Web Appendix:
Modification by frailty status of ambient air pollution effects on lung function in older adults in the Cardiovascular Health Study

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1 Single imputation of missing frailty information

Grip strength was not assessed in 1990–1991, so we carried forward the value recorded in 1989–1990. Reason for weight change was not assessed in 1991–1992, so we assigned unintentional weight change to those participants who had lost weight that year and had self-reported unintentional weight change in the 2 years before or after this exam. Physical activity was assessed by questionnaire at only 3 exam years (1989–1990, 1992–1993, and 1996–1997). We filled in low physical activity status at other years by using previously developed generalized boosted models (1, 2) that predict low physical activity status using other measures of physical activity assessed yearly (number of city blocks walked per week, usual walking pace outside the home, flights of stairs climbed up last week, number of hours seated or lying down in a typical 24 hour period). Prediction models were developed using baseline data and validated using followup data. At baseline for both cohorts, the area under the receiver operating characteristic curve (AUC)–a measure of the discriminant ability of the model ranging from 0.5 to 1, with values of 1 indicating perfect discrimination–was 0.80 for men and women. Applying the models to 1996–1997 data, the AUC were 0.79 for men and 0.77 for women in Cohort 1, and 0.67 for men and 0.72 for women in Cohort 2.

2 Study locations and exposures

Study locations. The study locations differed in terms of topography (Forsyth County: generally flat with rolling hills, Sacramento County: generally flat, and Pittsburgh: substantial differences in elevation due to river gorges) and the spatial dispersion of participants' residences (Forsyth County: $\sim$ 40 km, Sacramento County: $\sim$ 20 km, and Pittsburgh: $\sim$ 10 km). Participants in Pittsburgh lived in primarily urban areas, while participants in the other two locations lived in a variety of urban, suburban, and rural settings.

Exposure assignments. Residence address histories were obtained by compiling addresses reported at annual clinical exams and mid-year telephone contacts between exams. Addresses were geocoded (with poor matches flagged), and compared across time to infer changes in address (moves). A surrogate move date was assigned 3 months prior to the date of contact at which the geocode changed, since exact move dates were not available. Amongst all Cohort 1 participants in the 3 communities over the entire CHS study period (1989-2000): 2751 had no record of a move, 855 had at least one move, and 292 had poor quality residence histories, resulting in exclusion. Amongst the 687 Cohort 2 participants, 533 were non-movers, 118 had moved, and 36 were excluded. Ambient air pollution concentrations were assigned to residential geocodes that accounted for moves. Spatial interpolations were accompanied by quality codes of 1 (highest

quality), 2, and 3 indicating that at least one monitoring station was located within 5 km, 5–25 km, or 25–50 km, respectively, of the residence geocode. Interpolation quality varied by community, with 85.2%, 62.6%, and 35.5% of residence locations across all observation times in Pittsburgh, Forsyth County, and Sacramento County that were included in this study having the highest quality score for current month PM_{10}.

3 Cumulative summary motivation

Consider Y_{ij} for participant i at observation j, baseline (x_{i0}) and time-varying covariates (z_{ij}), and a random intercept $U_i \sim N(0, \tau^2)$. To investigate change over time in Y_{ij}, a standard longitudinal model can be reformulated as a function of time t, replacing age_{ij} with t:

$$\begin{aligned} Y_{ij} &= \beta_0 + \beta_1 x_{i0} + \beta_2 \text{age}_{ij} + \beta_3 x_{i0} \times \text{age}_{ij} + \beta_4 z_{ij} + U_i + \varepsilon_{ij} \quad (1) \\ Y_i(t) &= \beta_0 + \beta_1 x_{i0} + \beta_2 t + \beta_3 x_{i0} \times t + \beta_4 z_i(t) + U_i + \varepsilon_i(t)\,. \quad (2) \end{aligned}$$

Taking the derivative reveals that *change* in $Y_i(t)$ is a function of the level of x_{i0} and change in $z_i(t)$:

$$Y_i'(t) = \beta_2 + \beta_3 x_{i0} + \beta_4 z_i'(t) + \varepsilon_i'(t)\,. \quad (3)$$

To allow the level of $z_i(t)$ to affect change in $Y_i(t)$, we define the following model for change

$$Y_i'(t) = \beta_2 + \beta_3 x_{i0} + \beta_4 z_i'(t) + \beta_5 z_i(t) + \varepsilon_i'(t) \quad (4)$$

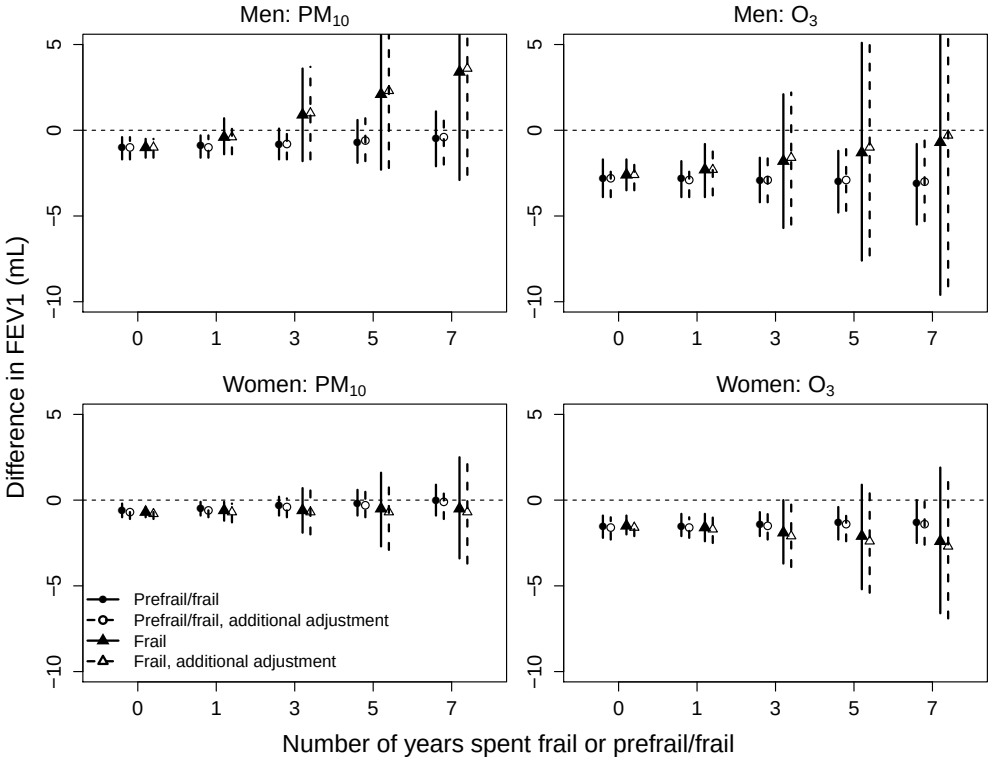
which can be translated back to the cross-sectional scale, with constant c_i, using integration:

$$Y_i(t) = c_i + \beta_2 t + \beta_3 x_{i0} t + \beta_4 z_i(t) + \beta_5 \int_0^t z_i(s) + \varepsilon_i(t)\,. \quad (5)$$

When $z_i(t)$ is measured at discrete times $(0, 1, \ldots, t-1, t)$, Equation 5 can be rewritten as:

$$Y_i(t) = c_i + \beta_2 t + \beta_3 x_{i0} t + \beta_4 z_i(t) + \beta_5 \sum_{s=0}^{t} z_i(s) + \varepsilon_i(t)\,. \quad (6)$$

4 Effects of cumulative exposures on FEV_1



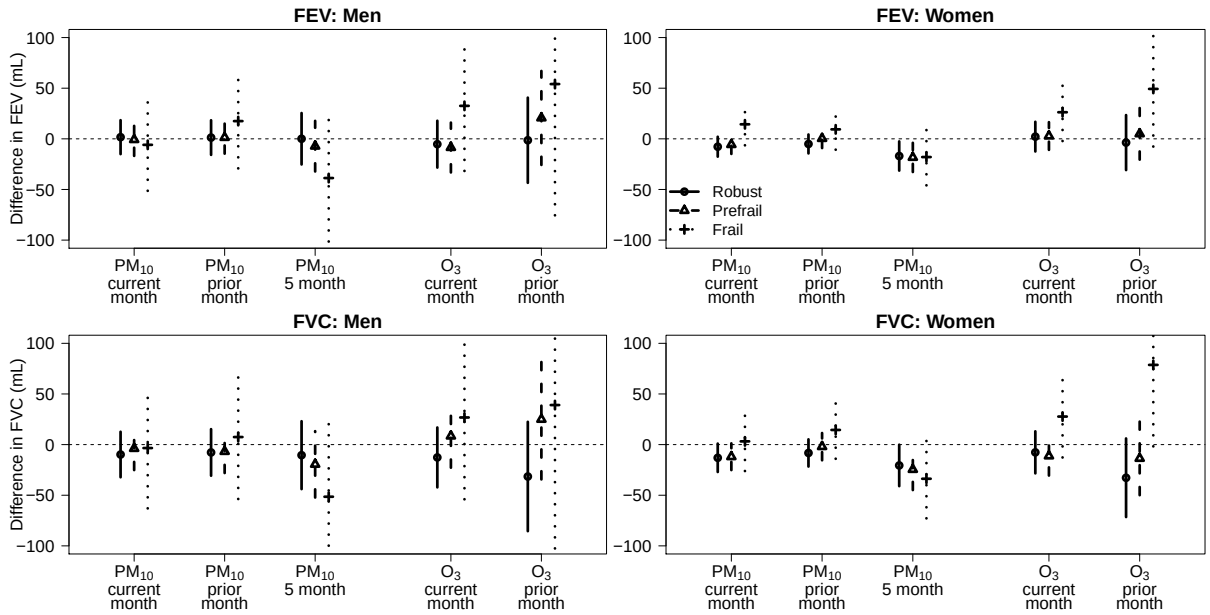
Web Figure 1: Difference in FEV_1 associated with a 1 month increase in typical pollution months according to the number of years spent frail or prefrail/frail, after adjusting for anthropometric, demographic and behavioral covariates (solid lines) and additionally adjusting for cardiovascular and respiratory disease covariates (dashed lines).

5 Excluding low quality PFT maneuvers

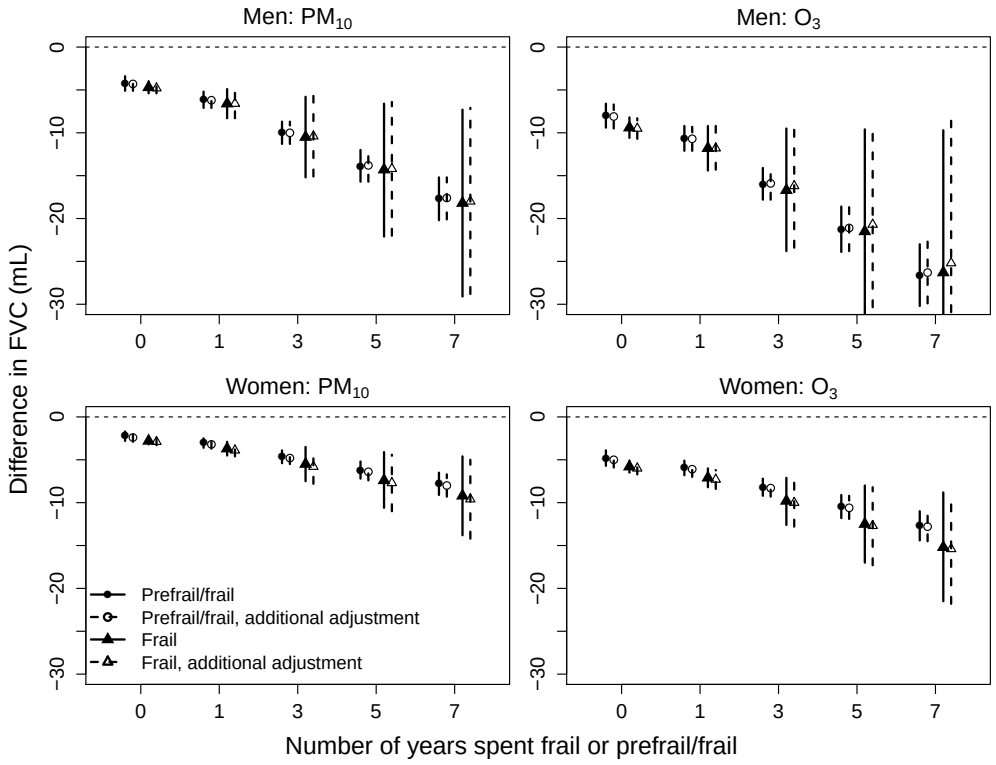
Excluding low quality PFT maneuvers differentially affected frail participants (observations excluded for robust: 10.0%, prefrail: 11.0%, and frail: 17.5%). When the low quality PFT were removed, associations with 5 month mean PM_{10} were attenuated, but still statistically significant in women (Table 1). The patterns of recent pollution associations according to current frailty status were similar, although the direction of the association did differ for recent O_3 in frail males (sample size was small and confidence intervals were wide, Figure 2). Typical pollution associations were quantitatively similar (both adjusting for frailty status or allowing for modification by years spent frail), with evidence of an interaction effect for FVC but not FEV_1 (Figures 3 and 4). An alternative to excluding low quality PFT is to downweight them, but this did not seem appropriate for this analysis because the variability in PFT was similar across quality grades.

Web Table 1: Difference in FEV_1 or FVC (mL) associated with a 10 $\mu g/m^3$ increase in recent PM_{10}, a 10 ppb increase in recent O_3 during O_3 season, or a 1 month increase in typical PM_{10} months or typical O_3 months during O_3 season after adjusting for anthropometric, demographic, behavioral covariates and current frailty status and excluding low quality PFT maneuvers.

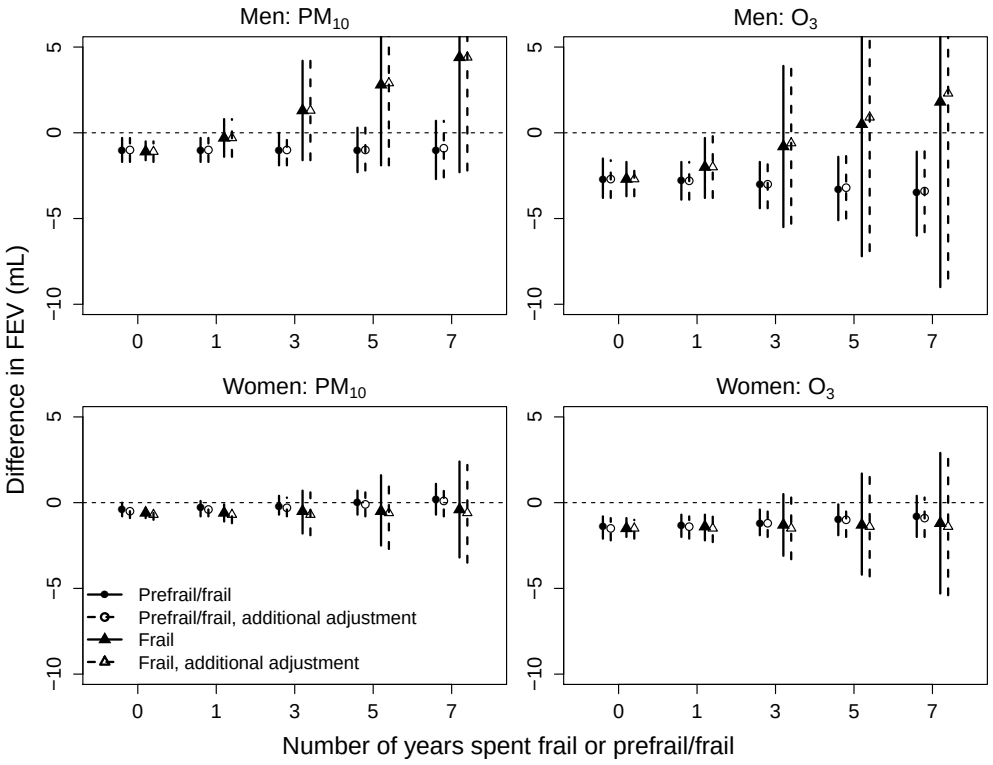
		FEV_1				FVC			
		Men		Women		Men		Women	
Pollutant	Summary	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
PM_{10}	Current month mean	0.0	(-12.6, 12.7)	-5.0	(-12.3, 2.3)	-6.5	(-23.3, 10.4)	-11.2	(-21.6, -0.7)
	Prior month mean	2.1	(-10.6, 14.9)	-1.5	(-8.7, 5.7)	-6.5	(-23.6, 10.7)	-3.6	(-13.9, 6.8)
	5 month mean	-5.3	(-26.2, 15.5)	-17.7	(-29.6, -5.7)	-16.9	(-44.4, 10.6)	-23.5	(-40.4, -6.5)
	Typical months	-0.9	(-1.5, -0.4)	-0.5	(-0.8, -0.1)	-4.7	(-5.3, -4.0)	-2.7	(-3.1, -2.3)
O_3	Current month mean	-4.5	(-22.6, 13.6)	4.9	(-5.9, 15.7)	-1.1	(-24.0, 21.7)	-5.8	(-21.0, 9.4)
	Prior month mean	10.1	(-24.1, 44.3)	4.9	(-15.4, 25.2)	-4.8	(-48.6, 39.0)	-14.1	(-43.1, 14.8)
	Typical months	-2.5	(-3.4, -1.5)	-1.2	(-1.7, -0.6)	-9.4	(-10.5, -8.3)	-5.6	(-6.3, -5.0)



Web Figure 2: Difference in FEV_1 or FVC (mL) associated with a 10 μg/m^3 increase in recent PM_{10} or a 10 ppb increase in recent O_3 during O_3 season according to current frailty status (robust: solid lines, prefrail: dashed lines, frail: dotted lines), after adjusting for anthropometric, demographic and behavioral covariates and excluding low quality PFT maneuvers.



Web Figure 3: Difference in FVC associated with a 1 month increase in typical pollution months according to the number of years spent frail or prefrail/frail, after adjusting for anthropometric, demographic and behavioral covariates (solid lines) and additionally adjusting for cardiovascular and respiratory disease covariates (dashed lines) and excluding low quality PFT maneuvers.



Web Figure 4: Difference in FEV_1 associated with a 1 month increase in typical pollution months according to the number of years spent frail or prefrail/frail, after adjusting for anthropometric, demographic and behavioral covariates (solid lines) and additionally adjusting for cardiovascular and respiratory disease covariates (dashed lines) and excluding low quality PFT maneuvers.

6 Multiple summary and multiple pollutant models

Web Table 2: Multi-summary or multi-pollutant model estimates of the difference in FEV_1 or FVC (mL) associated with a 10 $\mu g/m^3$ increase in recent PM_{10}, a 10 ppb increase in recent O_3 during O_3 season, or a 1 month increase in typical PM_{10} months or typical O_3 months during O_3 season after adjusting for anthropometric, demographic, behavioral covariates and current frailty status. Horizontal lines demarcate different models.

		FEV_1				FVC			
		Men		Women		Men		Women	
Pollutant	Summary	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
PM_{10}	Current month mean	0.0	(-1.4, 1.4)	-0.4	(-1.3, 0.5)	1.1	(-1.0, 3.2)	-0.2	(-1.5, 1.2)
	5 month mean	-0.2	(-2.5, 2.1)	-1.7	(-3.1, -0.2)	1.2	(-2.2, 4.6)	-0.3	(-2.5, 1.8)
	Typical months	-0.9	(-1.5, -0.3)	-0.7	(-1.0, -0.4)	-4.1	(-4.8, -3.4)	-2.6	(-3.1, -2.2)
O_3	Current month mean	-1.5	(-3.6, 0.6)	-0.0	(-1.4, 1.3)	1.3	(-1.9, 4.4)	-0.6	(-2.7, 1.5)
	Typical months	-1.8	(-3.2, -0.5)	-1.1	(-1.8, -0.3)	-8.9	(-10.5, -7.2)	-6.0	(-7.1, -4.9)

References

[1] Friedman J. Greedy function approximation: A gradient boosting machine. *Ann Stat.* 2001; 29(5):1189–1232.

[2] Eckel SP. *Quantifying individual and city level modification of the health effects of air pollution in older adults*. Ph.D. thesis, Johns Hopkins University, 2009.