Manual 20

Surveillance of Dementia in the ARIC Cohort

Version 2.2

January 9, 2025

Summary of Version Changes in the Dementia Surveillance Protocol

Minor changes to wording and page and section numbering have been made. Substantial changes have been made as follows:

Date	Section	Modification
Jan 2025	3.3	Updates were made in the Quality Assurance section of the manual to reflect the updates made in Nov 2022 when QC/Cert recordings shifted from being posted to the ARIC website to being uploaded to the Microsoft Teams OneDrive (Sharepoint) described in Memo #075.2022.
	3.4	Dementia surveillance discontinues when a living participant is classified as having dementia according to the Dementia Classification Committee OR with 2 IMPAIRED SIS OR 1 IMPAIRED ADS. No additional SIS or AD8 interviews are required. In this instance, the interviewer is notified about a participant's dementia status when "None-DEM" is displayed in the tracing sheet report in the "Type of Dementia Surveillance to Collect" field in the tracing sheet.
	3.5	1. The interviewer should attempt to collect the SIS if the Tracing Sheet displays "ADS" and a LAR/proxy/informant is unable to be interviewed. 2. If the participant or LAR/proxy mentions wanting to complete the SIS, unprompted by the interviewer, the interviewer's first response is to share with the participant that the SIS is not needed at this time. If the participant or LAR/proxy insists, the interviewer may collect the SIS.
Sep 2022	3 Table 1a	Updated recommendation from the ARIC Neurocognitive Classification Committee to attempt to collect the SIS(E/O) when the AD8 is recommended to be collected but the interviewer is unable to collect it.
	3	A related recommendation was made by the ARIC Neurocognitive Classification Committee to collect the dementia surveillance instruments annually. The delays associated with complying with sIRB re-consenting has disrupted the typical interviewing schedule for AFU. If the annual interview is missed (which was the traditional time to collect dementia surveillance), collect the SIS/ADS at the semi-annual interview.
Jun 2019	3.4	The tracing sheet reports now display which dementia surveillance instrument to collect during the interview.
Jun 2019	3.5	Dementia surveillance discontinues when a living participant is classified as having dementia according to the Dementia Classification Committee OR with 2 IMPAIRED SIS OR 1 IMPAIRED ADS.

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SURVEILLANCE OF DEMENTIA IN THE ARIC COHORT

1. BACKGROUND AND RATIONALE

With the aging of the ARIC cohort and the extended focus on aging-related outcomes, ascertainment of incident neurodegenerative diseases in general, and dementia in particular, is a priority in ARIC. Thus, ARIC and ARIC-NCS collaborate to determine the presence of prevalent dementia in the ARIC study participants by several means, set out in this protocol manual. In those attending ARIC Visit 5 (Stages 1-3), Visits 6 or 7, prevalent mild cognitive impairment (MCI) and dementia were ascertained and classified based on procedures described in ARIC-NCS protocols Manuals 16 and 17 (https://sites.cscc.unc.edu/aric/cohort-manuals). A cognitive assessment was also done using Telephone Interview for Cognitive Status (TICS) in those unable to attend Visit 5 but willing to undergo a phone assessment.

The prevalence of dementia in deceased cohort members and in those not participating in Visit 5 and unavailable for a TICS interview was estimated as described in Section 2 using a modified Clinical Dementia Rating Scale interview to proxy informants, referred to here as the Dementia Rating Interview for living participants (DRL) and the Dementia Rating Interview for deceased participants (DRD) forms (https://sites.cscc.unc.edu/aric/cohort-forms-forms). Subsequent to the completion of the ARIC-NCS cohort examination/ARIC Visit 5, new cases of dementia are prospectively identified through a short phone-based assessment tied to ARIC's annual phone follow-up (AFU) call. These prospective dementia ascertainment procedures are described in Section 3.

2. RETROSPECTIVE ASCERTAINMENT OF DEMENTIA IN THE ARIC COHORT

The retrospective ascertainment of potential cases of dementia targeted ARIC cohort members who were not examined at ARIC visit 5/NCS and declined (or where unable) to complete the TICS, and for whom cognitive impairment was suspected based on any of the following sources:

- an interviewer's assessment recorded on the ARIC Contact Information Update (CIU) form (starting with Visit 5 recruitment)
- an ICD-9 dementia hospital discharge code (defined in Appendix A) recorded on the Cohort Eligibility (CEL) form at any point since the start of cohort surveillance
- a self-report of dementia diagnosis on the semi-annual follow-up interview (starting with the introduction of the question on the GEN v1 on January 1, 2012)
- the reliance on a proxy or other contact for the annual or semiannual follow-up interview (based on most recent interview prior to data retrieval)
- the lack of a TICS attributed to hearing loss. A random sample (n~100) of all others who declined the TICS also was included. The first set of lists was distributed in July 2013, based on data retrieved July 24, 2013. A second set of lists was distributed in November 2013 after completion of the TICS. The lists were based on data available as of November 20, 2013.

Cohort participants who died before attending the visit were selected for the retrospective ascertainment of dementia if known to have died on or after January 1, 2004 and having no V5

data, if cognitive impairment was suspected based on a CEL form with an ICD-9 dementia discharge code or a DTH (Death Certificate) form with an ICD-9 or ICD-10 death code (ICD-10 codes are defined in Appendix B). A random sample of 100 other participants who died on or after January 1, 2004 and before attending ARIC's visit 5 examination also was included. Deceased participants identified through CEL were included in the lists distributed in July and November 2013. A set of lists of deceased participants identified through DTH was distributed in March 2014 based on data retrieved March 26, 2014.

3. PROSPECTIVE ASCERTAINMENT OF DEMENTIA IN THE ARIC COHORT

Prospective ascertainment of dementia will be conducted in the entire living, non-demented cohort as part of annual follow-up (AFU) calls to identify possible dementia cases on an ongoing basis.

One of two brief instruments will be administered on the participant or their designated proxy or other contact person during the annual phone follow-up (AFU calls only, not semi-AFU). The instrument to be administered will be determined algorithmically with input from the person completing the AFU interview. The Six Item Screener (SIS) will be administered directly to the participant whenever possible, and the ADS (AD8 Dementia Screening Interview) will be administered to a knowledgeable proxy informant in cases where a proxy or other contact person is the primary AFU contact.

There will be instances when the result of the last dementia surveillance instrument is 'Not Scored.' The reason the test was not scored will also be displayed on the tracing sheet to help inform the data collector about the last dementia surveillance data collection. The information may be helpful and provide justification for not collecting the instrument that is recommended by the algorithm. For example, there may be situations where the recommended instrument to collect is the ADS and the interviewer is unable to collect it. In that instance the interviewer should collect the SIS despite the recommendation on the tracing sheet. See table 1a for the recommended dementia surveillance instrument to collect for all data collection scenarios when the participant is alive. Carefully review the banded rows to learn about using discretion in the data collection.

In summer 2022, the ARIC Neurocognitive Classification Committee recommended that the dementia surveillance instrument be collected annually. The delays associated with complying with sIRB re-consenting disrupted the typical interviewing schedule for AFU. If the annual interview is missed due to the sIRB reconsenting, the Committee recommends to collect the dementia surveillance instrument in the semi-annual interview, especially if the last dementia surveillance collection was done in the previous contact year. More generally, the goal is to ensure that one dementia surveillance assessment is completed each year. This can be done at either the annual or the semi-annual follow-up. In the event that a given interview is missed, for whatever reason, the very next scheduled interview should include dementia surveillance, regardless if it is the annual or the semi-annual call.

Table 1a. Data Collection Decision Algorithm for Living Participants

Participant Status	Dementia Surveillance Respondent	Neurocognitive Instrument to Collect
Alive and not impaired	ARIC cohort member	SIS
Alive and one SIS IMPAIRED OR last dementia surveillance instrument was SIS with a 'Not Scored' result Note: the SIS is not scored when 1) the SIS is not attempted (SIS1=No) 2) 3 or more questions on the SIS are missing responses	Proxy/informant/other	ADS
Alive and last dementia surveillance instrument was ADS with a 'Not Scored' result Note: the ADS is not scored when 1) the ADS is not attempted (ADS1=No) 2) Too many missing responses on ADS	Proxy/informant/other OR ARIC cohort member	**Interviewer's discretion:** ADS or SIS
Alive and last dementia surveillance instrument was SIS IMPAIRED AND the ADS is **UNABLE to be collected**	ARIC cohort member	**Interviewer's discretion:** SIS
Alive and classified as having dementia	No interview	No interview

For deceased, non-demented participants, the ADS will be administered during the final interview of proxies and four questions about neurological diagnoses (currently asked in the ARIC Medical Conditions Update form) will also be asked.

The ADS is not administered following a study participant's death if 1) an IMPAIRED score is recorded on the ADS prior to the interview of the decedent's proxy, 2) two SIS interviews were scored as IMPAIRED prior to the death interview, or 3) an ADS was administered within 1 year of the participant's death, and this ADS was scored as NOT IMPAIRED. See table 1b for the recommended dementia surveillance instrument to collect for all data collection scenarios for deceased participants. Carefully review the banded row to learn about using discretion in the data collection.

Table 1b. Data Collection Decision Algorithm for Deceased Participants

Participant Status	Dementia Surveillance Respondent	Neurocognitive Instrument to Collect
Deceased and last dementia surveillance instrument was SIS with either a NOT IMPAIRED OR a NOT SCORED result	Proxy/informant/other	ADS + Neurological Dx questions
Deceased and an ADS administered within 1 year of the participant's death was scored as NOT IMPAIRED	No interview	No interview
Deceased and last dementia surveillance instrument, either SIS or ADS, had an IMPAIRED result	No interview	No interview
Deceased and last dementia surveillance instrument was the ADS, collected when the participant was alive, with a NOT SCORED result	Proxy/informant/other	**Interviewer's discretion:** None OR ADS + Neurological Dx questions

Participant Status	Dementia Surveillance Respondent	Neurocognitive Instrument to Collect
Deceased and classified as having dementia	No interview	No interview

Dementia cases will continue to be identified through ARIC's clinic exams, prospective dementia surveillance, and community surveillance network (ie. via hospital discharge codes and DTH form codes).

3.1. The Six Item Screener

3.1.1. Rationale

The SIS is a short instrument developed to identify cognitive impairment in older adults.[1] SIS items were derived from the widely used Mini Mental State Examination (MMSE). It is readily administered over the phone (e.g., performed by phone in the Reasons for Geographic and Racial Differences in Stroke study; REGARDS)[2] and has excellent diagnostic properties that are comparable to the full MMSE. Diagnostic performance can be adjusted by selecting a cut-point which best matches study objectives. Sensitivity and specificity for diagnosis of dementia is excellent. For example, using a cut-point of 3 or more errors, sensitivity was reported as 88.7% and specificity as 88.0%.[1]

3.1.2. Administration: SIS

The SIS is administered by phone by certified interviewers. No equipment is required for administration.

3.2. The AD8

3.2.1. Rationale

The AD8 is a brief instrument developed to discriminate between normal aging and dementia.[3] The items were derived from the Clinical Dementia Rating (CDR) interviews, a gold standard dementia rating system. The AD8 was designed to be administered as an informant-based interview, completed by a spouse or other knowledgeable informant. It is short, easily scored, and readily administered over the phone. The AD8 has been shown to reliably differentiate between demented and non-demented individuals. For example, using a cut-point of two items endorsed, sensitivity was reported as 85% and specificity as 86%.[3]

3.2.2. Administration: ADS (AD8 Dementia Screening Interview)

The ADS is administered by phone by certified interviewers. No equipment is required for administration.

3.3. Quality Assurance

Prior to the administration of the SIS and ADS, interviewers are trained and certified to a common level of proficiency. Training includes a webinar to introduce the procedures and forms to the follow-up interviewers. Following training, interviewers practice locally on volunteers. Once the interviewer feels that administration has been mastered, the interviewer will audio-tape 3 SIS and 3 ADS assessments, conducted on age-appropriate volunteers, and enter data into the CDART certification server. The 3 audio-taped SIS and 3 audio-taped ADS assessments are then uploaded to Microsoft Teams/SharePoint site (refer to ARIC memo 075.2022 on the ARIC website - https://aric.cscc.unc.edu/aric9/memo - for instructions) for review by their local lead psychometrist along with a corresponding PDF of the completed forms that were entered into CDART CERT by the field centers. Practice and Certification assessments are not performed on ARIC participants. Examiner certification for the SIS and ADS is achieved by the successful

administration of the 6 certification assessments reviewed and approved by the site's lead psychometrist. The field center follow-up supervisor is responsible for notifying the data coordinating center of any new personnel who may require training and certification. Training for dementia surveillance will be part of training for AFU.

Maintaining proficiency in the administration of the neurocognitive measures requires regular exposure to the protocol. To maintain certification, the AFU interviewers participate in an AFU round robin process. The round robin process is defined in a memo which should be followed by the site staff.

3.4. Data Management in CDART

The ADS or SIS is administered at the end of the AFU interview. The participants' responses are entered into CDART directly, or recorded on the paper versions of the forms for delayed data entry into CDART.

The Annual Participant Tracing Sheet and Semi-annual Participant Tracing Sheet provide information to the interviewer regarding participant cognitive status, which dementia surveillance instrument and result was last collected and which, if either, instrument should be collected during the interview. The fields that provide this information are described in the next table.

Field Name	Content Description
Last Dementia Surveillance Test and Result	Last Dementia Surveillance Test and Result gives SIS or ADS results collected from the last dementia surveillance interview, if SIS or ADS has been collected from either the PPT or their proxy. The results displayed will be 1) Impaired, 2) Not impaired, or 3) Not scored. If no SIS or ADS has ever been collected, 'None' is displayed.
Type of Dementia Surveillance to Collect	This field provides information as to whether dementia surveillance interview is expected to be done for the follow-up contact and if so, what type of dementia surveillance form needs to be collected. It has a value of 1) None-DEM, 2) SIS, 3) ADS*, None-ADS Not Scored. *If ADS cannot be administered, please try to collect the SIS instead, despite the recommendation

- A SIS will be listed in the report to collect if the
  - participant has never received any AFU dementia surveillance interview,
  - participant's previous dementia surveillance results, either SIS or ADS, have shown only NOT IMPAIRED
- An ADS will be listed if the participant has had 1 IMPAIRED SIS result and no IMPAIRED ADS results.

- Neither instrument will be collected if an ARIC participant has a dementia or IMPAIRED classification based on ARIC exams or 2 IMPAIRED SIS results or 1 IMPAIRED ADS result. Tracing sheet displays “None-DEM” in Type of Dementia Surveillance to Collect.

3.5. Transition to Proxy Status and Discontinuation of Dementia Surveillance

For participants whose last SIS interview status is ‘IMPAIRED’ or 'Not Scored' or the ‘Cognitive Problems’ field is printed as ‘Yes’, and the instrument to be collected is the ADS, the interviewer should make a polite attempt to convert from participant interviews to proxy/informant interviews for future follow-up calls. If the participant declines this suggestion, his/her wishes are respected, and an attempt to convert to a proxy/informant can be revisited at a future call. If the Tracing Sheet displays “ADS” and a LAR/proxy/informant is unable to be interviewed, the interviewer should collect the SIS.

At the end of the interview with a proxy/informant/other person, the interviewer is asked to answer three questions assessing the interviewee’s knowledge and reliability, and referencing any extenuating circumstances that might have influenced the interview.

Discontinuation of dementia surveillance.

Administration of the SIS or ADS is discontinued if

1) the participant has been classified as having dementia based on ARIC exam classification,
2) an IMPAIRED score is recorded on the ADS, or
3) two SIS interviews are scored as IMPAIRED.

As mentioned in Section 3, the ADS is not administered following a study participant’s death if

1) an IMPAIRED score is recorded on the ADS prior to the participant death interview,
2) two SIS interviews were scored as IMPAIRED prior to the death interview, or
3) an ADS was administered within 1 year of the participant’s death, and this ADS was scored as NOT IMPAIRED.

Scenarios that may lead to more than one impaired SIS scores may result from:

1) a case where, after the initial impaired SIS, the participant declines engagement of a proxy/informant and thus continues to answer the SIS on subsequent calls, or
2) if the participant agrees to engage a proxy/informant but the call is conducted with both the participant and proxy/informant on the call. In this case, since the participant is on the phone, the participant is administered the SIS rather than the ADS, even though a proxy/informant was engaged. In the latter scenario, the SIS is administered to the participant only after the proxy is no longer on the line.

Scenarios that may lead to collecting a SIS when the Type of Dementia Surveillance to Collect is “None-DEM”:

1) if the participant or LAR/proxy mentions wanting to complete the SIS, unprompted by the interviewer, the interviewer's first response is to share with the participant that the SIS is not needed at this time. If the participant or LAR/proxy insist, the interviewer may collect the SIS.

References

1. Callahan CM, Unverzagt, FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Medical Care. 2002; 40:771-781.
2. Unverzagt FW et al. Vascular Risk Factors and Cognitive Impairment in a Stroke-free Cohort. Neurology. 2011; 77:1729-1736.
3. Galvin JE, Rose CM, Powlishta KK, et al. the AD8. A brief informant interview to detect dementia. Neurology. 2005; 65:559-564.

APPENDIX A

ICD-9-CM Codes Consistent with Dementia Diagnosis

290 Dementias
* 290.0 Senile dementia uncomplicated
* 290.1 Presenile dementia
* 290.10 … uncomplicated
* 290.11 … with delirium
* 290.12 … with delusional features
* 290.13 … with depressive features
* 290.2 Senile dementia with delusional or depressive features
* 290.20 Senile dementia with delusional features
* 290.21 Senile dementia with depressive features
* 290.3 Senile dementia with delirium
* 290.4 Vascular dementia
* 290.40 … uncomplicated
* 290.41 … with delirium
* 290.42 … with delusions
* 290.43 … with depressed mood
* 290.8 Other specified senile psychotic conditions
* 290.9 Unspecified senile psychotic condition

294 Persistent mental disorders due to conditions classified elsewhere
* 294.0 Amnestic disorder in conditions classified elsewhere
* 294.1 Dementia in conditions classified elsewhere
* 294.10 … without behavioral disturbance
* 294.11 … with behavioral disturbance
* 294.2 Dementia, unspecified
* 294.20 … without behavioral disturbance
* 294.21 … with behavioral disturbance
* 294.9 Unspecified persistent mental disorders due to conditions classified elsewhere

[Not included: 249.8 Other persistent mental disorders due to conditions classified elsewhere]

331 Other cerebral degenerations
* 331.0 Alzheimer's disease
* 331.1 Pick's disease
* 331.11 Pick's disease
* 331.19 Other frontotemporal dementia
* 331.2 Senile degeneration of brain
* 331.7 Cerebral degeneration in diseases classified elsewhere
* 331.8 Other cerebral degeneration
* 331.82 Dementia with lewy bodies
* 331.83 Mild cognitive impairment, so stated
* 331.89 Other cerebral degeneration
* 331.9 Cerebral degeneration unspecified

APPENDIX B

ICD-10 CODES CONSISTENT WITH DEMENTIA DIAGNOSIS

F00 Dementia in Alzheimer's disease
F00.0 Dementia in Alzheimer's disease, early onset
F00.1 Dementia in Alzheimer's disease, late onset
F00.2 Dementia in Alzheimer's disease, atypical or mixed
F00.9 Dementia in Alzheimer's disease, unspecified

F01 Vascular dementia
F01.0 Vascular dementia of acute onset
F01.1 Multi-infarct dementia
F01.2 Subcortical vascular dementia
F01.3 Mixed subcortical and cortical vascular dementia
F01.5 Vascular dementia
F01.50 Vascular dementia without behavioral disturbance
F01.51 Vascular dementia with behavioral disturbance
F01.8 Other vascular dementia
F01.9 Vascular dementia, unspecified

F02 Dementia in other diseases classified elsewhere
F02.0 Dementia in Pick's disease
F02.1 Dementia in Creutzfeldt-Jakob disease
F02.2 Dementia in Huntington's disease
F02.3 Dementia in Parkinson's disease
F02.4 Dementia in human immunodeficiency virus (HIV) disease
F02.8 Dementia in other diseases classified elsewhere
F02.80 Dementia in other diseases classified elsewhere without behavioral disturbance
F02.81 Dementia in other diseases classified elsewhere with behavioral disturbance

F03 Unspecified dementia
F03.9 Unspecified dementia
F03.90 Unspecified dementia without behavioral disturbance
F03.91 Unspecified dementia with behavioral disturbance

F05.1 Delirium superimposed on dementia

F06.7 Mild cognitive disorder

G31.0 Frontotemporal dementia
G31.01 Pick’s disease
G31.83 Dementia with Parkinsonism
G31.09 Other Frontotemporal dementia
G31.83 Lewy Body Dementia
G31.84: Mild cognitive impairment, so stated
G31.1 Senile degeneration of brain, not elsewhere classified

G30 Alzheimer’s disease
G30.0 Alzheimer’s disease with early onset

G30.1 Alzheimer's disease with late onset
G30.8 Other Alzheimer's disease
G30.9 Alzheimer's disease, unspecified