Alzheimer's disease (AD)

AD is a progressive neurodegenerative disease responsible for 60-70% of dementia cases. Over 95% of AD is caused by multiple genetic (and environmental) factors.

Polygenic risk scores (PRS)

PRS integrate multiple genetic variants associated with a disease (here AD) in a single score, predicting an individual's likelihood of developing this disease.

Disease modifying treatment (DMT)

DMTs are treatments that delay, slow down or reverse disease progression by targeting underlying causes or mechanisms. Up until now, no DMT for AD is available.

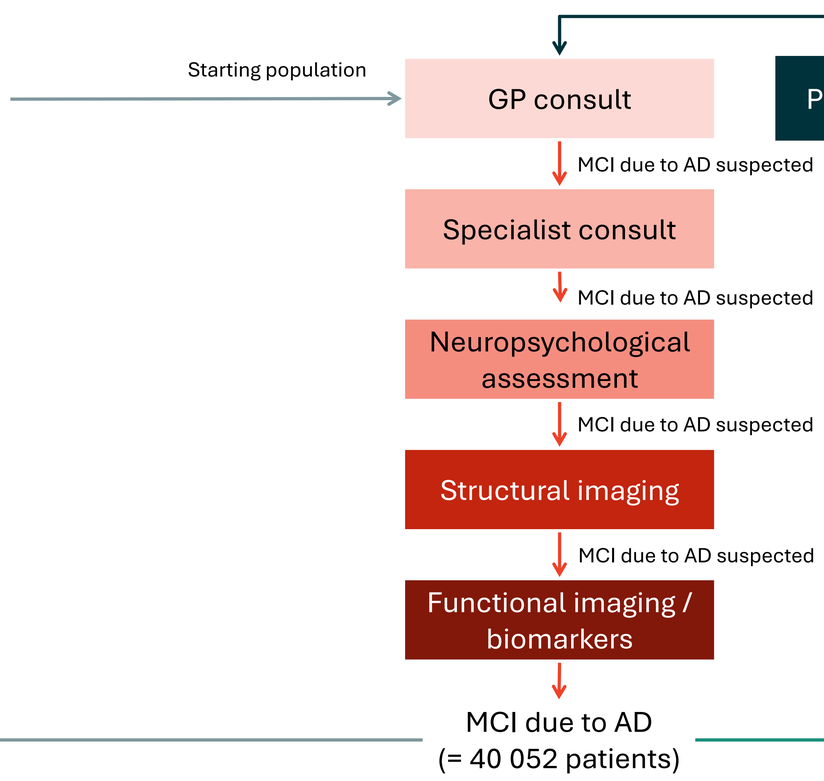
How can PRS support early diagnosis of Alzheimer's disease?

The diagnostic process for mild cognitive impairment (MCI) due to AD was mapped and translated in a decision tree, comparing

Current diagnostic pathway of MCI | **Diagnostic pathway of MCI with PRS**

Population at risk in Flanders (Belgium)

357 606 65+ patients with subjective cognitive impairment (SCM)



357 606
(i.e., same starting population as applied in the current diagnostic pathway)

In the current diagnostic pathway

544 MCI cases are expected to be identified, representing

1.4% of all Flemish 65+ people with MCI due to AD

If PRS assessment preceded the diagnostic pathway

848 MCI cases were to be identified (i.e., 304 more than the current diagnostic pathway)

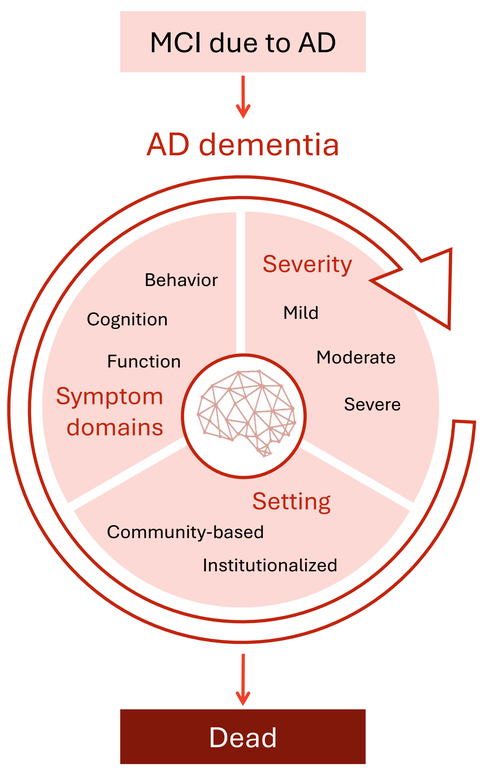
2.1% of all Flemish 65+ people with MCI due to AD

The current diagnostic pathway of MCI involves multiple steps. Even when AD is suspected, further testing is not always performed.

Screening with PRS increases the likelihood of early diagnosis of AD in patients with MCI, although the absolute impact is limited.

Can PRS screening be cost-effective? Under which circumstances?

The end points of the decision tree were linked to a Markov model, leveraging the open-source model of Green et al. (2019):



A hypothetical DMT

In both alternatives, DMT is assumed to

reduce the probability of developing AD with **30%**

during a 5-year period, after which MCI to AD progression returns to normal pace,

at a cost - for the healthcare payer (incl. patient shares) - of **10 000** €/year .

Comparison made in the model

Current diagnostic pathway of MCI (no PRS) + DMT vs. **Diagnostic pathway of MCI with PRS** + DMT

Then the ICER becomes...

When a DMT for AD becomes available under afore-mentioned conditions

284 061 €/QALY

When a DMT for AD becomes available under afore-mentioned conditions
AND the diagnostic pathway improves*

70 796€/QALY

When a DMT for AD becomes available, but at a cost of €5.000 per year,
AND the diagnostic pathway improves*

39 251€/QALY

*90% probability of undergoing functional imaging or biomarkers, instead of 10%

Clinical implications

Combining PRS, a static measure, with more dynamic measures (e.g. biomarkers, transcriptomics, or epigenomics) might bring extra insights into the pathophysiological mechanisms of AD.

As long as no DMT for AD is available, PRS will have limited use in clinical practice.

When a DMT becomes available, PRS is only helpful if the diagnostic pathway of MCI becomes less costly and/or more efficient in diagnosing patients.

Health-economic implications

The cost-effectiveness of PRS-screening heavily depends on the overall MCI diagnostic pathway and DMT availability.

The actual merit of a value model lies in its adaptability, creating the possibility to evolve together with further research in PRS.

This study demonstrates the feasibility of an early health-economic evaluation of PRS as a screening tool for AD.

Abstract reference:

Werbrouck A[1], Verdonck C[1], Abakkouy Y[2], Cleynen I[2], Vandenberghe R[3], Vermeersch S[1], & Schoonaert L[1] (2024). Exploring the Implementation of Polygenic Risk Scoring in Alzheimer's Disease: An Early Value Model

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