

Long-term Risk Of New-onset Dementia Following Covid-19

Among Adults Aged ≥50 Years

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COVID-19 may increase the risk of new-onset dementia 2–4 years after infection, particularly by accelerating clinical conversion among cognitively vulnerable older adults. This increased dementia risk was observed despite little difference in average cognitive decline, supporting a threshold rather than uniform deterioration model.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	CONTACT
Concerns persist regarding the long-term cognitive consequences of SARS-CoV-2 infection, yet evidence on incident dementia remains inconsistent, often limited by short follow-up and lack of pre-pandemic cognitive data. Reverse causation is a major concern, as individuals with subtle pre-existing impairment may be more vulnerable to infection. We examined whether COVID-19 is associated with new-onset dementia (NOD) occurring 2-4 years after infection among adults aged ≥50 years, leveraging objectively measured pre-pandemic cognition to better account for baseline vulnerability and to clarify whether COVID-19 confers sustained excess dementia risk.	We analysed data from the English Longitudinal Study of Ageing. COVID-19 status was ascertained during the 2020 COVID-19 sub-study using contemporaneous symptom- and test-based criteria. Participants with dementia at the start of the incident-dementia risk period (Wave 10) were excluded, and uninfected controls were required to remain COVID-negative through 2024. Incident all-cause dementia was identified by self- or proxy-reported physician diagnosis between Waves 10 and 11, corresponding to approximately 2-4 years post-infection. Poisson regression with robust standard errors estimated adjusted incidence rate ratios (IRRs), controlling for sociodemographic, lifestyle, clinical covariates, and a pre-pandemic global cognitive composite. Two-wave cognitive trajectories (Wave 9 to Wave 11) across four domains were examined using linear mixed-effects models.	Among 1,791 participants followed from the COVID-19 sub-study baseline for a median of 3.8 years, 16 developed NOD. Prior COVID-19 infection was associated with a higher incidence of NOD compared with uninfected participants (adjusted IRR 2.83, 95% CI 0.99-8.00), with consistently elevated point estimates across analyses. Excluding hospitalised cases yielded a similar or stronger association (IRR 3.26, 1.19-9.45). In contrast, average cognitive trajectories across memory, orientation, and verbal fluency did not differ significantly by infection status. Stratified analyses showed that individuals who developed NOD had lower baseline cognition and markedly steeper decline regardless of infection status.	COVID-19 was associated with increased risk of NOD 2-4 years after infection despite minimal differences in population-average cognitive decline. Findings support a threshold model in which COVID-19 accelerates clinical conversion to dementia among vulnerable individuals rather than inducing uniform cognitive deterioration, including after non-hospitalised infection.	d.shan@lancaster.ac.uk  ALZHEIMER'S ASSOCIATION 