CHAPTER 7

RANDOMIZATION

Study Documents Referred to in this Chapter:

- Telephone Screening Interview
- SPPB
- Informed Consent
- Demographics
- Blood Pressure, Radial Pulse and Weight
- 400 m Walk Test
- MMSE
- Medical, Hospital Admission History
- ECG
- Physical Exam
- Study Eligibility Checklist

CHAPTER 7

RANDOMIZATION

7.1. RANDOMIZATION OVERVIEW

Randomization can only occur after all eligibility requirements have been met and after key baseline data have been measured.

Randomization is stratified by clinical center and by gender. This will ensure nearly equal sample sizes for the two intervention groups within each center and for men and women. Stratification by center is important because we expect that the cohorts recruited by centers will vary, depending on local populations and recruitment strategies. Stratification by gender is important because we anticipate their may be differences in how women and men respond to the intervention.

Clinic sites will routinely determine the randomization assignment for each participant by using the LIFE web-based data management system. Because internet connections are occasionally not available, the LIFE DMAQC center has developed a back-up randomization process that is not dependent on the internet.

7.2. RANDOMIZATION PROCEDURE

The following forms must be entirely entered in the LIFE database prior to randomization.

Telephone Screening Interview
- Telephone Screening Interview Form

Screening Visit 1
- SPPB Battery
- 400 m Walk Test
- MMSE
- Physical Exam

Screening Visit 2
- Study Eligibility Checklist

These forms contain eligibility requirements and key data that are required on all participants.

As each form is entered, an eligibility check can be performed to confirm that all elements of the form have been completed and to confirm eligibility or partial eligibility. This may be important to confirm, for example, that a Screening Visit 2 should be scheduled.

If the eligibility check is not successful (i.e., it shows the screenee is currently ineligible), several steps should be taken. First, you should confirm that the data were entered correctly by comparing the hard copy of the form with the data screens (or compare with the report that indicates areas of ineligibility). If an error has been made in data entry, the screens can be corrected and the eligibility check can be run again. Any corrections that are made to the eligibility screens after the eligibility check is run will be documented in the system in a "journal file" and reviewed periodically by the DMAQC and study committees. Second, you should confirm that all activities have occurred within the allowable time (see Allowable Time between Activities, below). If it appears that the participant is indeed ineligible, determine whether it is a temporary ineligibility (e.g., blood pressure out of range) and discuss this with the participant. Re-screening can be conducted at a later date.

The randomization computer program requires that the LIFE DMAQC server, the clinic computer, and the phone lines are all operational. In the event of a failure of any of these systems, web-based randomization cannot be performed. The following steps should be followed. First, inform _L.C._ at the DMAQC (phone___, or email___), particularly if you are having difficulty reaching the DMAQC server. If you are unable to reach _L.C._, please contact _L.H._ (phone ___, or email___) Second, if you can delay randomization, do so. (It may be only a short time before the system is operational again.) If randomization must be performed immediately (e.g., an intervention group is due to begin the following

day), the DMAQC has a back-up plan for randomizing without the computer system: contact _L.C._.

The process of implementing the LIFE randomization computer program is described in Chapter 23, Data Management.

In the event you have made an error in randomization, i.e. with data entry or printing a form, contact _L.C._ at the DMAQC.

7.3. RANDOMIZATION ERRORS and ISSUES

Occasionally the clinic or the DMAQC uncovers information that indicates that a randomized participant was not eligible. One reason for this is that a participant may not have revealed information that made him/her ineligible until after the randomization. Alternatively, a data entry error may have been made that has led to an incorrect eligibility assessment.

When a randomization error is known to have occurred: (1) a memorandum signed by the Program Coordinator and Principal Investigator must be sent to the DMAQC as soon as the situation is uncovered and (2) the participant remains a part of the LIFE study. The DMAQC will be monitoring the frequency and type of randomization errors and reporting them regularly to the Data Safety Monitoring Board.

Another situation that may arise is that the status of a participant with respect to eligibility criteria determined at Screening Visit 1 changes by the time of Screening Visit 2. For example, a screenee has a cardiovascular event after Visit 1 but prior to Visit 2. If this happens, the individual is no longer eligible and the appropriate Visit 1 form may be edited to reflect this. If, however, a change in

eligibility criteria is not detected until after randomization, the individual is a study participant and should be followed. However, a safety assessment may be required to ensure that the assigned study intervention is appropriate.

Once a participant is randomized, NO CHANGES CAN BE MADE to the specific items determining eligibility in the screening forms in the database; the database will not allow this. Data that is listed on the form, but not required to determine eligibility can be changed at the Field Center. If you discover an error to an eligibility item that has been entered, these changes can be made by the DMAQC. In this situation, _L.C._ at the DMAQC should be contacted to determine the correct action to take. If the entered data needs to be corrected, this can only be done at the DMAQC after written notice of the needed change is received by _L.C._ (phone ___, or email___).

7.4. ALLOWABLE TIME BETWEEN ACTIVITIES

The allowable time from the date of informed consent (Informed Consent Form) to randomization is four weeks. The randomization program will not permit randomization of a participant who does not meet this criterion.

The allowable time from the date of randomization to the date of the first individual intervention is also four weeks. The DMAQC will monitor these activities and provide regular reports to the study leadership.