Capturing 2024 Revised Criteria for Diagnosis and Staging of AD Across the ADRC Program

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Background

- Revised criteria for diagnosing and staging AD were published after development of UDSv4

- Capturing these criteria will aid future analyses of NACC data
  - Classify who does/does not meet AD biomarker criteria
  - Enable biological staging of AD
  - Test criteria in future studies

- NACC convened a task force to determine how to capture revised criteria in ADRC participants

Taskforce Goals and Recommendations

Goals:

- Capture biomarkers considered diagnostic in plasma, CSF and PET

- Capture biological and clinical staging of AD

TABLE 2. Intended uses for imaging, CSF, and plasma biomarker assays.

Intended use	CSF	Plasma	Imaging
Diagnosis			
A: (Aβ proteinopathy)	—	—	Amyloid PET
T_1: (phosphorylated and secreted AD tau)	—	p-tau217	—
Hybrid ratios	p-tau181/Aβ42, t-tau/Aβ42, Aβ42/40	%p-tau217	—

TABLE 3. Biological staging.

	Initial-stage biomarkers	Early-stage biomarkers	Intermediate-stage biomarkers	Advanced-stage biomarkers
	(A)	(B)	(C)	(D)
PET	Amyloid PET	Tau PET medial temporal region	Tau PET moderate neocortical uptake	Tau PET high neocortical uptake
	$A+T_2-$	$A+T_{2MTL}+$	$A+T_{2MOD}+$	$A+T_{2HIGH}+$

Jack CR Jr, Andrews JS, Beach TG, Buracchio T, Dunn B, Graf A, Hansson O, Ho C, Jagust W, McDade E, Molinuevo JL, Okonkwo OC, Pani L, Rafii MS, Scheltens P, Siemers E, Snyder HM, Sperling R, Teunissen CE, Carrillo MC. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimers Dement. 2024 Aug;20(8):5143-5169. doi: 10.1002/alz.13859. Epub 2024 Jun 27. PMID: 38934362; PMCID: PMC11350039.

Taskforce Goals and Recommendations

Temporary plan:

- Capture criteria-related data via an optional form that will be added to UDSv4 packet *after* the initial UDSv4 rollout
- Results shared via ADRC Portals and accessible via Cohort Selection Tool on NACC Data Platform
- Incentivize Centers to complete form by capturing submissions on a leaderboard

Future goals:

- Integrate data collection into Form D1b
- Auto-populate biomarker and criteria data using information from the NACC Data Platform

Pilot Form: Plasma & CSF biomarkers

- Revised AA criteria include many Core 1 fluid biomarkers (e.g., plasma p-tau 181, p-tau 231, and CSF Aβ42)

- **New form will focus on the subset considered sufficient for diagnosis**
  - Plasma: p-tau 217 or %p-tau 217
  - CSF: p-tau 181/Aβ42, t-tau/Aβ42, Aβ42/40

1. Were plasma biomarkers used in the etiologic diagnosis?

☐ 0 No **(SKIP TO QUESTION 2)**
☐ 1 Yes

If yes, select all plasma biomarkers that were used:

1a. ☐ 1 p-tau 217
If checked:

1a1. p-tau 217 result

☐ 0 Normal
☐ 1 Abnormal

1a2. Where were the p-tau 217 values used in the diagnosis analyzed?

☐ 1 Analyzed by NCRAD
☐ 2 Analyzed locally **(CONTINUE TO QUESTION 1a2a)**

1a2a. How were p-tau 217 values analyzed?

☐ 1 NCRAD validated protocol
☐ 2 Non-NCRAD validated protocol

2. Were CSF biomarkers used in the etiologic diagnosis?

☐ 0 No **(SKIP TO QUESTION 3)**
☐ 1 Yes

If yes, select all CSF biomarkers that were used:

2a. ☐ 1 p-tau 181/ Aβ42
If checked:

2a1. p-tau 181/ Aβ42

☐ 0 Normal
☐ 1 Abnormal

2a2. Where were the p-tau 181/ Aβ42 values used in the diagnosis analyzed?

☐ 0 Analyzed by NCRAD
☐ 1 Analyzed locally **(CONTINUE TO QUESTION 2a2a)**

2a2a. How were p-tau 181/ Aβ42 values analyzed?

☐ 1 NCRAD validated protocol
☐ 2 Non-NCRAD validated protocol

Pilot Form – Amyloid PET and Tau PET

- New UDS form will include imaging results (elevated or not elevated) for:
  - Core 1 Amyloid PET
  - Core 2 Tau PET
    - Not elevated – Stage A
    - Elevated only in MTL - Stage B
    - Elevated in neocortex - Stage C & D

3. Was Amyloid PET used in the etiologic diagnosis?

☐ 0 No **(SKIP TO QUESTION 4)**
☐ 1 Yes

3a. Amyloid PET result:

☐ 0 Not elevated
☐ 1 Elevated

3b. How were amyloid PET values obtained *(select all that apply)*?

☐ 1 Visual read
☐ 1 Quantitative

3c. Where were amyloid PET values obtained?

☐ 1 Local
☐ 2 Central (SCAN, CLARiTI, ADNI, LEADS)

Pilot Form - Biomarker Criteria for AD

Form will ask whether the participant meets the biological criteria for AD based on a positive Core 1 biomarker

7. Did the participant meet the AA biological biomarker criteria for Alzheimer's based on a positive Core 1 biomarker?	☐ 0 No **(END FORM HERE)** ☐ 1 Yes
8. Which Core 1 biomarker was used to make this determination *(select all that apply)?*	**Imaging:** ☐ 1 Amyloid PET **Plasma:** ☐ 1 p-tau217 ☐ 1 %p-tau217 **CSF:** ☐ 1 p-tau181/Aβ42 ☐ 1 t-tau/Aβ42 ☐ 1 Aβ42/40 **Other ((SPECIFY):** _____

Pilot Form - Biological Staging

- Form will include biological and clinical staging for participants who meet AD criteria
- Biological staging filled in based on biomarker information entered at the beginning of the form (e.g., via REDCap calculation)

Section 2 – Biological staging for individuals on the Alzheimer's disease continuum

Use the information above to select the biological stage of the participant:

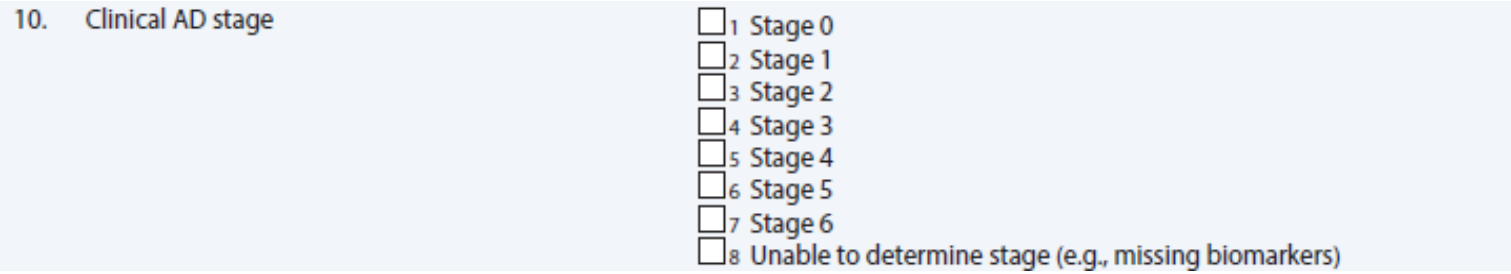
**Goal is to calculate the biomarker from the responses above (through algorithm in REDCap or by entering data into a future NACC calculator on web (similar to CDR calculator))*

	Initial-stage biomarkers	Early-stage biomarkers	Intermediate- to advanced-stage biomarkers	
PET	Amyloid PET	Tau PET medial temporal region	Tau PET moderate to high neocortical uptake	
	$A+T_{2-}$	$A+T_{2MTL+}$	$A+T_{2MOD+2HIGH+}$	
Core 1 fluid	CSF Aβ42/40, p-tau181/Aβ42, t-tau/Aβ42, and accurate Core 1 plasma assays can establish that an individual is in biological stage A or higher, but cannot discriminate between PET stages A–D at present.			
9. Select the biological stage of the participant:	☐ 1 (A)	☐ 1 (B)	☐ 1 (C-D)	☐ 1 Unable to determine stage (e.g., missing biomarkers)

Pilot Form - Clinical Staging

Clinical staging similar to criteria ADRCs already use to diagnose MCI, subjective decline, etc.

- **Stage 0 –** Asymptomatic, deterministic gene
- **Stage 1 –** Asymptomatic, biomarker evidence only
- **Stage 2 –** Transitional decline: Mild detectable change, but minimal impact on daily function
- **Stage 3 –** Cognitive impairment with early functional impact
- **Stage 4 –** Dementia with mild functional impairment
- **Stage 5 –** Dementia with moderate functional impairment
- **Stage 6 –** Dementia with severe functional impairment



10. Clinical AD stage

☐ 1 Stage 0
☐ 2 Stage 1
☐ 3 Stage 2
☐ 4 Stage 3
☐ 5 Stage 4
☐ 6 Stage 5
☐ 7 Stage 6
☐ 8 Unable to determine stage (e.g., missing biomarkers)

Are you interested in piloting this form?

Please fill out the short survey below!

Thank you to the Revised AA Criteria Task Force!

- Sanjay Asthana, MD
- Suzanne Craft, PhD
- Gil Rabinovici, MD
- Sudeshna Das, PhD
- William Jagust, MD
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- Sterling Johnson, PhD
- Sarah Biber, PhD
- Walter Kukull, PhD

Thank you!

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NACC

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