

**VCU**

SARS-CoV-2 infection increases risk of subsequent diagnosis of dementia in patients with obstructive sleep apnea

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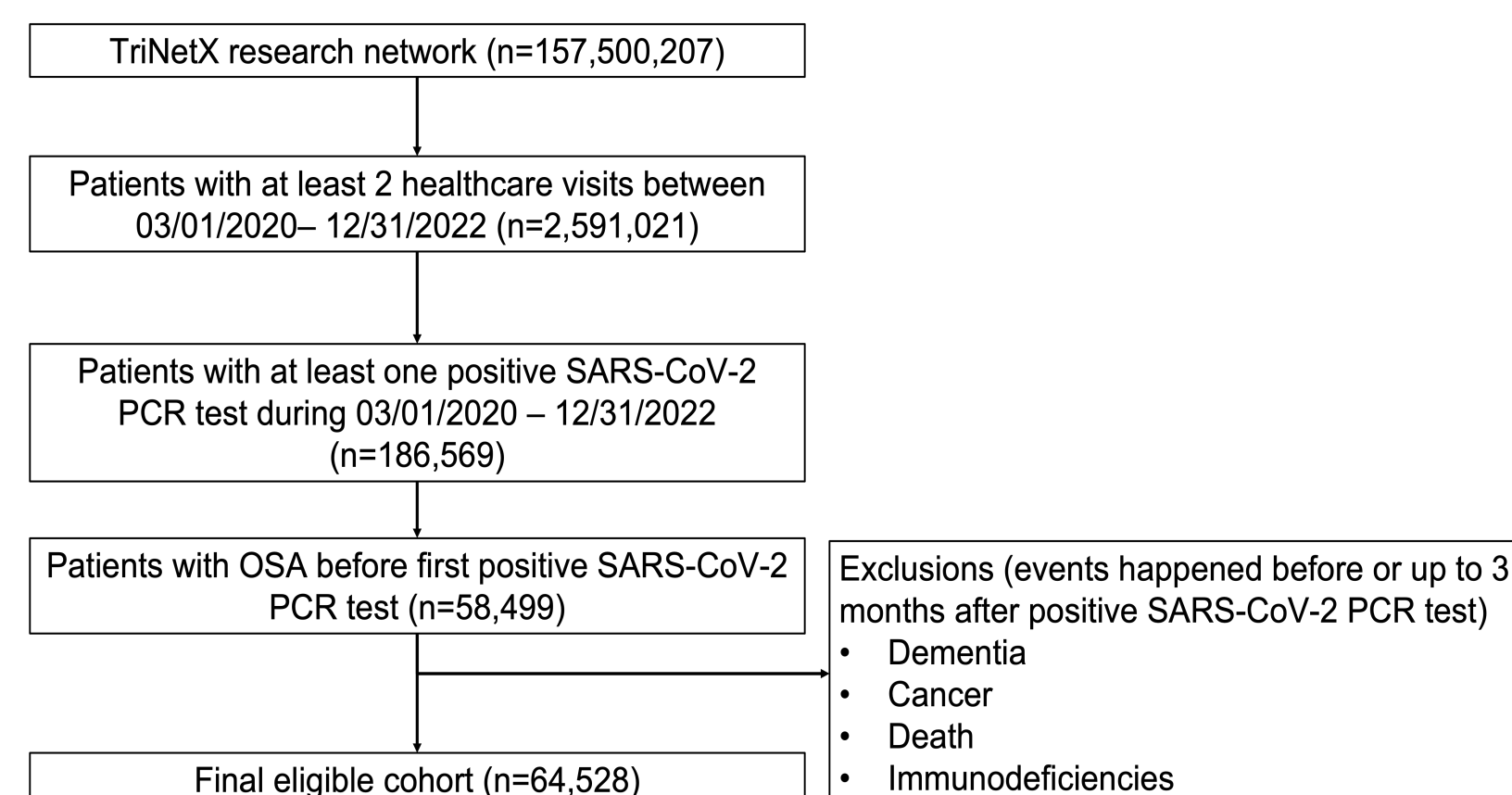
Objective

- SARS-CoV-2 and obstructive sleep apnea (OSA) have been independently linked to increased risk of neurodegenerative disease.^{1,2}
- Prior studies suggest that SARS-CoV-2-related neurological complications are most pronounced within 6–12 months post-infection.³
- The combined impact of OSA and SARS-CoV-2 on dementia risk is not well understood despite overlapping pathophysiological mechanisms that may accelerate neurodegeneration.
- This study aims to analyze the impact of SARS-CoV-2 infection on diagnosis of dementia in patients with OSA.

Methods

- TriNetX database was queried for adults with OSA with either positive or negative SARS-CoV-2 PCR tests between 03/01/2020 - 12/31/2022 (Figure 1)
- Patients with cancer or immune deficiency prior to COVID-19 diagnosis were excluded.
- The cohorts were propensity score-matched for multiple variables.
- Measures of association and a Kaplan-Meier analysis of dementia diagnosis were calculated after a 3-month wash-out period to 5 years post-PCR test.

Figure 1: Flowchart of Cohort Creation



Figures and Results

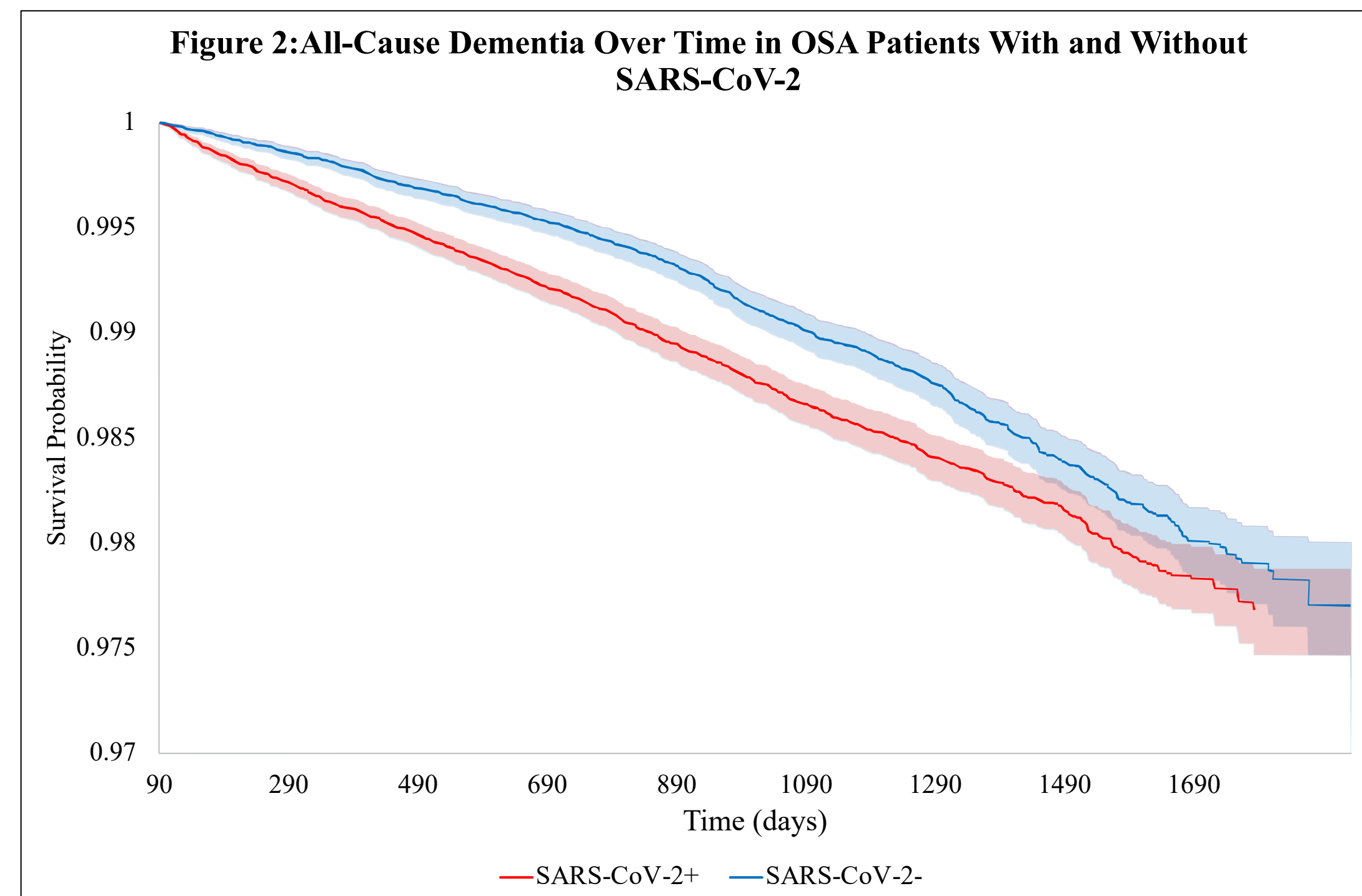


Table 1: Dementia outcomes in OSA Patients With and Without SARS-COV-2

Outcome	SARS-COV-2 (n=64,528); n (%)	No SARS-COV-2 (n=64,528); n (%)	RR (95% CI)
All-cause dementia	947 (1.468%)	753 (1.167%)	1.258 (1.144-1.383)
Alzheimer's disease	187 (0.29%)	183 (0.284%)	1.022 (0.834-1.252)
Vascular dementia	190 (0.294%)	135 (0.206%)	1.407 (1.129-1.754)
Lewy body dementia	30 (0.046%)	25 (0.039%)	1.2 (0.706-2.04)
Frontotemporal dementia	26 (0.04%)	24 (0.037%)	1.083 (0.622-1.887)

Table 2: Dementia Outcomes in Sub Analyses

	CPAP vs No CPAP (n=84,625)	Vaccination vs No Vaccination (n=4,088)	Hospitalization vs No Hospitalization (n=11,183)
	RR (95% CI)	RR (95% CI)	RR (95% CI)
All-cause dementia	0.949 (0.769-1.170)	1.032 (0.73-1.46)	1.532 (1.302-1.803)
Alzheimer's disease	0.5 (0.284-0.880)	0.813 (0.391-1.687)	0.981 (0.672-1.432)
Vascular dementia	0.914 (0.567-1.475)	1.455 (0.676-3.13)	1.705 (1.176-2.471)
Lewy body dementia	1 (0.416-2.402)*	1 (0.416-2.402)*	1 (0.416-2.402)*
Frontotemporal dementia	1 (0.417-2.399)*	1 (0.416-2.402)*	1 (0.416-2.402)*

Conclusion

- SARS-CoV-2 was associated with increased risk of earlier all-cause dementia diagnosis in OSA, with the greatest effect observed for vascular dementia, highlighting a potential acceleration of neurodegenerative processes. Increase risk persisted up to 5 years.
- In a subgroup analysis comparing patients with CPAP use to those without, there was no significant difference in dementia risk.
- Vaccination prior to infection did not significantly modify dementia risk, and treatment with Paxlovid, remdesivir, or dexamethasone was not associated with significant changes in risk.
- OSA patients who were hospitalized during SARS-CoV-2 infection, defined as hospitalization from 1 week before to 2 weeks after infection, exhibited a significantly higher risk of developing dementia compared to OSA patients who were not hospitalized during SARS-CoV-2 infection, suggesting that infection severity may compound neurological vulnerability in OSA patients.
- Proposed mechanisms include synergistic disruption of glymphatic clearance, vascular dysfunction, and neuroinflammatory pathways shared by OSA and SARS-CoV-2.
- Clinical awareness of cognitive symptoms in post-COVID OSA patients is warranted, and further prospective studies are needed to elucidate mechanisms and identify protective interventions.

Citations

- Shan, D., Wang, C., Crawford, T. *et al.* Association between COVID-19 infection and new-onset dementia in older adults: a systematic review and meta-analysis. *BMC Geriatr* 24, 940 (2024). <https://doi.org/10.1186/s12877-024-05538-5>
- Wei Lin, Yu-Kai Lin, Fu-Chi Yang, Chi-Hsiang Chung, Je-Ming Hu, Chang-Huei Tsao, Zi-Xeng Weng, Chien-An Ko, Wu-Chien Chien, Risk of neurodegenerative diseases in patients with sleep disorders: A nationwide population-based case-control study, *Sleep Medicine*, Volume 107, 2023, Pages 289-299, ISSN 1389-9457, <https://doi.org/10.1016/j.sleep.2023.05.014>.
- Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry*. 2021 May;8(5):416-427. doi: 10.1016/S2215-0366(21)00084-5. Epub 2021 Apr 6. PMID: 33836148; PMCID: PMC8023694.

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