

Rational use of neuroimaging in dementia

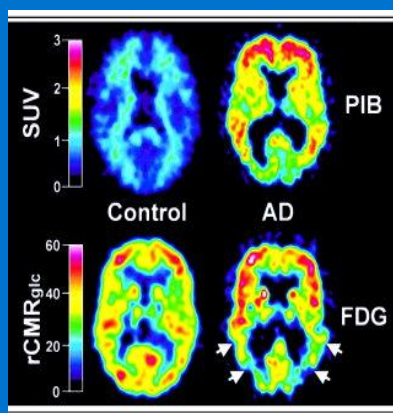
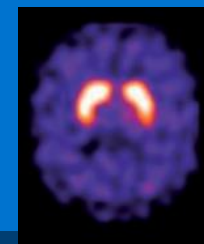
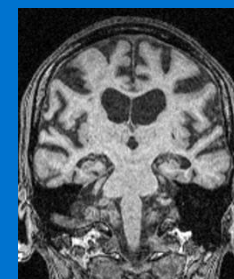
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NIHR National Specialty Lead for Dementia

Department of Psychiatry

University of Cambridge



Current biomarkers for Dementia

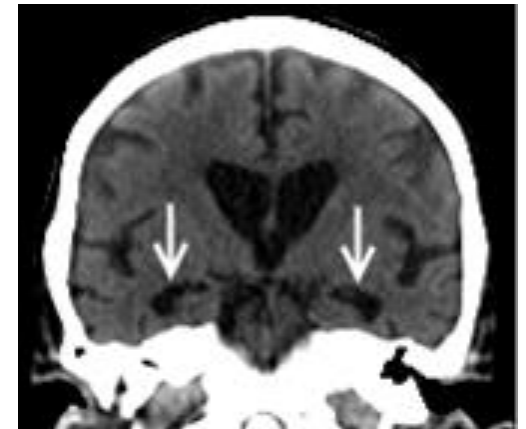
- **Structural imaging (CT/ MRI)**
- **Perfusion (HMPAO) SPECT**
- **Glucose (FDG) PET**
- **Dopamine (FP-CIT) SPECT**
- Amyloid PET – **limited availability in UK**
- Tau PET – **FDA approved May 2020**
- **CSF**
- Blood biomarkers – **not clinically available**

Bold = NICE recommended

Dementia diagnosis in specialist dementia diagnostic services

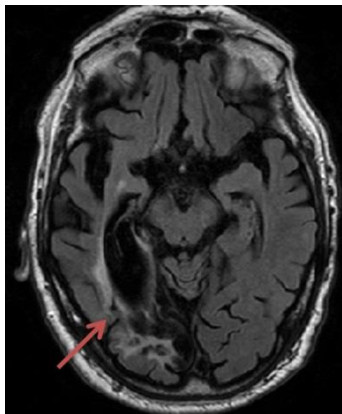
- Offer structural imaging to rule out reversible causes of cognitive decline and assist with subtype diagnosis, unless dementia is well established and the subtype diagnosis is clear
- Do not rule out dementia based solely on the results of CT or MRI scans

*Don't forget coronal CT to see MTA
(sens and spec around 80%)*

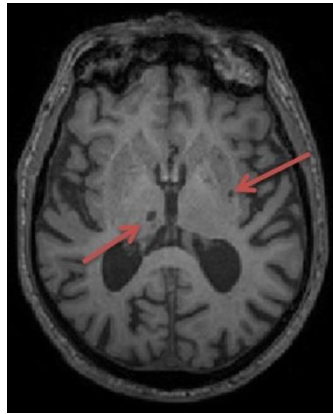


Diagnosing vascular dementia

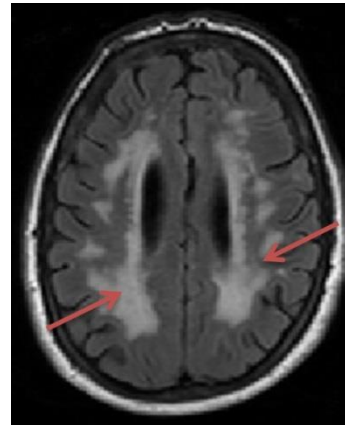
- If the dementia subtype is uncertain and vascular dementia is suspected, use MRI.



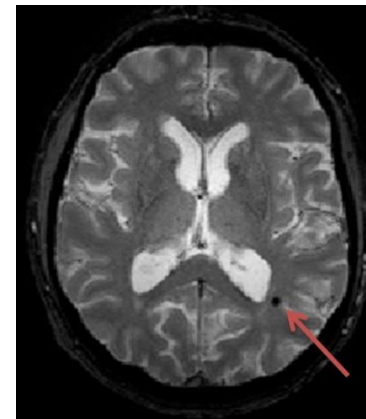
Cortical infarcts



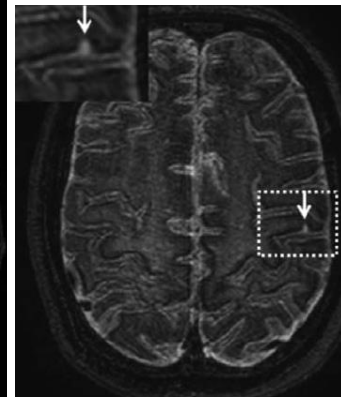
Lacunar
Infarcts



Extensive
>25%) WML



Microbleed
(T2*)



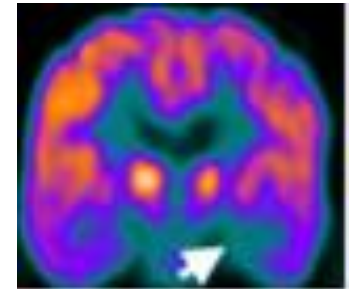
Microinfarct

Markers of small vessel disease

Diagnosing Alzheimer's disease

If the diagnosis is uncertain and Alzheimer's disease is suspected, consider either:

- **FDG-PET** (sensitivity and specificity around 85%) - or perfusion SPECT (single-photon emission CT) if FDG-PET is unavailable

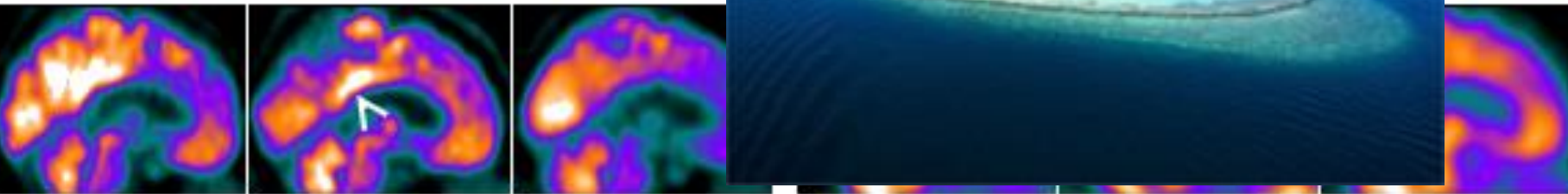
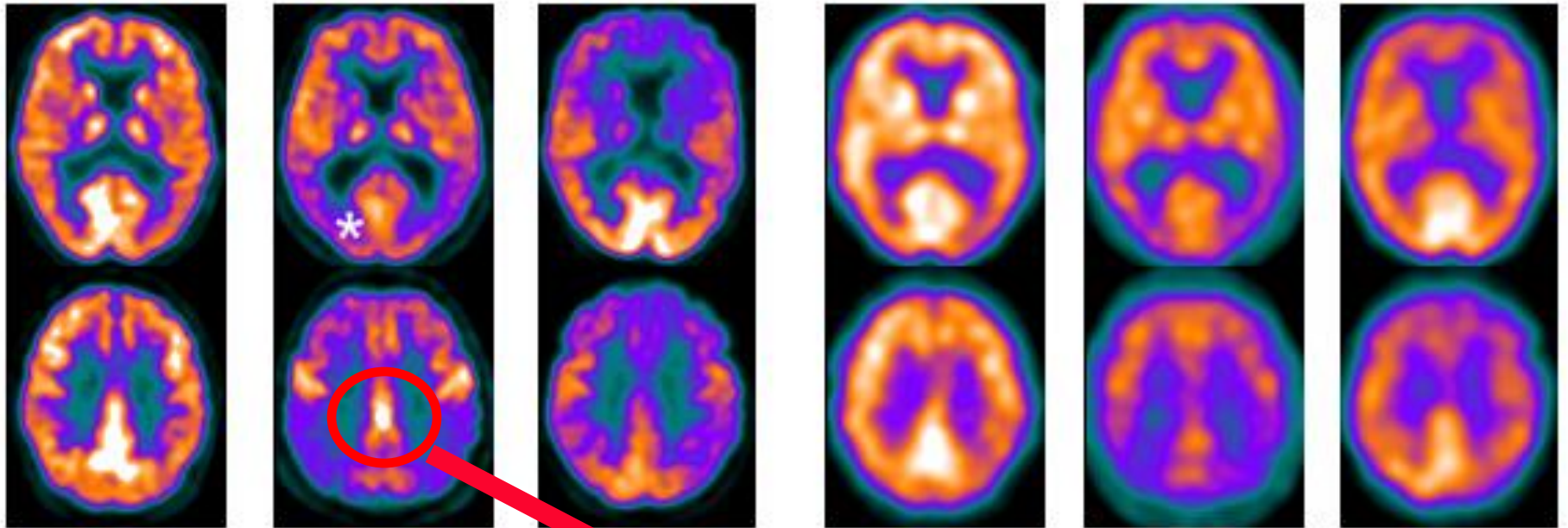


or

- Examining **CSF** for phosphorylated-tau 181 and total tau and either amyloid beta 1-42 or a ratio of amyloid beta 1-42 and amyloid beta 1-40

FDG PET

SPECT



Control

DLB

AD

Control

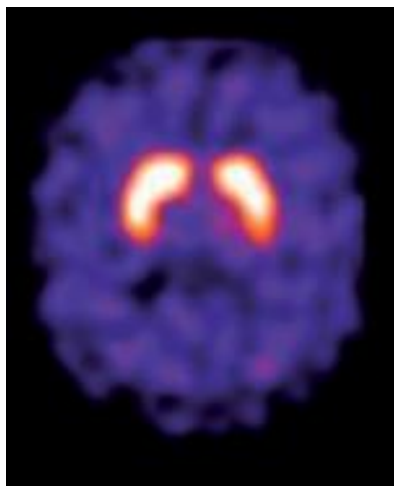
DLB

AD

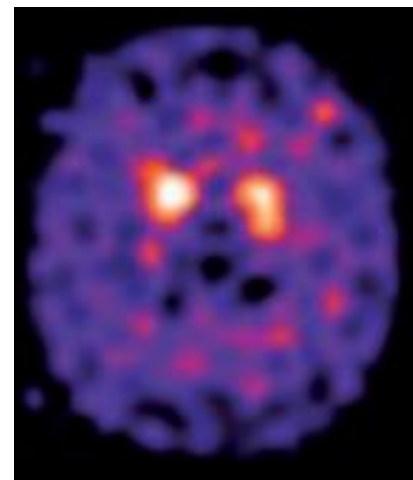


Diagnosing dementia with Lewy bodies

- If the diagnosis is uncertain and dementia with Lewy bodies is suspected, use dopaminergic (^{123}I -FP-CIT) SPECT (sensitivity 80%; specificity 90%)



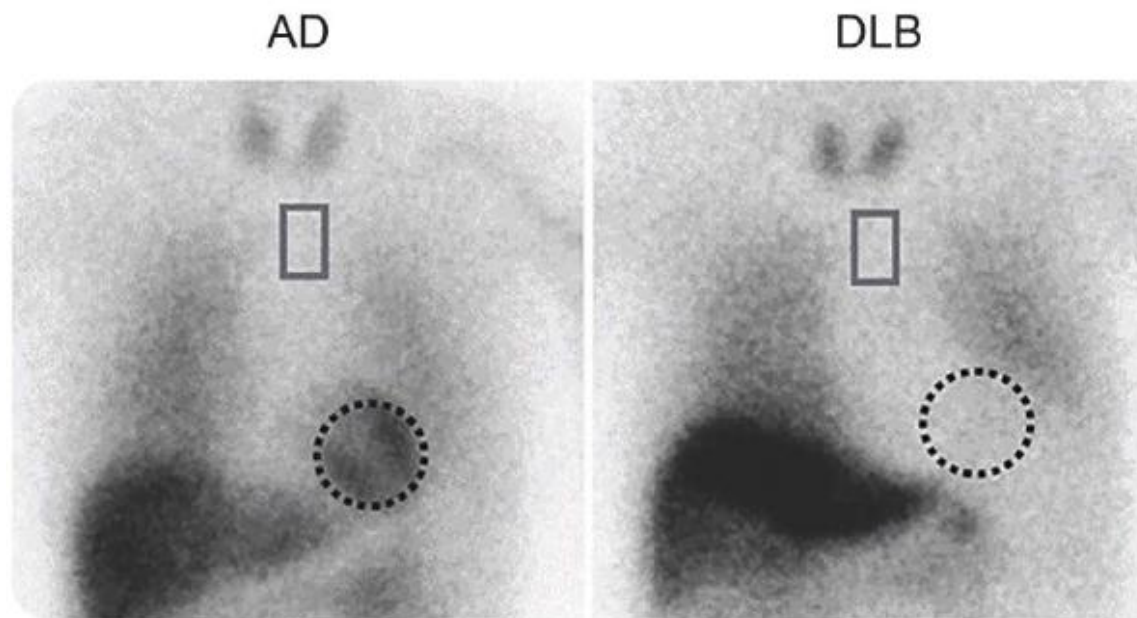
Normal



Dopamine deficit in DLB

Diagnosing dementia with Lewy bodies

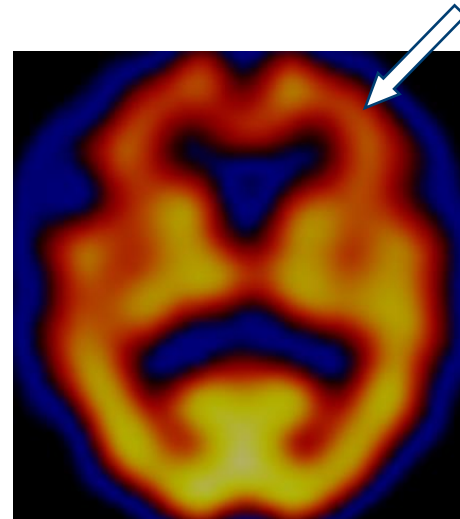
- If ^{123}I -FP-CIT SPECT is unavailable, consider ^{123}I -MIBG cardiac scintigraphy (sensitivity 70%; specificity 90%)



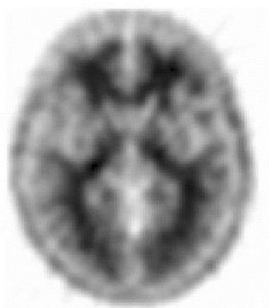
Diagnosing frontotemporal dementia

If the diagnosis is uncertain and frontotemporal dementia is suspected, use either:

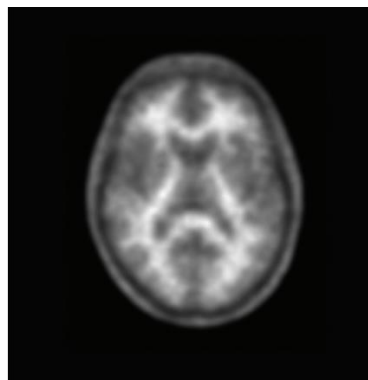
- FDG-PET or
- Perfusion SPECT



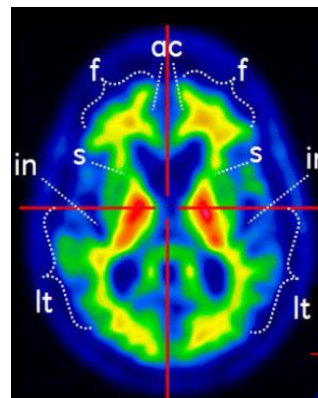
Amyloid imaging in Dementia



**Flurbetapir
(Amyvid)**

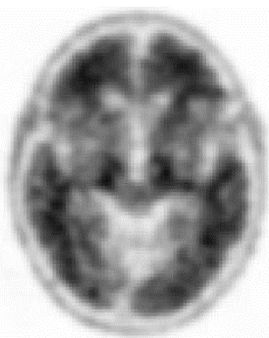


**Flurbetaben
(NeuraCeq)**

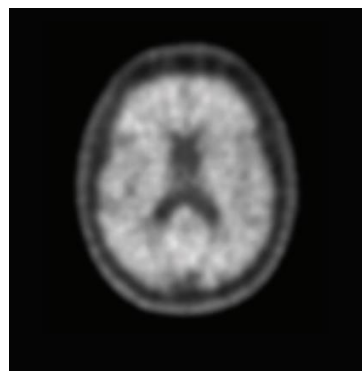


**Flutemetamol
(Vizamyl)**

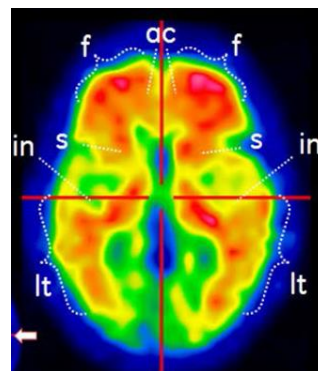
**Negative scan:
normal**



**Flurbetapir
(Amyvid)**

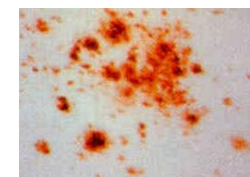


**Flurbetaben
(NeuraCeq)**



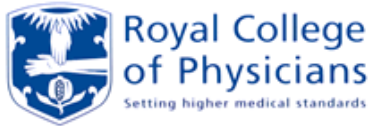
**Flutemetamol
(Vizamyl)**

**Positive scan:
Amyloid present
(AD, DLB, old age)**



What does NICE say about the use of amyloid imaging?

Evidence-based indications for PET-CT: Amyloid imaging



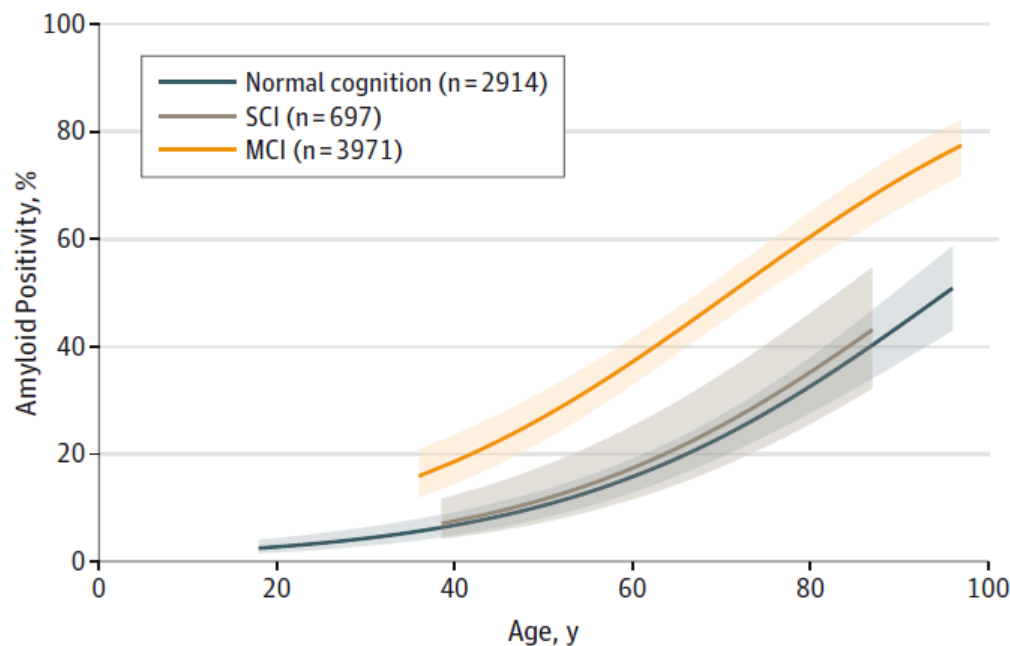
- Use in highly selected patients where:
 - Alzheimer's dementia (AD) is a possible diagnosis but this remains uncertain after comprehensive evaluation by a dementia expert and conventional imaging work-up, and
 - Knowledge of the presence or absence of amyloid is expected to increase diagnostic certainty and influence patient management
- Appropriate uses: unexplained dementia, unusual clinical presentation, very young age of onset
- Inappropriate uses: established AD, in those with no cognitive impairment or as a screening test

Prevalence of Cerebral Amyloid Pathology in Persons Without Dementia

A Meta-analysis

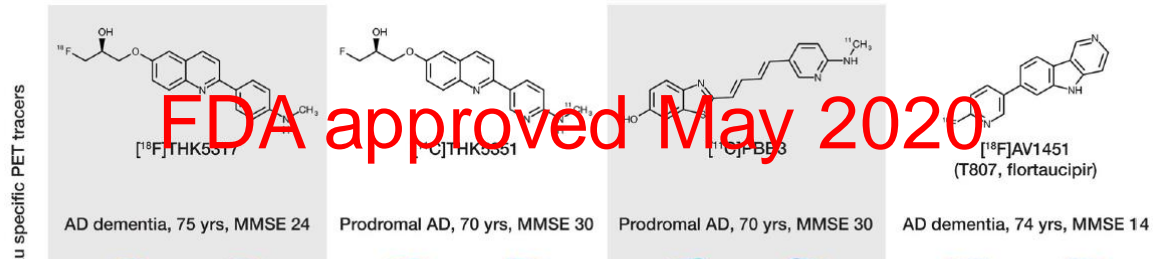
Willemijn J. Jansen, MSc; Rik Ossenkoppele, PhD; Dirk L. Knol, PhD; Betty M. Tijms, PhD; Philip Scheltens, MD, PhD; Frans R. J. Verhey, MD, PhD; Pieter Jelle Visser, MD, PhD; and the Amyloid Biomarker Study Group

55 studies of 8694 people



Rates:
10% at 50 yo
20% at 70 yo
40% at 90 yo

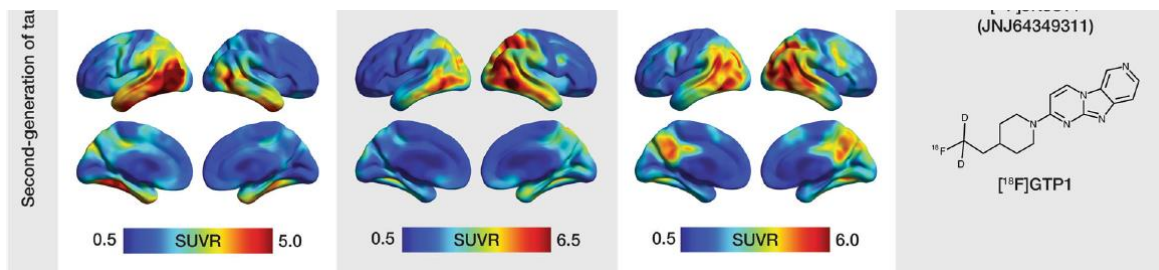
Tau tracers



TAUVID™ (flortaucipir F 18 injection), for intravenous use
Initial U.S. Approval: 2020

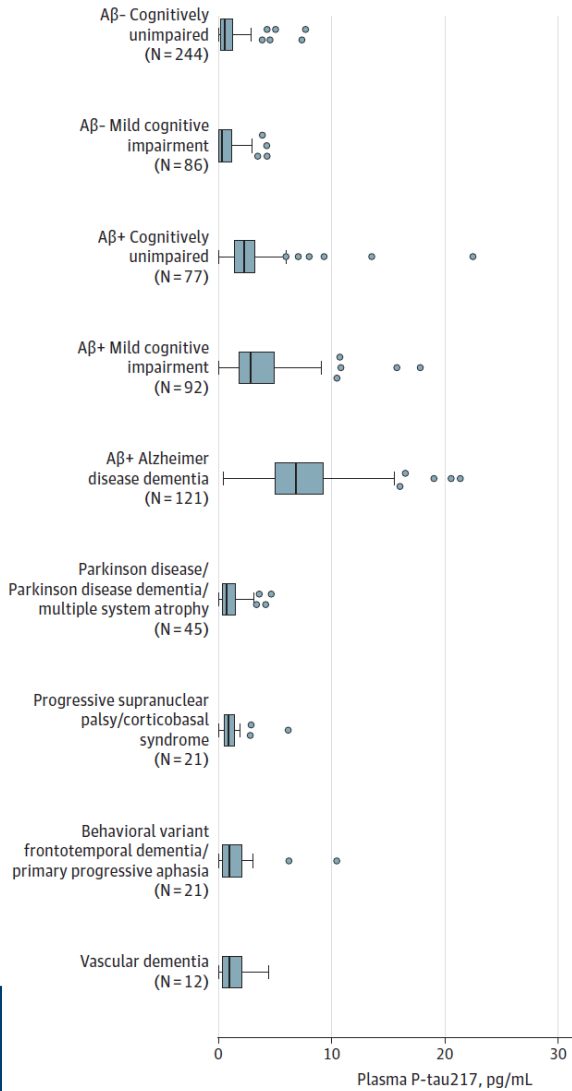
----- INDICATIONS AND USAGE -----

TAUVID is a radioactive diagnostic agent indicated for positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs) in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD). (1)

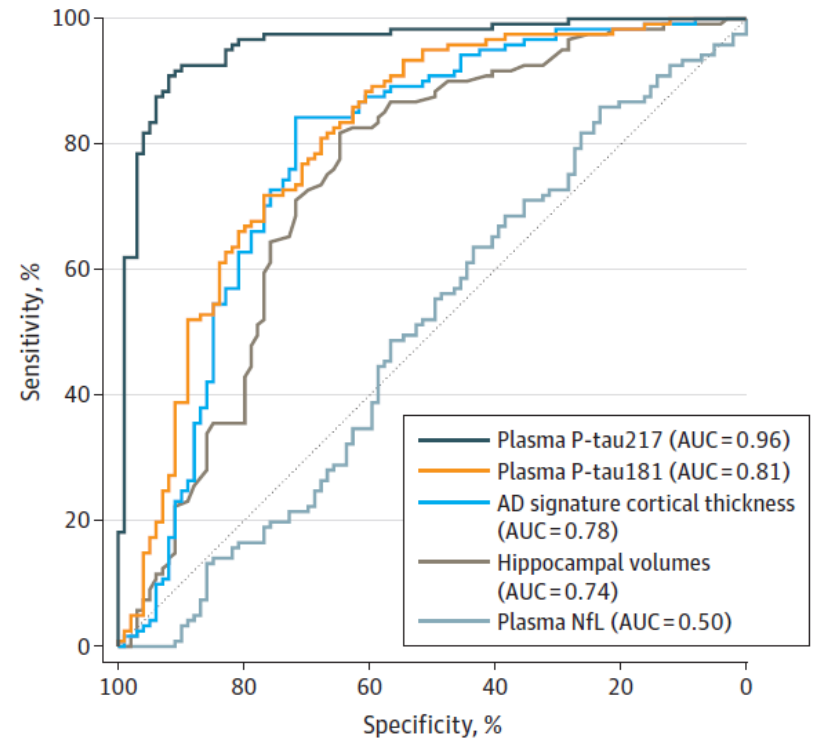


Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders

A Levels of P-tau217 in plasma across diagnostic groups



B AD dementia vs other neurodegenerative diseases: comparison of plasma P-tau217 vs other plasma and MRI biomarkers



Conclusions

- CT, MR, Perfusion SPECT and Glucose PET are established clinical tools
- FP-CIT and MIBG (heart) can help with DLB
- Amyloid imaging not in wide clinical use in the UK
- Tau ligands starting to be licensed
- CSF biomarkers available (but limited)
- Blood biomarkers may be validated soon
- The value of a test depends on how it is used