Long Life Family Study Mortality Investigation

Background and Overview

In April 2014, the LLFS Steering Committee established the Morbidity and Mortality Committee as a new committee. The M and M committee was charged to develop the quality of the morbidity and mortality data in LLFS and to harmonize these outcomes with the Framingham Heart Study (FHS) and other cohort studies to replicate findings. The M and M committee reviewed the procedures in several studies including FHS and Health, Aging, and Body Composition Study and recommended several protocol changes that will increase the opportunities to review health outcome data.

It was determined that the study needed to establish the date, location and cause of death for all decedents. To confirm feasibility, a pilot was proposed at the University of Pittsburgh Field Site. While this was underway, the informed consent was modified to include the collection of medical records during the study. Also, three questionnaires were revised to obtain more detailed information about health events and allow event adjudication to occur at a future date, should resources be identified. These questionnaires were the Panel 5 medical history update, the Panel 16 annual telephone contact, and the Panel 18 Decedent Proxy Interview (DPI) which included a narrative from the proxy of the symptoms, sequence and details of the death.

The steering committee discussed the success of the pilot project at the February 2017 meeting. It was agreed that understanding cause of death in a study of exceptional longevity was important to the study, and to pursue the classification with the other US sites. All investigators (Study PIs) agreed to initiate the same type of investigation at the Boston and New York centers (collection of death certificates and medical records). Sites also agreed to complete a modified Decedent Proxy Interview with the families of the subjects dying prior to exam 2 to supplement information on diagnoses, symptoms, treatment, and circumstances of death which would add important information lacking in the pilot cases. In addition to developing the modified DPI, a death certificate abstraction form was created. A National Death Index search will validate deaths, and eventually provide a more complete list of decedents. Adjudication packets will include the death certificate, medical records from the most recent hospitalization or other treating facility, and the narrative interview from the family. This will provide critical information necessary to adjudicate the deaths outside health care facilities (ie.at home) because a recent medical record will be available, and a narrative will provide important details about the sequence of events. In addition, 30% of records requested in the pilot were unobtainable, and some records provide information that is insufficient to determine cause of death.

The M and M committee developed and piloted the LLFS Underlying Cause of Death Adjudication Form to have a standardized form to collect information on the cause of death on each participant. Forms from the Framingham Heart Study and Health Aging and Body Composition Study were reviewed. The form includes location of death, underlying cause, immediate cause, contributing cause, and conditions present at death. In addition, supporting documents present to the review panel were documented. The M and M committee empaneled an Adjudication Committee consisting of physician investigators from each site. The form was pilot tested using deaths from the Pittsburgh site and refined at a face-to-face adjudication committee meeting at the February 2017 steering committee meeting.

Procedures for Mortality Investigation

Identifying LLFS deaths at each site - The National Death Index (NDI) will be used to validate known deaths, and identify deaths in lost-to-follow up subjects. The NDI application was submitted by the coordinating center (CC) in collaboration with the field centers, and approved. The CC will submit lists of known deaths with identifiers to NDI, providing matches at varying levels of confidence. Spreadsheets of the NDI data of decedents including the identifiers will be distributed to the 3 US field centers with sufficient information to confirm the matches. The first submission to NDI was submitted in the spring 2017 which included deaths-only through 2015, because NDI data are approximately 2 years behind. Subsequent submissions will include lost-to-follow up subjects as well as known deaths.

Obtaining death certificates with cause of death – When the NDI data were received, it was confirmed that location of death was not included, and therefore it would be necessary to obtain death certificates. Once field centers validate the NDI deaths matched to the LLFS participants, death certificates with cause of death will be obtained. Families may be asked to provide photocopies of death certificates. Death certificate requests standardly require full name, date of death, date of birth, county of death, and social security number, if available. Certificates range in price but average $10-$30 each, and non-certified copies are sufficient. Some states require applications for research while others are open access. Information to obtain death certificates from individual states can be found at https://www.cdc.gov/nchs/w2w/index.htm , or can be located by searching the web for 'vital records' in any specified state.

Obtaining medical records from health care facilities (acute care hospital, nursing home, and hospice) - Based on the location of death listed on the death certificate, field centers will request copies of 1) discharge/death summary, and 2) admission history and physical exam, from the medical records department of the facility where the subjects died, or from the hospitalization prior to death if subjects died at home. Since an authorization to release medical records to the study was not obtained from subjects during the early period prior to exam 2, the HIPAA regulations for the "Partial Waiver for Deceased Subjects" may be used (see appendix). This permits providers/facilities to release medical records on research subjects if the research is dependent on those records to complete the scope of work. A copy of the field center IRB approval letter for study should accompany the request along with specifying the name and date of birth of the subject, the date of admission/discharge/death, and the two documents being requested (see appendix). For medical records requested for subjects signing an authorization to release records to the study (at the time of exam 2), the release should be included with the request for records. A copy of the death certificate should also be included to confirm the subject is deceased, and therefore the request falls under the 'Partial Waiver' criteria. Each field center will develop a system for tracking requested and received records, and pursue those that are not completed. This can be done by adding a column(s) to the spreadsheets indicating dates requests were made and responses by facilities.

Some field centers included in their informed consent an option for subjects to agree to allow the study access to medical records. For those participants opting out/refusing to allow LLFS access to medical records, there should be no attempt to collect medical records from a health care facility. Death certificates may be obtained and, if a willing proxy is available, supplemental DPI information may be collected with a narrative.

Decedent Proxy Interview – The Decedent Proxy Interview (DPI) has been modified to include more details about hospitalizations prior to death, and an open field to collect a narrative to capture information surrounding the death from the family member's perspective. The expanded DPI was implemented at the start of visit 2. Cognitive decline and dementia are often not well documented in hospital records, and this subjective detail will supplement the clinical information especially for deaths at home. Each site will determine if their IRBs should review the process of recontacting families if an earlier version of the DPI was collected. A merged version of the old and expanded DPI questions will be produced for deaths pre-exam 2, while the post exam 2 deaths have already incorporated the expanded questions in the DPI. For pre-exam 2 recalls, sites should prioritize the calls based on the location of death as follows:

1. Deaths at home
2. Deaths for which location of death was not determined (ex. death certificate could not be obtained)
3. Deaths in nursing homes and hospices
4. Deaths in acute care hospitals

For deaths at home or where location of death could not be determined (ex. no death certificate), information from the DPI should be used to obtain a medical record, as described in the previous step.

Preparing adjudication packets – Field centers will create a packet for each decedent including:

1. Completed cover page indicating ID, acrostic, date of death, and checklist of attachments.
2. Death certificate with cause of death
3. Medical record from last treatment facility
4. DPI including narrative interview

The 'comment' field on the cover page may be used to provide additional information, explain missing information, or anything useful to the adjudicators. Field centers should scan each packet as ".pdf", and label every page with study ID and acrostic. The file name should be the same as the label on each page using the ID and acrostic (ex. 312345679_JONEP). Identifiers must be redacted using Adobe Acrobat Pro or other similar software, and uploaded to LLFS secured server. Identifiers include names of patient and family, personal phone numbers, addresses, emails, day and month of birth, identifying numbers such as social security, insurance and medical record numbers. Do not redact subject age, hospital or physician names, and dates of admission, discharge, tests or treatments, as these are relevant to adjudication of the events. For death certificates, location of death should not be redacted if it includes the name of a medical facility, but it must be redacted if the death was at a residence and the address of the home is in this field. Detailed information on redaction may be found at: https://privacyruleandresearch.nih.gov/pr_08.asp

Procedures for uploading packets: Due to our security policy to protect HIPPA information, the uploaders will be operating in the "blind" and will not be able to see the directories, nor the files being uploaded to the FTP server. Any persons wishing to upload the files should contact the DMCC Project Manager, LeAnne Kniepkamp (l.kniepkamp@wustl.edu) with the name and email address of the new user. LeAnne will then work with the DMCC IT department to grant permission for access.

Once access has been granted, new users wishing to upload files should connect via an FTP client to ftp.dsg.wustl.edu. Your user name will be anonymous and your password will simply be your email address.

Once connected, change your directory to **escondite**. From there you can upload any files that you wish. Once uploaded, email LeAnne who will verify the files have been uploaded in full. Once the files have been verified, DMCC IT will then move the files over to the downloaded directory where the downloaders can retrieve them. This verification process is required. Please note this process is not instantaneous and there will be some lag time.

Abstraction of Death Certificate – Field centers will abstract each death certificate onto the 'Death Certificate Abstract Form' and data enter the information into the Red Cap data system.

Adjudication – Packets will be downloaded for adjudication by the M and M committee members and classified for underlying and immediate cause of death, contributing causes and conditions present at death. Each death will be assigned two adjudicators (a primary and a secondary) who will independently review the case and complete the adjudication form. If the underlying cause of death is a match, then the remaining fields of the adjudication form will be accepted from the primary adjudicator. If the underlying cause of death is not a match (discordant), then the adjudicators will be notified and asked to discuss the case by email or conference call until they come to agreement on the underlying cause. The remaining fields of the adjudication form will be accepted from the primary adjudicator. Adjudicators may be primary or secondary adjudicators, and will be paired with different adjudicators for the various cases.

Appendix A

Partial Waiver of Consent

Reference: http://www.cga.ct.gov/2013/rpt/2013-R-0124.htm

Permitted Disclosures

....The privacy rule also permits disclosure of protected health information without the patient's authorization, subject to various conditions and limitations, for 12 national priority purposes — categories where disclosure is permitted due to the important uses for such information in contexts outside of health care. Such categories include, among other things, (1) disclosures required by law, (2) public health activities, (3) health oversight activities, (4) judicial and administrative proceedings, (5) law enforcement purposes, **(6) research**, and (7) serious threats to health or safety (45 C.F.R. § 164.512).

...The privacy rule establishes various conditions for researchers who seek protected health information. For example, if someone requests a deceased person's protected health information for research purposes without the personal representative's authorization, the researcher must provide the covered entity with representations that the (1) use or disclosure being sought is solely for research on the protected health information of decedents and (2) information being sought is necessary for the research. The researcher must also provide documentation of the person's death if the covered entity requests it (45 C.F.R. § 164.512(i)(1)(iii)). HHS's website has more information on requirements for researchers: http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/research.html.

Below is the federal law that is referenced in the highlighted paragraph (which details the legality of using an IRB-approved waiver of consent for release of PHI of decedents for research purposes):
http://www.law.cornell.edu/cfr/text/45/164.512

Title 45, CFR 46.116(d):
"...(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
(1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation."