Manual 34 Appendices

Appendices are identified by section number in Manual 34, and are found in the secure section of the ARIC study Website under
[Researchers > Cohort Studies > Current and Archived Visit Documents > Manuals]

Appendix 1. MRI Summary of Results Template Letters

A. Template Letter – No Change

MRI Summary of Results for Participants and their Physicians

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in this study at our Field Center. We appreciate your willingness to join us in this important study.

Since your last brain MRI exam on ***[MM/DD/YYYY],*** there has been no significant change. This means that there were no new abnormalities, and any abnormality that was reported in your last exam was seen again and appeared stable.

Thank you again for your participation in this study.

B. Template Letter – Change

MRI Summary of Results for Participants and their Physicians

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in this study at our Field Center. We appreciate your willingness to join us in this important study.

We have reviewed the images from your MRI exam. The findings are below:

Abnormality or alert	Description
Acute infarction	An acute infarction (stroke) was seen on your MRI scan.
Subacute infarction	A subacute infarction (stroke) was seen on your MRI scan. This may have occurred a while ago.
Acute subdural or epidural hematoma	An acute subdural or epidural hematoma was noted on your MRI scan.
Subarachnoid hemorrhage	A subarachnoid hemorrhage (bleeding from a blood vessel in your brain) was observed on your MRI scan.
Acute intraparenchymal hematoma	An acute intraparenchymal hematoma (hemorrhage in the brain) was seen on your MRI scan.

Abnormality or alert	Description
Obstructive hydrocephalus	An obstructive hydrocephalus (an abnormal accumulation of cerebrospinal fluid in your brain) was seen on your MRI scan.
Significant space occupying lesion (i.e., tumor)	A significant space-occupying lesion was observed on your MRI scan.
Benign tumor with no mass effect	A benign tumor with no mass effect (no pressure or swelling) was seen in your brain during your MRI scan. This likely does not pose a risk to your health.
Communicating hydrocephalus	A communicating hydrocephalus – an abnormal accumulation of cerebrospinal fluid in your brain – was seen in your brain during your MRI scan.

[Brain Reading Center comment]

This is new since your last brain MRI exam on ***[MM/DD/YYYY]***. Because the study does not provide any clinical diagnosis or treatment, we offer to send our brain MRI report to your physician or provider, when requested. If you do not have a personal physician or do not know where to find one, please call the ARIC center where you had your visit. We encourage you to review these results with your physician to determine whether the results should be studied further.

Thank you again for your participation in this study.

C. Template Letter – No Prior Scan, Normal

MRI Summary of Results for Participants and their Physicians

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in this study at our Field Center. We appreciate your willingness to join us in this important study.

We have reviewed the images from your MRI exam. There were no alerts or abnormalities found by the brain reading center.

Thank you again for your participation in this study.

D. Template Letter – No Prior Scan, Alert/Abnormality

MRI Summary of Results for Participants and their Physicians

Date: [run date]

Participant's name: **Birth Date:**
Date of MRI: **ID:**

Thank you for taking part in this study at our Field Center. We appreciate your willingness to join us in this important study.

We have reviewed the images from your MRI exam. The findings are below:

Abnormality or alert	Description
Acute infarction	An acute infarction (stroke) was seen on your MRI scan.
Subacute infarction	A subacute infarction (stroke) was seen on your MRI scan. This may have occurred a while ago.
Acute subdural or epidural hematoma	An acute subdural or epidural hematoma was noted on your MRI scan.
Subarachnoid hemorrhage	A subarachnoid hemorrhage (bleeding from a blood vessel in your brain) was observed on your MRI scan.
Acute intraparenchymal hematoma	An acute intraparenchymal hematoma (hemorrhage in the brain) was seen on your MRI scan.
Obstructive hydrocephalus	An obstructive hydrocephalus (an abnormal accumulation of cerebrospinal fluid in your brain) was seen on your MRI scan.
Significant space occupying lesion (i.e., tumor)	A significant space-occupying lesion was observed on your MRI scan.
Benign tumor with no mass effect	A benign tumor with no mass effect (no pressure or swelling) was seen in your brain during your MRI scan. This likely does not pose a risk to your health.
Communicating hydrocephalus	A communicating hydrocephalus – an abnormal accumulation of cerebrospinal fluid in your brain – was seen in your brain during your MRI scan.

[Brain Reading Center comment]

Because the study does not provide any clinical diagnosis or treatment, we offer to send our brain MRI report to your physician or provider, when requested. If you do not have a personal physician or do not know where to find one, please call the ARIC center where you had your visit. We encourage you to review these results with your physician to determine whether the results should be studied further.

Thank you again for your participation in this study.

Appendix 2. MRI Summary of Results Template Letters with Visit 10 Neurocognitive Testing Results

A. Visit 10 Neurocognitive Template Letter – Atypical

Visit 10 Neurocognitive Testing Results

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in the ARIC Study. The results of the tests you took related to memory and concentration are lower than expected for your age, and suggest that you may be experiencing some problems with memory or concentration. There are many possible conditions that may cause these difficulties, and our testing only represents results from your recent visit.

Testing results may vary from visit to visit, which may explain if your results are different from your last report, but based on your test results, we recommend that you notify your personal physician or health care clinic to discuss whether you might benefit from further medical evaluation. We would be glad to assist with an appropriate referral if you do not have a personal physician or other source of health care.

We are grateful for your time and effort as a member of ARIC. Sincerely,

B. Visit 10 Neurocognitive Template Letter – Typical

Visit 10 Neurocognitive Testing Results

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in the ARIC Study. The results for the tests you recently took related to memory and concentration are within the expected range for someone your age. Testing results may vary from visit to visit, which may explain if your results are different from your last report.

We are grateful for your time and effort as a member of ARIC.

C. Visit 10 Neurocognitive Template Letter – Undetermined

Visit 10 Neurocognitive Testing Results

Date: [run date]

Participant's name: **Birth Date:**
Date of visit to the ARIC field center: **ID:**

Thank you for taking part in the ARIC Study. Regrettably, because a limited number of measures could be completed during the exam, we are unable to provide an interpretation of the tests you recently took related to memory and concentration.

We are grateful for your time and effort as a member of ARIC.

Appendix 3. ARIC Amyloid PET Disclosure Outline

Overview of reasons for new amyloid PET disclosure policy

Traditionally, amyloid PET results were not shared with participants because they would not lead to any actionable change in their management and treatment. Within the past several years, new potential treatments are available for individuals who have cognitive impairment (mild cognitive impairment or mild dementia) and evidence of elevated amyloid on brain PET. Although the purpose of this new policy is *not* to provide treatment recommendations, it is in this context that the study has moved to a model where results are offered to those potential individuals who are within this cognitive status group.

Overview of results disclosure process

(1) The coordinating center will generate a report that lists all participants who had a PET scan in ARIC any time since November 1, 2022 and whose cognitive status is determined as dementia or mild cognitive impairment (MCI) by *algorithmic* diagnosis (see *NOTE* below).

(2) These ARIC participants on the above list will be sent a letter offering a conversation with a local expert to provide them with their PET results.

(3) Participants who respond to the letter and request results will be scheduled to speak with a local expert. Participants will be strongly encouraged to invite a family member who is a caregiver or proxy to join the disclosure call.

(4) The local expert will have a video or phone call with the participant +/- any family members. After a screen for suicidality, the local expert will proceed with disclosing results and answering any questions.

(5) Participants will be provided with a list of local resources (for all who request results, whether positive or negative) and, if requested, a copy of the “short form” of the PowerPoint that was shared with them by video call (or phone call).

(6) After completion of the phone or video disclosure, a followup letter of results will be provided to the participant and, if requested, their physician.

PET results

(1) PET results will depend on qualitative reads and will be read as “positive” (elevated) or “negative” (not elevated).

(2) The PET reading center at Washington University will generate these qualitative reads by November 15, 2024 (for the first half of top-priority scans within the proposed disclosure period) and February 2025 (for the second half of scans from the proposed disclosure period).

(3) Going forward, PET scans will be read for qualitative results (elevated/not elevated) within 3 months of scan acquisition, for scans acquired from November 15, 2024 onwards.

(4) For PET scans with uncertainty of the read, “probable positive” and “probable negative” will be provided by the reading center to the coordinating center. These will be considered “positive” (elevated) and “negative” (not elevated), respectively, for the purposes of disclosure to the participant and the local expert, if requested.

Letter asking for results interest to participants

(1) A standard letter template will be available and should be sent by mail to those individuals using the list of participants and the **CDART PET Scan Summary of Results Report**.

   a. Field center will record the date the letter asking for results interest is sent to the participant in **PSR Q1**.

(2) Each field center will send out letters for individuals on the report for their site.

(3) There is no need to followup on the letter with a call or query for those participants who do not contact the field center with interest for a meeting.

Participant calls in response to the letter asking for results interest

(1) Participants who call the field center in response to having received a letter should be scheduled for a meeting with the local expert.

   a. Field center will record the scheduling information in **PSR Q2 and Q2a**.

(2) Sites may need to identify preferred scheduling blocks of time for the local expert ahead of time, to facilitate scheduling once participants start calling in. Each field center will determine the best scheduling approach to account for the local expert's preferences.

(3) During the call, the preference is to schedule a video visit for the local expert disclosure (e.g. Zoom); if not possible, a telephone visit should be scheduled instead.

(4) Participants should be strongly encouraged to have a family member join them for the video or phone call with the local expert. ***"Because the expert will provide you with a fair amount of information, we recommend that you have a family member or someone that you are comfortable with hearing your results join for the call."***

(5) Some participants may not receive a letter (people with normal/typical cognition or with a PET scan prior to the reporting window) and may still reach out asking for results. If they call asking for results, these individuals should be offered a video or phone call with a local expert to discuss their results, with the same above preferences (2, 3 and 4, above).

   a. For participants who reach out for results and whose results have not been read yet by the PET reading center, a list of these participant ID's will be expedited to Washington University for a request for an earlier read, with the goal of having these scans read within 1 month.

(6) Ideally, video or phone visits should be scheduled within 4 weeks of the participant calling in. This may not be feasible in the initial roll-out of results reporting, but an attempt to keep this lag relatively short (within 6-8 weeks maximum) is preferred.

(7) It is recommended that, for those participants requesting a video visit, they be asked if they have used Zoom before and if they would like a brief instruction on how to use the Zoom platform. Sites are welcome to offer a "practice" Zoom session to help participants' comfort with the system. In the event that a Zoom meeting is scheduled, these should be scheduled and created by the field center staff.

(8) For Zoom meetings, staff should ask the participant what email address should be used for them to send a Zoom link to. This meeting link should also be sent to the local expert and, if preferred for local scheduling, a calendar invite should be sent to the local expert with the link included. Staff should not email the participant and local expert in the same email (please do not share the local expert's direct contact information with the participant).

(9) For phone meetings, staff should ask the participant the best phone number to use to contact them on the scheduled day/time. This number should be provided to the local expert, also ideally as a calendar invite to the local expert. The expert's phone number *should not* be given directly to the participant.

Disclosure visit

(1) We recommend that the local expert allocate up to 45 minutes for the disclosure visit. We anticipate they will take closer to 15-20 minutes in most cases.

(2) Prior to the visit, confirmation from the coordinating center and field center is required to confirm what the participant's disclosure result is.

   a. *The CC will provide a list of participant ID and PET disclosure results to field center and local expert.*

(3) The table below lists the PowerPoint that corresponds with the participant's reporting results.

PET Reporting Results	Type of Presentation Disclosure	Location on ARIC Website
Normal - Negative	PETDisclosure_COGNORMAL_NEG.pptx	[Researchers > Supporting Documents > V11 / NCS > **PET Disclosure Session PowerPoints (For Discussion Session with Expert)]**
Normal - Positive	PETDisclosure_COGNORMAL_POS.pptx	
Dementia - Negative	PETDisclosure_DEM_NEG.pptx	
Dementia - Positive	PETDisclosure_DEM_POS.pptx	
MCI - Negative	PETDisclosure_MCI_NEG.pptx	
MCI - Positive	PETDisclosure_MCI_POS.pptx	

(4) At the start of the call, the local expert should introduce him/herself, disclose their affiliation with the ARIC study, and state that they understand the participant is interested in learning their results from their PET scan.

(5) Prior to starting the PowerPoint disclosure materials, the local expert should state, ***"People respond to news about their health in different ways, so before we get started, I would like to ask some questions about your mood. Is that okay?"***

(6) After verification to proceed, the local expert should ask the following questions: ***"Are you having any thoughts of harming yourself at this time?" and "Would you harm yourself if you learned your brain showed changes consistent for Alzheimer's disease?"*** If the participant answers in the affirmative, it is recommended that the local expert consider rescheduling the appointment. Example of what to say if the local expert is not comfortable moving forward with disclosure: ***"I'm hesitant to proceed with this visit. I heard you mention [example], and that gives me pause. I want you to be in a good place to learn these results, and I don't think today is the day. There may be an opportunity in the future to learn these results. How do you feel about what I've said?"***

(7) Also, if the participant answers in the affirmative or there is any uncertainty and no family member joined the call, it should be recommended to reschedule at a time when a family member can join. Ultimately, the decision as to whether to proceed with disclosure is at the local expert's discretion.

(8) Prior to proceeding with results, the local expert should ask the participant again if they have any concerns about proceeding with getting their results or if they are still comfortable moving forward with the results. If the participant says they are no longer

interested in getting results, an example of what to say if the participant is not comfortable moving forward with disclosure: **"*I want you to feel comfortable and in charge of learning your results. This is your decision. You will not be letting anyone down if you don't learn your result today. I respect your decision and want you to choose what's best for you. You may also have the opportunity to learn this result in the future, if you want.*"**

(9) If the scheduled meeting is a Zoom call, the local expert should have the correct PowerPoint template loaded up, with confirmation of the correct results prior to the meeting. If it is a telephone call, the local expert should still follow the PowerPoint template sequence and information.

(10) At the end of the review of the results and materials, the local expert should ask the participant and family members if there are any questions. The response should not focus on specific recommendations or specific treatment recommendations, but more information can be provided in response to followup questions about the results that were given.

(11) At the end, the local expert can say that a letter restating the results will be sent to the participant by mail. The local expert should then ask the participant if they would like the results sent to their physician. The local expert should ask the participant if they want a copy of the slides that were shown (or, a set of material that summarizes the information presented, if the call was a phone and not video call), and if they want a list of local resources (consider having staff join the call at the end so they can ask about receiving followup materials and confirm address to send materials).

(12) Participants may ask for community referrals. In addition to local resources, each site should have a set of possible names for referral available.

(13) After the call, the local expert should communicate back to the field center staff if the disclosure took place, and if the participant requested a copy of the informational slides and results to their physician.

Post Disclosure

(1) After receiving verification (from the local expert) of the disclosure having taken place, the field center should record the disclosure took place in **PSR Q4 and Q4a.**

(2) Then the field center should run the **CDART PET Scan Summary of Results Report** and print the results letter to the participant.

a. If the participant requested that their physician should receive a letter, print the results letter for the physician and send the letter to the physician.

b. If the participant requested the informational slides, then print a copy of the slides and the cover letter for the disclosure slides. These materials should be included alongside the results letter sent to the participant.

PET Reporting Results	Type of Presentation Disclosure	Location on ARIC Website
Normal - Negative	ShortPETDisclosure_COGNORMAL_NEG.pptx	[Researchers > Supporting Documents > V11 / NCS > **PET Disclosure Session Shortened PowerPoints (For Participants Requesting Copy of Slides)]**
Normal - Positive	ShortPETDisclosure_COGNORMAL_POS.pptx	
MCI - Negative OR Dementia - Negative	ShortPETDisclosure_MCIorDEM_NEG.pptx	
MCI - Positive OR Dementia - Positive	ShortPETDisclosure_MCIorDEM_POS.pptx	
	Cover Letter for PET Disclosure Slides.docx	

(3) Field center should record whether the letter was sent to the participant and the date in **PSR Q5 and Q5a**.

(4) Verification will need to be done to assure that the correct results letter and physician results letter and educational materials are sent by mail to the participant.

(5) If the participant calls back with followup questions, field center staff should ask what the nature of the questions are. If they are logistic types of questions, the staff should attempt to answer (e.g., if results letter was sent, if there is a request for local resources). In general, the study would like to minimize the need for followup questions for the local expert and refer participants to their personal doctors for any followup questions.

NOTE
Please note, the diagnosis used to trigger an offer to disclose results is based on the *algorithmic diagnosis* in ARIC. It is not based on the neurocognitive status nor the expert-adjudicated diagnosis.

Algorithmic diagnosis is a computer-determined MCI/dementia syndromic diagnosis that uses decline, number of failed domains, CDR, and FAQ scores. To receive an algorithmic diagnosis of MCI or dementia, a participant must have met at least one of the following:

- Failed the MMSE, OR
- Have significant cognitive decline AND failed at least one domain (Cognitive decline is the slope of all their non-missing global cognition factor scores from V5 onwards)

Neurocognitive status is based on domain (memory, language, executive function) failure. The following conditions result in the letter shared with the participant.

- If a participant fails at least 2 domains or the MMSE, then they receive an "Atypical" letter.
- If a participant fails 1 domain, they receive a "Typical" letter.
- If a participant fails 0 domains, then they receive a "Typical" letter.
- If there is not enough information, then they receive an "Undetermined" letter.
- If a participant has had a dementia classification ascertained from a previous ARIC visit, then they receive a "No results" letter.

The expert-adjudicated diagnosis is determined by expert physicians and neuropsychologists who review the available cognitive data, the informant interviews (when available), and the pattern of the cognitive data over multiple visits. These diagnoses are made into clinical categories (normal/MCI/dementia).

All in all, the key differences between algorithmic diagnosis and neurocognitive results and expert-adjudicated diagnoses are:

1. The neurocognitive results letters do not account for cognitive decline. The results letters are based exclusively on domain failures or a failed MMSE.
2. The number of domain failures needed to reach a given result is different. Neurocognitive results require at least two failed domains to get an Atypical result, while the algorithmic diagnosis only requires at least one failed domain (plus cognitive decline) to get a diagnosis of MCI or dementia.
3. The algorithmic diagnoses are generated more quickly than the expert-classified diagnoses, which is why they are being used for this notification.

FAQ

Q1: *A spouse pair gets PET scans but only one receives a letter asking if they want results. They call and ask why only one got a letter.*

A1: Hypothetical response: “These letters offering the chance to get PET results are only sent to people with a PET scan during a certain time period but also with a certain range of cognitive testing results. This means that not everyone with a PET scan will get a letter. However, we are still able to set you up with a local expert, even if you did not get a letter, if you would like.”

Q2: *A participant calls in response to the letter and asks if you (staff) can provide results by phone and skip the expert call.*

A2: Hypothetical response: “Because the results from these scans are a little more challenging to understand and interpret, we prefer to have the results provided by experts who can do a better job answering your questions. I don’t actually know your results.”

Q3: A relative who is not an LAR calls in response to the letter (or otherwise) and asks for their family member’s results.

A3: Hypothetical response: “We are not able to disclose the results of these tests to someone other than the person who had the PET scan or a legally authorized representative.”