

Supplementary Online Content

Paulin LM, Gassett AJ, Alexis NE, et al. Association of long-term ambient ozone exposure with respiratory morbidity in smokers. *JAMA Intern Med*. Published online December 9, 2019. doi:10.1001/jamainternmed.2019.5498

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eTable 1. Relationship Between 10-Year Ozone Concentration and Health Outcomes in Current and Former Smokers (n=1874)

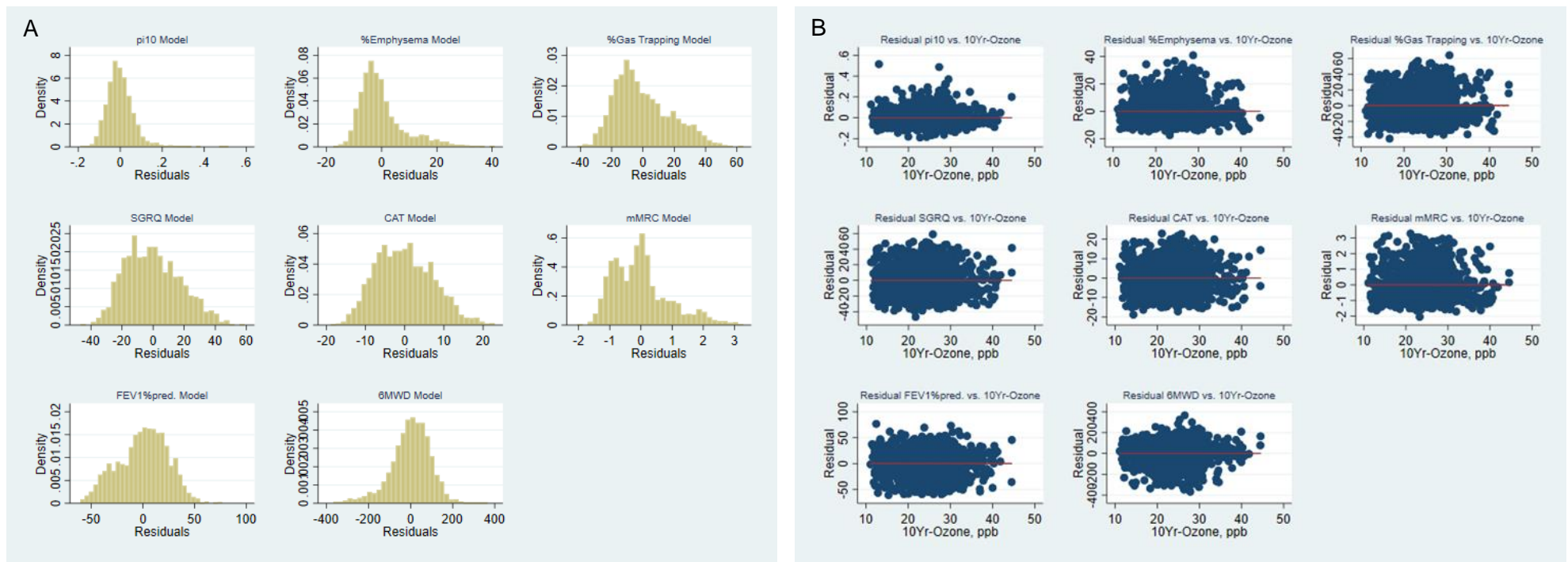
eTable 2. Relationship Between 10-Year Ozone Concentration and Health Outcomes in Current and Former Smokers (n=1874) With and Without Inclusion of 10-Year PM_{2.5} Concentration

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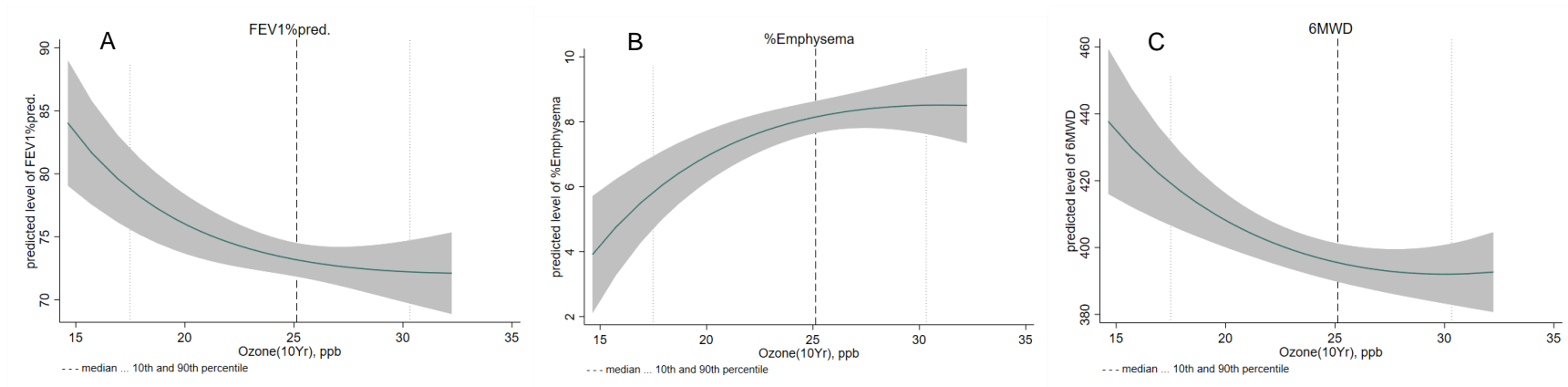
eTable 4. Relationship Between Warm Season 10-Year Ozone Concentration (April-September) and Health Outcomes in Current and Former Smokers (n=1874)

This supplementary material has been provided by the authors to give readers additional information about their work.

Figure 1. Regression Diagnostics. Distribution of Residual Based on Fully Adjusted Regression Model (A); Scatter Plot of Residual Versus 10-Year Ozone (B)

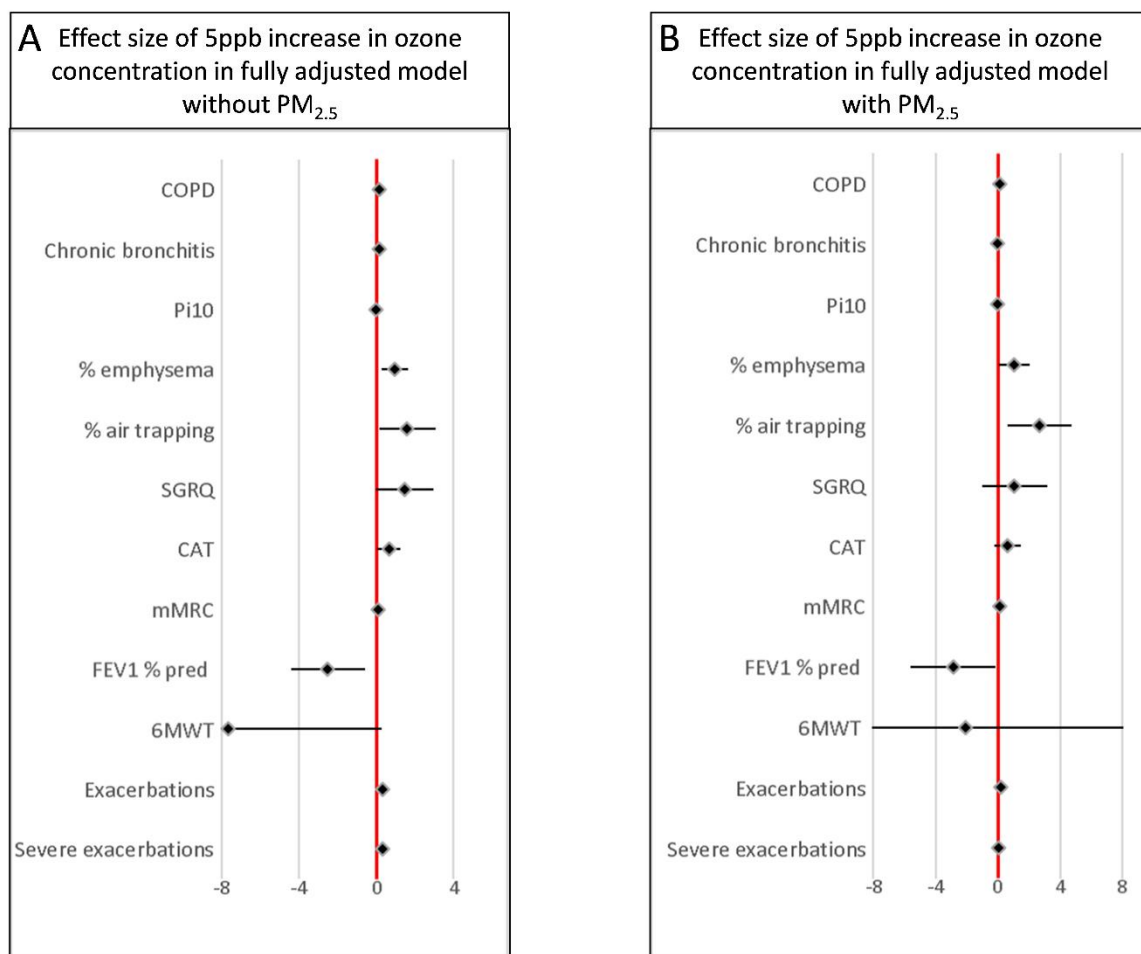


eFigure 2. Fractional Polynomial Approach to Explore the Shape of the Relationship Between Historical Ozone Concentration and FEV₁% Predicted (A); % Emphysema (B); and 6 MWT (C)



Potential nonlinearity is suggested in the relationship between ozone concentration and FEV₁% predicted, %Emphysema, and 6MWD by fractional polynomial approach. Point estimates and 95% confidence intervals depict average predicted level of outcome at the observed level of ozone concentration, adjusting for other covariates, constructed using a best-fitting fractional polynomial model to more flexibly identify ozone-outcome functional shape.

eFigure 3. Effect Size of Relationship Between 5 ppb Increase in 10-Year Ozone Concentration and Health Outcomes Without Inclusion of 10-Year PM_{2.5} Concentration (A); With Inclusion of PM_{2.5} in Model (B)



BMI= body mass index, VGDF= vapors, gas, dust or fumes; mMRC=modified Medical Research Council questionnaire; SGRQ=St. George's Respiratory Questionnaire; CAT=COPD assessment test; 6MWT=6-minute walk test-distance; PM_{2.5}=Particulate matter with an aerodynamic diameter of 2.5 microns and less

eTable 1. Relationship Between 10-Year Ozone Concentration and Health Outcomes in Current and Former Smokers (n=1874)

Estimated change in outcome per 5ppb increase in 10-year average ozone concentration	Minimally adjusted model (age, race, gender, and study site)			Moderately adjusted model (age, race, gender, study site, and personal and neighborhood income)			Fully adjusted model (age, race, gender, study site, BMI, current smoking status, pack years, VGDF exposure, education, and personal and neighborhood income)		
	Effect estimate	95% CI	p	Effect estimate	95% CI	p	Effect estimate	95% CI	p
Respiratory disease risk									
COPD (OR)	1.06	0.90, 1.25	0.460	1.13	0.95, 1.34	0.174	1.16	0.97, 1.40	0.103
Chronic bronchitis (OR)	1.01	0.87, 1.18	0.858	1.11	0.94, 1.30	0.211	1.14	0.96, 1.35	0.139
CT-measured outcomes									
Pi10	-0.001	-0.007, 0.004	0.569	0.001	-0.004, 0.007	0.601	0.0001	-0.005, 0.006	0.865
% emphysema	0.93	0.22, 1.63	0.010	0.91	0.16, 1.66	0.017	0.94	0.25, 1.64	0.007
% air trapping	1.22	-0.26, 2.70	0.105	1.60	0.05, 3.16	0.044	1.60	0.16, 3.04	0.030
Respiratory morbidity									
SGRQ	-0.41	-1.85, 1.03	0.579	1.40	-0.08, 2.88	0.064	1.47	0.01, 2.93	0.048
CAT	-0.10	-0.69, 0.49	0.740	0.66	0.06, 1.27	0.032	0.65	0.05, 1.26	0.035
mMRC	0.03	-0.04, 0.10	0.448	0.10	0.02, 0.17	0.010	0.10	0.03, 0.17	0.008
FEV ₁ % predicted	-0.99	-2.84, 0.86	0.294	-2.36	-4.30, -0.41	0.018	-2.50	-4.42, -0.59	0.010
6MWT	3.57	-4.13, 11.27	0.364	-8.01	-15.95, -0.07	0.048	-7.65	-15.57, 0.27	0.058
Exacerbations									
Any exacerbation in 12 months prior to enrollment (OR)	1.27	1.06, 1.52	0.009	1.33	1.10, 1.61	0.003	1.37	1.12, 1.66	0.002
Severe exacerbation in 12 months prior to enrollment (OR)	1.29	1.03, 1.63	0.029	1.38	1.08, 1.76	0.010	1.37	1.07, 1.76	0.014

BMI= body mass index, VGDF= vapors, gas, dust or fumes; mMRC=modified Medical Research Council questionnaire; SGRQ=St. George's Respiratory Questionnaire; CAT=COPD assessment test; 6MWT=6-minute walk test-distance. Boldface entries indicate a statistically significant correlation with a p value less than 0.05.

eTable 2. Relationship Between 10-Year Ozone Concentration and Health Outcomes in Current and Former Smokers (n=1874) With and Without Inclusion of 10-Year PM_{2.5} Concentration

Estimated change in outcome per 5ppb increase in 10-year average ozone concentration	Fully adjusted model (age, race, gender, study site, BMI, current smoking status, pack years, VGDF exposure, education, personal income, and neighborhood income)			Fully adjusted model (age, race, gender, study site, BMI, current smoking status, pack years, VGDF exposure, education, personal income, neighborhood income, and 10-year average PM _{2.5} concentration)		
	Effect estimate	95% CI	p	Effect estimate	95% CI	p
Respiratory disease risk						
Odds of COPD (OR)	1.16	0.97, 1.40	0.103	1.16	0.89, 1.50	0.267
Chronic bronchitis (OR)	1.14	0.96, 1.35	0.139	1.01	0.79, 1.28	0.967
CT-measured outcomes						
Pi10	0.0001	-0.005, 0.006	0.865	-0.001	-0.009, 0.007	0.801
% emphysema	0.94	0.25, 1.64	0.007	1.03	0.05, 2.01	0.039
% air trapping	1.60	0.16, 3.04	0.030	2.66	0.62, 4.70	0.011
Respiratory morbidity						
SGRQ	1.47	0.01, 2.93	0.048	1.08	-0.98, 3.14	0.303
CAT	0.65	0.05, 1.26	0.035	0.64	-0.21, 1.49	0.140
mMRC	0.10	0.03, 0.17	0.008	0.12	0.02, 0.23	0.023
FEV ₁ % predicted	-2.50	-4.42, -0.59	0.010	-2.86	-5.58, -0.15	0.039
6MWT	-7.65	-15.57, 0.27	0.058	-2.04	-13.25, 9.16	0.721
Exacerbations						
Any exacerbation in 12 months prior to enrollment (OR)	1.37	1.12, 1.66	0.002	1.26	0.95, 1.66	0.105
Severe exacerbation in 12 months prior to enrollment (OR)	1.37	1.07, 1.76	0.014	1.06	0.73, 1.53	0.774

BMI= body mass index, VGDF= vapors, gas, dust or fumes; mMRC=modified Medical Research Council questionnaire; SGRQ=St. George's Respiratory Questionnaire; CAT=COPD assessment test; 6MWT=6-minute walk test-distance. Boldface entries indicate a statistically significant correlation with a p value less than 0.05.

eTable 3. Relationship Between Historical Ozone Concentration and Health Outcomes in Current and Former Smokers (n=1874) With Varying Exposure Averaging Times

	Estimated change in outcome per 5ppb increase in 1-year average ozone			Estimated change in outcome per 5ppb increase in 5-year average ozone			Estimated change in outcome per 5ppb increase in 10-year average ozone		
	Effect estimate	95% CI	p	Effect estimate	95% CI	p	Effect estimate	95% CI	p
Respiratory disease risk									
Odds of COPD (OR)	1.14	0.97, 1.35	0.115	1.11	0.94, 1.32	0.220	1.16	0.97, 1.40	0.103
Chronic bronchitis (OR)	1.03	0.88, 1.21	0.687	1.11	0.95, 1.30	0.190	1.14	0.96, 1.35	0.139
CT-measured outcomes									
Pi10	0.0003	-0.005, 0.005	0.891	-0.0001	-0.006, 0.004	0.820	0.001	-0.005, 0.006	0.865
% emphysema	1.19	0.55, 1.84	<0.001	0.99	0.33, 1.65	0.003	0.94	0.25, 1.64	0.007
% air trapping	1.90	0.58, 3.23	0.005	1.52	0.17, 2.87	0.027	1.60	0.16, 3.04	0.030
Respiratory morbidity									
SGRQ	1.59	0.22, 2.96	0.023	1.50	0.11, 2.89	0.034	1.47	0.01, 2.93	0.048
CAT	0.57	0.01, 1.13	0.047	0.67	0.10, 1.24	0.021	0.65	0.05, 1.26	0.035
mMRC	0.07	-0.001, 0.14	0.053	0.07	-0.002, 0.14	0.058	0.10	0.03, 0.17	0.008
FEV ₁ % predicted	-2.19	-3.96, -0.42	0.015	-1.81	-3.61, -0.01	0.049	-2.50	-4.42, -0.59	0.010
6MWT	-2.29	-9.69, 5.11	0.544	-4.09	-11.59, 3.41	0.285	-7.65	-15.57, 0.27	0.058
Exacerbations									
Any exacerbation in 12 months prior to enrollment (OR)	1.34	1.12, 1.61	0.001	1.34	1.11, 1.60	0.002	1.37	1.12, 1.66	0.002
Severe exacerbation in 12 months prior to enrollment (OR)	1.20	0.94, 1.52	0.144	1.24	0.98, 1.57	0.076	1.37	1.07, 1.76	0.014

Adjusted for age, race, gender, study site, BMI, current smoking status, pack years, VGDF exposure, education, personal income, and neighborhood income. BMI= body mass index, VGDF= vapors, gas, dust or fumes; mMRC=modified Medical Research Council questionnaire; SGRQ=St. George's Respiratory Questionnaire; CAT=COPD assessment test; 6MWT=6-minute walk test-distance. Boldface entries indicate a statistically significant correlation with a p value less than 0.05.

eTable 4. Relationship Between Warm Season 10-Year Ozone Concentration (April-September) and Health Outcomes in Current and Former Smokers (n=1874)

Estimated change in outcome per <u>5ppb</u> increase in 10-year average ozone concentration	Entire year			Warm season only		
	Effect estimate	95% CI	p	Effect estimate	95% CI	p
Respiratory disease risk						
Odds of COPD (OR)	1.16	0.97, 1.40	0.103	1.18	0.98, 1.41	0.085
Chronic bronchitis (OR)	1.14	0.96, 1.35	0.139	1.12	0.95, 1.33	0.188
CT-measured outcomes						
Pi10	0.001	-0.005, 0.006	0.865	0.001	-0.004, 0.007	0.684
% emphysema	0.94	0.25, 1.64	0.007	0.95	0.25, 1.64	0.008
% air trapping	1.60	0.16, 3.04	0.030	1.75	0.30, 3.20	0.018
Respiratory morbidity						
SGRQ	1.47	0.01, 2.93	0.048	1.54	0.07, 3.01	0.041
CAT	0.65	0.05, 1.26	0.035	0.78	0.17, 1.38	0.012
mMRC	0.10	0.03, 0.17	0.008	0.12	0.04, 0.19	0.002
FEV ₁ % predicted	-2.50	-4.42, -0.59	0.010	-2.68	-4.61, -0.76	0.006
6MWT	-7.65	-15.57, 0.27	0.058	-6.76	-14.78, 1.26	0.099
Exacerbations						
Any exacerbation in 12 months prior to enrollment (OR)	1.37	1.12, 1.66	0.002	1.37	1.13, 1.67	0.002
Severe exacerbation in 12 months prior to enrollment (OR)	1.37	1.07, 1.76	0.014	1.35	1.05, 1.74	0.020

Adjusted for age, race, gender, study site, BMI, current smoking status, pack years, VGDF exposure, education, personal income, and neighborhood income. BMI= body mass index, VGDF= vapors, gas, dust or fumes; mMRC=modified Medical Research Council questionnaire; SGRQ=St. George's Respiratory Questionnaire; CAT=COPD assessment test; 6MWT=6-minute walk test-distance. Boldface entries indicate a statistically significant correlation with a p value less than 0.05.