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Appropriate Use Criteria for Amyloid and Tau PET Imaging 2025: A Clinician Summary

The Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging developed new and updated appropriate use criteria (AUC) for amyloid and tau positron emission tomography (PET) imaging in diagnosing and managing cognitive decline. Driven by advances in amyloid-lowering therapies and broader access to amyloid PET scans, as well as expanded coverage under certain circumstances by the Centers for Medicare and Medicaid Services, these evidence- and expert-informed criteria provide clinician guidance on when amyloid and tau PET scans are most clinically valuable and when their use may be less beneficial. These criteria provide an update to the 2013 Amyloid PET AUC, and introduce for the first time AUC for clinical use of tau PET.

The AUC aims to optimize the diagnostic utility and management value of amyloid and tau PET while emphasizing the essential role of a comprehensive clinical evaluation.

The updated **Appropriate Use Criteria (AUC)** are published in *The Journal of Nuclear Medicine* and *Alzheimer's & Dementia: The Journal of the Alzheimer's Association.*

For related guidance, see additional **AUC for CSF biomarkers** and **appropriate use recommendations (AURs) for blood-based AD biomarkers**.

Key Principles for Appropriate Use of PET Imaging

Crucially, amyloid and tau PET imaging are considered appropriate only when **both** of the following conditions are met:

1. Alzheimer's disease is a suspected cause of cognitive impairment, but the diagnosis remains uncertain even after a thorough evaluation by a dementia specialist.
2. Knowing whether amyloid or tau pathology is present will clarify the diagnosis and influence patient management.

Additional Factors to Consider

- **Disease stage:** PET scans are generally more informative in earlier stages of cognitive decline.
- **Age and APOE4 status:** The prevalence of amyloid positivity in cognitively unimpaired individuals increases with age and is higher in individuals carrying 1 or 2 copies of the apolipoprotein E ε4 (*APOE4*) risk allele — positive amyloid PET results should be interpreted with this context in mind.
- **Shared decision-making:** The decision to pursue PET imaging should be discussed with patients and care partners, with consideration for their preferences, potential psychological impact, and financial implications.

PET Technology for Amyloid and Tau Imaging

Positron emission tomography (PET) is a molecular imaging technique that uses radiopharmaceuticals (radioactive imaging agents) to detect and measure specific targets in the body. In the brain, PET can visualize amyloid plaques and tau neurofibrillary tangles (NFTs), hallmarks of Alzheimer's disease.

- **How it works:** PET radiopharmaceuticals, labeled with positron-emitting radionuclides (like fluorine-18), bind to amyloid plaques or tau NFTs. The emitted positrons interact with electrons, producing detectable signals that allow for visualization and quantification of these protein aggregates.
- **Amyloid PET Tracers:** Three FDA-approved fluorine-18 amyloid tracers are available: florbetapir (Amyvid), florbetaben (Neuraceq), and flutemetamol (Vizamyl). These tracers help estimate amyloid plaque density.
- **Tau PET Tracer:** Flortaucipir (Tauvid) is an FDA-approved fluorine-18 tracer that estimates the density and distribution of tau NFTs.
- **Interpretation:** Visual interpretation remains the primary method for clinical use, supplemented by quantitative measures like standardized uptake value ratios (SUVRs) in research settings. Standardized scales like the Centiloid scale for amyloid PET help compare results across different tracers and methods.
- **Importance of Quality:** Accurate and reliable PET imaging requires standardized procedures, qualified personnel (certified nuclear medicine physicians and technologists), and accredited imaging facilities. Appropriate training in image interpretation for amyloid and tau PET is crucial for accurate results.

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Clinical Scenarios for Use of Amyloid and Tau PET Imaging

To guide appropriate use of amyloid and tau PET imaging, 17 clinical scenarios covering various patient presentations are provided below. Amyloid and tau PET imaging were judged as independent modalities for each scenario. The scenarios are grouped by disease stage, and each imaging type is rated separately to help health care providers determine if amyloid or tau PET is appropriate.

While positive PET scans can accurately detect amyloid plaques or tau NFTs, negative scans do not definitively rule out their presence. Importantly, a positive scan does not singularly confirm an Alzheimer's diagnosis, and clinical correlation is essential.

Key: A = Appropriate   U = Uncertain   RA = Rarely Appropriate

Table 1: Cognitively Unimpaired (CU)

Scenario	Amyloid	Tau	Rationale (Key Points)
Not at Increased Risk	RA	RA	Amyloid common, individual prediction uncertain; elevated tau unlikely if person is cognitively unimpaired; Limited utility without prevention.
At Increased Risk * *Based on age, known APOE4 genotype, or multigenerational family history*	RA	RA	Higher risk, but prevention recommendations apply regardless; Tau unlikely elevated.

Table 2: Subjective Cognitive Decline (SCD)

Scenario	Amyloid	Tau	Rationale (Key Points)
Not at Increased Risk	RA	RA	Possibly increased MCI risk, but variable timeframe; Limited amyloid prognostic value; Tau rare.
At Increased Risk * *Based on age, known APOE4 genotype, or multigenerational family history*	U	RA	SCD may be early AD; Amyloid may inform, but risk/timeframe uncertain; Tau unlikely elevated.

Table 3: Mild Cognitive Impairment (MCI)

Scenario	Amyloid	Tau	Rationale (Key Points)
≥65, Typical AD	A	U	Amyloid confirms/rules out AD; Tau positive predictive value (PPV) high, negative predictive value (NPV) uncertain.
AD Suspected, Predicting future decline	A	A	Elevated amyloid predicts progression to dementia; Elevated tau associated with decline.

Table 4: Dementia

Scenario	Amyloid	Tau	Rationale (Key Points)
<65, AD Suspected	A	A	High amyloid PET accuracy in young-onset AD; Elevated tau helpful for AD detection.
Atypical Features	A	A	Amyloid PET excludes/confirms AD in atypical cases; Tau patterns match clinical symptoms.
Established AD, Monitoring	RA	U	Amyloid doesn't track severity/progression; Tau correlates with cognition, serial scan utility uncertain.
Prodromal or DLB	RA	U	Amyloid positive in many DLB, does not distinguish from AD; Tau may indicate AD contribution.
Conclusive CSF	RA	U	CSF usually sufficient for amyloid; tau PET may add regional and staging information.
Equivocal CSF	A	U	Amyloid PET clarifies amyloid status; tau PET may add value.
AD Suspected, Predict future decline	U	A	Amyloid less useful for prognosis; Tau correlates with severity/decline.

Table 5: Other Indications

Scenario	Amyloid	Tau	Rationale (Key Points)
Eligibility for Amyloid Therapy	A	A	Confirms amyloid for therapy; Tau may predict benefit.
Monitoring Amyloid Therapy	A	U	Tracks amyloid reduction; Limited tau data in monitoring therapy.
Non-Medical Use	RA	RA	Inappropriate for legal/insurance/employment.
Suspected Dominantly Inherited Alzheimer's Disease (DIAD)	RA	RA	Genetic testing is standard; PET not a substitute.

Important Note: While the AUC provides recommendations for both amyloid and tau PET, the current criteria for tau PET are based primarily on expert opinion due to limited clinical data. As more research emerges, these recommendations may evolve.

Combined Amyloid and Tau PET Imaging

While these AUC focus on each modality individually, combining amyloid and tau PET can provide complementary information. Amyloid PET is more sensitive for early disease detection, while tau PET is more specific for AD, can be used for disease staging and correlates better with cognitive symptoms. Combining them can increase diagnostic confidence and may be particularly useful in certain situations, such as:

- When amyloid PET is positive, but there is diagnostic uncertainty
- In cognitively unimpaired individuals at increased risk of AD

Further research is needed to fully understand the optimal use of combined amyloid and tau PET.

Conclusion

These amyloid and tau PET AUC provide guidance for health care professionals evaluating patients with cognitive concerns. Applying these criteria may help clinicians make appropriate and effective use of these valuable imaging tools. A comprehensive clinical evaluation, however, remains essential for diagnosis and management of cognitive decline. PET imaging should be used to complement, not replace, this essential assessment and clinician judgment.

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For additional information and professional resources, visit **alz.org/ALZPro**.

About the Workgroup & Methodology

These AUC were developed by a multidisciplinary workgroup convened by the Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging. The workgroup identified key research questions to guide a systematic literature review, performed by Oregon Health & Science University, on clinical amyloid and tau PET, developed 17 clinical scenarios, and rated each by consensus as "rarely appropriate," "uncertain," or "appropriate." Ratings were assessed and voted on for amyloid and tau use separately.

About the Alzheimer's Association

The Alzheimer's Association is a worldwide voluntary health organization dedicated to Alzheimer's care, support and research. Our mission is to lead the way to end Alzheimer's and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support. Our vision is a world without Alzheimer's and all other dementia®. Visit **alz.org** or call 800.272.3900.

About SNMMI

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is a global nonprofit organization dedicated to advancing nuclear medicine, molecular imaging, and theranostics through its education and research programs. Founded in 1954, SNMMI brings together professionals from all parts of the field to drive innovation, establish practice standards, and enhance education in precision medicine, improving patient care through advanced imaging and therapies that transform diagnosis and treatment. For more information, visit **SNMMI.org**.

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