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- Individuals with suspected cognitive decline usually first present in primary care.
- Although much research focuses on Alzheimer's disease (AD) diagnostic accuracy, the clinical priority in this setting is often to identify if any neurocognitive disorder could be present before initiating further steps, and, only secondly, to assess whether AD is a potential diagnosis.

- Investigate which combination of blood-based biomarkers, cognitive tests & clinical questionnaires in primary care is optimal for the two-step approach: the diagnosis of
 - (1) any symptomatic neurodegenerative disease and, if positive,
 - (2) AD vs. non-AD

- 660 primary care patients from **BioFINDER**
undergoing cognitive evaluation with full data available on 03-Dec-2025 (Fig.1A).
- Main outcome: clinical diagnosis of mild cognitive impairment (MCI) or dementia due to any neurodegenerative disease established at a memory clinic, including
 - comprehensive clinical work-up, CSF/PET AD biomarkers, but blinded to the blood-based biomarkers and cognitive tests in primary care.
- Examined predictors, collected in primary care, included plasma and imaging biomarkers, brief clinical questionnaires, and cognitive tests (Fig.1B).

	Neurodegenerative disease	Non-neurodegenerative disease	Total
N	420	240	660
Cognitive status			
SCD	0 (0%)	217 (90.4%)	217 (32.9%)
MCI	215 (51.2%)	17 (7.1%)	232 (35.2%)
Dementia	205 (48.8%)	6 (2.5%)	211 (32.0%)
Age	78.6 (6.05)	71.7 (8.17)	76.1 (7.65)
Sex (female)	219 (52.1%)	122 (50.8%)	341 (51.5%)
Education (years)	10.8 (3.17)	12.5 (3.30)	11.4 (3.32)
Aβ positive (CSF/PET)	261 (62.1%)	63 (26.3%)	324 (49.1%)
MMSE score	24.8 (3.56)	28.1 (2.21)	26.0 (3.32)
Underlying etiology	AD: 273 (65.0%) VaD: 100 (23.8%) Other: bvFTD, DLB, FTD, PSP, rlvFTD, svPPA	Alcohol, Anxiety, Depression, Epilepsy, normal pressure hydrocephalus, other psychiatric disorder, Parkinson's disease, Post resection, TBI, Tumor	

The diagram illustrates the study design, which includes four main components:

- Demographic information:**
 - Age
 - Sex
 - Education (years)
- Plasma biomarkers:**
 - Lumpyulse p-tau217
 - Lumpyulse NFL
- MRI/CT:**
 - Fazekas grading of white matter lesions
 - Global cortical atrophy
 - Infarcts
 - Medial temporal lobe atrophy
- Cognitive testing / Brief questionnaires:**
 - MMSE
 - MoCA
 - ADAS-Cog
 - Trail Making Test A/B
 - Letter F fluency
 - Animal fluency
 - Symbol digit modalities test
 - Cognitive Function Instrument (informant)
 - Functional Activities Questionnaire
 - Informant based questions on memory/parietal/temporal/frontal/subcortical symptoms

- Optimal predictors were selected using recursive feature elimination, and final logistic regression models were evaluated using the Akaike Information Criterion.
- As sensitivity analyses digital cognitive assessments were explored (BioCog¹; CANTAB²; iADL³).

 anika.wuestefeld@med.lu.se
 [anika-wuestefeld](https://www.linkedin.com/in/anika-wuestefeld)



References: ¹ Tidemann & Karlsson et al., Nat Med, 2025; ² Fray, Robbins & Sahakian, Int. J. Geriatr. Psychiatry, 1996; ³ Dubbelman et al., Neuropsychology, 2024