



Varicella-Zoster Vaccination Is Associated with Lower Alzheimer's Disease Prevalence and Cognitive Impairment in a Puerto Rican Cohort



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VZV vaccination may be a protective factor against Alzheimer's disease and cognitive decline in older Puerto Rican adults.

INTRODUCTION

- Alzheimer's disease (AD) affects approximately 12% of adults aged ≥ 65 years, in Puerto Rico (PR).
- Emerging evidence suggests that neuroinflammation and latent viral reactivation may contribute to AD pathogenesis.
- Varicella-zoster virus (VZV), a neurotropic herpesvirus, has been implicated in central nervous system inflammation and vascular injury.
- However, Caribbean Hispanic populations remain underrepresented in this area of research.
- We examined whether VZV vaccination is associated with AD diagnosis and cognitive outcomes in older Puerto Rican adults.

RESULTS

- AD was present in 56 participants (61.5%).
- Vaccinated individuals had a significantly lower prevalence of AD compared to unvaccinated individuals (27.9% vs 91.7%, $p < 0.001$), corresponding to markedly reduced odds of AD ($OR \approx 0.04$).
- Vaccinated participants also demonstrated less severe cognitive impairment, with lower rates of moderate-to-severe impairment on MoCA (37.2% vs 68.1%, $p = 0.008$) and a higher proportion without dementia on CDR (69.8% vs 12.8%, $p < 0.001$).
- However, vaccinated individuals were younger and had higher educational attainment, and unvaccinated participants exhibited greater cognitive severity and higher use of dementia-related medications, suggesting important baseline differences between groups.
- No significant differences were observed in GDS scores or APOE genotype distribution.

CONCLUSION

- Zoster vaccination was associated with lower AD prevalence and less severe cognitive impairment in this cohort.
- However, given the cross-sectional design and substantial baseline differences between groups, these findings may reflect confounding, including age, education, and disease severity, as well as potential reverse causation and healthcare utilization bias.
- These results highlight the need for longitudinal studies with careful temporal characterization of vaccination exposure to determine whether VZV vaccination may influence Alzheimer's disease risk or progression.

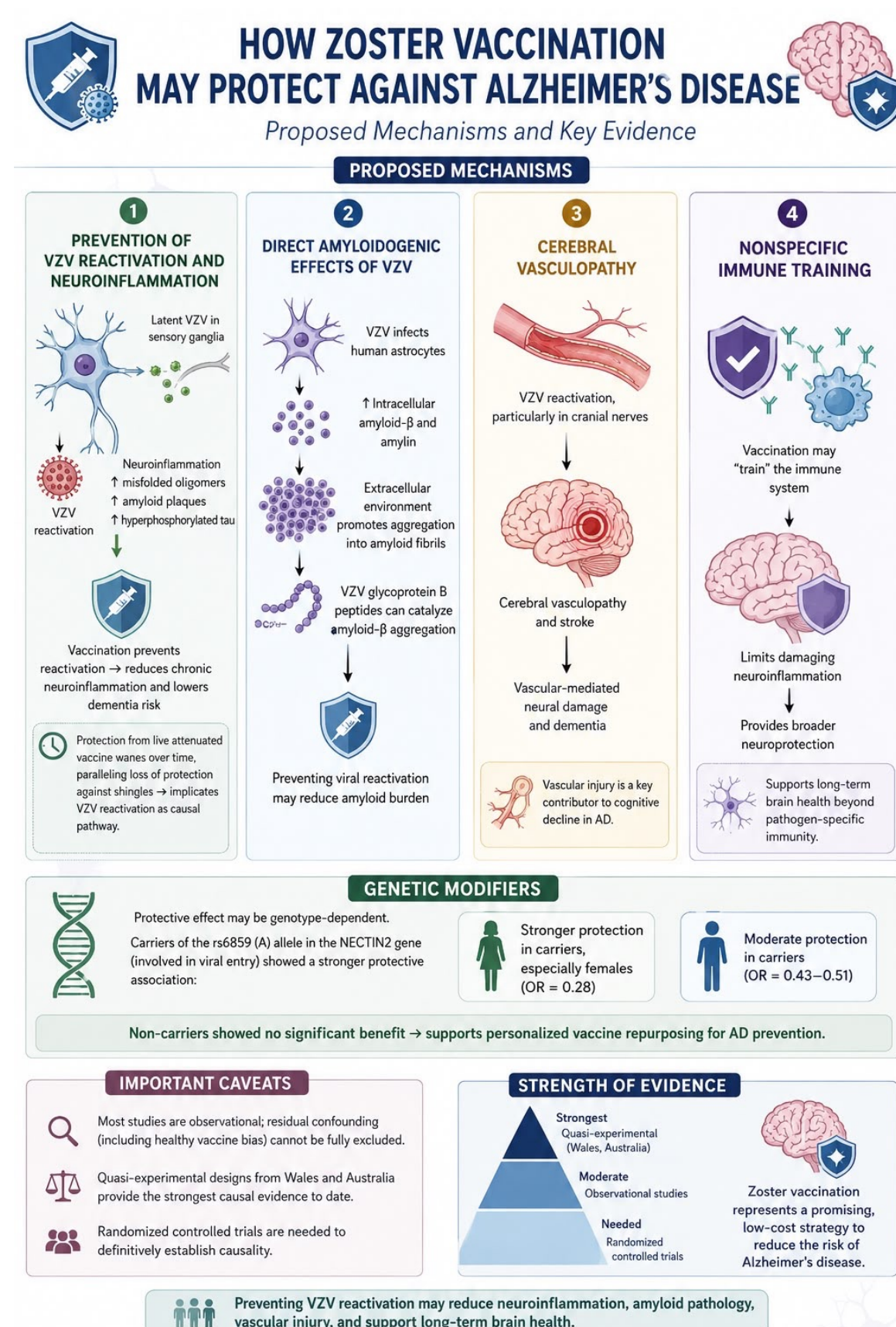
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METHODS

- Cross-sectional analysis of 91 adults from the Association-Gut-Microbiome-AD cohort.
- Participants were categorized by zoster vaccination status (vaccinated $n=43$; unvaccinated $n=48$).
- AD diagnosis was determined from clinical records, and cognitive status was assessed using the MoCA, CDR, and Depression scales
- Group differences were evaluated using chi-square, Fisher's exact, and t-tests, as appropriate.

	Varicella Vaccination			p-value ¹
	No n=48 N (%)	Yes n=43 N (%)	Total n=91 N (%)	
Cognitive				
AD Diagnosis²				
No	4 (8.3)	31 (72.1)	35 (38.5)	<0.001
Yes	44 (91.7)	12 (27.9)	56 (61.5)	
MOCA status¹				0.008
Normal	3 (6.4)	3 (7.0)	6 (6.7)	
Mild	12 (25.5)	24 (55.8)	36 (40.0)	
Mod/Severe	32 (68.1)	16 (37.2)	48 (53.3)	
CDR status¹				<0.001
None	6 (12.8)	30 (69.8)	36 (40.0)	
Mild	0 (0.0)	1 (2.3)	1 (1.1)	
Mod/Severe	21 (44.7)	2 (4.7)	23 (25.6)	
Other	20 (42.6)	10 (23.3)	30 (33.3)	
GDS status¹				0.060
Normal	40 (85.1)	42 (97.7)	82 (91.1)	
Mild	7 (14.9)	1 (2.3)	8 (8.9)	
APOE¹				0.650
E2E2	0 (0.0)	1 (2.4)	1 (1.1)	
E2E3	2 (4.2)	4 (9.8)	6 (6.7)	
E2E4	0 (0.0)	1 (2.4)	1 (1.1)	
E3E3	32 (66.7)	23 (56.1)	55 (61.8)	
E3E4	13 (27.1)	11 (26.8)	24 (27.0)	
E4E4	1 (2.1)	1 (2.4)	2 (2.3)	

Abbreviations: MOCA=; CDR=; GDS=; APOE=.

¹ P-value was obtained using Fisher's Exact Test.

² P-value was obtained using Pearson's Chi-Square.

³ P-value was obtained using T-Test.