

Lower Baseline Pulmonary Function Preferentially Increases Risk for Non-AD Dementia

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BACKGROUND

- Prior research supports robust associations between poorer pulmonary function, measured by peak expiratory flow (PEF), and increased risk for subsequent all-cause dementia.^{1,2}
- Yet whether this association varies by underlying dementia etiology is unclear.³
- While some studies support a vascular-mediated pathway linking lower PEF to higher degrees of generalized brain atrophy and lacunar infarcts,⁴ others have demonstrated associations with dementia independent of vascular comorbidities, including a higher risk for Alzheimer's Disease (AD).⁵
- We aimed to evaluate whether baseline PEF predicts all-cause dementia in a longitudinal population-based cohort, and whether this association may vary by dementia etiology.

METHODS

- The sample included 5,973 participants from the Wisconsin Longitudinal Study (WLS) with known dementia status at the 2025 data collection timepoint (aged ~85 years).
- Pulmonary functioning was defined as max PEF obtained across 3 trials at the 2011 data collection wave (2011; aged ~71 years).
- Dementia status and clinically suspected etiology was determined through a multi-disciplinary consensus panel, and by proxy (Dementia Questionnaire) for those without objective cognitive assessments available.
- Binomial logistic regression tested associations between baseline PEF and dementia versus no dementia (MCI and cognitively unimpaired); multinomial logistic regression evaluated associations between cognitively unimpaired (CU) and cognitively impaired groups (MCI and dementia) parsed by primary AD versus non-AD etiology.
- All models accounted for missing data using multiple imputation, and controlled for age (year of birth), sex, height, and adolescent IQ.

RESULTS

TABLE 1 Baseline Characteristics and Unadjusted Comparisons

Characteristic	Overall N = 5973 ¹	Dementia N = 936 ¹	Non-dementia N = 5,037 ¹	p-value ²	CU N = 4,259 ¹	Non-AD Etiology N = 325 ¹	AD Etiology N = 1,334 ¹	p-value ³
Age (in 2020)	82.3 (3.9)	83.8 (3.4)	82.0 (4.0)	<0.001	81.8 (4.1)	83.0 (3.5)	83.6 (3.2)	<0.001
Sex (female)	3,265 (55%)	528 (56%)	2,737 (54%)	0.2	2,399 (56%)	147 (45%)	695 (52%)	<0.001
Height (inches) Unknown	67.2 (3.8) 73	66.9 (3.8) 17	67.3 (3.8) 56	0.014	67.2 (3.8) 48	67.6 (3.9) 3	67.1 (3.8) 22	0.091
Adolescent IQ (std)	0.20 (0.99)	-0.02 (1.01)	0.24 (0.98)	<0.001	0.32 (0.96)	0.00 (0.97)	-0.11 (0.99)	<0.001
Peak Flow Max (L/s) Unknown	6.89 (2.19) 657	6.47 (2.20) 121	6.96 (2.18) 536	<0.001	6.93 (2.18) 456	6.86 (2.35) 35	6.76 (2.19) 161	0.10

¹ Mean (SD); n (%) ² Wilcoxon rank sum test; Pearson's Chi-squared test ³ Kruskal-Wallis rank sum test; Pearson's Chi-squared test

NOTE: Non-Dementia group includes both normal cognition and mild cognitive impairment (MCI); Cognitively Unimpaired (CU) group includes normal cognition only; Alzheimer's Disease (AD)

FIGURE 1

**Logistic Regression Predicting All-Cause Dementia Status
(Reference Group: Non-Dementia)**

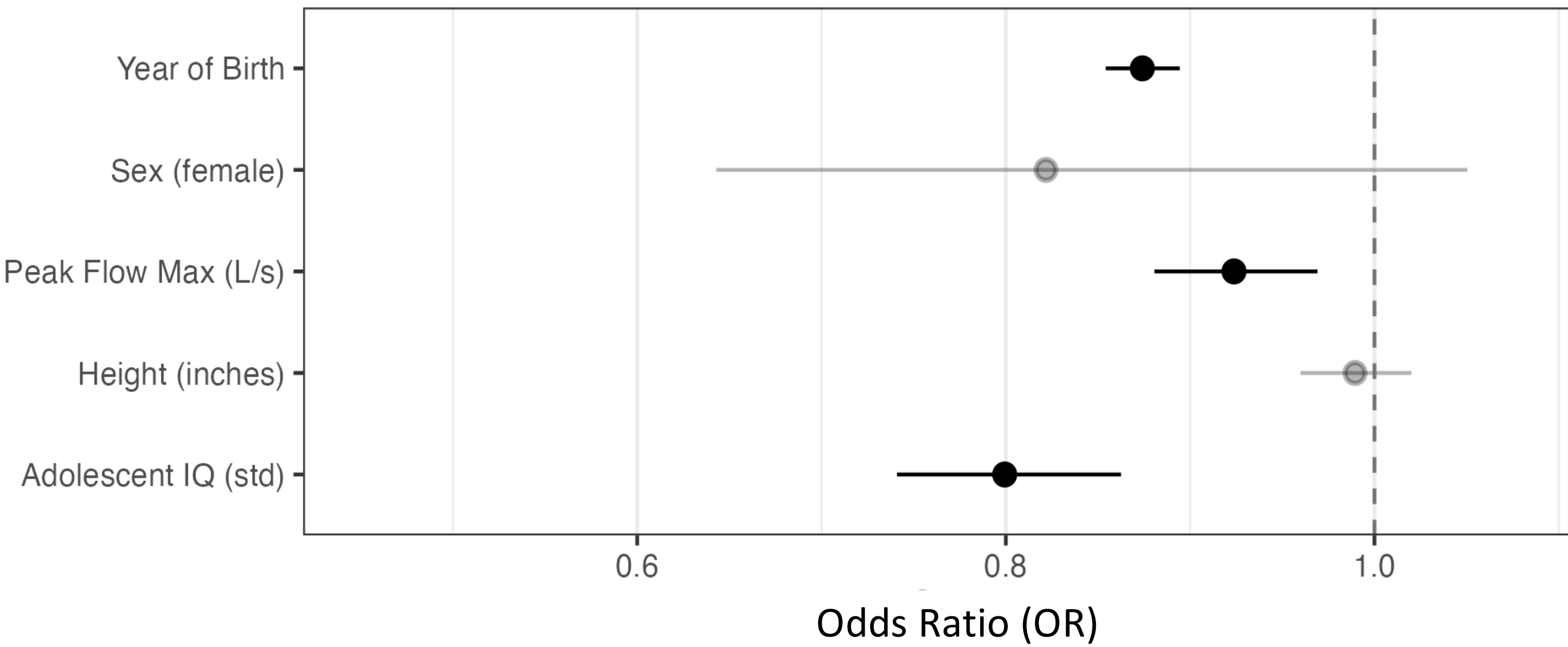
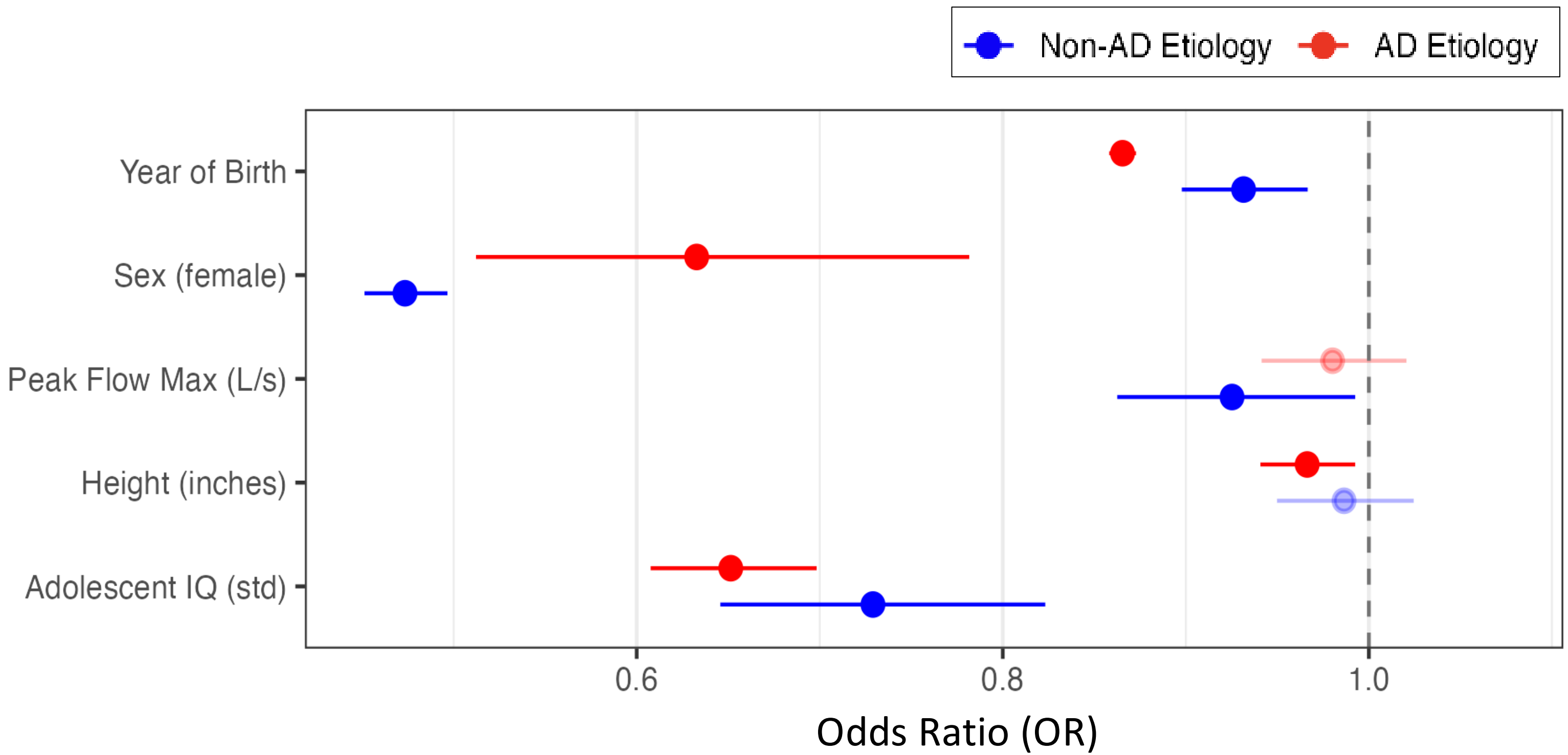


FIGURE 2

**Logistic Regression Predicting Alzheimer's Disease (AD) and Non-AD Etiology
(Reference Group: Cognitively Unimpaired)**



RESULTS...

TABLE 1 In unadjusted groupwise comparisons, participants with all-cause dementia tended to be older, have lower adolescent IQ, of shorter stature and poorer pulmonary functioning (PEF max) at the 2011 data collection wave, but did not meaningfully differ by sex.

FIGURE 1 Higher PEF (reflecting better pulmonary function), younger age (higher birth year), and higher adolescent IQ associated with reduced odds of subsequent all-cause dementia

FIGURE 2 Participants with cognitive impairment due to AD etiology did not meaningfully differ in baseline PEF from those who did not develop cognitive impairment, although tended to be older, more likely female, and had lower adolescent IQ.

Participants with cognitive impairment due to a non-AD etiology tended to show lower baseline PEF when compared to those who did not develop cognitive impairment. Those with a non-AD etiology also tended to be older, female, and had lower adolescent IQ.

CONCLUSIONS

- Findings support a growing body of literature establishing pulmonary function as a significant and potentially modifiable risk factor for late-life dementia.
- Although lower baseline pulmonary function significantly associated with greater odds of all-cause dementia, this association appears to be preferentially driven by participants with a primary non-AD etiology, which in this sample tends to reflect cerebrovascular disease.

ACKNOWLEDGEMENTS

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Funding Source: NIH-NIA R01AG060737
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