

Sharing Amyloid PET Results Back to Research Participants

Nathaniel Chin, MD

Preparation Prior to Meeting with the Participant

- Amyloid PET result
- Review the “Note to File”
- Review ADRC summary visit
 - Cohort (Unimpaired, MCI, Dementia)
 - Medical, Social, and Family history along with medications
 - MRI brain scan and lab results
 - Cognitive testing summary
 - Clinician impressions and comments from consensus conference
- Psychological questionnaire
- Talk with research coordinator about any changes not documented
 - What was discussed or clinical questions asked

Case 1: Impaired, Elevated amyloid

- 79M, BA, worked in management.
- Family hx: Father with AD (sx onset 78) and Mother with LBD (sx onset 89)
- Clinical dx of dementia (possible CVD +/- AD). Sx onset 74.
- Cognitive complaints gradually worsening over time
- Medical hx: CVA (2014), paroxysmal A fib, HTN, HLD, OSA, GERD, Asthma (remote), depression and anxiety, RLS, BPH
- Meds: Apixaban 5 mg, diltiazem 120 mg qd, HCTZ 12.5 mg qd, fluoxetine 40 mg qd, omeprazole 10 mg daily, rosuvastatin 40 mg daily, multiple supplements

Case 1:

21 years of research participation

- Visits 1-5: Cognitively unimpaired stable
 - *Note: CVA occurred during this time*
- Visit 6-7: Mild Cognitive Impairment
- Visit 8: Dementia

Pertinent PE findings: mildly increased tone UE, mild L intention tremor, and slow/stiff gait with cane use

Imaging/Labs

- Research MRI- Remote infarct R PCA medial temporal territory, moderately advanced chronic small vessel disease
- Labs- Lipid panel, HS-CRP wnl

ADRC/WRAP PET Study Disclosure Semi-Structured Interview

ADRC / WRAP (circle one) #: _____

Date: _____

PRE-DISCLOSURE:

- 1) Have you had any experience with Alzheimer's disease? YES NO

If **yes**, please describe:

If **yes**, do you think that experience will impact how you receive your amyloid PET scan result?

- 2) What do you plan to do with your amyloid PET result?

- 3) On a scale of 1-5, how interested in enrolling in a clinical trial involving an Alzheimer's related medication?

(1) Definitely Not Interested (2) Not Interested (3) Neutral (4) Interested
 (5) Very interested

- 4) Do you have any questions or concerns that should be addressed before learning your result?

YES NO

If **yes**, probe for specific questions:

Pre disclosure script:

Now that we've answered those questions we're at a point where I'm going to share with you the result of your amyloid PET scan. I will show you your copy of the result with the explanation below. While sharing your results, I will be using language that most research centers across the country are using. We feel it's important to follow this standardized language so that we're clear and concise. I wanted you to know this in advance because it may sound a little mechanical but we'll talk about what all of this means afterward and you'll have plenty of time to ask questions. Are you ready to hear your results now?

DISCLOSURE:

- Give results summary sheet (with result box checked off) to participant
- Reveal result using standardized language on result summary
- Pause to gather post disclosure information

During Disclosure: Notes about Disclosure Process. (Behavioral observations, re-teaching needed, etc.). How was the participant's reaction/body language? (Comment on initial reaction, if anxious or still calm, if asking good questions, etc.)

ADRC/WRAP PET Study
Summary of Brain Amyloid Research Test Result

This fact sheet summarizes your brain amyloid research scan result. You received this test as part of your participation in the Wisconsin Alzheimer's Disease Research Center or the Wisconsin Registry for Alzheimer's Prevention (WRAP). If you have any questions about this information, please contact [REDACTED]

Participant name _____ ADRC# or WRAP# (circle one) _____

- Your amyloid level was measured by a PET Scan on _____ (DATE)
- Your brain amyloid test result was:
 - Elevated Not Elevated

Amyloid Test Summary Points

- What does it mean if my amyloid scan result is **Elevated**?
 - Your result means the scan detected amyloid plaques in your brain.
 - Your result cannot definitively confirm or diagnose the cause of your dementia. However, it does support the likelihood that Alzheimer's disease is a cause of your dementia.
 - This result cannot determine if you have other changes occurring in your brain such as vascular disease, Parkinson's disease, or Lewy body disease.

- What does it mean if my amyloid scan result is **Not Elevated**?
 - Your result means the scan did not detect amyloid plaques in your brain.
 - It is possible that amyloid plaques are present but not at an elevated level.
 - Your result means your dementia is not due to Alzheimer's disease. Another disease is more likely to be the cause of your dementia.
 - This result cannot determine if you have other changes occurring in your brain such as vascular disease, Parkinson's disease, or Lewy body disease.

Term	Definition
Amyloid	Hallmark protein of Alzheimer's disease that accumulates to form beta-amyloid plaques.
Alzheimer's Disease	The most common cause of dementia in adults over the age of 65. Alzheimer's disease is a brain disease characterized by beta-amyloid plaques and neurofibrillary tangles.
Dementia	A <u>clinical</u> syndrome diagnosed when a person has memory or other thinking problems that interfere with their ability to perform normal daily activities. Dementia can be caused by many diseases (e.g., strokes, Parkinson's disease) but Alzheimer's disease is the most common cause in older adults.
Mild Cognitive Impairment	A <u>clinical</u> syndrome diagnosed when a person has memory or other thinking problems, but these problems are not severe enough to interfere with their ability to perform normal daily activities. Mild cognitive impairment can be caused by many diseases (e.g., Alzheimer's disease, strokes, Parkinson's disease) as well as other reversible conditions (e.g., sleep disturbance, medication effects).
Research brain scan (e.g., amyloid PET)	A research brain scan is used to identify <i>increased risk</i> for Alzheimer's disease.
Clinical brain scan (e.g., MRI, FDG-PET)	A brain scan in a medical clinic is used as part of a <i>diagnosis</i> of Alzheimer's disease in people with thinking problems.

POST-DISCLOSURE:

Post disclosure script: *I want to make sure I've explained things clearly to you and the information on that sheet makes sense.*

1) Can you tell me what you've heard and what your amyloid result is? What does that mean to you and how do you interpret this result?

2) Is this the result you expected?

3) What questions do you have about your result?

4a) [For cognitively unimpaired] Do you have any questions about your risk of having Alzheimer's disease?

4b) [For cognitively impaired] Do you have any questions about how this result impacts your clinical/research diagnosis of MCI/dementia?

Below are some examples of prompting questions the clinician can use based on issues that may come up:

[These questions are optional based on participant needs but can be helpful to elicit additional information]

Effect on Family:

- Will you share your result with family or friends? If so, who? If not, why not?

- Will you share your result with a healthcare provider?

Concern about discrimination/privacy:

- As you learned during the consent process, there is legal protection from discrimination once you learn your genetic information. This is called GINA. We don't have this yet for biomarker information and don't know what the future holds. With that in mind, did you come to the visit today with any concerns about discrimination or privacy?

Preventative measures:

- Will your result change any of your current activities or future plans? Which ones?
- Does learning your result change your interest in enrolling in Alzheimer's related clinical trials? (yes, no)

Key points made to participant

- Results do not change diagnosis of dementia
- Increased likelihood of AD contributing to dementia
 - Tau biomarker result needed to confirm AD diagnosis
- Other diseases may also be present
 - TDP-43, alpha-synuclein, vascular disease
- Other factors may still cause cognitive symptoms
 - Review key factors like sleep, medications, mood
- Care options
 - Discussed going to the memory clinic & talking to Area Agency on Aging
 - Discuss implications of sharing results with providers and medical records
 - Answered questions on lecanemab

What if they had MCI instead of Dementia?

- Meaning may be different to the participant
- Potential key differences
 - Participants more eager to learn results
 - More focus on risk of progression
 - More focus on understanding other causes and interventions

Amyloid Test Summary Points

- What does it mean if my amyloid scan result is **Elevated**?
 - Your result means the scan detected amyloid plaques in your brain.
 - Your result means that you may have Alzheimer's disease but cannot definitively diagnose someone with Alzheimer's disease. To have Alzheimer's disease you need to have brain changes of both amyloid plaques and neurofibrillary tangles.
 - Your result means you are at an *increased risk* for developing dementia due to Alzheimer's disease. However, this result does not mean you will definitely develop dementia.
 - This result does not change the fact that you have mild cognitive impairment.

For example:

Cholesterol	Amyloid
High cholesterol <i>increases the risk</i> of having heart disease, but having high cholesterol does not mean a person will definitely have a heart attack	Elevated amyloid <i>increases the risk</i> of developing Alzheimer's disease dementia, but elevated amyloid does not mean a person will definitely develop dementia.

- At present, researchers and clinicians can use amyloid scans to identify *increased risk* for Alzheimer's disease and progression to dementia, but do not know how to provide specific information on each person's exact amount of risk.
 - This result cannot determine if you have other changes occurring in your brain such as vascular disease, Parkinson's disease, or Lewy body disease.
- What does it mean if my amyloid scan result is **Not Elevated**?
 - Your result means the scan did not detect amyloid plaques in your brain. This result means brain changes indicative of Alzheimer's disease were not detected.
 - You are not at an *increased risk* at this time for developing dementia due to Alzheimer's disease based on your scan result.
 - You may develop elevated amyloid plaques in the future.
 - You could still develop Alzheimer's disease dementia in the future.
 - It is possible that amyloid plaques are present but not at an elevated level.
 - This result does not change the fact that you have mild cognitive impairment.

Post-Disclosure Support for Impaired Participants

- “What do we do now?”
- Resources and referrals overview with team social worker
 - Education: cognition, AD, lifestyle, caregiving, etc
 - Advanced care planning: Advance directives and legal planning
 - Community resources and supports
 - Connect with memory clinic for assessment
- Care partner support
 - Support groups and caregiver information

Case 2: Unimpaired, Elevated Amyloid

- 64 Black woman, MS, working in business (planning to retire)
- Family hx: No cognitive disorders in parents or siblings
- No clinical evaluation for cognition
- Cognitive complaints starting the past 2 years, gradual
- Medical hx: Prediabetes, HTN, HLD, depression, anxiety, Graves disease, sleep apnea w/ CPAP, insomnia, chronic pain, osteoarthritis
- Meds: Metformin 500 mg daily, atorvastatin 20 mg daily, carvedilol 6.25 mg BID, enalapril 10 mg daily, sotalol 80 mg twice daily, spironolactone 12.5 mg daily, **Tylenol PM**, duloxetine 60 mg daily, **tramadol 50 mg PRN**-uses at least once daily, levothyroxine 112 mcg daily, supplements

Case 2:

3 research visits: normal cognition on cognitive testing

Participant reporting changes in attention, short term memory, word finding and multitasking. No functional impairments, mild slowing in some areas.

Study partner denies problems with memory and thinking. Reported participant under more stress at work.

Imaging/Labs

- MRI 9/8/21: Normal, prominent perivascular spaces, white matter change Ok for age. CHS 2.
- HLD 30, triglycerides 155, glucose 110 – BMI 26.2

ADRC/WRAP PET Study
Summary of Brain Amyloid Research Test Result

This fact sheet summarizes your brain amyloid research scan result. You received this test as part of your participation in a study linked with the Wisconsin Alzheimer's Disease Research Center or the Wisconsin Registry for Alzheimer's Prevention (WRAP). If you have any questions about this information, please contact [REDACTED]

Participant name _____ ADRC or WRAP # _____

- Your amyloid level was measured by a PET Scan on _____ (DATE).
- Your brain amyloid test result was:
 Elevated Not Elevated

Amyloid Test Summary Points

- What does it mean if my amyloid scan result is **Elevated**?
 - Your result means the scan detected amyloid plaques in your brain
 - Your result means you are at an *increased risk* for developing dementia due to Alzheimer's disease
 - An elevated result does not mean you have Alzheimer's disease
 - An elevated result does not mean you will definitely develop dementia from Alzheimer's disease

For example:

Cholesterol	Amyloid
High cholesterol <i>increases the risk</i> of having heart disease, but having high cholesterol does not mean a person will definitely have a heart attack	Elevated amyloid <i>increases the risk</i> of developing Alzheimer's disease dementia, but elevated amyloid does not mean a person will definitely develop dementia.

- At present, researchers and clinicians can use amyloid scans to identify *increased risk* for Alzheimer's disease, but do not know how to provide specific information on each person's exact amount of risk.
- What does it mean if my amyloid scan result is **Not Elevated**?
 - Your result means the scan did not detect amyloid plaques in your brain
 - It is possible that amyloid plaques are present but not at an elevated level
 - You are not at an *increased risk* at this time for developing dementia due to Alzheimer's disease based on your scan result
 - You may develop elevated amyloid plaques in the future
 - You could still develop Alzheimer's disease dementia in the future
 - This result only shows amyloid levels at the time the test was done. It is possible that your amyloid levels could change in the future.

Disclosure summary document: Unimpaired

Key points made to participant

What do we know about the result?

- Elevated amyloid is not a clinical diagnosis
- Is not Alzheimer's since AD is defined by amyloid and tau pathology
- Increases the *risk* of AD and AD dementia

Key points made to participant (cont.)

*What do we **not** know regarding the result?*

- We don't know the individual amount of risk
 - Unclear who with amyloid progresses to tau
 - Unclear who with amyloid and tau develops symptoms
 - Nun study
 - Importance of resilience in the brain
- Result does not speak to other potential brain changes
 - TDP-43, Lewy bodies, alpha-synuclein, vascular
- Other factors can still cause cognitive symptoms
 - Review key factors like OSA, medications, mood, chronic pain
 - Caution ppt to not think every memory lapse is due to amyloid

Limitations of the result

- Meaning for people of color remains unclear
 - Majority of biomarker studies involve White participants

Next Steps for cognitively unimpaired ppts

- Talk to PCP re: symptoms, consider memory referral based on that evaluation
 - Discuss implications of sharing with providers and medical record
 - Insurances, employment
- Risk reduction counseling
- Sharing results with family
- Clinical trials