

TRAJECTORIES OF PLASMA BIOMARKERS AND THEIR RELATIONSHIP WITH AMYLOID-BETA PET AND COGNITIVE DECLINE IN THE GENERAL POPULATION

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Background

Plasma biomarkers may enable early detection and monitoring of Alzheimer's disease pathology^{1,2}; however, longitudinal biomarker studies in the general population remain limited.

Aim

To determine trajectories of plasma biomarkers in the general population and their associations with amyloid-beta positron emission tomography (Aβ-PET), cognitive decline, and incident mild cognitive impairment (MCI).

Conclusion

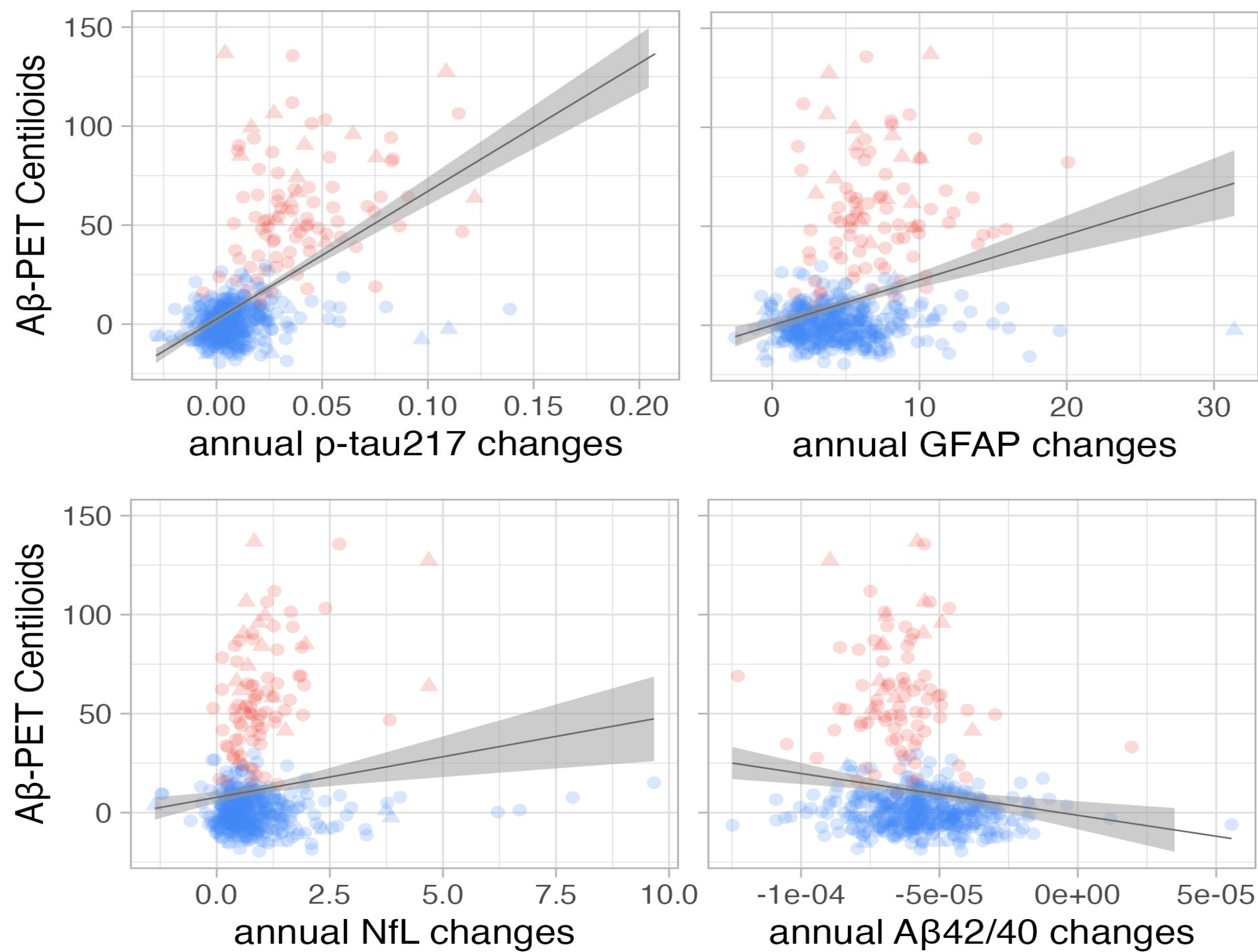
Longitudinal plasma p-tau217 changes showed the strongest association with Aβ burden, and longitudinal increases in p-tau217 and NfL were associated with faster cognitive decline and incident MCI.

Methods

- Two **population-based longitudinal cohort** studies
- Rhineland Study** (Germany; mean follow-up 5 years; baseline 2016-2020; intermediate 2020; follow-up 2022-2024)
- Rotterdam Study** (the Netherlands; mean follow-up 9 years; baseline 2010-2016; Aβ-PET 2018-2021; follow-up 2021-2024)
- Plasma biomarkers:** Simoa p-tau217, Aβ42/40, GFAP, NfL

Statistical analyses:

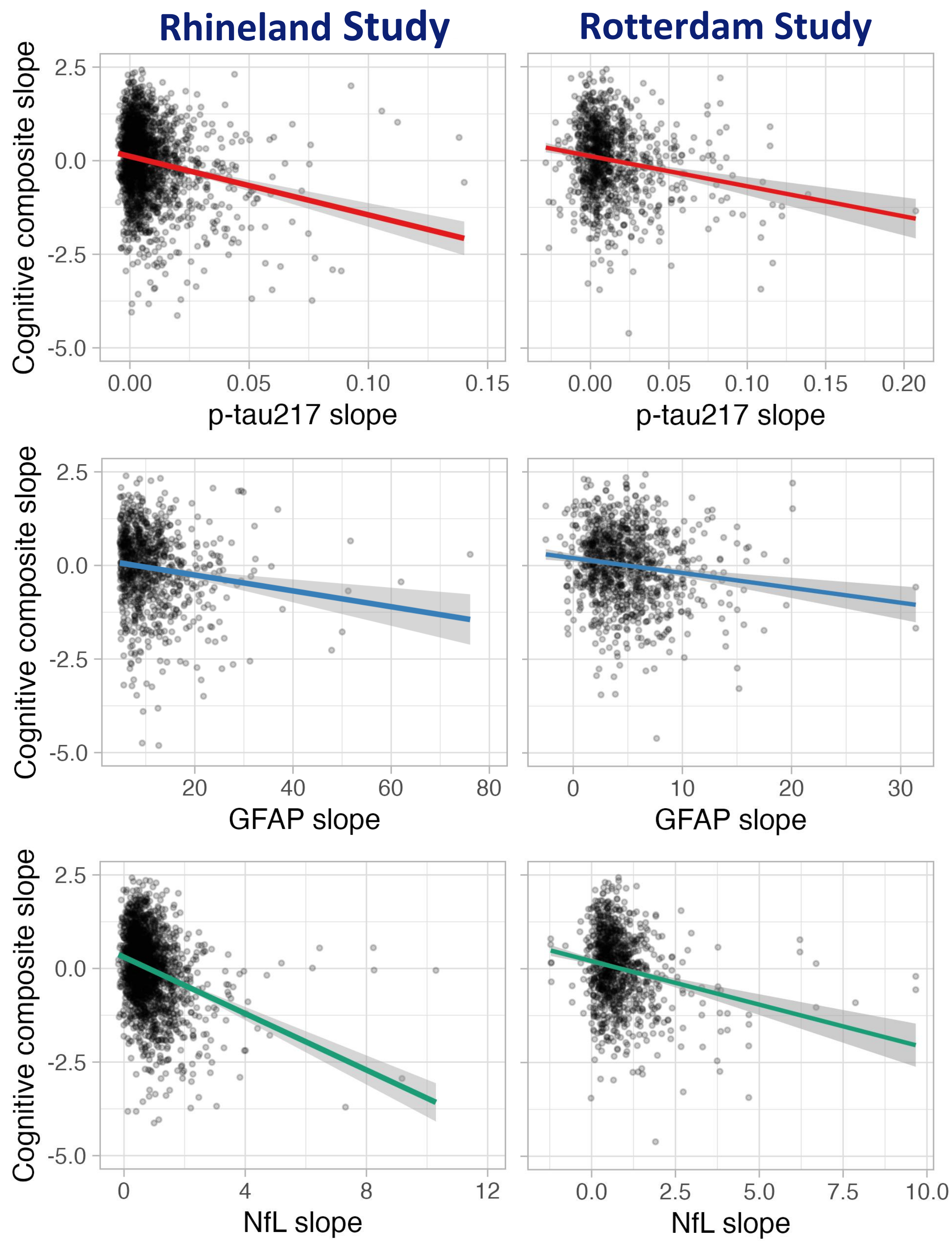
- Aβ-PET** (Rotterdam only): Linear regression models adjusted for demographics + APOE ε4
- Cognitive decline:** LME models and linear regression of LME-derived biomarker and cognitive slopes. Adjusted for demographics; + APOE ε4, eGFR, BMI, diabetes, hypertension; + baseline plasma biomarkers
- Incident MCI:** Firth's penalized logistic regression adjusted for demographics



- p-tau217 → +145% Centiloids (per 1 SD)
 - GFAP → +44% Centiloids
 - Aβ42/40 ratio → -26% Centiloids
 - NfL → +26% Centiloids
- Aβ-PET status
● Negative
● Positive

Results

- Rhineland Study:** 3,965 participants (mean age 54.1 [13.0] years; 57% female)
- Rotterdam Study:** 584 participants (62.2 [5.5] years; 50% female)
- Longitudinal p-tau217 changes** showed the strongest association with Aβ-PET burden.
- Longitudinal increases in **p-tau217** and **NfL** were associated with faster cognitive decline and incident MCI, with NfL providing information beyond baseline levels



References:

- Hansson O, Edelmayer RM, Boxer AL, Carrillo MC, Mielke MM, Rabinovici GD, Salloway S, Sperling R, Zetterberg H, Teunissen CE. The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease. *Alzheimer's & Dementia*. 2022;18(12):2669–2686.
- Teunissen CE, Verberk IMW, Thijssen EH, Vermunt L, Hansson O, Zetterberg H, van der Flier WM, Mielke MM, del Campo M. Blood-based biomarkers for Alzheimer's disease: towards clinical implementation. *The Lancet Neurology*. 2022;21(1):66–77.