Atherosclerosis Risk in Communities Study

Visit 7 Manual 17

ARIC Neurocognitive Exam

06 February 2019

Study website - https://www2.cscc.unc.edu/aric/

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Updates to Neuroclassification since Visit 6

This table describes the changes made to the neuroclassification process for Visit 7.

Modification Date	Modification
01/31/2018	Determine rate of cognitive decline using visit 6 data or visit 5 data in the absence of visit 6 data.
01/31/2018	The selection algorithm moved from real time determination to a job run at the Coordinating Center.
01/31/2018	Drop Visit 5 procedure for full committee review.
10/31/2018	Drop cases from advancing to classification review when the algorithmic diagnosis is the same as the reviewer diagnosis from the previous visit's review.
10/31/2018	Packet changes - Included test information from V6, historical diagnoses added, and added BLESSED items.
02/06/2019	Added instructions for running the DCF query report into the procedural overview (Appendix 3).

List of Abbreviations

ARIC	Atherosclerosis Risk in Communities Study
CA	Community Affairs
CSCC, CC	Collaborative Studies Coordinating Center
CDI	Clinical Dementia Rating form - Informant
CDP	Clinical Dementia Rating form - Subject
CDR	Clinical Dementia Rating
DEM	Dementia
DMS	Data Management System
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSS	Digital Symbol Substitution
DWR	Delayed Word Recall
FAQ	Functional Assessment Questionnaire
HH	Home and Hobbies
JPS	Judgment and Problem Solving
LTCF	Long-term Care Facility
M, MEM	Memory
MCI	Mild Cognitive Impairment
MMSE	Mini-Mental Summary Exam
MRI	Magnetic Resonance Imaging
NACC	National Alzheimer's Coordinating Center
NCS	Neurocognitive Summary form
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association
NPI	Neuropsychiatric Inventory form
O	Orientation
PC	Personal Care
QC	Quality Control
QxQ	Question by Question instructions
REM	Rapid Eye Movement pattern
RMSE	Root-Mean-Squared error
UDS	Uniform Data Set
WF	Word Fluency

1. OVERVIEW

The ARIC Visit 7 Neurocognitive Study (ARIC V7 NCS) is the 7th ARIC examination, to be completed in 2018-2019 on the survivors of the ARIC cohort. The design includes follow-up cognitive testing at ages where cognitive decline accelerates or manifests across several domains, allowing capture of a large number of both incident dementias and pre-dementia cognitive impairments. Its overall objectives are to determine the prevalence of cognitive impairments and the associations of mid-life vascular risk factors and markers with later-life cognitive impairments and cognitive change.

Participants are invited for exams in clinic or in their homes or long-term care (LTC) facilities. Additional information about participant's cognitive and functional status is sought from informants when necessary on a subset of the examined participants. An expert committee reviews data and classifies cognitive status (normal, mild cognitive impairment, or dementia).

This overview lists the ARIC NCS neurocognitive components with reference to corresponding Exam 7 Manual of Procedure (MOP) sections where the procedures are described in detail.

Manual 16 and Manual 17 for Visit 5 and Manual 17 for Visit 6 provide an historical overview of previous neurocognitive examinations in ARIC.

1.1. Eligibility

All surviving ARIC participants are eligible for ARIC NCS.

1.2. Recruitment

Recruitment begins during the ARIC Annual Follow-up interview. Details are found in V7 NCS Manual 2.

2. STAGE 2 SELECTION FOR ARIC EXAM 7

2.1. Overview

ARIC V7 NCS has two stages. Stage 1 includes the full cognitive test battery collected at the visit 7 exam. Stage 2 consists of informant interviews and is limited to only those participants who meet cognitive criteria for poor cognitive performance. Stage 2 is conducted by telephone shortly after the exam. A participant must attend visit 7 to be eligible to be selected to Stage 2.

Participants with a diagnosis of Dementia (Level 1) at visits 5 or 6 complete Block A of the cognitive battery but not Block B, and are exempt from selection to Stage 2. Home and LTCF-based visits complete Block A only. See ARIC Manual 2, section 10 for a description of the neurocognitive testing blocks.

Participants with a low score on the prorated MMSE at visit 7, defined as <21 if Caucasian or <19 if African American, complete both Block A and Block B. The prorated MMSE score is calculated as (30*number of correct questions on MMSE)/(30-number of questions refused).

Participants with the following characteristics are selected for Stage 2:

- Cognitive Domain Failure on any of three cognitive domains
- **AND** Definite Global Cognitive Decline from visit 6 to visit 7 or visit 5 to visit 7 in the absence of visit 6 data.

Cognitive Domain Failure is defined in Section 2.2.a.
Definite Global Cognitive Decline from visit 6 to visit 7 or visit 5 to visit 7 in the absence of visit 6 data is defined in section 2.2.b.

Sites identify participants who are selected for Stage 2 data collection using the CDART report, V7 Selection to Stage 2. The selection process is the same for both clinic- and home-based visits.

> *Note that unlike ARIC visit 5, no cognitively normal controls are selected for Stage 2. This is because sufficient data were collected at visit 5 to demonstrate that there was essentially no added yield (no missed MCI/dementia cases) by collecting Stage 2 assessments when cognitive test scores were normal. Thus at visit 6 and 7, Stage 2 is limited to those that meet the cognitive criteria described previously.*

Note that the stage 2 selection criteria, cognitive domain failure (Section 2.2.a) and visit 6 (or V5 in the absence of V6) to visit 7 cognitive decline (Section 2.2.b),are used to determine MCI or dementia diagnoses at visit 7 (section 4.4).

There may be some participants who come to visit 7 and do not complete any neurocognitive tests, or perhaps only the MMSE. In this case the participant is automatically selected to Stage 2.

2.2 Calculation of Cognitive domain failure and definite global cognitive decline

2.2.a. Cognitive Domain Failure

Three cognitive domains (and their component tests), as defined by Gross(1) are:

- Memory (3 tests: Delayed Word Recall [DWR], Logical Memory I and II (summed), and Incidental Learning),
- Language (3 tests: Word Fluency [WF or FAS], Animal Naming, Boston Naming),

- Executive Functioning (3 tests: Trail Making Test A, Trail Making Test B, and Digit Symbol Substitution [DSS]).

(1) Gross AL, Power MC, Albert MS, Deal JA, Gottesman RF, Griswold M, Wruck LM, Mosley TH, Jr., Coresh J, Sharrett AR, Bandeen-Roche K. Application of Latent Variable Methods to the Study of Cognitive Decline When Tests Change over Time. Epidemiology. 2015;26(6):878-87. doi: 10.1097/EDE.0000000000000379. PubMed PMID: 26414855.

Each participant's three domain scores are calculated and compared to norms established using a robust Normative Sample of participants who completed visit 5. "Cognitive Domain Failure" is defined as a domain Z score relative to the Normative Sample of worse than -1.5 for any one or more of the three domains.

As described below, domain scores are calculated if at least one of the tests in the domain is completed. If no tests are completed in a domain, then the domain score is set to missing. In the case where 1 or more of the 3 domain scores are set to missing, Cognitive Domain Failure is set to "Yes".

> *Note that cognitive failure is defined more precisely and accurately at visit 6 and 7 than at visit 5, both because it is based on cognitive domains rather than single tests and also because the criteria for failure are derived entirely using norms from a large subpopulation of the ARIC population themselves and do not require assuming that any externally-derived norms are appropriate.*

Step A. Normative Sample Creation

The Normative Sample used is comprised of n=2609 ARIC Visit 5 (V5) participants who do not have any of the following exclusions.

Clinical neurologic disease at V5

1. Stroke hospitalization as of V5

2. History of neurological disease at or before V5 (multiple sclerosis, Parkinson's disease or brain tumor)

Diagnosed or self-reported memory problems or factors affecting cognition at V5

3. Using medications for dementia at V5

4. Low MMSE (prorated MMSE<22, where the prorated MMSE is scored as 30*number of correct responses / (30 – Total number of questions not attempted due to refusal or disability))

5. Self-report memory problems at V5 identified on the Subjective Memory Form (SMF) responses to questions 1 and 3 is often (3) or very often (4)

6. Dementia discharge codes prior to V5
   a. Includes all codes with the first 3 digits='290'

   b. Includes all codes with the first 5 digits='294.0', '294.1', '294.2', '294.9', '331.0', '331.1', '331.2', '331.7', '331.9'

c. Also Includes codes '331.8', '331.82', '331.83', '331.89'

7. Diagnosis of dementia (level 3 definition) at V5

8. Depression (CES-D summary score>=8, summed over items 1-11 on the CES-D, items 5 and 8 are reverse scored) at V5

9. ApoE4/4

10. Substantial decline in neurocognitive tests DWR, DSS, or WF
    - Change in DWR, DSS and WF test scores at V5 was calculated as the change for each test at V5 from the mean of the visit 2 and visit 4 test scores.
    - Participants were excluded if their change score was in the worst 10% on any one test or between the worst 10-20% on at least two tests.
    - These percentiles are calculated from all visit 5 participants. The 10 and 20 % cut points for the individual tests are shown in the table below

Normative Sample Cut-points for Change from Average (visit 2, visit 4) to visit 5

	DWR	DSS	WF
20th percentile	-3	-14.5	-8
10th percentile	-3.5	-18.5	-11.5

Results derived in job UC691101

11. Diagnosis of MCI, or unknown cognitive status at V5

Additional exclusions based on information collected after V5

12. ARIC Semi-annual Follow Up General Interview version A (GEN) response to any one question of 1a, 1c, or 1d is “Yes”

13. Dementia or memory problems ascertained in the time (min. 2.3 years) following visit 5
    a. Hospitalizations following V5 including additional dementia-related ICD-9 codes (defined in item 6a-6c above)

    b. Dementia death code found including the following list ('F00', 'F00.0', 'F00.1', 'F00.2', 'F00.9', 'F01', 'F01.0', 'F01.1', 'F01.2', 'F01.3', 'F01.5', 'F01.50', 'F01.51', 'F01.8', 'F00.9', 'F02', 'F02.0', 'F02.1', 'F02.2', 'F02.3', 'F02.4', 'F02.8', 'F02.80', 'F02.81', 'F03', 'F03.9', 'F03.90', 'F03.91', 'F05.1', 'F06.7', 'G31.0', 'G31.1', 'G31.01', 'G31.09', 'G31.83', 'G31.84', 'G30', 'G30.0', 'G30.1', 'G30.8', 'G30.9')

    c. ARIC dementia surveillance using the Six-item Screener (SIS) and the AD8 (ADS) (impaired indicated as determined in the algorithm of the ADER dataset derived variables LAST_SIS_RESULT or LAST_ADS_RESULT, or any ADS12 through ADS15 = Y)

    d. Memory problems self-reported at annual follow-up after visit 5 (any MCU13a-MCU13d=Y)

    Note that the ARIC Semi-annual Follow Up General Interview version E (GNE) questions were not used in defining the normative sample because the GNE went into production concurrently with the normative sample development in January 2016.

Exclusions to normative sample based on missing values for variables in prediction models

14. Race other than Caucasian or African American

15. Unknown education level or WRAT score that is either missing or <10

> *Note that exclusion numbers 12 and 13, which exclude dementias occurring shortly after visit 5 are what characterize the normative sample as "robust", i.e. defined as "normal" with greater specificity than if only visit 5 exclusions were applied.*

Visit 5 Normative Sample Exclusion Criteria

Substantial cognitive decline prior to visit 5 Defined as **Normative sample exclusion criteria**	**N (not mutually exclusive)**	**Additive decrease in N from previous exclusion**
1. Stroke hospitalization as of Visit 5	267	6271
2. History of neurological disease	404	5979
3. Use of cholinomimetics at Visit 5	137	5887
4. Prorated MMSE < 22	374	5656
5. Self-report memory problems at Visit 5	1548	4474
6. Dementia discharge codes prior to Visit 5	81	4461
7. Dementia diagnosis at Visit 5	349	4414
8. Depression as of Visit 5	637	4135
9. APOE e4/4 allele carrier	144	4063
10. Decline in neurocognitive tests	1943	3094
11. MCI diagnosis or Unknown Diagnosis	1783	2739
12. Impairment identified in GEN	35	2738
13. Impairment identified in follow-up	864	2645
14. Race other than black or white	18	2639
15. Missing WRAT and/or Education, WRAT score < 10	226	*2609

*****Number of Participants in normative sample. Results derived in job UC691102

Step B. Calculation of Visit 7 Cognitive Domain Z Scores

Step B has 2 sub-parts:

1. Each participant's three Visit 7 domain scores (normed to visit 5 $Z_{V5}V7$) are calculated using a formula of weighted sums based on factor analysis of all visit 5 data (Gross et al Epidemiology 2015), as shown in Section 2.3, below, and Appendix 2**.** As described in 2.3, if all tests are missing in a domain, the domain score is set to missing.

2. Domain $Z_{V5}V7$ scores are converted to Z scores relative to the Normative Sample ($Z_{NS}V7$) as the $Z_{V5}V7$ value minus the participant's (PPT) predicted mean from the Normative Sample ($Z_{V5}NS$) divided by the root-mean-squared error (RMSE) from race-specific linear regression models of $Z_{V5}V5$ for the normative sample adjusted for age, education and WRAT score, as described in the following steps:

2.1 Visit 5 Domain score values ($Z_{V5}V5$) for each participant in the Normative Sample were calculated by Gross et al (2015).

2.2 Race-specific (African American, Caucasian) linear regression models for each domain score adjusted for age (continuous), education (< HS, HS, >HS) and WRAT score at Visit 5 (continuous) were computed from the Normative Sample domain scores ($Z_{V5}V5$) as follows:

Coefficients and 95% CI for Linear Regression Model of Domain Scores

Domain	Race	Intercept	Education < HS	Education: HS	V7 Age (yrs) - 75	V5 WRAT - 45	RMSE
Memory	African Am.	0.289 (0.215, 0.363)	-0.274 (-0.432, -0.116)	-0.147 (-0.271, -0.023)	-0.030 (-0.040, -0.019)	0.022 (0.015, 0.029)	0.576
	Caucasian	0.438 (0.392, 0.484)	-0.270 (-0.382, -0.157)	-0.156 (-0.214, -0.097)	-0.035 (-0.040, -0.030)	0.032 (0.026, 0.037)	0.593
Language	African Am.	-0.044 (-0.123, 0.035)	-0.570 (-0.739, -0.400)	-0.312 (-0.444, -0.179)	-0.039 (-0.050, -0.027)	0.037 (0.029, 0.045)	0.615
	Caucasian	0.569 (0.532, 0.606)	-0.416 (-0.506, -0.326)	-0.111 (-0.158, -0.064)	-0.039 (-0.043, -0.034)	0.024 (0.020, 0.028)	0.473
Executive Function	African Am.	0.160 (0.086, 0.235)	-0.348 (-0.508, -0.188)	-0.286 (-0.411, -0.160)	-0.028 (-0.039, -0.017)	0.046 (0.038, 0.053)	0.583
	Caucasian	0.454 (0.412, 0.496)	-0.323 (-0.427, -0.220)	-0.196 (-0.249, -0.142)	-0.026 (-0.031, -0.021)	0.044 (0.040, 0.049)	0.543

Intercept corresponds to Education > HS, Age=75, WRAT=45; entries are estimates and 95% CIs, RMSE = Model root mean squared error. Results derived in job UC691102.

2.3 For each participant, a Z score relative to the Normative Sample ($Z_{NS}V7$) for each domain is calculated as the $Z_{V5}V7$ value minus that person's predicted mean from the above equation divided by the root-mean-squared error (RMSE).

2.4 A small percentage of participants have missing values for education or Visit 5 WRAT score. In these situations, when applying the prediction formula, education will be set to < HS and WRAT will be set to the median WRAT score according to age (70-74, 75-79, 80+), race, and education level (< HS, HS, > HS). Predicted scores for Asian or Native American participants were calculated using the Caucasian-specific formula.

In the final step to determine Domain Failure, the Domain $Z_{NS}V7$ scores are compared relative to the cut-point of -1.5. A person with one or more domain scores < -1.5 is considered a Cognitive Domain Failure. In addition, a person with one or more missing domain scores is considered a Cognitive Domain Failure.

2.2.b. Definite Cognitive Decline from Visit 6 (or 5) to Visit 7

Definite cognitive decline from visit 6 (or visit 5 in the absence of V6 data) to visit 7 is defined as an average annual decline of 0.055 standard deviations or more in the General Cognitive

Performance score, which is the combination of all 10 of the ARIC neurocognitive tests administered in both visits, as described in Gross (Epidemiology 2015), This consists of the items in the memory, language, and executive functioning domain plus the digit span backwards test. The standard deviation used is cross-sectional (i.e. based on ARIC visit 5 scores, not on change in scores over time.

External data, a meta-analysis performed by Gross based on 8 established aging cohorts, suggest that a decline in a global score of 0.055 standard deviations per year would select 50-60% of persons older than 75 years who become demented within 5-6 years and approximately 10% of comparable persons who do not develop dementia in that time.

Exploratory evaluation of change in the General Cognitive Performance factor from Brain MRI to Visit 5 (both scores scaled to Visit 2, provided by Gross, difference = Z_{V2}V5 – Z_{V2}MRI) for 645 participants with a non-missing score at both time-points suggests that this cut-point would have selected 78% of persons who met Dementia/MCI definition at visit 5, and 58% of comparable persons who do not develop dementia/MCI at visit 5 (2016 01 19 Sens Spec Cutpoints.sas).

Steps are as follows:

1. A participant's visit 7 General Cognitive Performance Score, also known as the global cognition score, (normed to visit 5 Z_{V5}V7) will be calculated using a formula of weighted sums based on factor analysis of all visit 5 data (Gross et al Epidemiology 2015), as shown in **section 2.3** below, and **Appendix 2.** The general cognitive performance score will be calculated as long as 1 neurocognitive test is present from the battery.

2. The participant's change in General Cognitive Performance Score per year is calculated as (Z_{V5}V7 - Z_{V5}V6)/(visit 7 date – visit 6 date/365.25). In the absence of visit 6 data, change in cognitive performance is calculated as (Z_{V5}V7 - Z_{V5}V5)/(visit 7 date – visit 5 date/365.25). The visit 5 score Z_{V5}V5 was calculated by Gross.

3. Participants with a change of -0.055 standard deviations per year or worse, or with a missing change score, are considered to have Definite Cognitive Decline.

4. If the General Cognitive Performance Score is missing because none of the items were completed or the participant missed visit 5 and visit 6, then the person will be considered Definite Cognitive Decline = Yes.

2.3 Calculation: Domain and General Cognitive Performance Scores Formulas for Calculation of Z_{V5}V7 Cognitive Domain Scores and General Cognitive Performance Score

Each participant's three domain scores and general cognitive performance score at visit 7 (Z relative to visit 5, Z_{V5}) is calculated using a formula of weighted sums based on factor analysis of visit 5 data from all participants (Gross et al Epidemiology 2015), using the below table. The table shows the coefficients for the domain and general cognition scores when all tests included in the battery have been completed. Appendix 2 contains the coefficients for all factor score equations when some neurocognitive tests are missing.

Values were provided by Gross. They were derived without regard to race (not "diff-adjusted").

The domain score is calculated as the sum across the items within the domain of the factor weight multiplied by the Z_{V5} score, which is obtained by subtracting the visit 5 mean from the

observed raw value and dividing by the visit 5 standard deviation. In the table below, the steps are simplified and the coefficients represent the factor weight divided by the visit 5 standard deviation, and the calculation is operationalized as the sum of the coefficient multiplied by the difference of the observed raw value minus the visit 5 mean. If all items in the domain or the general cognitive performance score are missing, then the score is set to missing.

Coefficients for calculation of V7 Domain Z_{V5}V7 scores from raw Visit 7 test scores

Cognitive Test	Memory Domain	Exec. Funct. Domain	Language Domain	General Cognitive Performance	Visit 5 Mean
Delayed Word Recall	0.147			0.033	5.196
Logical Memory I, II (summed)	0.033			0.006	37.960
Incidental Learning	0.119			0.031	3.304
Trail Making A		0.008		0.004	189.802
Trail Making B		0.006		0.004	111.656
Digit Symbol Substitution		0.030		0.018	37.750
Digit Span Backwards				0.037	5.522
Animal Naming			0.088	0.020	16.010
Boston Naming			0.050	0.025	24.571
Word Fluency (FAS)			0.027	0.007	32.625

Results provided by Gross January 2016
Domain Z_{V5} scores calculated by summing down columns of coefficient*(raw value – V5 mean).
Coefficients to be used when one or more items are missing are documented in Appendix 4.

3. NEUROLOGICAL INTERVIEWS (STAGE 2)

3.1. Overview

The neurologic interviews completed as part of Stage 2 include the Clinical Dementia Rating Scale (CDR) and the Neuropsychiatric Inventory (NPI). The CDR includes the CDR Participant (CDP, administered to all participants, is described in MOP 2), the CDR Informant (CDI), and the CDR Summary (CDS). The CDI and CDS are described in this MOP. In addition, the Functional Activities Questionnaire (FAQ) is used in determining a participant's level of daily functioning, but does not have a dedicated interview or form- rather, all FAQ items are embedded within the CDR interview and recorded on the CDI. Each of the measures described below are well-validated, standardized instruments that have been widely used in both clinical and epidemiologic studies of dementia and cognitive function, and include some of the measures recommended in the Uniform Data Set (UDS) implemented in 2005 across all National Institute on Aging-sponsored Alzheimer's Disease Centers.

3.2 CLINICAL DEMENTIA RATING (CDR)

3.2.1 Rationale

The CDR scale includes the CDR Informant and CDR Participant interviews, and two scores: the standard CDR summary score and the standard CDR sum-of-boxes. Since subject and

informant responses must be recorded in categories of severity which unavoidably require subjective judgment, interviewers need good training and adequate QA to assure adequate standardization. The CDR gives important information about daily functioning, and it is a required element in the determination as to whether an individual is demented or has mild cognitive impairment, or is normal. The CDP is administered to all participants and is described in MOP 2. This form (CDP) will need to be referred to, along with the CDI, when the CDR scoring is being completed (on the CDS form). Because some subjective assessments are needed in order to make the CDR scoring determinations, only staff members who have experience in neurocognitive testing, who have previously undergone CDR certification, or who have a nursing degree would be considered for CDR certification.

3.2.2 Administration: CDR Informant

The CDR Informant form is administered by a certified staff member while an informant, usually identified by the participant, is seated, in a quiet private area without the subject present, whether in the clinic or at home, LTC facility. No equipment is required for administration. The CDR informant (CDI) is administered by the psychometrist.

3.2.3. Administration: CDR summary score

The certified staff member will score the CDR after completion of these two components (participant (CDP) and informant (CDI)), and will not score them in the presence of the subject or informant. A scoring algorithm will be taught to study staff based on the responses to the questions on both the CDR subject and the CDR informant; this will be completed in the event of a missing informant, as well.

The study staff member will be primarily responsible for generating the CDR box scores, ranging from 0 (normal) to 3 (severe impairment) for each of the following 6 areas, for the standard CDR: memory (M), orientation (O), judgment and problem solving (JPS), community affairs (CA), home and hobbies (HH), and personal care (PC).

The online training module described above teaches how to translate a participant's responses into box scores, with the following basic guidelines: 0=no impairment; 0.5= questionable impairment; 1= mild impairment; 2= moderate impairment; 3=severe impairment. The standard CDR sum-of-boxes is simply a sum of the first 6 CDR box scores (with total possible range from 0 to 18). The standard Global CDR is calculated based on a formula generated at Washington University, where the CDR online training is administered. This standard Global CDR will only be used for publication purposes and will not be part of the classification or selection process. This website: http://www.biostat.wustl.edu/~adrc/cdrpgm/index.html generates a global CDR score based on individual box scores, and the same formula used to generate scores from this website are used to generate Global CDR scores based on box scores in the ARIC-NCS study.

The basic formula to generate a global CDR score is as follows: memory (M) is considered the primary category, with others considered secondary. The global CDR is the same as the M score if at least 3 secondary categories are given the same score as M; however, if 3 or more secondary categories have a score greater or less than the M score, the global CDR score equals the score of the majority of secondary categories on whichever side (scores below or scores above) of M has the greater number of secondary categories. If three of these secondary categories are scored on one side (below or above) of M and two are on the other side of M, CDR=M. When the M score is 0.5 (or greater); the global CDR cannot be 0. Instead, when M=0.5, the global CDR can be 1 if 3 or more of the other categories are scored at a 1 or greater. If M=0, the global CDR=0 unless there is a score of 0.5 or greater in two or more secondary categories (in which case CDR=0.5).

3.2.4. Administration: Functional Assessment Questionnaire (FAQ) Score

Although the Functional Assessment Questionnaire (FAQ) score is not administered as a distinct scale, the items for the FAQ are embedded within the CDR, and scoring ranges from a 0 (normal function) to 1 (has difficulty, but does by self), to 2 (requires assistance, to an FAQ of 3 (dependent), depending on the specific response. There are 9 items from the CDR which are also FAQ questions (there are 10 FAQ questions; one CDR question encompasses two FAQ questions). The following items on CDR are used for the FAQ: CDR informant items 17, 18, 22, 25, 26, 31, 35 (scored twice: covers two FAQ questions), 36, and 37. The total FAQ score, used for classification, is the sum of the 10 individual scores.

3.2.5. Quality Assurance

Online training and certification for the CDR is required (www.adrc.wustl.edu). After selecting "Begin CDR Training", the user will be asked to register after which they will have access to 9 videos, each approximately 30 minutes in duration. The trainee should plan to review these videos over several days. Two audio-taped recordings of the CDR interviews (Informant and Subject interviews) per trainee will be reviewed by the neurologic QC reviewer with oversight by a study neurologist for certification. See ARIC Visit 7 Manual 12 for additional details on neurologic quality assurance and quality control.

3.3. NEUROPSYCHIATRIC SCALE

3.3.1 Rationale: Neuropsychiatric Inventory (NPI)

The NPI consists of questions relating to personality and behavioral changes. Certain types of dementia (such as frontotemporal dementia) may be more likely based on the presence or absence of some of these behavioral changes, or the presence of significant depression in combination with a high CES-D score (from visit 7 exam) might increase the likelihood that apparent memory or other cognitive problems are actually due to depression, rather than dementia.

3.3.2 Administration: NPI

This scale is completed after the CDR with the informant (CDI) only, and is done with the informant, seated, in a quiet private space (either in clinic or at home, or by telephone). The participant should not be present. No special equipment is needed.

3.3.3 Quality Assurance

Certification and recertification are performed as described above. The NPI should be audio recorded with the CDI.

4. DIAGNOSIS AND ADJUDICATION OF MCI AND DEMENTIA

4.1. Rationale

The diagnosis of cognitive impairment is the centerpiece of ARIC-NCS. Using a variety of sources of information, our diagnostic reviewers will review data on each ARIC-NCS participant and render a syndromic diagnosis of normal cognition, mild cognitive impairment (MCI) or dementia (DEM).

The bases for the syndromic diagnoses of MCI and DEM are well-established. Current criteria for MCI (Albert, 2011) and dementia (McKhann, 2011) prominently included ARIC investigators. Current MCI criteria are a considerable advance in clarity and flexibility compared to prior versions of MCI criteria. In the case of DEM, the new criteria for all-cause dementia are based on DSM-IIIR and the dementia criteria of the 1984 NINCDS-ADRDA criteria (McKhann, 1984), but reflect the advances of the past 25 years in the field.

4.2. Personnel

Drs. Knopman, Albert, Coker, Gottesman, Mosley, and Windham will serve as diagnostic reviewers. Diagnoses of all subjects will be reviewed by two diagnostic reviewers.

Diagnosis will be assigned independently by 2 of these diagnostic reviewers. When possible, one reviewer will be a physician and one will be a neuropsychologist. Discordant cases will be assigned to a 3rd independent adjudicator (either Albert or Knopman). Cases with substantive differences may be discussed during the Neurocognitive Classification Committee teleconferences.

Because all reviewers previously participated in adjudications in ARIC visit 5 and visit 6, a formal retraining is not necessary. However, after all reviewers have completed diagnostic assessments in 10 cases (all of which were also reviewed by 2 other adjudicators), diagnostic data will be reviewed and discussed among the 6 reviewers on a conference call. If there are systematic disagreements, the reasons will be reviewed and case law formulated to achieve concordance.

The Classification Committee will have access to the following materials on each subject:

4.3. Information and Tools available to Members of Classification Committee

1. Demographic information: race, sex, age

2. Table containing historical algorithmic and syndromic diagnoses since visit 5.

3. Neuropsychiatric information (from clinic, home, long-term care)

    A. Current neurocognitive tests: Raw scores, (adjusted) cognitive domain (Z) scores, and the reason for any missing tests (i.e., recorded by the examiner at the visit as due to physical disability, etc.).

    B. Previous neurocognitive tests: Raw scores (without adjustment), for comparison with current raw scores. Note: included are DSS, DWR, WFT test scores from all previous occasions as well as the more detailed cognitive battery administered in the ARIC Brain MRI study and visit 5.

    C. Cognitive Decline: Decline in General Cognitive Performance from visit 6 to 7 (or V5 to V7 in the absence of V6 data) (defined in 2.2.b).

    D. Psychometrist comments, verbatim.

E. BLESSED items.

4. Study partner/ subjective memory (clinic, home, long-term care)

   A. CDR informant, including FAQ questions embedded; scanned complete CDI (should be given on paper) Also, any CDI "notes" from the DMS.

   B. CDR score sheet; CDS: need each box score, as well as total scores.

   C. NPI: study partner; NPI form: list each item that has a "yes" along with its severity score. No need to list items with a "No." The NPI is included in the packet to provide information to the reviewer about the participant. No item on the NPI is used for determining the syndromic diagnosis.

   D. FAQ compiled score: CDI25 + CDI26 + CDI31 + CDI35 + CDI36 + CDI37 + CDI37 + CDI18 + CDI17 + CDI22 where CDI numbered items are questions on the CDR – Informant (CDI) form

4.4. Operational criteria

All Participants who are not considered definitely cognitively normal will be reviewed by the Dementia/MCI Classification Committee with the exceptions of those participants whose visit 7 algorithmic diagnosis is the same as the previous V6 (or V5 in the absence of V6 data) reviewer diagnosis or as noted in table 4.1.

Syndromic Diagnosis

Mild Cognitive Impairment (MCI).

An MCI diagnosis is assigned in persons without dementia who meet the 3 criteria below:

1. FAQ $\leq$ 5 or CDR Sum of Boxes $\leq$ 3 (Note the FAQ data is based on an analysis of NACC database by Teng et al 2010, and CDR Sum of Boxes based on unpublished analysis of NACC data), and
2. At least one neuropsychological cognitive domain Z score < -1.5 Z (see section 2.2.a), and
3. Definite Cognitive Decline in General Cognitive Performance score (see section 2.2.b).

(Subjective complaint by subject not necessary.)

Note that we will not ask diagnostic reviewers to distinguish MCI subtypes.

Also note that the above criteria are the "ideal." In actual practice there will be cases that are close to but not strictly adherent to the above criteria that will be diagnosed with MCI. As shown in Table 4.1 below, an MCI diagnosis may also be assigned in specific instances where some of the four diagnostic elements (decline, domain failures, CDR and FAQ) are discordant.

Dementia

Diagnosis can be made either:

A. By a low MMSE score (<21 for Caucasians or <19 for African Americans), even in the absence of more complete cognitive testing.

B. By meeting all three of the following criteria:

1. FAQ > 5 or CDR SUM OF BOXES > 3, and
2. At least two neuropsychiatric cognitive domain scores < -1.5 Z (see section 2.2.a) and
3. Definite cognitive decline (see section 2.2.b).

As with MCI; there may be instances where subjects are diagnosed with dementia whose data does not strictly conform to the above criteria. As shown in Table 5.1, a dementia diagnosis may also be assigned in specific instances where the diagnostic elements are in conflict.

Normal

Participants failing to meet criteria for MCI or dementia are classified “normal”.

Computer-generated algorithmic diagnoses

The table below shows the possible combinations of decline (yes/no/missing), number of failed domains (0, 1, >1, or missing), CDR sum of boxes (0, >0 but ≤3, >3, missing) and FAQ (≤5, >5, missing). Where the criteria above are met, a diagnosis will be assigned by computer, and the table designates these cases as automatic diagnoses. In all other instances, which are expected to occur infrequently, data may be inconsistent, and the computer will provide only a “probable” or “uncertain” diagnosis. In all cases the Classification Committee will assign its own preferred diagnosis, which might differ from the computer diagnosis. The algorithmic diagnosis is available in the reviewer packet.

Every PPT who comes to V7 will be assigned an algorithmic diagnosis according to the table. The rows are mutually exclusive; each PPT will be assigned to only 1 row in the table.

Table 4.1. Computer Generated Algorithmic Diagnoses

Stratum	Decline[1]	Failed domain[2]	CDR sum of boxes	FAQ	Algorithm Dx[3]	Selected to Stage 2	Requires Review
1	PPT diagnosed with dementia at V5 (DEMDXL1_51=1)				Dem	No	No
2	MMSE score (prorated) less than 21 for white participants ***or*** MMSE score (prorated) less than 19 for black participants				Dem	No	No
3	N	ANY	uncollected	uncollected	NL	No	No
4	Y or Y due to missing	0	uncollected	uncollected	NL	No	No
5	Y or Y due to missing	1 failed OR at least 1 missing	0, missing	≤5, missing	MCI	Yes	yes
6	Y or Y due to missing	1 failed OR at least 1 missing	0	>5	Prob MCI	Yes	yes
7	Y or Y due to missing	1 failed OR at least 1 missing	>0 but ≤3	≤5, missing	MCI	Yes	yes
8	Y or Y due to missing	1 failed OR at least 1 missing	>0 but ≤3	>5	Prob MCI	Yes	yes
9	Y or Y due to missing	1 failed OR at least 1 missing	>3	≤5	Prob Dem	Yes	yes
10	Y or Y due to missing	1 failed OR at least 1 missing	>3	>5, missing	Prob Dem	Yes	yes
11	Y or Y due to missing	>1	0, missing	≤5, missing	MCI	Yes	yes
12	Y or Y due to missing	>1	0	>5	Prob MCI	Yes	yes
13	Y or Y due to missing	>1	>0 but ≤3	≤5	MCI	Yes	yes
14	Y or Y due to missing	>1	>0 but ≤3	>5, missing	Prob MCI	Yes	yes

Stratum	Decline[1]	Failed domain[2]	CDR sum of boxes	FAQ	Algorithm Dx[3]	Selected to Stage 2	Requires Review
15	Y or Y due to missing	>1	>3	≤5	Prob Dem	Yes	yes
16	Y or Y due to missing	>1	>3	>5, missing	Dem	Yes	yes

1 Definite cognitive decline is described in section 2.2.b of manual. Meeting the decline criteria is necessary for selection to stage 2 data collection. The criteria may be met if the annual decrease exceeds 0.055 SD/year OR if decline is missing for the PPT.
2 Number of failed domains is described in section 2.2.a of the manual. A domain is failed if any one domain z score <-1.5 OR if the domain score is missing.
3 The algorithmic diagnosis will be assigned according to the following hierarchy: 1) PPTs diagnosed with dementia at V5, 2) PPTs with low, race specific prorated MMSE (row 0); then 3) according to the PPTs domain failure, cognitive decline, CDR sum of boxes, and FAQ (rows 3+).

4.5. Case Law

Clarifications to diagnostic criteria made after initiation of the review process will be documented in this section as case law.

1. For cases with full neuropsych data but missing CDR and FAQ, a syndrome dx would be:
   - Normal if neuropsych domain scores are all >-1.5 Z
   - Dementia if MMS<21 for whites and <19 for blacks
   - All other cases will have to be reviewed.

Primary Review

Participants are selected for primary review if they meet the operational criteria (see Section 4.4)

Adjudication Review

Cases are selected for adjudication review if the original reviewers do not reach agreement. A list of cases and a set of case packets for cases needing adjudication is sent to one of the two adjudication reviewers (**note:** if either of the two adjudication reviewers served as a primary reviewer for a case requiring adjudication review, the case is sent to the other adjudication reviewer). The adjudication reviewer examines the case packet and the DCFs of the original reviewers and determines the syndromic diagnosis; two outcomes are possible, either singly or in combination:

- The adjudicator records his/her diagnoses in an “Adjudication” DCF
- If the adjudication reviewer feels that diagnostic classification is too complex, the case may be discussed on the monthly Neurocognitive Classification Committee teleconference.

Appendix 1. CDR: 0/0.5/1/2/3: Level of impairment

	0 (None)	0.5 (Questionable)	1 (Mild)	2 (Moderate)	3 (Severe)
Memory	No memory loss, or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss, more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
Judgment and problem solving	Solves everyday problems, handles business and financial affairs well; judgment good in relation to past performance	Slight impairment in these activities	Moderate difficulty in handling problems, similarities and differences; social judgment usually maintained	Severely impaired in handling problems, similarities and differences; social judgment usually impaired	Unable to make judgments or solve problems
Community Affairs	Independent function at usual level in job, shopping, volunteer and social groups	Life at home, hobbies and intellectual interests slightly impaired	Unable to function independently at these activities, although may still be engaged in some; appears normal to casual inspection	No pretense of independent function outside the home; appears well enough to be taken to functions outside the family home	No pretense of independent function outside the home; appears too ill to be taken to functions outside the family home
Home and Hobbies	Life at home, hobbies and intellectual interests well maintained	Life at home, hobbies, and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies and interests abandoned.	Only simple chores preserved; very restricted interests; poorly maintained	No significant function in the home.

	0 (None)	0.5 (Questionable)	1 (Mild)	2 (Moderate)	3 (Severe)
Personal Care	Fully capable of self-care		Needs prompting	Requires assistance in dressing, hygiene, keeping of personal effects	Requires much help with personal care; frequent incontinence

Appendix 2. Domain and General Cognition Score Coefficients

Factor score coefficients needed for computations of domain and general cognitive performance when some cognitive tests are missing.

Table 1: Memory

Pattern of missing tests*	Delayed Word Recall	Logical Memory	Incidental Learning
001	NULL	NULL	0.272
010	NULL	0.05	NULL
011	NULL	0.04	0.145
100	0.332	NULL	NULL
101	0.239	NULL	0.194
110	0.177	0.04	NULL
111	0.147	0.033	0.119

*0 INDICATES TEST IS MISSING AND 1 INDICATES TEST IS PRESENT

Table 2: Executive Functioning Domain

Pattern of missing tests*	Trails A	Trails B	Digit Symbol Substitution
001	NULL	NULL	0.068
011	NULL	0.008	0.037
100	0.025	NULL	NULL
101	0.013	NULL	0.046
110	0.012	0.009	NULL
111	0.008	0.006	0.03

*0 INDICATES TEST IS MISSING AND 1 INDICATES TEST IS PRESENT

Table 3: Language Domain

Pattern of missing tests*	Semantic Learning	Boston Naming Test	Word Fluency
001	NULL	NULL	0.057
010	NULL	0.12	NULL
011	NULL	0.077	0.041
100	0.152	NULL	NULL
101	0.108	NULL	0.032
110	0.115	0.065	NULL
111	0.088	0.05	0.027

*0 INDICATES TEST IS MISSING AND 1 INDICATES TEST IS PRESENT

Table 4: Global Cognition

Pattern of missing tests*	Delayed Word Recalled	Logical Memory	Incidental Learning	Trails A	Trails B	Digit Symbol Substitutio	Digit Span Backwards	Semantic Learning	Boston Naming	Word Fluency
0000000010	NULL	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.134	NULL
0000000100	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.132	NULL	NULL
0000000101	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.096	NULL	0.034
0000000110	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.079	0.097	NULL
0000000111	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.065	0.079	0.023
0000001010	NULL	NULL	NULL	NULL	NULL	NULL	0.161	NULL	0.108	NULL
0000001101	NULL	NULL	NULL	NULL	NULL	NULL	0.145	0.079	NULL	0.028
0000001110	NULL	NULL	NULL	NULL	NULL	NULL	0.123	0.067	0.083	NULL
0000010000	NULL	NULL	NULL	NULL	NULL	0.066	NULL	NULL	NULL	NULL
0000010100	NULL	NULL	NULL	NULL	NULL	0.053	NULL	0.059	NULL	NULL
0000010101	NULL	NULL	NULL	NULL	NULL	0.045	NULL	0.05	NULL	0.018
0000010111	NULL	NULL	NULL	NULL	NULL	0.036	NULL	0.04	0.049	0.014
0001000110	NULL	NULL	NULL	0.012	NULL	NULL	NULL	0.056	0.069	NULL
0001001111	NULL	NULL	NULL	0.01	NULL	NULL	0.08	0.044	0.054	0.016
0001011110	NULL	NULL	NULL	0.007	NULL	0.031	0.062	0.034	0.042	NULL
0001011111	NULL	NULL	NULL	0.007	NULL	0.028	0.057	0.031	0.038	0.011
0001111111	NULL	NULL	NULL	0.005	0.004	0.021	0.043	0.023	0.029	0.008
0010010100	NULL	NULL	0.081	NULL	NULL	0.047	NULL	0.052	NULL	NULL
0010010101	NULL	NULL	0.071	NULL	NULL	0.041	NULL	0.045	NULL	0.016
0010010111	NULL	NULL	0.057	NULL	NULL	0.033	NULL	0.037	0.045	0.013
0011010110	NULL	NULL	0.053	0.007	NULL	0.031	NULL	0.034	0.042	NULL
0011010111	NULL	NULL	0.048	0.007	NULL	0.028	NULL	0.031	0.038	0.011
0011011101	NULL	NULL	0.053	0.007	NULL	0.031	0.062	0.034	NULL	0.012
0011011110	NULL	NULL	0.049	0.007	NULL	0.028	0.058	0.032	0.039	NULL

Pattern of missing tests*	Delayed Word Recalled	Logical Memory	Incidental Learning	Trails A	Trails B	Digit Symbol Substitutio	Digit Span Backwards	Semantic Learning	Boston Naming	Word Fluency
0011011111	NULL	NULL	0.045	0.006	NULL	0.026	0.053	0.029	0.036	0.01
0011110010	NULL	NULL	0.042	0.006	0.005	0.025	NULL	NULL	0.034	NULL
0011110111	NULL	NULL	0.036	0.005	0.004	0.021	NULL	0.023	0.029	0.008
0011111010	NULL	NULL	0.04	0.006	0.005	0.023	0.047	NULL	0.032	NULL
0011111111	NULL	NULL	0.034	0.005	0.004	0.02	0.041	0.022	0.027	0.008
0100000110	NULL	0.018	NULL	NULL	NULL	NULL	NULL	0.065	0.08	NULL
0100001100	NULL	0.022	NULL	NULL	NULL	NULL	0.147	0.081	NULL	NULL
0100001101	NULL	0.018	NULL	NULL	NULL	NULL	0.12	0.066	NULL	0.023
0100001110	NULL	0.016	NULL	NULL	NULL	NULL	0.105	0.057	0.07	NULL
0100001111	NULL	0.014	NULL	NULL	NULL	NULL	0.09	0.049	0.061	0.017
0101000110	NULL	0.014	NULL	0.011	NULL	NULL	NULL	0.049	0.06	NULL
0101001110	NULL	0.012	NULL	0.01	NULL	NULL	0.081	0.44	0.054	NULL
0101001111	NULL	0.011	NULL	0.009	NULL	NULL	0.072	0.039	0.048	0.014
0101011111	NULL	0.008	NULL	0.006	NULL	0.026	0.052	0.029	0.035	0.01
0101111011	NULL	0.007	NULL	0.005	0.004	0.021	0.043	NULL	0.029	0.008
0101111111	NULL	0.006	NULL	0.005	0.004	0.02	0.04	0.022	0.027	0.008
0110011110	NULL	0.01	0.053	NULL	NULL	0.031	0.063	0.034	0.042	NULL
0110011111	NULL	0.009	0.049	NULL	NULL	0.028	0.057	0.031	0.039	0.011
0111010111	NULL	0.008	0.044	0.006	NULL	0.026	NULL	0.029	0.035	0.01
0111011110	NULL	0.008	0.045	0.006	NULL	0.026	0.053	0.029	0.036	NULL
0111011111	NULL	0.007	0.042	0.006	NULL	0.024	0.049	0.027	0.033	0.01
0111111010	NULL	0.007	0.037	0.005	0.004	0.022	0.044	NULL	0.03	NULL
0111111110	NULL	0.006	0.035	0.005	0.004	0.02	0.041	0.022	0.027	NULL
0111111111	NULL	0.006	0.033	0.005	0.004	0.019	0.038	0.021	0.026	0.007
1000000000	0.282	NULL	NULL	NULL	NULL	NULL	NULL	NULL	NULL	NULL
1000000001	0.189	NULL	NULL	NULL	NULL	NULL	NULL	NULL	NULL	0.041

Pattern of missing tests*	Delayed Word Recalled	Logical Memory	Incidental Learning	Trails A	Trails B	Digit Symbol Substitutio	Digit Span Backwards	Semantic Learning	Boston Naming	Word Fluency
1000000100	0.176	NULL	NULL	NULL	NULL	NULL	NULL	0.108	NULL	NULL
1000000101	0.135	NULL	NULL	NULL	NULL	NULL	NULL	0.083	NULL	0.029
1000000111	0.095	NULL	NULL	NULL	NULL	NULL	NULL	0.058	0.072	0.021
1000001010	0.125	NULL	NULL	NULL	NULL	NULL	0.14	NULL	0.094	NULL
1000001110	0.099	NULL	NULL	NULL	NULL	NULL	0.111	0.061	0.075	NULL
1000001111	0.084	NULL	NULL	NULL	NULL	NULL	0.095	0.052	0.064	0.018
1000010000	0.107	NULL	NULL	NULL	NULL	0.059	NULL	NULL	NULL	NULL
1000010001	0.09	NULL	NULL	NULL	NULL	0.05	NULL	NULL	NULL	0.02
1000010101	0.076	NULL	NULL	NULL	NULL	0.042	NULL	0.046	NULL	0.016
1001001111	0.066	NULL	NULL	0.009	NULL	NULL	0.074	0.041	0.05	0.014
1001010110	0.056	NULL	NULL	0.008	NULL	0.031	NULL	0.034	0.042	NULL
1001011100	0.062	NULL	NULL	0.008	NULL	0.034	0.07	0.038	NULL	NULL
1001011111	0.048	NULL	NULL	0.006	NULL	0.026	0.054	0.029	0.036	0.01
1001111110	0.039	NULL	NULL	0.005	0.004	0.022	0.044	0.024	0.029	NULL
1001111111	0.036	NULL	NULL	0.005	0.004	0.02	0.041	0.022	0.028	0.008
1010010000	0.094	NULL	0.089	NULL	NULL	0.052	NULL	NULL	NULL	NULL
1010010001	0.081	NULL	0.077	NULL	NULL	0.045	NULL	NULL	NULL	0.018
1010010010	0.073	NULL	0.069	NULL	NULL	0.04	NULL	NULL	0.055	NULL
1010010100	0.078	NULL	0.075	NULL	NULL	0.43	NULL	0.048	NULL	NULL
1010010101	0.069	NULL	0.066	NULL	NULL	0.038	NULL	0.042	NULL	0.015
1010010111	0.057	NULL	0.054	NULL	NULL	0.031	NULL	0.035	0.043	0.012
1010011111	0.053	NULL	0.05	NULL	NULL	0.029	0.059	0.032	0.04	0.011
1011010111	0.048	NULL	0.046	0.006	NULL	0.027	NULL	0.029	0.036	0.01
1011011101	0.052	NULL	0.05	0.007	NULL	0.029	0.059	0.032	NULL	0.011
1011011110	0.049	NULL	0.047	0.007	NULL	0.027	0.055	0.03	0.037	NULL
1011011111	0.045	NULL	0.043	0.006	NULL	0.025	0.051	0.028	0.034	0.01

Pattern of missing tests*	Delayed Word Recalled	Logical Memory	Incidental Learning	Trails A	Trails B	Digit Symbol Substitutio	Digit Span Backwards	Semantic Learning	Boston Naming	Word Fluency
1011110111	0.037	NULL	0.035	0.005	0.004	0.02	NULL	0.022	0.028	0.008
1011111110	0.037	NULL	0.035	0.005	0.004	0.02	0.042	0.023	0.028	NULL
1011111111	0.035	NULL	0.033	0.005	0.004	0.019	0.039	0.021	0.026	0.008
1100000101	0.111	0.019	NULL	NULL	NULL	NULL	NULL	0.068	NULL	0.024
1100000110	0.096	0.016	NULL	NULL	NULL	NULL	NULL	0.059	0.072	NULL
1100000111	0.082	0.014	NULL	NULL	NULL	NULL	NULL	0.05	0.062	0.018
1100001101	0.096	0.016	NULL	NULL	NULL	NULL	0.108	0.059	NULL	0.021
1100001110	0.085	0.014	NULL	NULL	NULL	NULL	0.095	0.052	0.064	NULL
1100001111	0.074	0.013	NULL	NULL	NULL	NULL	0.083	0.045	0.056	0.016
1100010111	0.056	0.009	NULL	NULL	NULL	0.031	NULL	0.034	0.042	0.012
1100011110	0.057	0.01	NULL	NULL	NULL	0.031	0.064	0.035	0.043	NULL
1101000111	0.065	0.011	NULL	0.009	NULL	NULL	NULL	0.04	0.049	0.014
1101001011	0.069	0.012	NULL	0.009	NULL	NULL	0.077	NULL	0.052	0.015
1101001101	0.074	0.013	NULL	0.01	NULL	NULL	0.083	0.045	NULL	0.016
1101001110	0.067	0.011	NULL	0.009	NULL	NULL	0.075	0.041	0.05	NULL
1101001111	0.06	0.01	NULL	0.008	NULL	NULL	0.067	0.037	0.045	0.013
1101011110	0.048	0.008	NULL	0.006	NULL	0.027	0.054	0.03	0.036	NULL
1101011111	0.044	0.008	NULL	0.006	NULL	0.025	0.05	0.027	0.034	0.01
1101101110	0.047	0.008	NULL	0.006	0.005	NULL	0.052	0.029	0.035	NULL
1101101111	0.043	0.007	NULL	0.006	0.005	NULL	0.048	0.026	0.032	0.009
1101110111	0.036	0.006	NULL	0.005	0.004	0.02	NULL	0.022	0.027	0.008
1101111111	0.034	0.006	NULL	0.005	0.004	0.019	0.039	0.021	0.026	0.008
1110010101	0.062	0.011	0.059	NULL	NULL	0.034	NULL	0.038	NULL	0.013
1110010111	0.052	0.009	0.049	NULL	NULL	0.029	NULL	0.032	0.039	0.011
1110011100	0.064	0.011	0.06	NULL	NULL	0.035	0.071	0.039	NULL	NULL
1110011110	0.053	0.009	0.051	NULL	NULL	0.029	0.059	0.032	0.04	NULL

Pattern of missing tests*	Delayed Word Recalled	Logical Memory	Incidental Learning	Trails A	Trails B	Digit Symbol Substitutio	Digit Span Backwards	Semantic Learning	Boston Naming	Word Fluency
1110011111	0.049	0.008	0.046	NULL	NULL	0.027	0.054	0.03	0.037	0.011
1110111111	0.037	0.006	0.035	NULL	0.004	0.02	0.041	0.023	0.028	0.008
1111010110	0.048	0.008	0.046	0.006	NULL	0.027	NULL	0.03	0.036	NULL
1111010111	0.045	0.008	0.042	0.006	NULL	0.025	NULL	0.027	0.034	0.01
1111011010	0.05	0.009	0.048	0.007	NULL	0.028	0.056	NULL	0.038	NULL
1111011101	0.048	0.008	0.046	0.007	NULL	0.027	0.054	0.03	NULL	0.011
1111011110	0.045	0.008	0.043	0.006	NULL	0.025	0.051	0.028	0.034	NULL
1111011111	0.042	0.007	0.04	0.006	NULL	0.023	0.047	0.026	0.032	0.009
1111110111	0.034	0.006	0.033	0.005	0.004	0.019	NULL	0.021	0.026	0.008
1111111011	0.035	0.006	0.034	0.005	0.004	0.02	0.04	NULL	0.027	0.008
1111111101	0.037	0.006	0.035	0.005	0.004	0.02	0.041	0.023	NULL	0.008
1111111110	0.035	0.006	0.033	0.005	0.004	0.019	0.039	0.021	0.026	NULL
1111111111	0.033	0.006	0.031	0.004	0.004	0.018	0.037	0.02	0.025	0.007

*0 INDICATES TEST IS MISSING AND 1 INDICATES TEST IS PRESENT

Appendix 3. Dementia Classification Review Instructions

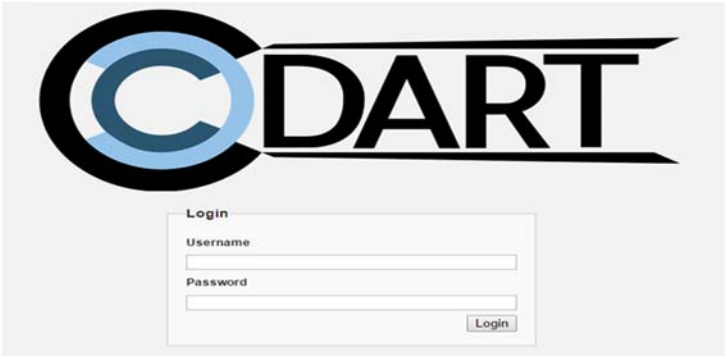
MOP 17: Appendix 3

Procedural Overview: Dementia Classification Review

CDART URL: https://cdart2.cscc.unc.edu/CDART2/login.jsp

ARICHelp Contact: Email (arichelp@unc.edu) or (877) 967-8732

1

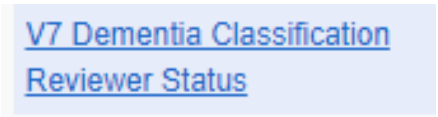


Login Screen: enter credentials

2

Click “Reports” and locate the “V7 Dementia Classification Reviewer Status Report” on the resulting screen.

3



Click report link to run.

4

1) Enter parameters. **Please select your reviewer ID only from the dropdown**

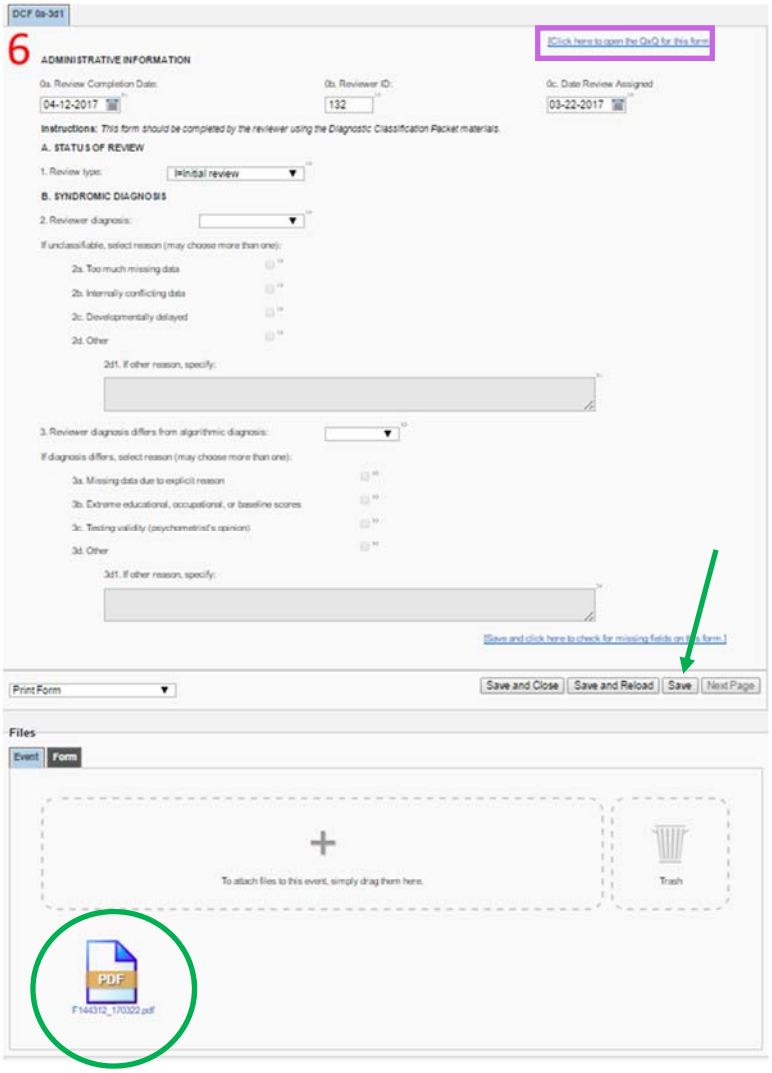
2) Select “Assigned” to create a list of assigned cases to review

3) Click “Ok” in bottom right of

5

Report result is a list of reviews to be completed. Click the report link to open the DCF.

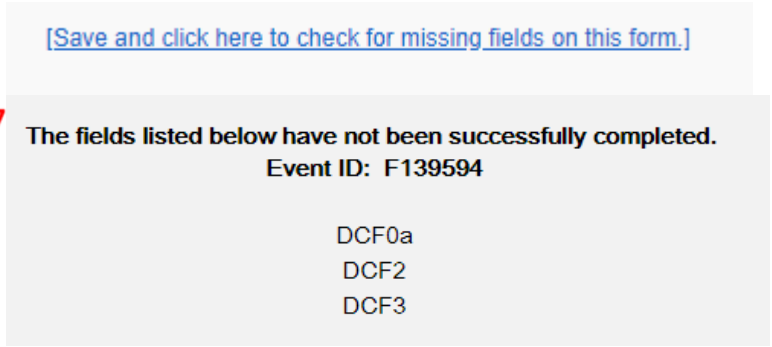
6



Double click on the pdf icon (green circle) to open the attached reviewer's packet. The packet will open in a new tab for you to toggle between the form and the packet. Use the information in the packet to complete the DCF. For DCF completion instructions, open the question-by-question (QxQ) by clicking the link in the top right corner of the screen (purple box) .

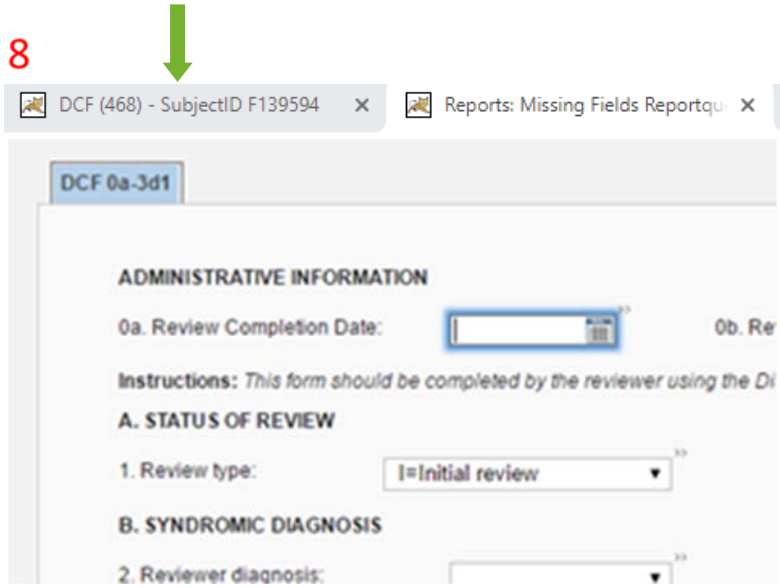
After data entry is complete, click "**SAVE**" (green arrow). Saving the form pushes the data to the database. It is important to **SAVE** frequently, because reports need saved data to display accurate information.

7



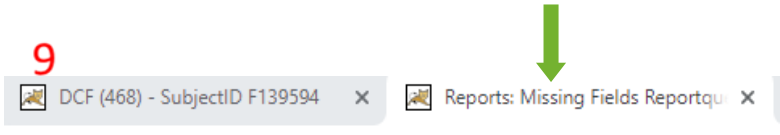
After you have completed the data entry and **SAVED** the form, click the link at the bottom of the DCF form to open the missing fields report. The missing fields report result opens in a new tab, and will show any fields in the form that do not have a value entered. The screenshot is an example that shows the DCF with three empty fields. Note: If the data you entered has not been **SAVED**, it will appear as missing.

8

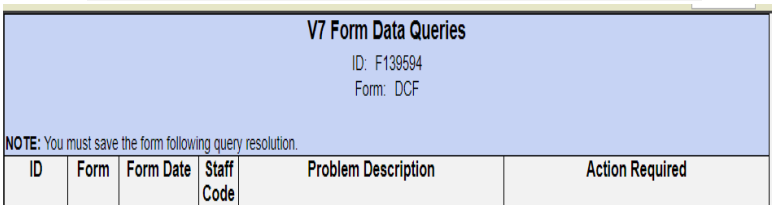


To address missing fields, return to the open DCF form (green arrow) and enter all missed data. **SAVE** the form.

9

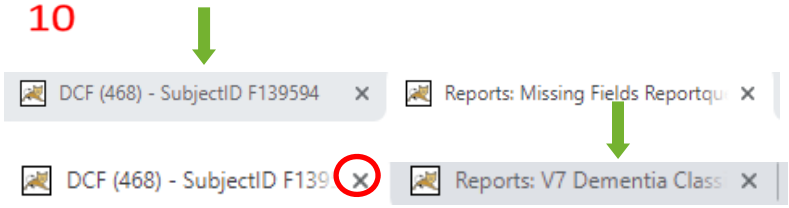


A Click here to run the DCF Query Report.



Return to the Missing Fields Report (green arrow) to run the DCF Query Report. Click the link (A). The query report describes any data entry errors and the action required to correct them.

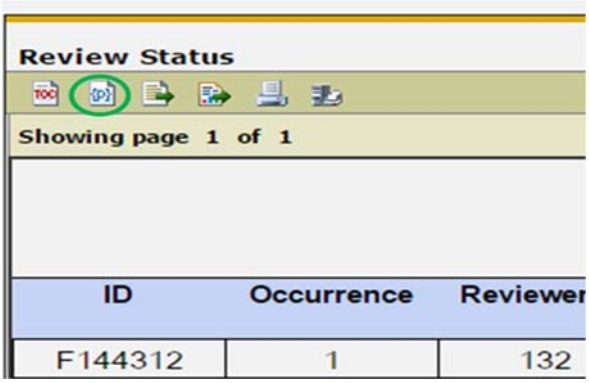
10



Return to the DCF to correct the data entry errors and then **SAVE** the form.

Once you have **SAVED**, you can close the DCF (red circle) and return to the V7 Dementia Classification Review Status Report tab that is still open (green arrow).

11



Refresh the Dementia Classification Review Status Report by clicking the icon (green circle). The pop-up box from step 4 will appear with your parameters already selected. Click “OK.” This will update the values in the table and drop the participant ID you just completed. You can then restart the process from step 5 with a different participant ID.