# Visit 6 Manual 17

## ARIC Neurocognitive Exam

05 Apr 2017

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

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## List of Abbreviations

| | |
|---|---|
| ARIC | Atherosclerosis Risk in Communities Study |
| CA | Community Affairs |
| 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 | 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 6 Neurocognitive Study (ARIC V6 NCS) is the 6th ARIC examination, to be completed in 2016-2017 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 6 Manual of Procedure (MOP) sections where the procedures are described in detail.

An historical overview of Visit 5 NCS may be reviewed in Manual 16 and Manual 17 for Visit 5.

## 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 V6 NCS Manual 2.

# 2. STAGE 2 SELECTION FOR ARIC EXAM 6

## 2.1. Overview

ARIC V6 NCS has two stages. Stage 1 includes the full cognitive test battery. Stage 2 consists of informant interviews and is limited to only those participants who meet cognitive criteria for poor cognitive performance. Depending on informant availability, Stage 2 may be conducted at the visit 6 exam or (by telephone) shortly after the exam. A participant must attend visit 6 to be eligible to be selected to Stage 2.

Participants with a diagnosis of Dementia (Level 1) at visit 5 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 6, 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 5 to visit 6.

Cognitive Domain Failure is defined in Section 2.2.a.
Definite Global Cognitive Decline from visit 5 to visit 6 is defined in section 2.2.b.

Selection for Stage 2 will be automated so that it can be implemented in real time at visit 6 as soon as visit 6 cognitive test scores are entered into the CDART database. This will facilitate immediate implementation of Stage 2, when needed. 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, Stage 2 is limited to those that meet the cognitive criteria (described above).*

Note that these two criteria, cognitive domain failure (Section 2.2.a) and visit 5 to visit 6 cognitive decline (Section 2.2.b) which are used for Stage 2 selection are also required for a diagnosis of MCI or dementia at visit 6 (section 4.4).

There may be some participants who come to visit 6 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. "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 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 6 Cognitive Domain Z Scores**

Step B has 2 sub-parts:

1. Each participant's three Visit 6 domain scores (normed to visit 5 $Z_{V5}V6$) 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 $Z_{V5}V6$ scores are converted to Z scores relative to the Normative Sample ($Z_{NS}V6$) as the $Z_{V5}V6$ 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 | V6 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 ($Z_{NS}V6$) for each domain is calculated as the $Z_{V5}V6$ 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 $Z_{NS}V6$ 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 domain scores = missing is considered a Cognitive Domain Failure.

### 2.2.b. Definite Cognitive Decline from Visit 5 to Visit 6

Definite cognitive decline from visit 5 to visit 6 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 6 General Cognitive Performance Score (normed to visit 5 $Z_{V5}$V6) 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 4.** 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 ($Z_{V5}$V6 - $Z_{V5}$V5)/(visit 6 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 did not attend visit 5, then the person will be considered Definite Cognitive Decline = Yes.

### 2.3 Calculation: Domain and General Cognitive Performance Scores Formulas for Calculation of $Z_{V5}$V6 Cognitive Domain Scores and General Cognitive Performance Score

Each participant's three domain scores and general cognitive performance score at visit 6 (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 V6 Domain $Z_{V5}V6$ scores from raw Visit 6 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; described in MOP 2 as this is administered to all participants), 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. 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 as part of stage

1, so 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. In the event that the informant does not accompany the subject in person to stage 1, the CDR informant can be administered by the study nurse over the telephone, as is standard for this portion of the CDR; this generally shortens the duration of the clinic visit.

### 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 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. I 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 a study neurologist for certification.

During the first 6 months of the study, 2 audiotaped sessions of the CDR interviews (CDR-Subject [CDP]; CDR-Informant CDI]) and associated documentation (PDF file from DMS for CDP, CDI, and CDR-Summary [CDS]), for each interviewer will be reviewed by a neurologic expert. After the initial 6 month period, the neurologic expert will review one session per interviewer, noting deviations from the standardized protocol. General feedback that pertains to all examiners will be provided on QC Committee conference calls. These calls will also provide an opportunity to discuss and problem-solve various exam issues that may arise.

## 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 Stage 1) 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, depending on the remainder of the visit). 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 diagnosis of normal cognition, mild cognitive impairment (MCI) or dementia (DEM). In the absence of neuroimaging at visit 6, only a syndromic diagnosis will be made. Information pertaining to criteria for etiologic diagnoses assigned at visit 5 may be found in MOP XX.

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). Substantive differences will be discussed by conference call with the entire Classification Committee for final diagnosis. Discordant cases will be settled by consensus. If a committee member cannot agree, the case will be tagged as discordant, with the primary diagnosis being the one agreed on by 2 of 3 reviewers.

Because all reviewers previously participated in adjudications in ARIC visit 5, 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. Additional test case reviews will depend on the outcome of the first exercise. Thereafter, a telephone conference call will occur 3 months after adjudication activities begin, in order to address issues that have arisen. A teleconference for the diagnostic reviewers will take place at least every 3 months over the course of the ARIC-NCS recruitment.

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. 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 5 to 6 (defined in 2.2.b).

D. Psychometrist comments, verbatim.

3. 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."

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.

***Syndromic Diagnosis***

Mild Cognitive Impairment (MCI).

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

1. FAQ ≤ 5 or CDR Sum of Boxes ≤ 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. That can and will be accomplished through the neuropsychological test results.

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 V6 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+).

**Etiologic Diagnosis**

Formal assignment of etiologic diagnosis is not being performed in ARIC V6 because we lack a face to face neurological examination as well as some other key elements from the history. However, at the completion of syndromic adjudication in ARIC V6, we will attempt to contact all persons with diagnoses of MCI or dementia and who had a stroke according to ARIC surveillance or other ARIC history information to ascertain 1) whether or not there was a temporal relationship of the onset of cognitive impairment to the stroke (within 1 year). We will then use that information along with information from imaging (presence of infarcts and burden of white matter hyperintensities) to derive a diagnosis algorithmically of cerebrovascular etiology for the cognitive impairment.

### 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; and/or
- If the adjudication reviewer feels that diagnostic classification is too complex, s/he refers the case to the full committee by entering a DCF in the Full Committee event.

If the adjudication reviewer does not refer the case to the full committee, review is considered complete and the DCF locked by the adjudicator.

***Full Committee Review***

Cases are selected for full committee review based on the adjudicator's opinion.

- The committee reviews the case packet material and determines a syndromic diagnosis.
- The adjudicator records the committee's diagnoses in a "Full Committee" DCF
- Review is complete

## 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

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

### Table 1: Memory

| MEMPATT | DWRMD | LOGMEMMD | INCLRNMD |
|---|---|---|---|
| 001 | 0 | 0 | 0.272 |
| 010 | 0 | 0.05 | 0 |
| 011 | 0 | 0.04 | 0.145 |
| 100 | 0.332 | 0 | 0 |
| 101 | 0.239 | 0 | 0.194 |
| 110 | 0.177 | 0.04 | 0 |
| 111 | 0.147 | 0.033 | 0.119 |

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

### Table 2: Executive Functioning Domain

| EFPATT | TMTAEFD | TMTBEFD | DSSEFD |
|---|---|---|---|
| 001 | 0 | 0 | 0.068 |
| 011 | 0 | 0.008 | 0.037 |
| 100 | 0.025 | 0 | 0 |
| 101 | 0.013 | 0 | 0.046 |
| 110 | 0.012 | 0.009 | 0 |
| 111 | 0.008 | 0.006 | 0.03 |

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

### Table 3: Language Domain

| LANGPATT | SEMANTLD | BNT30LD | FASLD |
|---|---|---|---|

| | | | |
|---|---|---|---|
| 001 | 0 | 0 | 0.057 |
| 010 | 0 | 0.12 | 0 |
| 011 | 0 | 0.077 | 0.041 |
| 100 | 0.152 | 0 | 0 |
| 101 | 0.108 | 0 | 0.032 |
| 110 | 0.115 | 0.065 | 0 |
| 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 |

| 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| 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 |
| 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 |

| 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| 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 |
| 1000000100 | 0.176 | NULL | NULL | NULL | NULL | NULL | NULL | 0.108 | NULL | 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| 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 |

| 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| 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 |
| 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 |

| 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| 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