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ORIGINAL ARTICLE

Indoor Pollution and Lung Function Decline in Current and Former Smokers
SPIROMICS AIR

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Abstract

Rationale: Indoor pollutants have been associated with chronic obstructive pulmonary disease morbidity, but it is unclear whether they contribute to disease progression.

Objectives: We aimed to determine whether indoor particulate matter (PM) and nitrogen dioxide (NO_2) are associated with lung function decline among current and former smokers.

Methods: Of the 2,382 subjects with a history of smoking in SPIROMICS AIR, 1,208 participants had complete information to estimate indoor PM and NO_2, using individual-based prediction models, in relation to measured spirometry at two or more clinic visits. We used a three-way interaction model between time, pollutant, and smoking status and assessed the indoor pollutant–associated difference in FEV_1 decline separately using a generalized linear mixed model.

Measurements and Main Results: Participants had an average rate of FEV_1 decline of 60.3 ml/yr for those currently smoking compared with 35.2 ml/yr for those who quit. The association of indoor PM with FEV_1 decline differed by smoking status. Among former smokers, every 10 $\mu g/m^3$ increase in estimated indoor PM was associated with an additional 10 ml/yr decline in FEV_1 ($P = 0.044$). Among current smokers, FEV_1 decline did not differ by indoor PM. The results of indoor NO_2 suggest trends similar to those for PM $\leqslant$2.5 μm in aerodynamic diameter.

Conclusions: Former smokers with chronic obstructive pulmonary disease who live in homes with high estimated PM have accelerated lung function loss, and those in homes with low PM have lung function loss similar to normal aging. In-home PM exposure may contribute to variability in lung function decline in people who quit smoking and may be a modifiable exposure.

Keywords: chronic obstructive pulmonary disease; indoor particulate matter; lung function decline

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At a Glance Commentary

Scientific Knowledge on the Subject: Indoor particulate matter has been associated with chronic obstructive pulmonary disease (COPD) morbidity, but it is unclear whether it contributes to the progression of disease. The goal of this study was to determine whether estimated indoor pollutant concentrations are associated with lung function decline among current and former smokers with and without COPD from the SPIROMICS AIR study.

What This Study Adds to the Field: Our study results highlight that former smokers with or without COPD who live in homes estimated to have high particulate matter ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$) concentrations have accelerated loss of lung function. Conversely, former smokers living in homes estimated to have low $PM_{2.5}$ concentrations have lung function loss similar to normal aging in never smokers. These study results suggest that in-home PM exposure may contribute to variability in annual lung function decline seen in people who successfully quit smoking and that indoor air quality improvement strategies may be an approach to preserve lung function.

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterized by lung injury and inflammation secondary to particulate and gaseous exposures. Accelerated lung function decline is a hallmark feature of COPD. Smoking is the primary exposure in high-income countries, and smoking cessation is associated with reduced incidence and slower progression of COPD; however, significant variability in lung function decline exists after accounting for cigarettes smoked (1). Furthermore, continued accelerated loss of lung function is seen even among those who quit smoking (2). It remains unclear which factors contribute to variability in lung function loss.

Exposure to both outdoor and indoor air pollution, including particulate matter ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$) and nitrogen dioxide (NO_2), has known adverse respiratory effects (3, 4). The indoor environment is of particular concern because most adults and patients with chronic lung diseases such as COPD spend the majority of their time indoors. Indoor $PM_{2.5}$ and NO_2 are composed of particles and gases of ambient origin that can infiltrate effectively into the home and those of indoor origin that can be generated by a variety of activities, including cooking and smoking, the presence of pets and pests, use of gas appliances, and resuspension of settled dusts. It has remained elusive whether chronic exposure to indoor $PM_{2.5}$ and NO_2 is associated with progression of disease, because direct measurement of long-term individual indoor pollutant exposure has been prohibitive as a result of complexity, burden, and cost of implementation in large-scale studies. As part of the SPIROMICS AIR study (Subpopulations and Intermediate Outcome Measures in COPD Study of Air Pollution), Zusman and colleagues developed an individual-based model to estimate each participant's long-term indoor exposure to $PM_{2.5}$ and NO_2 across the SPIROMICS cohort using direct indoor pollutant measurements in a subset of homes, estimates of ambient origin infiltrated concentrations, and questionnaire-based behavioral and residence data (5). The goal of the present analysis is to determine whether estimated indoor $PM_{2.5}$ and NO_2 concentrations were associated with annual lung function decline among current and former smokers with COPD from SPIROMICS followed longitudinally for up to 3 years.

Methods

Study Population

SPIROMICS is a multicenter cohort study of current and former smokers (≥20 pack-years) aged 40–80 years with or without COPD (6). COPD status was based on post-bronchodilator (post-BD) $FEV_1/FVC < 70\%$. Participants had baseline visits between 2010 and 2015 and up to three annual follow-up visits. SPIROMICS AIR is an ancillary study providing air pollution and other environmental characterizations across study sites (7). Of the 2,382 participants with a history of smoking with or without COPD in SPIROMICS AIR, 1,208 participants had complete information to estimate indoor pollutants ($PM_{2.5}$ and NO_2) and spirometry at two or more clinic visits (*see* Figure E1 in the online supplement).

Exposure Assessment

Indoor home $PM_{2.5}$ and NO_2 concentrations were estimated using an individual-based prediction model as previously described (5), and the major predictors are noted in Table E1. Cross-validation in a subset of homes showed that approximately 60% of the variation in each indoor pollutant concentration was explained by model predictions (5). The in-home secondhand smoke (SHS) exposure was captured by indoor nicotine concentration, which was estimated using a similar modeling approach including self-reported SHS questionnaires (5). Two-week mean concentrations of ambient $PM_{2.5}$ and ambient NO_2 were estimated using spatiotemporal modeling (8, 9) and averaged across 1 year dating back to each study visit, and estimates of indoor pollutant concentrations resembled this 2-week average concentration. Occupational exposure was ascertained by self-reported exposure to vapors, gas, dust, or fumes in the longest-held job (10).

Participant Characterization

The primary outcome was an annual rate of decline in post-BD FEV_1 in milliliters per year. Pre-BD FEV_1 annual decline is shown

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as a secondary outcome. Spirometry was performed using a pneumotachograph spirometer (KoKo, NSPIRE Healthcare) following American Thoracic Society guidelines (11).

Cumulative smoking history was defined as pack-years smoked. At each study visit, participants were defined as "current smokers" if they reported cigarette smoking within 1 month of the study visit. Quantity smoked at each visit was reported by average packs per day smoked. Neighborhood socioeconomic status was indicated by Area Deprivation Index (ADI) (12, 13).

Statistical Analysis

To assess lung function decline by indoor $PM_{2.5}$, we performed linear regression of FEV_1 on time, indoor $PM_{2.5}$, and their interaction using a generalized linear mixed model. To evaluate analyses separately by smoking status, we used a three-way interaction model between time, indoor $PM_{2.5}$, and smoking status, and we assessed the $PM_{2.5}$ difference in FEV_1 decline separately by smoking status, which was considered time varying. All analyses were adjusted by baseline absolute FEV_1; COPD status; demographics; pack-years; vapors, gas, dust, or fumes; and study site as fixed effects and by time-varying estimated current average packs per day of smoking, indoor NO_2, ambient $PM_{2.5}$ and NO_2, and neighborhood ADI, as well as two-way interactions with time for each covariate except study site (*see* the METHODS section in the online supplement). To assess lung function decline by indoor NO_2, the same analysis was repeated but using indoor NO_2 as the main exposure and adjusting by the same covariates except adjusting by indoor $PM_{2.5}$ in place of indoor NO_2. To check on the linearity assumption and to flexibly illustrate the functional shape of lung function and time, a restricted cubic spline model was run, modeling time as cubic splines in its interaction with indoor pollutants and smoking status, adjusted by covariates.

Sensitivity analyses included covariate adjustment for SHS exposure as indicated by estimated indoor nicotine concentration, and $PM_{2.5}$-FEV_1 or NO_2-FEV_1 decline was assessed within former smokers who showed an estimated indoor nicotine concentration below 0.01 $\mu g/m^3$. In addition, FEV_1 decline was assessed using pre-BD FEV_1 values. Sex effect modification on indoor pollutant difference in FEV_1 decline by smoking status was also assessed using a four-way interaction model (sex × time × indoor pollutant × smoking status). Analyses were repeated including only those participants with COPD ($n = 769$).

Results

The participants with a history of smoking with or without COPD ($n = 1{,}168$) had a mean age of 65 years, were mostly White (80%), were mostly educated beyond high school (62% with some college or above), had a mean of 50 pack-years of smoking, and 34% reported currently smoking, with the mean (SD) estimated indoor nicotine concentration being 0.14 (0.8) $\mu g/m^3$ (Table 1). The baseline mean (SD) estimated indoor $PM_{2.5}$ and NO_2 were 11.3 (9.7) $\mu g/m^3$ and 11.7 (5.1) ppb, respectively, and the median (Q1, Q3) concentrations were 8.4 (4.8, 15.0) $\mu g/m^3$ and 10.7 (7.9, 14.3) ppb, respectively. The estimated indoor $PM_{2.5}$ concentration was weakly correlated with indoor NO_2 concentration ($\rho = 0.18$; $P < 0.001$) and with either outdoor $PM_{2.5}$ ($\rho = 0.15$; $P < 0.001$) or NO_2 concentration ($\rho = 0.16$; $P < 0.001$), whereas indoor NO_2 was moderately to strongly correlated with outdoor $PM_{2.5}$ and NO_2, respectively (Table E2). On average, participants were examined for 3.3 (SD, 1) years with the median (Q1, Q3) of 3.2 (2.3, 4.0) years, including the baseline year. In comparison with the entire SPIROMICS AIR participants with a history of smoking ($n = 1{,}558$), the analytic sample had higher absolute FEV_1 (2.15 [0.85] L vs. 1.79 [0.78] L) and FEV_1 percent predicted (76.4 [24.8] vs. 62.7 [22.9]) and were younger, more likely to be female, to be non-White, and to have had education beyond high school and reported fewer smoking pack-years and resided in neighborhoods with lower ADI; otherwise, there were no significant differences (Table E3).

Participants residing in homes with greater than median estimated indoor $PM_{2.5}$ concentration were younger and more likely to be non-White, to have lower educational attainment and income, and to be currently smoking and showed higher estimated indoor nicotine level but no difference in baseline lung function compared with those residing in homes with lower than median indoor $PM_{2.5}$ concentration (Table 1). Among the subgroup who were former smokers at baseline, fewer participants resided in high $PM_{2.5}$ homes (33% resided in homes with $PM_{2.5}$ estimated to be >8.4 $\mu g/m^3$). Former smokers residing in high $PM_{2.5}$ homes were younger, had lower income, and were more likely to show higher estimated indoor nicotine level and reside in a more disadvantaged neighborhood (Table 1).

Annual Decline in FEV_1

Among participants with a history of smoking with or without COPD, FEV_1 declined by an average of 46.6 ml per year (95% confidence interval [CI], 41.7–51.6). Adjusting for covariates and allowing for change in smoking status across time (66%, 66%, 69%, and 73% were former smokers at visits 1, 2, 3, and 4, respectively), as expected, the average rate of FEV_1 decline was steeper for those currently smoking (60.3 ml/yr [95% CI, 49.9–70.6]) than for those not currently smoking (35.2 ml/yr [95% CI, 25.3–45.1]). The association of indoor $PM_{2.5}$ with annual FEV_1 decline differed by smoking status, such that the indoor $PM_{2.5}$ was associated with annual FEV_1 decline among former smokers but not among current smokers (Table 2).

Former Smokers: Annual Decline in FEV_1 by Indoor $PM_{2.5}$

Among former smokers, every 10 $\mu g/m^3$ increase (approximately a 1-SD increase) in estimated indoor $PM_{2.5}$ was associated with an additional 10.0 ml per year decline in FEV_1 (95% CI, 0.2–19.8). This resulted in participants residing in the "lowest" indoor $PM_{2.5}$ concentration homes, as represented by fifth percentile $PM_{2.5}$ level, equivalent to 1.7 $\mu g/m^3$, showing an FEV_1 decline of 27.7 ml per year (95% CI, 15.7–39.8), whereas those who resided in the "highest" indoor $PM_{2.5}$ concentration homes, as represented by the 95th percentile $PM_{2.5}$ level, equivalent to 31.3 $\mu g/m^3$, showed an FEV_1 decline of 58.4 ml per year (95% CI, 33.2–83.7) (Table 2). The linearity test using restricted cubic spline modeling showed that the linearity assumption for FEV_1 decline is reasonable ($P_{\text{spline test}} = 0.95$) (Figure E2).

The results remained robust with and without adjustment for estimated indoor nicotine exposure (Table 2). Furthermore, in additional subgroup analyses limited to former smokers without SHS exposure (indicated by estimated indoor nicotine level below 0.01 $\mu g/m^3$), the results remained similar to those for all former smokers (*see* Table E5). Also, when using pre-BD FEV_1 instead of post-BD FEV_1, the results remained robust in both primary and SHS

Table 1. Baseline Participant Characteristics, All Participants with a History of Smoking with or without COPD

	All	All			Former Smokers Only		
	All ($N = 1,168$)	Low Indoor PM (<8.4 μg/m³*) ($n = 584$)	High Indoor PM (≥8.4 μg /m³*) ($n = 584$)	*P* Value	Low Indoor PM (<8.4 μg/m³*) ($n = 516$)	High Indoor PM (≥8.4 μg /m³*) ($n = 250$)	*P* Value
Age, yr	64.64 ± 8.52	66.91 ± 7.30	62.37 ± 9.05	<0.001	67.70 ± 6.66	66.07 ± 7.92	0.003
Height, cm	169.68 ± 9.62	169.69 ± 9.76	169.66 ± 9.48	0.959	169.91 ± 9.90	169.83 ± 9.59	0.923
Sex, *n* (% female)	559 (47.9%)	275 (47.1%)	284 (48.6%)	0.598	242 (46.9%)	112 (44.8%)	0.585
Race, *n* (% White)	933 (79.9%)	502 (86.0%)	431 (73.8%)	<0.001	453 (87.8%)	210 (84.0%)	0.149
Education, n (%high school graduate or above)	728 (62.3%)	394 (67.5%)	334 (57.2%)	<0.001	345 (66.9%)	159 (63.6%)	0.372
Income							
<$35,000	354 (30.3%)	156 (26.7%)	198 (33.9%)	<0.001	124 (24.0%)	63 (25.2%)	0.001
$35,000–$74,999	362 (31.0%)	207 (35.4%)	155 (26.5%)		192 (37.2%)	66 (26.4%)	
≥$75,000	222 (19.0%)	129 (22.1%)	93 (15.9%)		124 (24.0%)	57 (22.8%)	
Decline to answer	230 (19.7%)	92 (15.8%)	138 (23.6%)		76 (14.7%)	64 (25.6%)	
Pack-years smoked, yr	49.77 ± 26.58	49.16 ± 22.94	50.39 ± 29.80	0.430	49.72 ± 23.52	55.80 ± 35.20	0.005
Currently smoking, *n* (% yes)	402 (34.4%)	68 (11.6%)	334 (57.2%)	<0.001	0 (0%)	0 (0%)	—
Average packs per day‡, count	1.37 ± 1.43	1.45 ± 1.90	1.30 ± 0.71	0.082	1.49 ± 2.01	1.53 ± 0.87	0.774
Occupational exposure†, *n* (% yes)	532 (45.5%)	259 (44.3%)	273 (46.7%)	0.411	227 (44.0%)	114 (45.6%)	0.675
Estimated indoor nicotine, μg/m³	0.14 ± 0.81	0.03 ± 0.08	0.25 ± 1.14	<0.001	0.02 ± 0.04	0.04 ± 0.10	0.001
Estimated ambient $PM_{2.5}$, μg/m³	9.10 ± 1.74	8.80 ± 1.73	9.40 ± 1.71	<0.001	8.75 ± 1.74	9.23 ± 1.70	<0.001
Estimated ambient NO_2‡, ppb	12.64 ± 6.60	11.51 ± 5.78	13.77 ± 7.15	<0.001	11.45 ± 5.98	13.61 ± 7.32	<0.001
Area Deprivation Index‡	33.64 ± 26.86	34.41 ± 26.66	32.88 ± 27.06	0.330	33.72 ± 26.54	26.96 ± 26.64	0.001
FEV_1, % predicted	76.41 ± 24.76	76.58 ± 24.87	76.24 ± 24.67	0.812	75.98 ± 24.98	72.78 ± 26.92	0.105
FEV_1, L	2.15 ± 0.85	2.14 ± 0.86	2.17 ± 0.84	0.649	2.12 ± 0.87	2.03 ± 0.85	0.148

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; NO_2 = nitrogen dioxide; PM = particulate matter; $PM_{2.5}$ = particulate matter ≤2.5 μm in aerodynamic diameter.

*Includes participants who were missing baseline time-varying analytic variable(s) but had two or more subsequent visits and thus included in our analytic sample; for these participants, the descriptive statistics for the time-varying variables are based on their earliest visit observations.

†Exposure to vapors, gas, dust, or fumes at the longest-held occupation.

‡A continuous measure ranging from 0 to 100 with 100 representing the worst neighborhood and 0 the best in terms of various neighborhood socio-economic measures at the census block-group level.

sensitivity analyses (Tables E6 and E7). These results suggest that accelerated loss of annual lung function among former smokers with high indoor $PM_{2.5}$ was not specifically attributable to SHS exposure and evident in both pre- and post-BD values. Furthermore, additional sensitivity analysis showed no statistically significant sex differences in the patterns observed for our primary model ($P_{\text{sex interaction}} = 0.23$). However, directionally, the association between indoor PM and lung function decline in former smokers appeared stronger in men than in women (Table E9).

When only participants with COPD were included, the primary results were similar (Table 2). On average, FEV_1 declined by 41.9 ml per year (95% CI, 36.0–47.9), and, adjusting for covariates, the decline was steeper for the current smokers (51.2 ml/yr [95% CI, 15.7–33.1]) than for the former smokers (30.0 ml/yr [95% CI, 18.0–42.0]). However, among the former smokers, the rate of decline significantly differed by the indoor $PM_{2.5}$ concentrations ($P_{\text{PM interaction}} = 0.012$); for example, among former smokers with COPD, every 10 μg/m³ increase in estimated indoor $PM_{2.5}$ was associated with an additional 15.2 ml/yr decline in FEV_1 (95% CI, 3.3–27.0), such that those residing in the "lowest" indoor PM concentration homes showed an annual FEV_1 decline of 18.8 ml (95% CI, 15.7–33.1) in comparison with those in the "highest" indoor PM concentration homes, showing an annual FEV_1 decline of 63.4 ml (95% CI, 33.6–93.1) (Figures 1 and E2). The results remained similar to those shown for the full cohort when taking into account SHS exposure (Tables 2 and E5) and/or examining pre-BD FEV_1 (Tables E6 and E7).

Current Smokers: Annual Decline in FEV_1 by Indoor $PM_{2.5}$

Among current smokers with a history of smoking, FEV_1 decline did not differ significantly by indoor $PM_{2.5}$ concentration ($P_{\text{two-way interaction}} = 0.87$) (Table 2). Using 5th and 95th percentile $PM_{2.5}$ levels, the annual rates of FEV_1 decline were 62.6 ml (95% CI, 46.7–78.6) and 64.5 ml (95% CI, 50.5–78.6) for those residing in the lowest and highest $PM_{2.5}$ concentration homes, respectively (Figure 2). Similarly, no indoor $PM_{2.5}$ difference in FEV_1 decline was found among COPD-only participants who were current smokers (Table 2 and Figure 2). Various sensitivity analyses also showed no indoor $PM_{2.5}$ difference in FEV_1 decline among current smokers (Tables 2 and E5–E7).

Table 2. Estimated Change in FEV_1 (in milliliters) per Year, by Estimated Indoor $PM_{2.5}$ Concentration

	Former Smokers			Current Smokers		
	Low Indoor $PM_{2.5}$ (95% CI)	High Indoor $PM_{2.5}$ (95% CI)	Interaction* *P* Value	Low Indoor $PM_{2.5}$ (95% CI)	High Indoor $PM_{2.5}$ (95% CI)	Interaction* *P* Value
Full cohort						
Main model†	−27.7 (−39.8, −15.7)	−58.4 (−83.7, −33.2)	**0.044**	−62.6 (−78.6, −46.7)	−64.5 (−78.6, −50.5)	0.871
Main model additionally adjusted for SHS‡	−27.9 (−40.0, −15.9)	−59.0 (−84.2, −33.8)	**0.042**	−62.4 (−78.3, −46.5)	−65.9 (−80.2, −51.6)	0.769
COPD-only cohort						
Main model†	−18.8 (−33.1, −4.4)	−63.4 (−93.1, −33.6)	**0.012**	−55.1 (−73.8, −36.3)	−57.4 (−73.4, −41.5)	0.855
Main model additionally adjusted for SHS‡	−18.4 (−32.8, −3.9)	−63.2 (−93.0, −33.5)	**0.012**	−54.9 (−73.7, −36.2)	−58.6 (−75.5, −41.7)	0.786

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter ⩽2.5 μm in aerodynamic diameter; SHS = secondhand smoke. Bold values indicate statistical significance $P < 0.05$.

*Two-way interaction of indoor $PM_{2.5}$ × time.

†The main model was adjusted by baseline covariates and time-varying covariates. The baseline covariates included COPD status (for the full-cohort model only); age; sex; race; education; income; pack-years; vapors, gas, dust, or fumes, height; baseline FEV_1; and study sites. The time-varying covariates included estimated coindoor pollutant (e.g., indoor NO_2 as a covariate in the indoor $PM_{2.5}$ model and vice versa), ambient 1-year $PM_{2.5}$ and ambient 1-year NO_2, average packs per day, and neighborhood poverty. In addition, the model was adjusted by two-way interaction of time with each of the covariates except study site.

‡Additionally adjusted by estimated indoor nicotine.

Current and Former Smokers: Annual Decline in FEV_1 by Indoor NO_2

The patterns of FEV_1 decline by indoor NO_2 were largely similar to those shown by indoor $PM_{2.5}$, with a general trend of steeper decline in FEV_1 associated with higher indoor NO_2 (vs. lower indoor NO_2) among former smokers ($P_{NO2\ interaction} = 0.084$) but not among current smokers ($P_{NO2\ interaction} = 0.51$) (Table E4). For example, among former smokers, the participants residing in homes with low indoor NO_2, indicated by 5th percentile indoor NO_2 concentration level, equivalent to 5.5 ppb, showed an estimated FEV_1 decline of 27.0 ml/yr (95% CI, 13.3–40.7), whereas their counterpart former smokers residing in homes with high indoor NO_2, indicated by 95th percentile indoor NO_2 concentration level, equivalent to 21.0 ppb, showed an estimated FEV_1 decline of 48.8 ml/yr (95% CI, 30.7–67.0). Among current smokers, annual FEV_1 decline was similar between those residing in low and high indoor NO_2, with 56.4 ml FEV_1 decline per year (95% CI, 39.9–72.9) for the participants residing in low indoor NO_2 and 67.3 ml decline per year (95% CI, 45.2–89.4) for the participants residing in high indoor NO_2. The results remained similar when taking into account SHS exposure (Table E4), whereas the trend for NO_2 difference in pre-BD FEV_1 decline was weaker than the trend in post-BD FEV_1 among former smokers (Table E8). There was no statistically significant sex difference ($P_{sex\ interaction} = 0.345$) in the above patterns, but the difference in FEV_1 decline by indoor NO_2 concentrations was shown among male but not female former smokers (Table E9). Among COPD-only participants, the results were largely similar to those shown for the full cohort (Tables E4 and E8).

Discussion

Lung function decline is a hallmark feature of COPD. Smoking cessation is associated with reduced incidence and slower progression of COPD; however, some former smokers continue to have accelerated loss of lung function. To date, factors that may drive continued loss of lung function among those who successfully quit cigarette smoking remain unclear. Our study results suggest that former smokers at risk for or with COPD who live in homes estimated to have high $PM_{2.5}$ concentrations have accelerated loss of annual lung function and have rates of

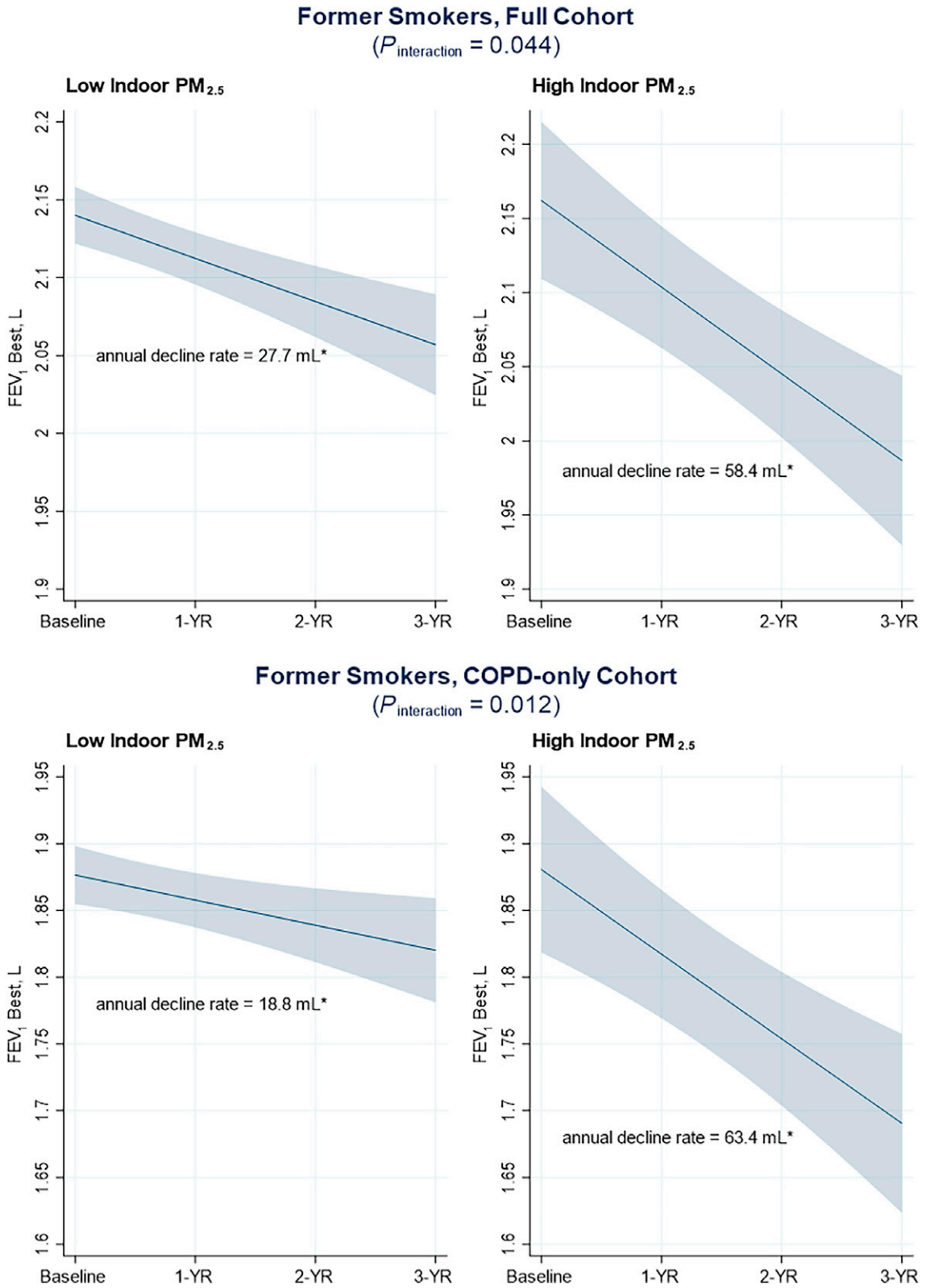

Figure 1. Among former smokers, decline in FEV_1 is steeper for those residing in homes with higher indoor particulate matter ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$) concentration. The chart compares the FEV_1 progression over time for those residing in homes with indoor $PM_{2.5}$ concentration at the 5th percentile (1.7 $\mu g/m^3$) versus the 95th percentile level (31.3 $\mu g/m^3$). * = annual decline rate was statistically significant; COPD = chronic obstructive pulmonary disease.

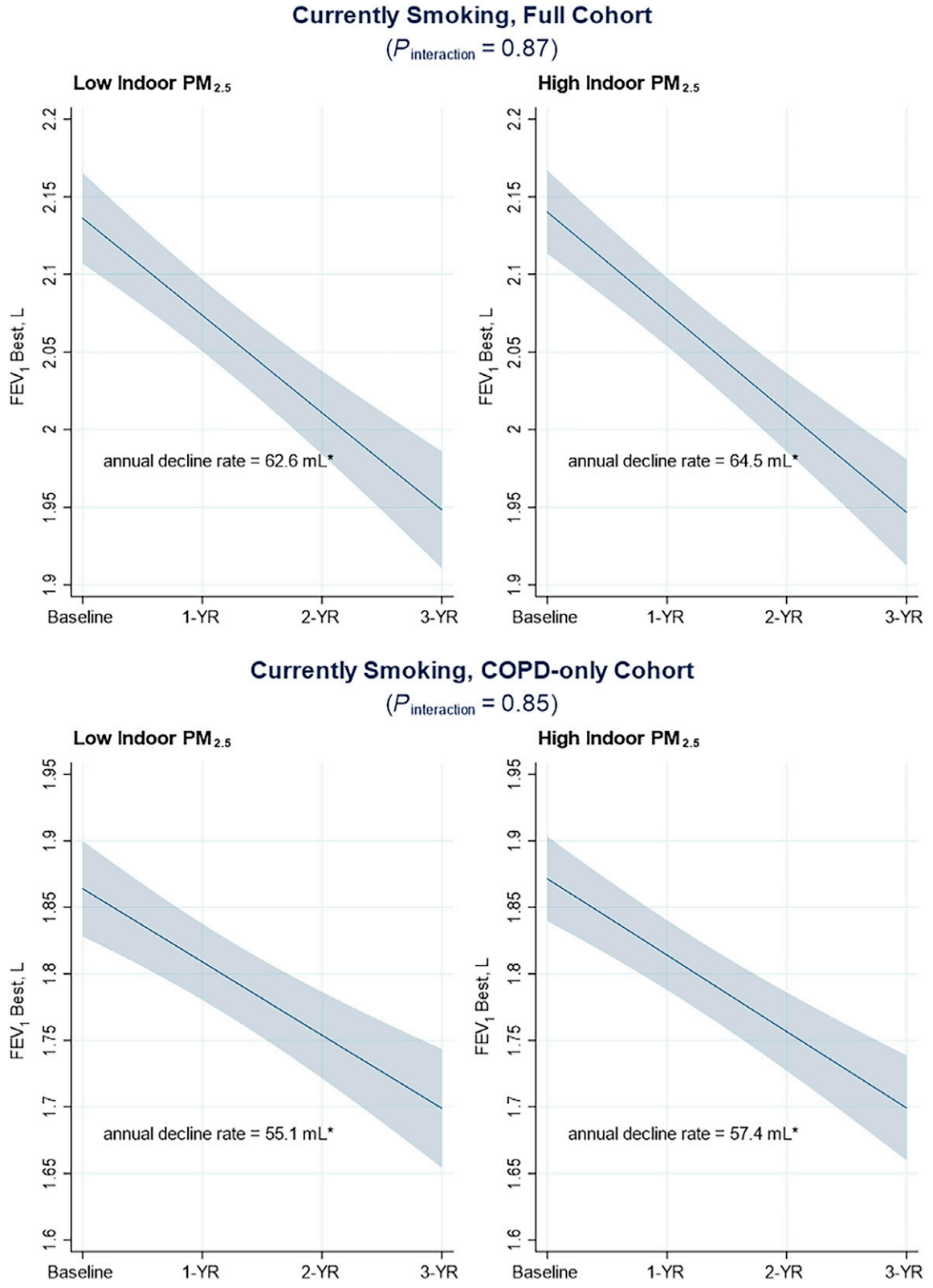

Figure 2. Among current smokers, there was no indoor particulate matter ⩽2.5 μm in aerodynamic diameter ($PM_{2.5}$) difference in FEV_1 decline. The chart compares the FEV_1 progression over time for those residing in homes with indoor $PM_{2.5}$ concentration at the 5th percentile (1.7 $\mu g/m^3$) versus the 95th percentile level (31.3 $\mu g/m^3$). * = annual decline rate was statistically significant; COPD = chronic obstructive pulmonary disease.

lung function decline similarly to those of individuals who continue to smoke. Conversely, former smokers living in homes estimated to have low $PM_{2.5}$ concentrations have lung function loss similar to normal aging in never smokers. Although indoor $PM_{2.5}$ is estimated to be higher in low-income neighborhoods and where smoking is present, the association between indoor $PM_{2.5}$ and annual lung function decline appears to be independent of SHS exposure and neighborhood poverty. These study results suggest that in-home $PM_{2.5}$ exposure may contribute to variability in annual lung function decline seen in people who successfully quit smoking and may be a modifiable environmental exposure.

Among all participants with a history of smoking, FEV_1 declined, on average, by approximately 47 ml per year, with current smokers having a faster rate of lung function decline of 60 ml per year than those currently not smoking, with 35 ml per year decline. Rates of lung function decline were similar among participants with COPD, in whom FEV_1 declined, on average, by approximately 42 ml per year, with a faster rate of decline for those currently smoking (52 ml/yr) than for those not currently smoking (30 ml/yr), and very similar to other longitudinal COPD cohorts (14). However, each 10 $\mu g/m^3$ estimated increment of indoor $PM_{2.5}$ concentration was associated with a 15 ml per year additional loss of lung function. Former smokers with COPD who resided in homes with the highest indoor $PM_{2.5}$ concentration, as represented by 95th percentile $PM_{2.5}$ level, equivalent to 31.3 $\mu g/m^3$, experienced an average FEV_1 decline of 63 ml per year, an estimate similar to that for current smokers with COPD. Conversely, former smokers who resided in low indoor $PM_{2.5}$ concentration homes had lower FEV_1 decline, showing an FEV_1 decline of 19 ml per year. This lung function decline is similar to or even lower than normal age-related lung function decline in never smokers, which is estimated to range between 10 ml/yr and 56 ml/yr in adults between the ages of 40 and 80, based on a systematic review of prospective cohort studies (15). These results suggest that indoor air quality improvement strategies specifically mitigating $PM_{2.5}$ levels may be an approach to minimize decline in lung function. Furthermore, although indoor PM concentrations are often higher in low-income homes, the results were independent of educational attainment, household income, and neighborhood poverty, suggesting that the association of $PM_{2.5}$ concentration and lung function decline is independent of socioeconomic status.

We developed residential indoor exposure prediction models for measured $PM_{2.5}$ and NO_2 based on meteorological, behavioral, residential, and ambient pollutant concentration data obtained from questionnaires, direct observations, and measurements. Smoking indoors is a major contributor to indoor PM concentrations. To determine whether the accelerated loss of lung function among former smokers with high indoor PM was attributable to SHS, additional analyses adjusted for the estimated indoor nicotine, which took into account various self-reported measures of SHS. It is possible that we did not accurately capture smoking in the home, but the results remained quantitatively similar to those for all former smokers, suggesting that the effect of indoor PM exposure is unlikely to be attributable solely to SHS. It is also relevant to note that a substantial portion of homes had estimated indoor $PM_{2.5}$ levels above the 2021 World Health Organization guideline recommendation of a 5 $\mu g/m^3$ annual limit (16), and even in homes deemed to have high $PM_{2.5}$ concentrations in SPIROMICS AIR as represented by 95th percentile $PM_{2.5}$ level, these levels are still considerably lower than levels of indoor particulate pollution resulting from solid fuel burning in the developing world (17, 18), and they provide the context that even lower indoor PM levels, often considered safe, may have significant health effects, given the considerable amount of time that adults with COPD spend in their homes (19).

Similar to $PM_{2.5}$, a substantial portion of homes had estimated indoor NO_2 levels above the 2021 World Health Organization guideline recommendation of a 5.1 ppb (or 10 $\mu g/m^3$) annual limit for NO_2 (16). The results of indoor NO_2 also suggest trends similar to those for $PM_{2.5}$ in that higher estimated levels of indoor NO_2 tended to be associated with accelerated loss of lung function among former smokers, adjusting for outdoor pollutant concentrations and indoor $PM_{2.5}$, although the results did not reach statistical significance. This may reflect a weaker association of NO_2 with lung function decline than that of $PM_{2.5}$, or it may be a result of differences in the accuracy of estimating pollutant concentrations leading to misclassification bias.

Given the large contribution of indoor sources to indoor PM and NO_2 concentrations, indoor air may be modifiable at the personal level by source reduction. For example, smoking, use of a wood fireplace, cooking, specific cleaning practices, and use of candles are significantly associated with a higher concentration of indoor fine particles (5, 20–24). Therefore, limiting or using increased ventilation while performing such activities may reduce exposures. Furthermore, use of an air cleaner/filter and living on the second floor or higher compared with living in a basement and the ground floor are associated with lower indoor $PM_{2.5}$ concentrations (5). Indeed, portable high-efficiency particulate-absorbing air cleaners can lead to a sustainable reduction over several months in indoor PM concentrations (25), and the results of a randomized clinical trial in COPD (26) suggest that portable air cleaners may lead to respiratory health benefits. Intervention studies are needed to determine whether long-term indoor pollutant reduction strategies can attenuate lung function decline among former smokers with COPD.

The effect of pollution exposure in current smokers is controversial. Some studies suggest that exposures are detrimental even among current smokers, and SHS exposure was associated with respiratory morbidity, such as exacerbation risk, respiratory symptoms, and functional status, among former and current smokers (27). However, our results suggest that indoor $PM_{2.5}$ estimates did not further influence lung function decline among current smokers. It is possible that the low level of pollution seen in SPIROMICS AIR homes was not adequate to augment the adverse effects of chronic cigarette smoking on lung function decline. Specifically, current smokers have accelerated lung function decline compared with former smokers (as noted by an average FEV_1 decline of 60 ml vs. 35 ml per year decline) and a larger inhaled particulate burden through smoking. Therefore, it is possible that larger differences in indoor PM exposure than observed in the present study are needed to contribute to further detectable loss of lung function among active smokers. It is also possible that it was challenging to adequately quantify the additive burden of indoor PM to smoking burden in smoking homes without direct measurement of PM and nicotine.

Limitations

Our study is subject to some limitations. It is possible that the error in $PM_{2.5}$ and NO_2 estimates in our analysis would lead to misclassification bias, and several factors impacting indoor pollutant concentrations were not captured, leading to potential residual confounding. For example, cooking and cleaning practices and use of candles have been associated with indoor $PM_{2.5}$ concentrations (23, 24) but were not well captured on the questionnaires, and detailed data on home air exchange rates were not available. Furthermore, several of the indoor sources of PM are dependent not only on housing characteristics but also on behaviors that may vary with time. Our indoor pollutant models explained about 60% of the variability in measured 1-week indoor pollutant concentrations and have been associated with an objective biological marker (i.e., black carbon deposition in sputum airway macrophages) (28); however, caution in interpretation of the results is still warranted. Given that indoor sources of fine particles are the major source of variation in indoor concentrations, rather than infiltrated ambient particles, direct indoor measurement is needed to definitively quantify the association between chronic exposure to indoor air particulates and lung health. It is possible that the association of long-term exposure to indoor pollution is even greater than estimated. Last, the SPIROMICS cohort includes too few never-smokers to estimate the effect of indoor PM among never-smokers, and other estimates of other indoor pollutants, such as volatile organic compounds, were not available. The ability to detect differences in the risk of indoor pollutant exposure by sex is limited by sample size; however, this does not suggest increased risk in women and potentially increased susceptibility among men.

Conclusions

In conclusion, indoor $PM_{2.5}$ exposure can adversely impact lung function decline among former smokers with or at risk of COPD. Indoor air exposures may account for continued accelerated loss of lung function among former smokers, and former smokers who resided in low indoor $PM_{2.5}$ concentration homes had lower FEV_1 decline consistent with normal aging, suggesting that indoor air quality improvement strategies may be an approach to preserve lung function. ■

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References

1. Drummond MB, Hansel NN, Connett JE, Scanlon PD, Tashkin DP, Wise RA. Spirometric predictors of lung function decline and mortality in early chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2012;185:1301–1306.
2. Oelsner EC, Balte PP, Bhatt SP, Cassano PA, Couper D, Folsom AR, *et al.* Lung function decline in former smokers and low-intensity current smokers: a secondary data analysis of the NHLBI Pooled Cohorts Study. *Lancet Respir Med* 2020;8:34–44.
3. Hansel NN, McCormack MC, Belli AJ, Matsui EC, Peng RD, Aloe C, *et al.* In-home air pollution is linked to respiratory morbidity in former smokers with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2013;187:1085–1090.
4. Hansel NN, McCormack MC, Kim V. The effects of air pollution and temperature on COPD. *COPD* 2016;13:372–379.
5. Zusman M, Gassett AJ, Kirwa K, Barr RG, Cooper CB, Han MK, *et al.* Modeling residential indoor concentrations of $PM_{2.5}$, NO_2, NO_x, and secondhand smoke in the Subpopulations and Intermediate Outcome Measures in COPD (SPIROMICS) Air study. *Indoor Air* 2021;31:702–716.
6. Couper D, LaVange LM, Han M, Barr RG, Bleecker E, Hoffman EA, *et al.*; SPIROMICS Research Group. Design of the Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS). *Thorax* 2014;69:491–494.
7. Hansel NN, Paulin LM, Gassett AJ, Peng RD, Alexis N, Fan VS, *et al.* Design of the Subpopulations and Intermediate Outcome Measures in COPD (SPIROMICS) AIR Study. *BMJ Open Respir Res* 2017;4:e000186.
8. Kirwa K, Szpiro AA, Sheppard L, Sampson PD, Wang M, Keller JP, *et al.* Fine-scale air pollution models for epidemiologic research: insights from approaches developed in the Multi-ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Curr Environ Health Rep* 2021;8:113–126.
9. Keller JP, Olives C, Kim SY, Sheppard L, Sampson PD, Szpiro AA, *et al.* A unified spatiotemporal modeling approach for predicting concentrations of multiple air pollutants in the Multi-Ethnic Study of Atherosclerosis and Air Pollution. *Environ Health Perspect* 2015;123:301–309.
10. Paulin LM, Diette GB, Blanc PD, Putcha N, Eisner MD, Kanner RE, *et al.*; SPIROMICS Research Group. Occupational exposures are associated with worse morbidity in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2015;191:557–565.
11. American Thoracic Society. Standardization of spirometry: 1994 update. *Am J Respir Crit Care Med* 1995;152:1107–1136.
12. Kind AJH, Buckingham WR. Making neighborhood-disadvantage metrics accessible—the neighborhood atlas. *N Engl J Med* 2018;378:2456–2458.

13. Galiatsatos P, Woo H, Paulin LM, Kind A, Putcha N, Gassett AJ, *et al.* The association between neighborhood socioeconomic disadvantage and chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2020;15:981–993.
14. Kanner RE, Anthonisen NR, Connett JE; Lung Health Study Research Group. Lower respiratory illnesses promote FEV_1 decline in current smokers but not ex-smokers with mild chronic obstructive pulmonary disease: results from the Lung Health Study. *Am J Respir Crit Care Med* 2001;164:358–364.
15. Thomas ET, Guppy M, Straus SE, Bell KJL, Glasziou P. Rate of normal lung function decline in ageing adults: a systematic review of prospective cohort studies. *BMJ Open* 2019;9:e028150.
16. World Health Organization. WHO global air quality guidelines: particulate matter (PM2. 5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide: executive summary. Geneva: WHO; 2021.
17. Diette GB, Accinelli RA, Balmes JR, Buist AS, Checkley W, Garbe P, *et al.* Obstructive lung disease and exposure to burning biomass fuel in the indoor environment. *Glob Heart* 2012;7:265–270.
18. Balmes JR. Household air pollution from domestic combustion of solid fuels and health. *J Allergy Clin Immunol* 2019;143:1979–1987.
19. Leech JA, Smith-Doiron M. Exposure time and place: do COPD patients differ from the general population? *J Expo Sci Environ Epidemiol* 2006; 16:238–241.
20. McCormack MC, Breysse PN, Hansel NN, Matsui EC, Tonorezos ES, Curtin-Brosnan J, *et al.* Common household activities are associated with elevated particulate matter concentrations in bedrooms of inner-city Baltimore pre-school children. *Environ Res* 2008;106:148–155.
21. Meng QY, Spector D, Colome S, Turpin B. Determinants of indoor and personal exposure to $PM_{2.5}$ of indoor and outdoor origin during the RIOPA study. *Atmos Environ (1994)* 2009;43:5750–5758.
22. Wallace LA, Mitchell H, O'Connor GT, Neas L, Lippmann M, Kattan M, *et al.*; Inner-City Asthma Study. Particle concentrations in inner-city homes of children with asthma: the effect of smoking, cooking, and outdoor pollution. *Environ Health Perspect* 2003;111: 1265–1272.
23. Maung TZ, Bishop JE, Holt E, Turner AM, Pfrang C. Indoor air pollution and the health of vulnerable groups: a systematic review focused on particulate matter (PM), volatile organic compounds (VOCs) and their effects on children and people with pre-existing lung disease. *Int J Environ Res Public Health* 2022;19:8752.
24. Vardoulakis S, Giagloglou E, Steinle S, Davis A, Sleeuwenhoek A, Galea KS, *et al.* Indoor exposure to selected air pollutants in the home environment: a systematic review. *Int J Environ Res Public Health* 2020;17:8972.
25. Lorizio W, Woo H, McCormack MC, Liu C, Putcha N, Wood M, *et al.* Patterns and predictors of air cleaner adherence among adults with COPD. *Chronic Obstr Pulm Dis (Miami)* 2022;9:366–376.
26. Hansel NN, Putcha N, Woo H, Peng R, Diette GB, Fawzy A, *et al.* Randomized clinical trial of air cleaners to improve indoor air quality and chronic obstructive pulmonary disease health: results of the CLEAN AIR Study. *Am J Respir Crit Care Med* 2022;205: 421–430.
27. Putcha N, Barr RG, Han MK, Woodruff PG, Bleecker ER, Kanner RE, *et al.*; SPIROMICS Investigators. Understanding the impact of second-hand smoke exposure on clinical outcomes in participants with COPD in the SPIROMICS cohort. *Thorax* 2016;71:411–420.
28. Tejwani V, Woo H, Liu C, Tillery AK, Gassett AJ, Kanner RE, *et al.* Black carbon content in airway macrophages is associated with increased severe exacerbations and worse COPD morbidity in SPIROMICS. *Respir Res* 2022;23:310.