

Genetic Liability to Alzheimer's Disease and Susceptibility to Childhood Infections

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No strong evidence was found for an association between genetic liability to Alzheimer's disease and common childhood infections.

INTRODUCTION

Accumulating evidence suggests microbial infections may play a role in the aetiology of Alzheimer's disease (AD)^{1,2}. A number of pathogens have been implicated, with the most studied being herpesviruses. However, the role of polygenic liability to AD or *APOE* ϵ 4 status has not been comprehensively studied against a broad range of infections.

This study aims to examine the association between genetic liability to AD and risk of common childhood infections.

METHODS

Sample: A subsample of 8,056 children with genetic and infections data available was selected from the Avon Longitudinal Study of Parents and Children (ALSPAC)^{3,4}, a population-based pregnancy cohort based in and around Bristol, United Kingdom.

Exposures: We calculated polygenic risk scores for Alzheimer's disease including and excluding the *APOE* region (PRS_{AD} and PRS_{AD_noAPOE}) and extracted *APOE* ϵ 4 carrier status.

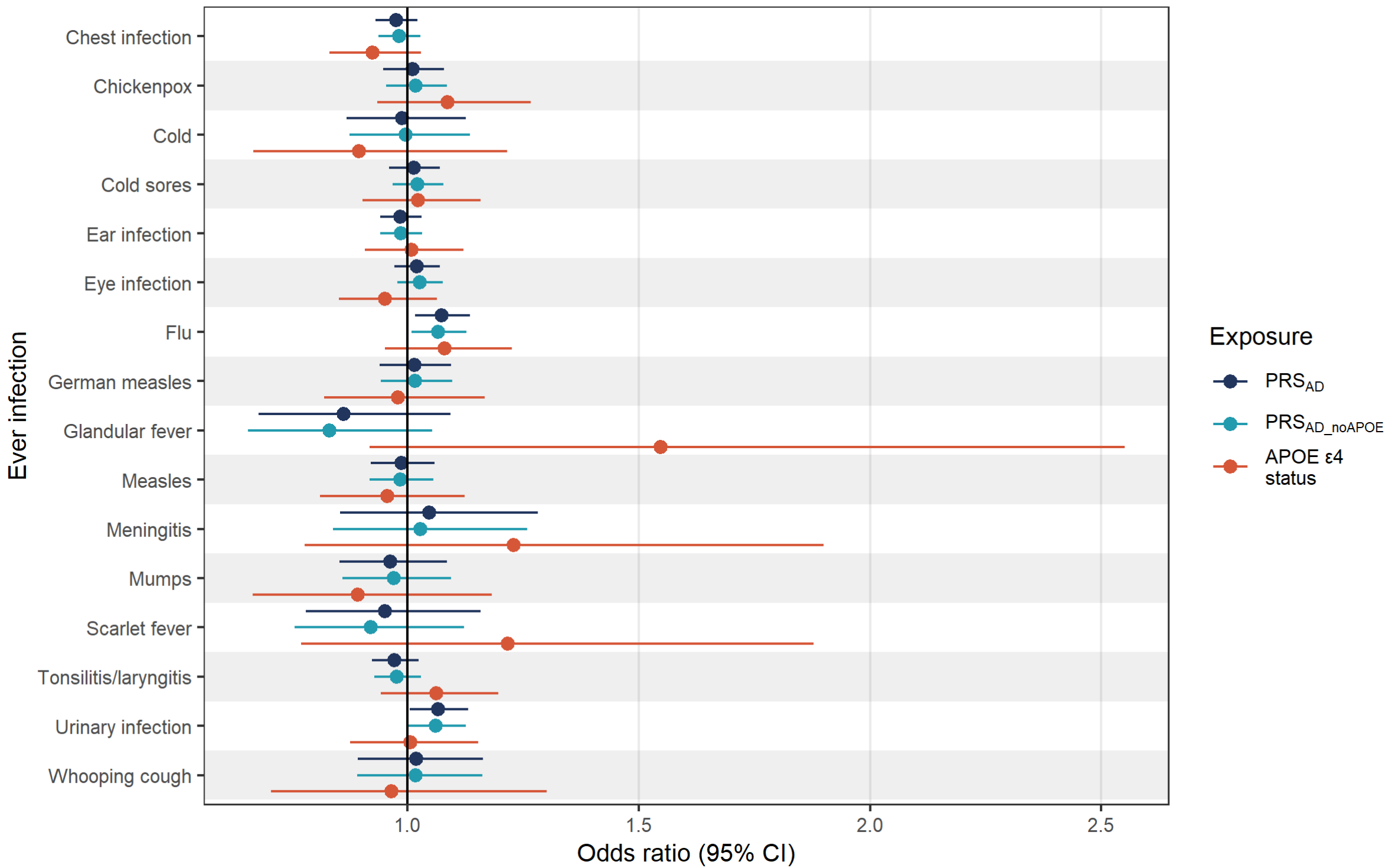
Outcomes: Variables for "ever infection", "number of infection episodes" and "overall infection burden" were derived from data on 16 infections from parent-completed questionnaires collected between the ages of 18 months and 13 years.

Analysis: We performed logistic, Poisson and zero-inflated negative binomial regressions, adjusting for sex and first 10 genetic principal components, and controlled the false discovery rate at 5% using the Benjamini-Hochberg procedure.

RESULTS

Childhood infections were common in our sample. PRS_{AD} and PRS_{AD_noAPOE} were associated with higher risks of flu and urinary infections; however, these associations did not survive correction for multiple testing. There appears to be a trend of *APOE* ϵ 4 being associated with higher risks of certain infections, but the confidence intervals are wide and should be further investigated in larger samples.

	n (%) or median [IQR]
Sex: female	3960 (49.2%)
Available infection data points	92 [58.75, 107.00]
Cold (ever)	6907 (96.7%)
Chickenpox (ever)	6956 (86.4%)
Ear infection (ever)	4301 (56.5%)
Chest infection (ever)	2952 (38.8%)
Eye infection (ever)	2553 (33.5%)
Tonsillitis/laryngitis (ever)	1971 (27.6%)
Flu (ever)	1616 (22.6%)
Cold sores (ever)	1693 (21.4%)
Urinary infection (ever)	1379 (18.1%)
Measles (ever)	889 (11.0%)
German measles (ever)	740 (9.3%)
Mumps (ever)	276 (3.4%)
Whooping cough (ever)	228 (3.0%)
Scarlet fever (ever)	99 (1.4%)
Glandular fever (ever)	69 (1.3%)
Meningitis (ever)	96 (1.2%)
Overall infection burden	8 [5, 12]



We found no evidence of an association of PRS_{AD}, PRS_{AD_noAPOE} or *APOE* ϵ 4 carrier status with the number of infection episodes or overall infection burden.

REFERENCES

¹Brutkiewicz et al. Trends Neurosci 2025;48(8):608-23. ²Ou et al. J Alzheimers Dis 2020;75(1):299-309. ³Boyd et al. Int J Epidemiol 2013;42(1):111-27. ⁴Fraser et al. Int J Epidemiol 2013;42(1):97-110.

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