

Association of Cardiovascular Risk Trajectory With Cognitive Decline and Incident Dementia

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Study Question

How does the longitudinal trajectory of cardiovascular risk affect the incidence of cognitive decline and dementia?

What Is Known and What This Paper Adds

Recent research has shown that cardiovascular disease (CVD) risk is associated with midlife cognitive decline and increased dementia risk. However, few studies have examined the relationship of longitudinal changes in multiple CVD risk factors with regard to cognitive variation and dementia. This study demonstrates that an accelerated, compared to a stable or average, trajectory of longitudinal CVD risk can increase the risk of both dementia incidence and episodic memory (EM) decline.

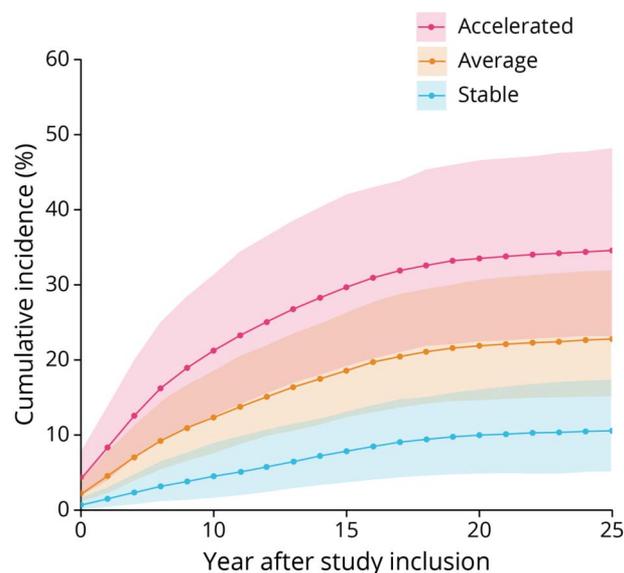
Methods

For this longitudinal study, we examined 1,244 healthy community-dwelling participants from the prospective cohort Betula study, based in Umeå, Sweden. At every 5-year time point (T) across 20 to 25 years, data on CVD risk, EM performance, and dementia status were measured. The primary outcome of the study was dementia risk in an elderly subgroup of the sample (≥ 70 years of age at study start, $n = 243$) and EM decline in a younger subgroup (35–65 years of age at study start, $n = 1,001$). Participants were split into 3 groups, each of which had similar CVD risk at study start yet exhibited diverging risk trajectories over time. The groups showed an average, accelerated, or stable CVD risk progression. Analysis was performed with bayesian additive regression testing, a semiparametric machine-learning method. Risk ratios (RRs) were calculated at each time point (i.e., T2–T5).

Results and Study Limitations

Participants with a stable cardiovascular risk trajectory were less likely to develop Alzheimer disease (RR at T2: 3.3 [95% CI 2.6–17.5]; RR at T5: 5.7 [95% CI 1.9–6.7]) or vascular dementia (RR at T2: 3.3 [95% CI 1.1–16.6]; RR at T5: 4.1 [95% CI 1.5–7.6]) compared to those in the accelerated trajectory group or to exhibit EM decline (RR at T2: 1.4 [95% CI 1–1.9]; RR at T5 1.2 [95% CI 1–1.5]). Tests of tertile or

Figure Dementia Incidence and CVD Risk Trajectory



Alzheimer disease incidence across 25 years in older individuals with accelerated, average, and stable cardiovascular disease (CVD) risk trajectories. Shaded areas represent 95% credible intervals.

quartile splits of CVD risk at baseline were not associated with outcome. A stable cardiovascular risk trajectory also appeared to partially mitigate Alzheimer disease dementia risk for *APOE* $\epsilon 4$ carriers. Limitations include a lack of neuroimaging or biomarker assessment in the diagnosis procedure and an inability to determine whether the sequence of EM decline leading to dementia is causally triggered by an accelerated CVD risk trajectory.

Study Funding and Competing Interests

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