Manual 16

ARIC Neurocognitive Study Overview

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Study website - **http://www.cscc.unc.edu/aric/**

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1. OVERVIEW

The ARIC Neurocognitive Study (ARIC NCS) is integrated operationally with the 5th ARIC examination, in 2011-13, of survivors of the 15,792 middle aged participants first seen in 1987-89, and it evaluates their cognitive performance. 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. Genetic markers and cerebral imaging features are also studied.

Participants are invited for exams in clinic or in their homes or long-term care (LTC) facilities. Those who cannot be examined in person are assessed by telephone. Additional information about participant's cognitive and functional status is sought from informants when necessary. Some participants are invited for further evaluation and brain MR imaging. An expert committee reviews data and classifies dementia, MCI and their subtypes.

This overview lists all ARIC NCS components with reference to corresponding Exam 5 Manual of Procedure (MOP) sections where the procedures are described in detail.

1.1. Eligibility

All surviving ARIC participants are eligible for ARIC NCS.

1.2. Recruitment

Recruitment begins during the ARIC Annual Follow-up interview (MOP 2, Section 3).

2. CLINIC EXAMS

2.1. Stage 1

The first part of the ARIC NCS clinic exam (Stage 1) is concurrent with ARIC Exam 5. The combined exam takes 6 to 7 hours. Participants who require further cognitive evaluation and comparison subjects are invited for separate visits (NCS Stages 2 and 3). Components of the clinic exam which are specific for NCS Stage 1 are listed in the table below:

Components of Stage 1 (clinic)	MOP/Section
Blood and urine collection and processing	7
MMSE	2/12
Neurocognitive test battery	2/12
Subjective memory	2/20
CES Depression	2/12
MRI exclusions	MRI exclusion form
Selection for Stages 2 and 3	17/1
Consent for Stage 2 (when eligible)	Not in 2/7
Exit interview	2/24

2.2. Selection for Stage 2 and 3

Before departure from Stage 1, the participant's cognitive status is evaluated by an automated computer algorithm for possible cognitive impairment based on their cognitive test performance at Stage 1, decline in test performance from earlier ARIC exams and evidence of functional decline. Those meeting criteria for possible cognitive impairment and a small comparison sample without impairment are invited for Stage 2 and 3 exams at separate visits. In some cases, informants will need to be interviewed in order to determine Stage 2 and 3 eligibility. These interviews are promptly scheduled (CDR informant interview telephone call, MOP17 Section 3). Persons with MRI contraindications are not eligible for Stage 3. Criteria for selection are described in MOP 17 Section 1, and the selection procedures are detailed in MOP 2 Section 3. Stage 3 scheduling of persons who do not have contraindications to MRI is coordinated with MRI facility availability.

2.3. Stage 2

Stage 2 components are listed in the table:

Components of Stage 2 (clinic)	MOP/Section
Neurologic and dementia history	2/21
Neurologic family history	2/21
Neurological examination: • Physical and neurological exam • Unified Parkinson's Rating Scale • Clinical Dementia Rating (CDR subject) • Hachinski Ischemic Scale	17/2-4
Retinal photography	14A
Informant interview • CDR informant and summary • Neuropsychiatric Inventory)	17/3-4
MRI Consent	13
Selection for MRI	17/1
Exit interview	MOP17/4

2.4. Stage 3

Stage 3 is cerebral MR imaging (MOP 13. It is scheduled on the same day as Stage 2 when possible.

3. HOME AND LONG-TERM CARE FACILITY (LTC) VISITS

All participants unable or unwilling to be examined in clinic are invited for NCS Stage 1 exams at home or LTC where they reside. Because the prevalence of dementia is expected to be higher for those seen at home, a short mental status screener will be administered by phone prior to the home exam (MOP 2 Section 3 and the Annual Follow-Up Interview manual). The phone screen will allow arrangement for a proxy or informant prior to the visit. NCS Stage 1 components for home and LTC exams are the same as for clinic exams. As in the clinic exam, the participant's cognitive testing results are evaluated by an automated computer algorithm for possible cognitive impairment (described above). If the participant is eligible, Stage 2 is

performed at the same visit. Relaxed criteria are used for selection for Stage 2 for the home exam compared to the clinic exam, because these examinees are expected to have a higher prevalence of cognitive impairment. Selection is described in MOP 17 Section 1.

Stage 2 exams are similar to those performed in clinic, except that there is no retinal exam, and no home or LTC examinees are scheduled for Stage 3. ARIC NCS components are listed in the table.

Components of Stage 1 (home/LTC)	**MOP/Section**
Screening and abbreviated exam for frail or severely impaired	2/4
Blood and urine collection and processing	7
Neurocognitive test battery/ subjective memory	2/12
Subjective memory	2/20
CES Depression	2/12
Selection for Stage 2	17/1
Exit interview	2/24
Components of Stage 2 (home/LTC)	
Neurologic and dementia history	2/21
Neurologic family history	2/21
Neurological examination: Physical and neurological exam Unified Parkinson's Rating Scale Clinical Dementia Rating (CDR subject) Hachinski Ischemic Scale	17/2-4
Informant interview CDR informant and summary Neuropsychiatric Inventory)	17/3-4
Exit interview	17/4

The Stage 1 NCS examination components which are also part of home visits in ARIC Exam 5, i.e. reception, consent, contact updates, height and weight, blood pressure, personal and medical history, and medication inventory are described in MOP 2.

4. TELEPHONE INTERVIEW (TICS)

Participants who cannot be scheduled for examination in either clinic or home/LTC are interviewed using the Telephone Interview for Cognitive Status. Scheduling the TICS requires a separate telephone call for those who schedule an examination but fail to appear (MOP 2 Section 3).

5. LABORATORY ASSAYS

Biospecimen Collection and Processing and instructions for shipping to the laboratories are described in MOP7. Methods of analyses are described in MOP8.

All ARIC visit 5 and NCS Stage 1 examinees will have the following assays:

> Cholesterol, triglycerides, HDL-cholesterol, calculated LDL-cholesterol when triglycerides are <400 mg/dL, Cystatin C, Uric acid, Troponin T, Hs CRP, NT=proBNP, , CBC, HbA1c, Blood creatinine, Urine albumin, and Urine creatinine. Those seen in clinic (but not at home or long-term care facility) will also have Glucose and Insulin assays.

These will be assayed as received, with clinically relevant reports back to participants, as specified in MOP2 Section 26.

All examinees selected for Stage 2 because of potential cognitive impairment, whether from clinic or home, will also have the following assays:

> Thyroid stimulating hormone and B12

These will be assayed as received, with clinically relevant reports back to participants as specified in MOP2 Section 26.

All examinees selected for Stage 2 from clinic (but not home) will have the following assays:

> B-amyloid 1-40 and B-amyloid 1-42, in blood from both the current visit and from ARIC visit 3, and D-dimer, Plasminogen, and vWF antigen from ARIC visit 3.

These will be analyzed in batches, with no expected participant reports.

See ARIC Visit 5 Manual 8 (Laboratory Methods), section 5.2, for details regarding these assays.

6. CLASSIFICATION

Classification Committee structure and operations, Dx criteria and methods, and assembly of records for classification are described in MOP17 Section 5.