQ

Before presenting Item 1 say: *"You have been identified by* [participant's name] *as someone who would be able to answer questions about his/her health and well-being. I would like to ask you some questions about* [participant's name] *memory and other health related items that may interfere with his/her daily living. The reason we are asking these questions is so we can get another perspective on [participant's name] health and well-being."* If this is a repeat follow-up, then add that we are interested in your perspective on [participant's name] changes since we last interviewed you on [insert date of last interview].

Note: For each question on the DQ, it is important to emphasize that we are most concerned about problems that are out of the ordinary for the participant as they relate to the course of his/her *entire lifetime*. For example, an informant answering questions about his/her 100-year-old relative may respond that difficulty with memory is "normal" for all 100-year-olds and, therefore, does not constitute a problem. While memory problems may not be out of the ordinary in terms of the participant's recent lifetime, they may be out of the ordinary in terms of the participant's entire lifetime. Therefore, the interviewer should probe for as much information as possible in order to determine whether the participant's problems are truly out of the ordinary for him/her and constitute a problem.

- Item 1: Memory Problem.
  - Ask: "***Does [participant's name] have any problems with his/her memory*?**" Mark the informant's answer, Yes or No. If the informant reports Yes, go on to ask about the date or age of onset (or indicate if it has already been recorded) and the other details.○ If the date/age of onset has not already been recorded, ask: ***"Around what time would you say this started?"*** Record the date in the space provided - Month and Year.
    - Informants rarely have an exact date that they can provide for this answer. However, you must use your interviewing skills to help them. Using events or holidays as benchmarks may help the informant. However, if the problems began after a stroke or some other event or accident, the exact date may be able to be produced. If they come up with a month, ask them if the problems began in the beginning, middle, or end of the month. If they come up with the year, help to narrow it down to the month or season. You may have to write in the margins to help record what is reported.
    - If an exact date is not possible to pin down, but you are able to get month and year, record the 15th of the month.
    - If the informant is able to narrow it down to a year, record June 15th of that year.
    - If the informant is able to narrow it down to a couple of years, choose the midpoint.
  - State: "***You said that their memory has not been the same since* [date of onset]. *Can you describe what kinds of problems they have been having with their memory?"*** Attempt to obtain as many details and descriptions as possible about the nature of the memory problems, and the effect they have had on the participant's life.
  - Ask: "***Who first noticed their memory problem(s)?"*** Record the relationship of the person to the participant and the circumstances surrounding the time in which they first noticed the problems.
- Continue with Items 2-7, asking: "***Does (participant's name) have any problems with_____ that interferes with daily living*?"** Mark the informant's answer, Yes or No.
  - Ask for an example for each item to which they respond "Yes".
  - If the informant reports "Yes", proceed with inquiring about the date of onset or age of onset (or indicate if it has already been recorded) and other details and examples.
- Item 8. Ask: ***"Would you say that these problems started all of a sudden or gradually (slowly)?"*** Circle the informant's answer and describe any details about the course of the problems that are provided. Note whether Q8 has already been recorded in previous administration of the DQ.
- Item 9: Ask: "***Would you say that there has been a steady decline in his/her memory since* [date of onset]*? Or has* [his/her] *memory been worse since* [date of onset] *and remained stable, or at the same level? Has there been further decline in memory since* [date of onset] *that is not***

gradual, but stepwise, like drops all of a sudden, then stable, then another drop…" Each of these questions try to probe into the course of the decline. Record the description that the informant agrees with and any details they provide you about the course of their memory problems.

- Examples on how to answer number 9:
  - Ask: ***"Would you say that the memory problems have been continuous or that there are some days when his/her memory is better than others?"*** Record the informant's characterization of whether there is fluctuation in their memory.
  - Ask: ***"Did the memory problems begin around the same time as a medical, emotional or physical event in his/her life, like the death of a loved one, an accident, or an illness?"***

  Record the informant's view of whether the onset of the memory problems coincided with an event.

▪ Ask: ***"Did the participant's memory problems start before or after his/her _____ problems began?"*** Record any details provided about the timing of the memory problems with a cerebrovascular event or onset of EPS.

- The informant should be read as much information as needed from the anchor descriptions in order to answer the question as accurately as they can. Make sure it is clear that they need to think about the statements in terms of [participant's name] ability to live on their own (independence).

- Items 10-12 Verbal Expression. Ask examples for each and date or age of onset (or indicate if it has already been recorded).
- Items 13-20 Daily Functioning. Ask the items as described and score not only those behaviors that are due to physical or sensory limitations but also to cognitive problems. For example, a participant with Parkinson's disease or severe arthritis may have difficulty with buttons and require complete assistance getting dressed. However, for someone who performs any aspects of their own dressing and who reports difficulty with buttons or remembering details, this would also be a "yes" in item 17 (trouble in dressing or self-care). In other words, it is possible for someone to have some physical limitations but to also have problems with cognitive function that interfere with these basic activities of daily function, and the functional problems related to cognitive decline would also be scored a 1 or "yes". Again, it is up to the interviewer to provide as much information and probes as possible for the informant to make their own decision about whether the participant is able to perform these activities.
  - The cause of daily functioning problems (e.g., participant is blind but knows how to dress him/herself), if known by the informant, should be noted after the "Notes and Examples" section. The interviewer should select the appropriate cause: "sensorimotor", "cognitive", "both", "other", or "unknown".
  - If the informant answers "Yes" on any items 1-15 or 16c-20, proceed with asking Items 21-25, unless the only endorsed items are 13-20 and are only due to sensorimotor impairments. If the Recognition of Problem questions have been previously recorded check the box and proceed to Item 26.
  - Item 16b – If the participant retired prior to the previous DQ administration and this information has already been recorded then check the box and proceed to Q17.
- Item 21-22. Ask: "***Who first noticed something wrong?"*** Record the relationship of the person to the participant and the circumstances surrounding the time in which they first noticed problems.
- Item 22. "Old Self" - please add **"*when these problem(s)* [was/were not] *present*"**.
- Item 23-25. These are self-explanatory; remember to record verbatim "*what cause was given*".
- Items 26(a-l) Stroke Questions. These questions are needed to gather more detailed information about stroke status. Questionnaires such as this one have been used in prior research as a practical, reliable, and valid method of determining stroke status. These questions are entirely self report and can be asked of their informant.
  - Items 26k and 26l do not need to be asked for participants who answered "No" to Q1-12 and answered "Yes" to Q13-15, 16c-20 only due to sensory or physical impairment. Also, the interviewer should note whether Items 26k and 26l have been previously recorded. If so, proceed to Item 27a.
- Item 27: Alcohol problems. This question pertains to significant persistent alcohol use, such as 3 or more drinks per day OR if alcohol use ever affected ability to function in personal, family or professional life.
- Items 28-29: Depression.
  - *For the following questions, I would like you to answer Yes or No.*
  - . . . you can also add , *"did participant feel sad, depressed, blue or down in the dumps?"*
  - Based on the informant's answers, each item will be marked as Yes or No.
  - During this interview, an informant may not answer a question with "yes" or "no", but

will describe the participant's feelings in more detail or recall an event. Write down what the informant says. Then, use your interviewing skills to encourage the participant to choose yes or no.

- Sometimes the participant will not narrow their answer to a yes or no after these types of prompts. In these cases, write down what the participant tells you in the margins of the page. This will allow discussion of "borderline" answers with the adjudication team. A general rule is that items will be marked as Yes even if the participant has the symptom only some of the time or if they tell you that the symptom is mild in intensity; however, if the participant does not give you a yes or no answer, you should write down their response as fully as possible in the margins in order to facilitate discussion.

- Questions 30-35. Self-explanatory. The interviewer should note whether driving cessation has been previously recorded. If so, proceed to Item 36.
- Question 36-37. Self-explanatory.
- Question 38. This question is not asked of the informant, but is rather answered by the interviewer. This question is based on the judgment of the informant's responses to this questionnaire. Please rate the reliability of the responses as "very reliable", "fairly reliable", "not very reliable" or "don't know". Please try to give a response and limit the use of don't know.

Phase 7 of the LLFS will begin in Summer 2018 when all field centers have IRB approval. This phase is post-Visit 2 and only includes annual telephone follow-up for all enrolled LLFS participants including newly enrolled for Visit 2. This telephone follow-up call will be similar to Phase 6 but with the following changes:

1) Panel 16, Question 15 (querying additional family members) will be removed as it is not relevant at this time. This also included deleting the "Additional Interested Relatives" table at the end of the panel.
2) The Pittsburgh Fatigability Scale (PFS) from Visit 2, Panel 3 will be added to Panel 16 for the next full year of follow-up. The PFS is a marker of exercise capacity, and also has been strongly predictive of change in physical function. The PFS will be telephone administered in contrast to self-administered at Visit 2. A central training session was conducted on August 7, 2018. After discussion, all field centers agreed that to ease administration of the PFS over the phone, research assistants could first ask the participant if they had done the activity in the past month (yes/no) and then query their associated physical and mental fatigue they experienced or imagined they would feel after completing all 10 activities.

Figure: When to administer the DQ.