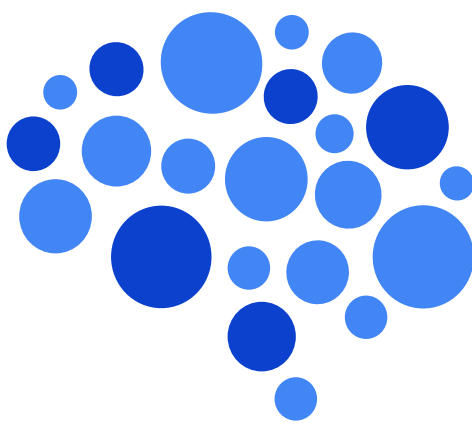


Evaluating the Elecsys in vitro diagnostic pTau217 plasma assay for the detection of amyloid pathology in primary and secondary care settings

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Sunday-1076
Exhibit Hall
12 July 2026 (07:30–16:15)

What does this mean for the Alzheimer's community?

- Implementation of plasma pTau217 as a simple, scalable blood-based test capable of both ruling in and ruling out amyloid pathology, with high performance across care settings, has the potential to revolutionise the Alzheimer's disease (AD) diagnostic pathway.
- Establishing the dual cutoffs for the Elecsys® Phospho-Tau (217P) Plasma immunoassay is a key step in the development of this assay as an in vitro diagnostic (IVD) tool.

Background

- Plasma tau phosphorylated at threonine 217 (pTau217) has consistently demonstrated high accuracy for identifying amyloid pathology and offers great potential as an accessible and minimally invasive tool to support the diagnosis or triage of individuals with suspected AD.^{1–3}
- Aim:** To evaluate the clinical performance of the Elecsys Phospho-Tau (217P) Plasma (pTau217p) assay (Roche Diagnostics International Ltd) as an IVD biomarker assay for detecting amyloid pathology across care settings.

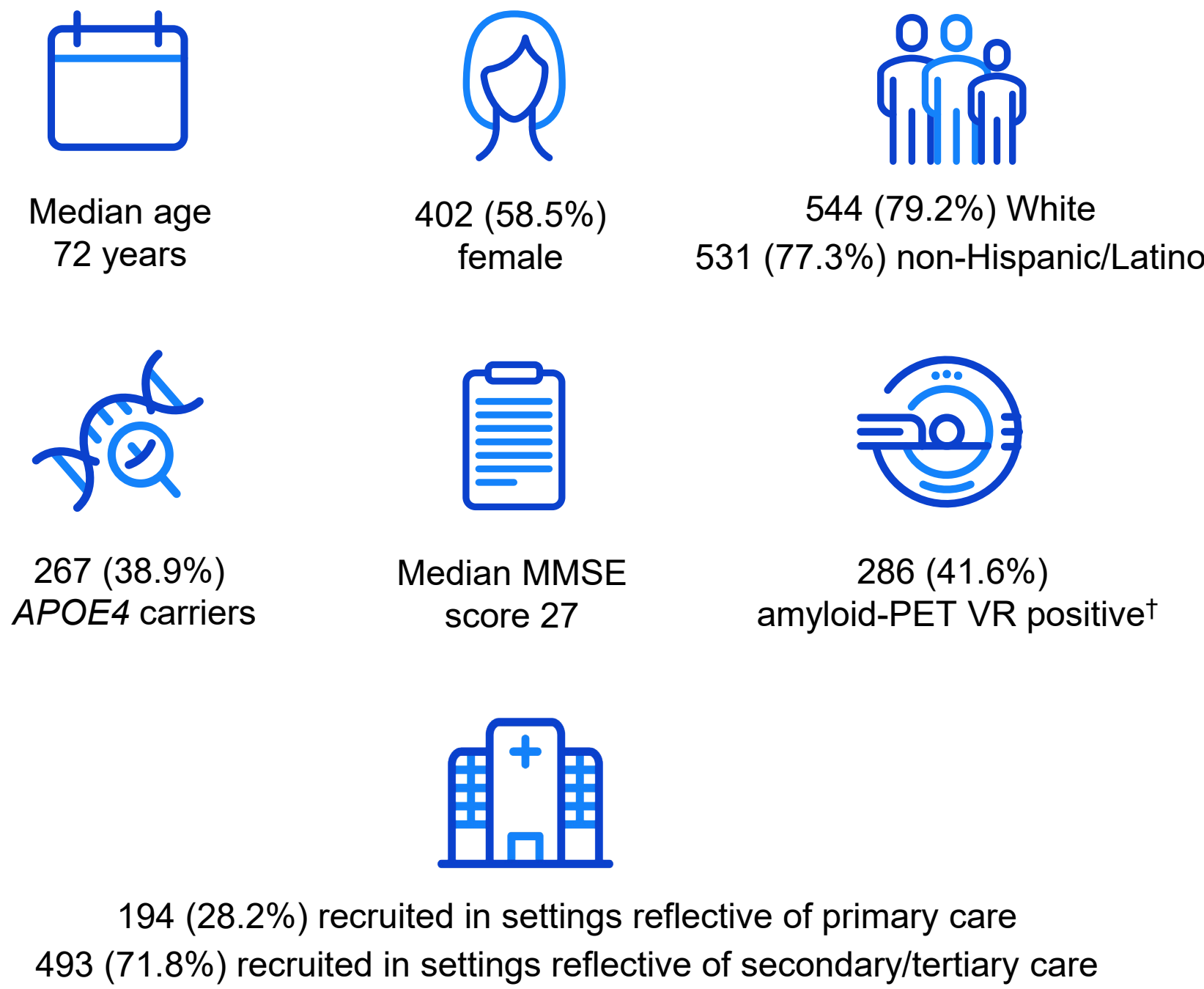
Methodology

- Non-interventional, observational study
- Adults with subjective cognitive decline (SCD), mild cognitive impairment (MCI) or mild dementia (MD) under evaluation for AD or other causes of cognitive decline
- Samples from two cohorts (N=687):
 - Cutoff establishment arm of the APPROACH study (RD006263; n=487)
 - Non-US screening subset from the TRAILBLAZER-ALZ 2 (TB2) study (NCT04437511; n=200)⁴
- Plasma pTau217 was measured using the pTau217p assay
- Discriminative ability of the pTau217p assay versus amyloid-positron emission tomography visual read (amyloid-PET VR) status assessed using receiver operating characteristic-area under the curve (ROC-AUC) analysis
- Two cutoffs for classifying pTau217p results into low, high and indeterminate likelihood of amyloid pathology were derived to achieve a combination of sensitivity/specificity ≥90% across care settings, per Global CEOi recommendations for acceptable performance of blood-based biomarker tests for clinical use⁵

Results

- The APPROACH cohort comprised diagnostically-naïve individuals from primary and secondary/tertiary care (SCD, MCI and MD), while the TB2 cohort was a clinical trial population (secondary/tertiary care) with more advanced disease (MCI and MD).
- Baseline characteristics are summarised in **Figure 1**.

Figure 1. Baseline characteristics (N=687*).



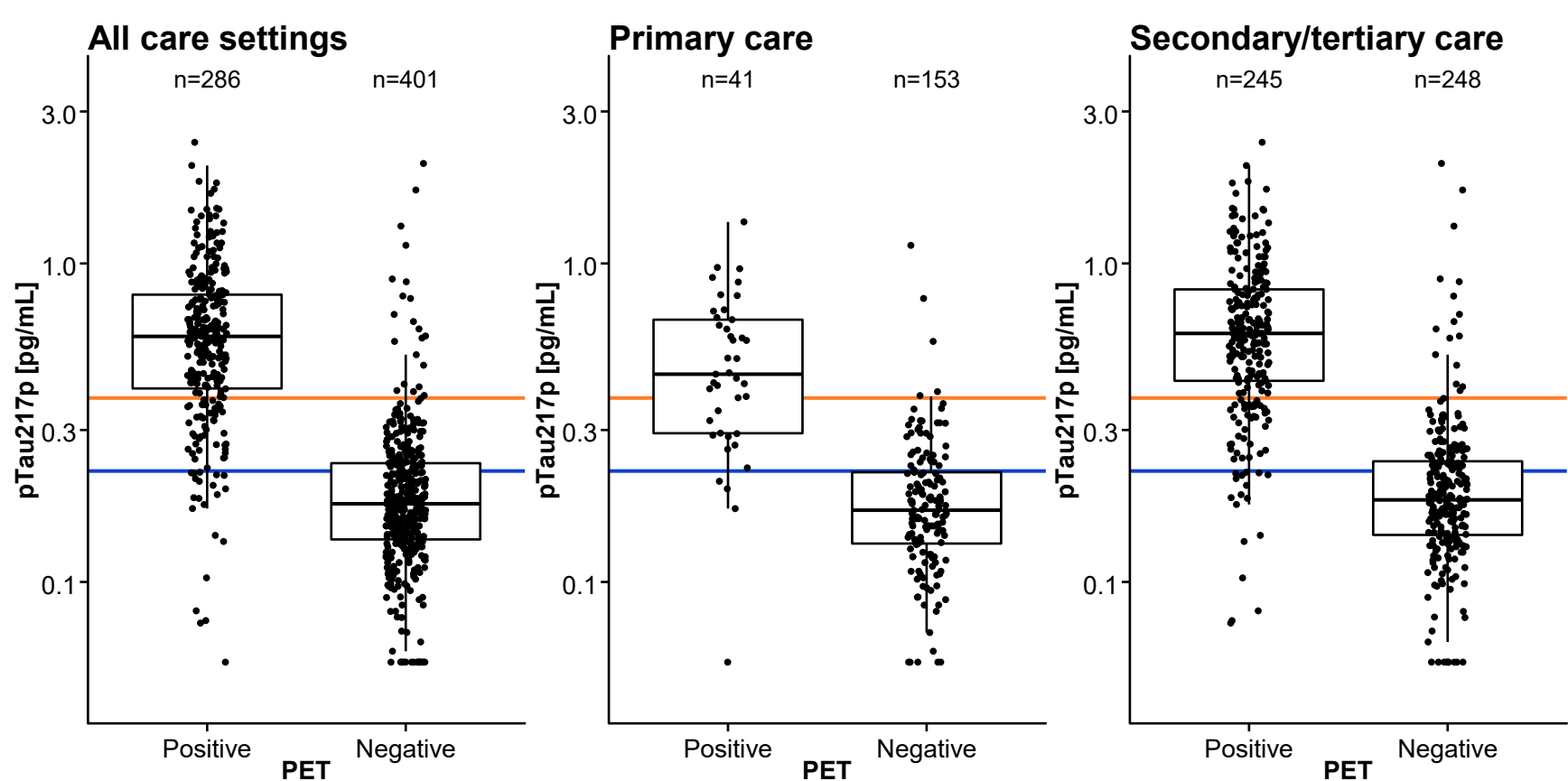
APOE4, Apolipoprotein E4 gene; MMSE, Mini-Mental State Examination.
*687 individuals with valid plasma and amyloid-PET VR results were included in this analysis.
†Amyloid pathology status determined by majority vote derived from the ratings of six individual expert readers from two different vendors, with cerebrospinal fluid biomarker adjudication used in the event of a 3-3 tiebreaker.

- The pTau217p assay demonstrated high accuracy for discriminating amyloid pathology across care settings (**Figures 2 and 3**), with an AUC of 0.923 overall (**Figure 3**).
- Lower and upper cutoffs established for pTau217p classification were 0.223 pg/mL and 0.378 pg/mL, respectively, to achieve sensitivity/specificity ≥90% across care settings (**Figure 3**).

Conclusions

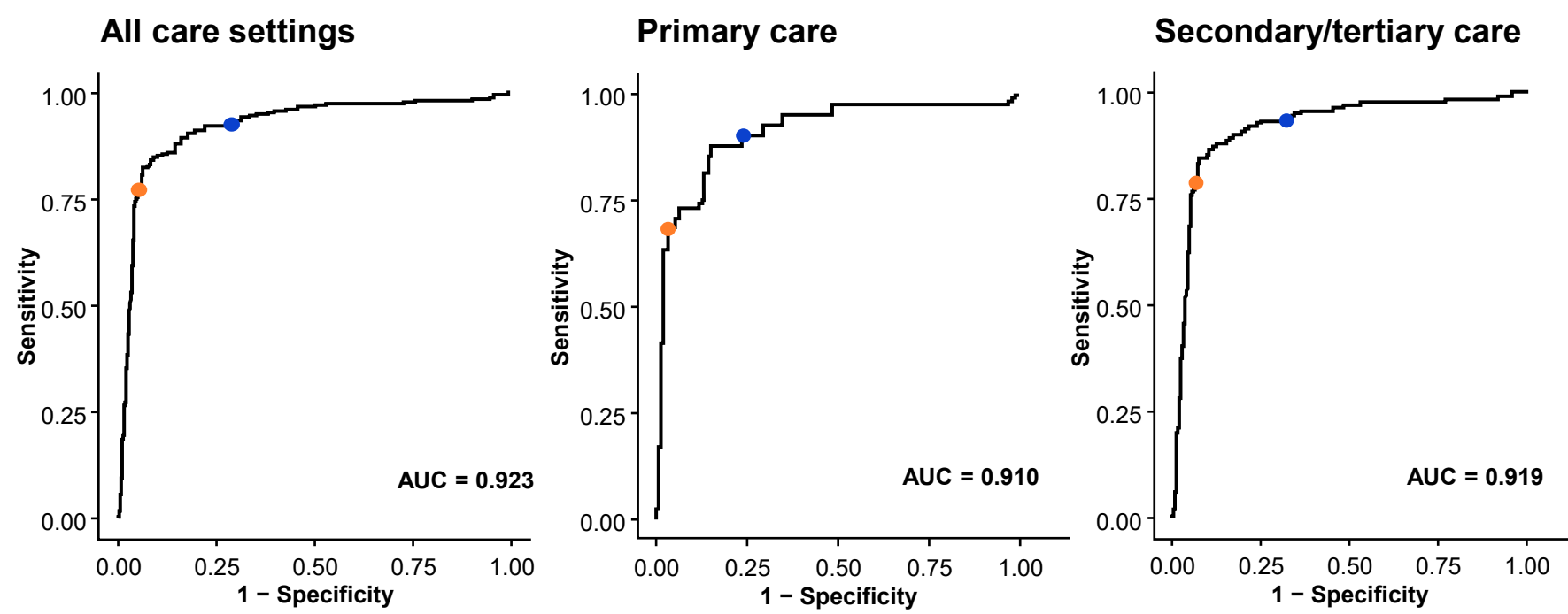
- The Elecsys pTau217p assay demonstrated high discriminative accuracy for distinguishing amyloid-positive from amyloid-negative participants, meeting Global CEO Initiative (CEOi) on Alzheimer's Disease recommendations.
- Upper and lower cutoffs of 0.378 and 0.223 pg/mL, respectively, were selected for classifying results into high, low and indeterminate likelihood of amyloid pathology, for validation in a separate study.

Figure 2. pTau217p distribution by amyloid-PET VR status, stratified by care setting.



The blue and orange lines indicate the final lower and upper cutoffs for the pTau217p assay, respectively. Cutoffs are validated in a separate study.

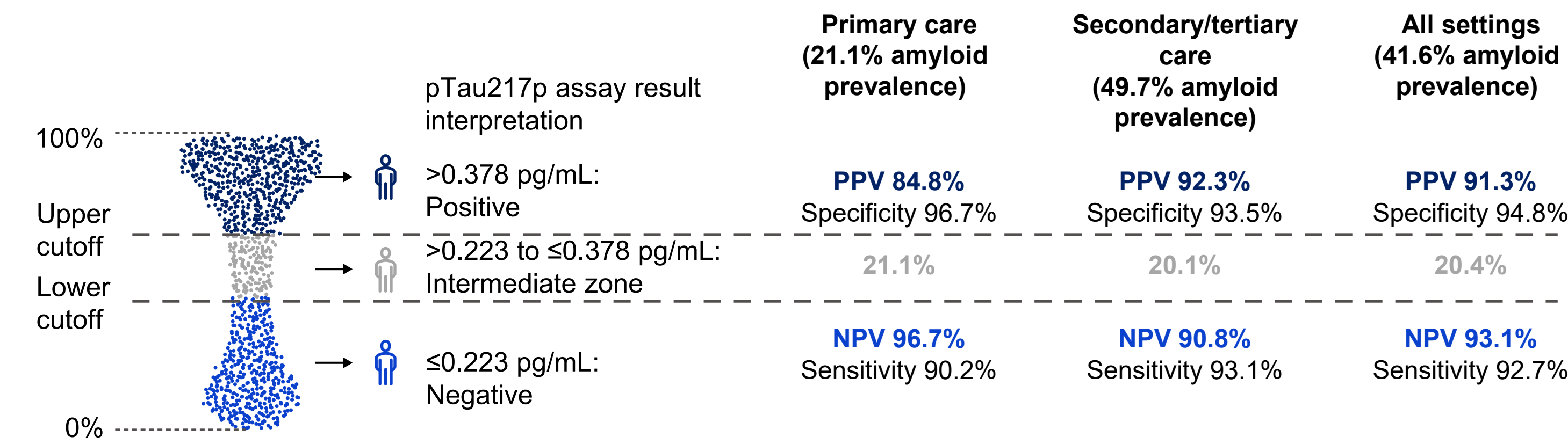
Figure 3. ROC-AUC analysis for pTau217p performance with respect to amyloid-PET VR status, stratified by care setting.



The blue and orange circles indicate the performance at the final pTau217p assay lower and upper cutoffs, respectively. Cutoffs are validated in a separate study.

- Based on a 41.6% amyloid positivity prevalence by amyloid-PET VR in this cohort, the pTau217p assay had a (**Figure 4**):
 - Negative predictive value (NPV) of 93.1% (sensitivity: 92.7%) for results below the lower cutoff of 0.223 pg/mL
 - Positive predictive value (PPV) of 91.3% (specificity: 94.8%) for results above the upper cutoff of 0.378 pg/mL.
- Overall, 20.4% of results fell in the intermediate zone (**Figure 4**).
- High performance was maintained regardless of care setting (**Figure 4**):
 - Primary care (amyloid prevalence 21.1%): PPV 84.8% at upper cutoff; NPV 96.7% at lower cutoff
 - Secondary/tertiary care (amyloid prevalence 49.7%): PPV 92.3% at upper cutoff; NPV 90.8% at lower cutoff

Figure 4. Performance characteristics of the pTau217p assay cutoffs across care settings.



Acknowledgements

- This study was funded by Roche Diagnostics International Ltd, Rotkreuz, Switzerland, and Eli Lilly and Company, Indianapolis, IN, USA.
- Third-party medical writing support, under the direction of the authors, was provided by Pozisa Majaja, MSc, of Ashfield MedComms (Johannesburg, South Africa), an Inizio company, and funded by Roche Diagnostics International Ltd, Rotkreuz, Switzerland.
- ELECSYS is a trademark of Roche. The Elecsys Phospho-Tau (217P) Plasma immunoassay is now an in vitro diagnostic-certified immunoassay available for clinical use in CE-mark accepting countries.

Disclosures

ADD: Employee of Roche Diagnostics International Ltd. SH: Employee of Roche Diagnostics GmbH and holds participation certificates of Roche Holding Ltd. NB: Employee of Roche Diagnostics GmbH and shareholder in F. Hoffmann-La Roche Ltd. DC: Employee of Roche Diagnostics Ltd. KB: During 2023–2025, served as a consultant, advisory board member, lecturer, educational material producer, and participant in educational programs for AC Immune, ALZPath, AnBio, Beckman Coulter, BioArctic, Eisai, Eli Lilly, Neurimmune, Novartis, Roche Diagnostics, Sunbird Bio, and Siemens Healthineers. He was also a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS) in the GU Ventures Program. Since September 2025, KB has been an employee of Eli Lilly and Company and has no other disclosures. OH: Employee of Eli Lilly and Company. MSC: Received grants paid to his institution and has served as a clinical trial site investigator for Roche Diagnostics International Ltd. He has received consultancy fees paid to his institution or served as an advisory board member for Eli Lilly, Grifols, Novo Nordisk, and Roche Diagnostics International Ltd. He has received research support from AdX Neurosciences, Almar Biosciences, ALZPath, Avid adropharmaceuticals Inc. (Eli Lilly and Company), Fujirebio, Janssen Research & Development, Meso Scale Discovery, and Roche Diagnostics International Ltd. He has received no personal compensation from these organisations or any other for-profit organisation. He has also served as a site investigator for Roche Diagnostics International Ltd for the study "A multicenter, prospective, non-interventional study to determine the cutoff and clinical performance of the Elecsys Amyloid Plasma Panel and its component assays; RD006263". No gifts or financial incentives of any kind have been provided to MSC. CWR: CEO, founder, and majority shareholder of Scottish Brain Sciences, Edinburgh, UK. He has received funding paid to his institution for projects, consultancy, or investigator fees from Actinogen, Biogen, Eisai, Eli Lilly, F. Hoffmann-La Roche Ltd, Janssen-Cilag GmbH, Kynexis, Linus, Merck, Novartis, Roche Diagnostics International Ltd, TauRx, and Thereni. NJA, MD: No conflicts. CCR: Received grants paid to his institution from Biogen, Cerveau Technologies, Eisai, Enigma Biomedical, F. Hoffmann-La Roche Ltd, and Novo Nordisk. He has provided consultation for Biogen, Cerveau Technologies, Eisai, Enigma Biomedical, F. Hoffmann-La Roche Ltd, Eli Lilly, Merck, and Novo Nordisk. He has also served as an advisory board member for Eisai Australia, Enigma Biomedical, F. Hoffmann-La Roche Ltd, and Eli Lilly Australia. He is an unpaid Director at Australian Dementia Network Ltd, which is supported by Austin Health and the National Health and Medical Research Council of Australia. ML, SW: Employees of Eli Lilly and Company. SP: Acquired research support for his institution from Avid Radiopharmaceuticals and Ki elements through ADDF. He has received consultancy or speaker fees from Danaher, Eisai, Eli Lilly, Novo Nordisk, Roche, and Sanofi.

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