Long Life Family Study Dementia Review

Background and Overview

In October 2018, the LLFS Steering Committee established a new committee, the Dementia Review Committee, to aid Stephanie Cosentino with the Administrative supplement received to establish and implement a dementia diagnosis procedure in LLFS and to continue the process as part of new funding. The Dementia Review committee was charged to establish and implement a dementia diagnosis procedure in LLFS, modeled after the Framingham Heart Study (FHS) and to compare rates of dementia across these two cohorts. The Dementia Review committee reviewed the procedures from FHS and recommended protocol changes that will allow similar processes for dementia diagnosis between LLFS and FHS.

The Dementia Review committee decided to use the Dementia Review forms used in FHS (short and long, see appendix). In addition, supporting documents from the DMCC (dementia reports), as well as scanned copies of additional participant data from the in-person and annual follow-up calls will be shared amongst the committee. The Dementia Review committee convened a panel consisting of investigators involved in dementia reviews for other studies, including Stephanie Cosentino (CU), Stacy Andersen (BU), Larry Honig (CU), Sandy Auerbach (FHS), and Diane Ives (PT).

Procedures for Dementia Review

Identifying cases for dementia review – Dementia review packets will be prepared for LLFS participants who demonstrate the presence of diagnostic triggers at ANY time including:

1) CDR >0
2) Cognitively impaired by the NACC-based algorithm (case_status = 1);
3) If CDR and algorithm are missing, report of a cognitive problem by an informant defined by endorsement of any item between #1 and 7 on the Dementia Questionnaire

Dementia Report from DMCC – Once the list of potential dementia participants is created (based on retrospective review of CDR, algorithm status, and DQ), the DMCC will:
- provide a list of the participants whose charts will need to be retrieved for dementia review at each site, and
- create a report for each participant (*Neuropsychology Summary)*. This report includes information entered into REDCap during in-person and follow-up phone calls, which is then used to create analysis datasets.
- Using these datasets, the DMCC extracts necessary information to aid with the dementia review process. These reports will be available for download at the sFTP site: **/LLFS_#/DementiaReview/ (where # is NY, BU, or PT).**

Dementia Review Packets for each participant – Prior to the bi-weekly dementia review calls, each site will create dementia review packets for participants to be presented on the call. These packets will be uploaded to the sFTP site by the Friday prior to the call. See following section ('**Preparing Documents for Review'**) for details on the preparation of the packets. Additionally, at each site, a draft of the *Dementia Review Form* (long or short, see appendix) should be completed as a starting point for discussion on the call. During the Dementia Review call, the dementia review form will be finalized. Each form will be entered into REDCap after the call by CU staff.

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**. Then change to the **DemRev** directory (case sensitive). 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 LeAnne accesses them. This verification process is required. Please note this process is not instantaneous and there will be some lag time.

Once packet upload has been verified, LeAnne will move the packets to the Password protected dropbox for downloading by adjudicators. LeAnne will send out credentials to the adjudicators prior to the January 22, 2019 call. After that date, if new adjudicators need access to the password protected dropbox, they will need to email LeAnne (l.kniepkamp@wustl.edu).

Adjudication During Dementia Review Panel Calls – Packets will be downloaded for adjudication by the Dementia Review committee members and classified as Normal Cognition, Mild Cognitive Impairment (MCI) or Dementia. Each dementia review case will be presented by the person at the site who completed the initial dementia review form. Discussion of the case and completion of the Dementia Review Form (long or short) will be decided on the call. Hard copies of the dementia review form will be put in the participants chart after data entry and will be entered into the REDCap data system after the call. The Dementia Review Meeting Notes template will be filled out by CU staff to record details of the cognitive status decision making process and forwarded to the participant's field center for placement in the chart. This form is not entered into REDCap.

Preparing Documents for Review

Each packet will include the Dementia Review Summary (see Appendix), the Neuropsychology Summary report from the DMCC, scanned documents from the charts, and a summary of all information coalesced. These will be saved as four separate files. The documents should be labelled and ordered as follows:

1. 1_Dementia Review Summary for Presentation_ID NUMBER_SITE_DR
2. 2_Neuropsychology Summary_ID NUMBER_SITE_DR
3. 3_Scanned Documents_ID NUMBER_SITE_DR
4. 4_Summary of Available Information_ID NUMBER_SITE_DR

For further details on the preparation of each of these documents, please see below.

Dementia Review Summary
The 'Synthesized Summary' section should include an overview of when cognitive symptoms were first recorded, an overview of the cognitive decline, and any transition dates. This should take the form of a table which lists all dates of contact in chronological order, with key cognitive details after each date. Here is an *example*:

Jan 2009 (V1)	Notes about V1 test scores, relevant medical conditions
Jan 2010 (AFU)	TICS (40/51), no DQ due to high TICS score
Jan 2011 (AFU)	TICS (20/51), notes about DQ findings, new relevant medical conditions
Jan 2014 (AFU)	TICS (20/51), notes about DQ findings, new relevant medical conditions
Jan 2016 (V2)	Notes about V2 test scores, changes in cognition, summary of DQ findings, CDR score [including domain e.g. memory]
Jan 2017 (AFU)	TICS refused, CDR score, notes about DQ findings

In the 'Synthesized Summary' section it should be indicated whether the person is male or female. It is important to include any DQ information in this section.

The 'Chart Summary' should include any other contributing factors and health-related / medical issues (not necessarily cognitive) (e.g., head injury, stroke, developmental disorder, Parkinson's disease, etc.). Age of diagnosis should be included. Smoking / drinking / problems with physical function may be included here. If the person is deceased, please include information from the Decedent Proxy Interview and Addendum here.

The 'Medical Records Summary' should only be completed if medical records have been obtained following death of the participant. Otherwise write 'N/A'.

The 'Neuropsychology Summary' should include a short paragraph or table detailing performance on key neuropsychological measures including (but not necessarily limited to): memory retention, animal fluency, Trails B, Digits backward.

The 'Behavioral Observations' should include comments from the tester and any qualitative information (e.g. types of errors) from the cognitive testing (e.g., 'semantic intrusions on HVLT', '7 perseverations on phonemic fluency', '4 LOS errors on Trails B'). Any behavioral peculiarities should be specified here. If there was nothing of note, write 'nothing of note'.

Scanned Documents: All V1 drawings (MMSE sentence, MMSE pentagons, DSST), V2 drawings (MMSE sentence, MMSE pentagons, DSST, all 4 trails items, Clock command, Clock copy), and all TICS should be scanned. When scanning documents to be circulated, all identifying information (e.g., names) needs to be redacted by using Adobe to place a black box over the information. Drawings should be labeled appropriately, for example 'V1 Pentagons', 'V1 Sentence', 'V2 Trails A' etc. using Adobe typewriter function.

Appendix

Dementia Review Form- Short (Form Version Date 04JAN2019)

Subject's ID number	⬚⬚⬚⬚⬚⬚⬚⬚
Date of Review (dd/mm/yyyy)	⬚⬚ / ⬚⬚ / ⬚⬚⬚⬚
Adjudicators:	
Review Number (n^th review)	⬚

Sources available for this review	Dates

Last Date of Documented Normal/Baseline Cognitive Status **(dd/mm/yyyy) U = Unavailable**	⬚⬚ / ⬚⬚ / ⬚⬚⬚⬚
Degree of Certainty Regarding Normal Cognitive Status Date **1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A**	⬚
Sources supporting normal cognitive status date	**Dates**

CT Scan Information

CT Scan Performed: 0 = No 1 = Yes D = Don't Know	☐
Date of the Most Recent CT Scan (dd/mm/yyyy) U = Unavailable	☐☐ / ☐☐ / ☐☐☐☐
CT Scan Results: 1 = Normal 2 = Atrophy only 3 = Single Stroke 4 = Two or more Strokes 5 = Other,_____ 6 = Small Vessel Ischemic disease U = Unavailable	☐

MRI Scan Information

MRI Scan Performed: 0 = No 1 = Yes D = Don't Know	☐
Date of the Most Recent MRI Scan (dd/mm/yyyy) U = Unavailable	☐☐ / ☐☐ / ☐☐☐☐
MRI Scan Results: 1 = Normal 2 = Atrophy only 3 = Single Stroke 4 = Two or more Strokes 5 = Other,_____ 6 = Small Vessel Ischemic disease U = Unavailable	☐

Cognitive Status at Time of Death 0 = No Dementia 0.5 = Cognitive Impairment – No Dementia 1.0 = Mild Dementia 1.5 = Greater than or equal to mild dementia 2.0 = Moderate Dementia 2.5 = Greater than or equal to moderate dementia 3.0 = Severe Dementia 4.0 = Alive U = Unavailable	☐.☐
Certainty of Cognitive Status at Death 1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A	☐

Sources supporting the cognitive status at death	**Dates**

Is a developmental disorder (e.g., intellectual disorder, learning disorder) suspected? 0 = No 1 = Yes D = Don't Know	☐

Dementia Review Form- Long (Form Version Date 04JAN2019)

Subject's ID number	☐☐☐ DemRev ☐☐☐☐
Date of Review (dd/mm/yyyy)	☐☐ / ☐☐ / ☐☐☐☐
Adjudicators:	
Review Number (nth review)	☐

Sources available for this review	Dates

Last Date of Documented Normal/Baseline Cognitive Status (dd/mm/yyyy) U = Unavailable	☐☐ / ☐☐ / ☐☐☐☐
Degree of Certainty Regarding Normal Cognitive Status Date 1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A	☐
Sources supporting normal cognitive status date	**Dates**

Cognitive Impairment 0 = No 1 = Yes D = Don't Know		
Sources supporting presence/absence of cognitive impairment	**Dates**	
Date of Cognitive Impairment Onset (dd/mm/yyyy) N = N/A U = Unavailable	☐☐ / ☐☐ / ☐☐☐☐	
Degree of Certainty Regarding Impairment Onset Date 1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A		☐
Sources supporting cognitive impairment onset date	**Dates**	

Cognitive Decline 0 = No 1 = Yes, Duration Less Than 1 Year 2 = Yes, Duration Greater Than 6 Months D = Don't Know		☐
Sources supporting the presence or absence of cognitive decline	**Dates**	

Probable Dementia Present 0 = No 1 = Yes D = Don't Know		
Sources supporting the presence or absence of dementia	**Dates**	

Date of Diagnosis of Mild Dementia (dd/mm/yyyy) N = N/A U = Unavailable	☐☐ / ☐☐ / ☐☐☐☐	
Degree of Certainty regarding Mild Dementia Date 1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A		☐
Sources supporting the date of mild dementia	**Dates**	

Date of Diagnosis of Moderate Dementia **(dd/mm/yyyy) N = N/A U = Unavailable** (Dementia Diagnosis Date)	☐☐ / ☐☐ / ☐☐☐☐
Degree of Certainty regarding Moderate Dementia Date **1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A**	☐

Sources supporting the date of moderate dementia	**Dates**

Date of Diagnosis of Severe Dementia **(dd/mm/yyyy) N = N/A U = Unavailable**	☐☐ / ☐☐ / ☐☐☐☐
Degree of Certainty regarding Severe Dementia Date **1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A**	☐

Sources supporting the date of severe dementia	**Dates**

Definite Stroke or TIA **0 = No 1 = Yes D = Don't Know**	☐
Parkinson's Disease **0 = No 1 = Yes D = Don't Know**	☐

CT Scan Information	
CT Scan Performed: **0 = No 1 = Yes D = Don't Know**	☐
Date of the Most Recent CT Scan **(dd/mm/yyyy) U = Unavailable**	☐☐ / ☐☐ / ☐☐☐☐
CT Scan Results: **1 = Normal 2 = Atrophy only 3 = Single Stroke 4 = Two or more Strokes 5 = Other,_____** **6 = Small Vessel Ischemic disease U = Unavailable**	☐

MRI Scan Information	
MRI Scan Performed: **0 = No 1 = Yes D = Don't Know**	☐
Date of the Most Recent MRI Scan **(dd/mm/yyyy) U = Unavailable**	☐☐ / ☐☐ / ☐☐☐☐
MRI Scan Results: **1 = Normal 2 = Atrophy only 3 = Single Stroke 4 = Two or more Strokes 5 = Other,_____** **6 = Small Vessel Ischemic disease U = Unavailable**	☐

Cognitive Status at Time of Death **0 = No Dementia 0.5 = Cognitive Impairment – No Dementia 1.0 = Mild Dementia 1.5 = Greater than or equal to mild dementia 2.0 = Moderate Dementia 2.5 = Greater than or equal to moderate dementia 3.0 = Severe Dementia 4.0 = Alive 7.0=died, unknown at final review U = Unavailable**	☐.☐
Certainty of Cognitive Status at Death **1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A**	☐

Sources supporting the cognitive status at death	Dates

Dementia Subtype (fill out at review only)

0 = None
1 = Alzheimer's Disease Without Stroke
2 = Alzheimer's Disease With Stroke
3 = Vascular Dementia Without Alzheimer's Disease
4 = Mixed Dementia Type (Alzheimer's Disease + Vascular Dementia)
5 = Frontotemporal Dementia
6 = Dementia with Lewy Bodies
7 = Dementia that does not fit any other Category (progressive)
8 = Dementia that does not fit any other Category (non-progressive)
9 = Cognitive Impairment – No Dementia
10 = Dementia – Uncertain
D = Don't Know

If answer is dementia due to inability to fit other categories, specify:

Severity Of Dementia Subtype

0 = None   1 = Mild   2 = Moderate   3 = Severe   D = Don't Know

For Cognitive Impairment (this only refers to impairment *during the MCI stage*), Code Subtype:

1= amnestic   2=non-amnestic   N=N/A   D=Don't Know

If Amnestic, Code Subtype:

1=amnestic only   2=amnestic plus   N=N/A   D=Don't Know

If 2 ("amnestic plus") code: 0= no   1= yes   D=Don't Know   N=N/A

executive function	abstract reasoning	visuospatial function	language	attention

If Non-Amnestic, Code Subtype:

1=single domain   2=multiple domain   N=N/A   D=Don't Know

If 1 ("single domain") or 2 ("multiple domain") code: 0=no   1= yes   D=Don't Know   N=N/A

executive function	abstract reasoning	visuospatial function	language	attention

Dementia Review Form Supplement

Criteria for DSM-IV	
Memory Impairment 0 = No 1 = Yes D = Don't Know [ ]	**If Memory Impairment, Code Subtype:** 1= Verbal and Non-verbal memory 2= Verbal 3= Non-verbal N= N/A D= Don't Know [ ]
Aphasia 0 = No 1 = Yes D = Don't Know	[ ]
Executive Dysfunction (planning, organizing, sequencing, abstracting) 0 = No 1 = Yes D = Don't Know	[ ]
Significant Impairment in Function (Social/Occupational) 0 = No 1 = Yes D = Don't Know	[ ]
Dementia by DSM-IV Criteria Memory Impairment, Impairment in one other Cognitive Domain, Functional Decline, Not Due to Delirium, Depression, or Schizophrenia 0 = No 1 = Yes D = Don't Know	[ ]
Dementia by ADDTC criteria Impairment in two or more Cognitive Domains, Functional Decline secondary to Cognitive Impairment 0 = No 1 = Yes D = Don't Know	[ ]
Symptoms Above Present for at least Six Months (refers to memory imp, aphasia, etc., *not* dementia) 0 = No 1 = Yes N = N/A D = Don't Know	[ ]

Cognitive Deficits Not Related to DSM-IV Criteria	
Language 0 = No 1 = Yes D = Don't Know	[ ]
Visuospatial Abilities 0 = No 1 = Yes D = Don't Know	[ ]
Attention 0 = No 1 = Yes D = Don't Know	[ ]

Alzheimer's Disease by NINCDS-ADRDA criteria (fill out at review only) **0 = No 1 = Yes D = Don't Know**	☐
Classification of Alzheimer's Disease (fill out at review only; note that, in certain cases, a pt. *can* have both probable AD and probable vascular dementia) **1 = Probable AD (dementia, progression, and no other etiology)** **2 = Possible AD (dementia, progression, unusual clinical features or other contributory etiologies)** **3 = Definite AD** **N = N/A D = Don't Know**	☐
If Possible AD, Code Subtype below: (fill out at review only) **1 = Mixed AD + Vascular** **2 = Mixed AD + Parkinsonism (includingdrug-induced)** **3 = Mixed AD + Other, Specify _____** **N = N/A D = Don't Know**	☐

Notes for coding Vascular dementia: Focal neurological signs suggestive of stroke include: weakness of an extremity, exaggerated DTRs, pseudobulbar palsy, extensor plantar responses, gait abnormalities, hemianopsia, facial weakness, dysarthria and sensory deficit if thought to be of vascular etiology.

1. Dementia Present (from page 3) **0 = No 1 = Yes D = Don't Know**	
2. Clinical Stroke Documented **0 = No Stroke 1 = Yes, One Stroke 2 = Yes, More Than One Stroke** **3= Terminal Stroke Only N = N/A**	
3. Suggestive Temporal Profile (onset of dementia less than 3 months after stroke, abrupt onset or fluctuating stepwise decline) **0 = No 1 = Yes N = N/A D = Don't Know**	
4. Imaging (CT or MRI) (code 'atrophy only' or 'mild white matter changes' as 0) **0 = No Stroke 1 = Yes, One Stroke 2 = Yes, More Than One Stroke** **3 = Yes, Extensive White Matter Changes N = N/A D = Don't Know**	
5. Focal Neurological Signs Suggestive of Stroke **0 = No 1 = Yes N = N/A D = Don't Know**	
Vascular Dementia Present **0 = No 1 = Yes D = Don't Know**	

If Vascular Dementia Present Code:
 	
   1 = Probable Vascular Dementia:
      Criteria: #1 and #2 and #3 = 1 ('Yes')
                #4 = 1 or 2 ('One or More Strokes')
      Possible Vascular Dementia:
   2 = #1 and #2 = 1 ('Yes')
      #3 = 0 or 9 ('No' or 'Don't Know')
      #4 or #5 = 1 ('Yes')
   3 = #1 and #2 and #3 = 1 ('Yes')
      #4 = 0 or 9 ('No Stroke' or 'Don't Know'')
   4 = #1= 1 ('Yes') and #4= 3 ('Extensive White Matter Changes') +
      diagnosis of Binswanger's disease
   5= #1= 1 ('Yes') and #4= 1, 2, or 3 and/or #5= 1 ('Yes') Or
      #1= 1 ('Yes') and #3= 1 ('Yes') and #4= 1, 2, or 3 and/or #5= 1
      ('Yes')
   N = N/A D = Don't Know	

Coma/Persistent Vegetative State Post Stroke, Until Death **0 = No 1 = Yes N = N/A D = Don't Know**	

*Other Causes of Dementia or Impairment

0 = None   1 = PD prior to dementia onset   2 = PD after dementia onset   3 = Dementia with Lewy Bodies

4 = PSP   5 = Shy-Dager syndrome   6 = Striato-nigral degeneration   7 = FTD with Parkinsonism

8 = Wilson's disease   9 = FTD (w/ and w/out atrophy on imaging)   10 = Cortiocobasal ganglionic degeneration

11 = Huntington's disease   12 = Spino-cerebellar degeneration   13 = Leukodystrophies

14 = Post cardiac arrest   15 = TBI   16 = Post infectious sequelae (after meningitis, encephalitis, ADEM)

17 = Malignancy (primary, secondary, para-neoplastic)   18 = Subdural hematoma   19 = NPH   20 = CJD

21 = Multiple sclerosis   22 = AIDS associated dementias   23 = Other infections (fungal meningitis, syphilis)

24 = Alcoholic dementia   25 = Toxic-Metabolic Encephalopathy   26 = Dementia – Uncertain Etiology

27 = Other Etiologies (specify
_____)

28 = History of Depression   29 = History of Alcohol/Drug abuse   N = N/A   D = Don't Know

1. [ ][ ]

2. [ ][ ]

3. [ ][ ]

Earliest Documented Date of Dementia ("demented by" date)
(dd/mm/yyyy)   N = N/A   U = Unavailable
Note: if the pt. has a "date of diagnosis of mild dementia," put Ns in this field and the next two. If the pt. is missing a "date of diagnosis of mild dementia," put the earliest documented date of dementia in the first line and then complete the rest of the boxes.

[ ][ ] / [ ][ ] / [ ][ ][ ]

Severity: 1.0 = Mild Dementia 1.5 = Greater than or equal to mild dem. 2.0 = Moderate Dementia 2.5 = Greater than or equal to moderate dementia 3.0 = Severe Dementia   N = NA U = Unavailable (Dementia is present, and the pt. is at least mild, but severity is uncertain)

[ ].[ ]

Degree of Certainty Regarding Dementia Date
1 = Slightly 2 = Somewhat 3 = Moderately 4 = Reasonably 5 = Highly N = N/A

[ ]

Sources supporting earliest documented date of dementia	Dates

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Is a developmental disorder (e.g., intellectual disorder, learning disorder) suspected? 0 = No 1 = Yes D = Don't Know	[ ]

<u>Dementia Review Summary</u>

Participant ID: **Site:**

Date of Birth: **Date of Death:**

Synthesized Summary *(incl. when the cognitive symptoms were first recorded, overview of cognitive decline, transition dates)*:

Highest level of education:
Occupation:
If not seen recently (e.g. missed AFU or visit), why:

Chart Summary *(incl. other contributing factors and health-related issues (not necessarily cognitive), e.g., stroke, head injury, smoking, medical issues, hypertension, developmental disorders, Parkinson's, etc)*:

Medical Records Summary *(if available)*:

Neuropsychology Summary: See printout from REDCap

Behavioral Observations *(incl. comments from tester, qualitative info (e.g. types of errors) on neuropsych tests, any peculiarities)*:

*Reasons for Non-Completion of Tests

1=poor hearing	6=unresponsive to task	11=experimenter error	16=anxiety
2= poor vision	7=fatigue	12=insufficient time	17=environmental distraction
3= unable to establish set	8=unable to write	13=poor effort	18=experimenter discretion
4= unable to maintain set	9=refused	14=disinterest/boredom	19=physical limitation
5= English not native language	10=frustration	15=depression	20=other
			25=digital pen buzz

Written by:
Written on:
Examiner number: