

Original Research

# Physical Activity, Air Pollution Exposure, and Lung Function Interactions Among Adults with COPD

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## Abstract

**Rationale:** Although physical activity is strongly encouraged for patients with chronic obstructive pulmonary disease (COPD), it is unknown if physical activity affects daily exposure to air pollution, or whether it attenuates or exacerbates the effects of pollution on the airways among adults with COPD.

**Methods:** Thirty former smokers with moderate-to-severe COPD in Boston were followed for 4 non-consecutive months in different seasons. We assessed daily lung function (forced expiratory volume in 1 second [FEV<sub>1</sub>] and forced vital capacity [FVC]), prior-day personal pollutant exposure measured by portable air quality monitors (fine particulate matter [PM<sub>2.5</sub>] nitrogen oxide [NO<sub>2</sub>], and ozone [O<sub>3</sub>]), and daily step count. We constructed multi-level linear mixed-effects models with random intercepts for person and person-observation month, adjusting for demographic/seasonal covariates to test if step count was associated with daily pollution exposure, and if associations between prior-day pollution and lung function differed based on prior-day step count. Where effect modification was found, we performed stratified analyses by tertile of step count.

**Results:** Higher daily step count was associated with higher same-day personal exposure to PM<sub>2.5</sub>, and O<sub>3</sub> but not NO<sub>2</sub>. Each interquartile range (IQR) increment in step count was associated with 0.97 μg/m<sup>3</sup> (95% CI: 0.30, 1.64) higher exposure to PM<sub>2.5</sub> and 0.15 parts per billion (95% CI: -0.05, 0.35) higher exposure to O<sub>3</sub> in adjusted models. We observed an interaction between prior-day NO<sub>2</sub> and step count on FEV<sub>1</sub> and FVC (P<sub>interaction</sub><0.05) in which the negative associations between NO<sub>2</sub> and lung function were reduced or absent at higher levels of daily activity. For example, FEV<sub>1</sub> was 28.5 mL (95% CI: -41.0, -15.9) lower per IQR of NO<sub>2</sub> in the lowest tertile of step count, but there was no association in the highest tertile of step count (-1.6 mL, 95% CI: -18.4, 15.2).

**Conclusion:** Higher physical activity was associated with modestly higher daily exposure to PM<sub>2.5</sub> and O<sub>3</sub> and may attenuate the association between NO<sub>2</sub> exposure and lung function.

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## Abbreviations:

**COPD**=chronic obstructive pulmonary disease; **EPA**=Environmental Protection Agency; **FEV<sub>1</sub>**=forced expiratory volume in 1 second; **FVC**=forced vital capacity; **IQR**=interquartile range; **NO<sub>2</sub>**=nitrogen dioxide; **O<sub>3</sub>**=ozone; **PAM**=personal air quality monitor; **PM<sub>2.5</sub>**=fine particulate matter; **ppb**=parts per billion; **SPACE**=Study of Pollution And COPD Exacerbation

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**Introduction**

Chronic obstructive pulmonary disease (COPD) is an irreversible, progressive lung disease characterized by chronic respiratory symptoms and airflow limitation.<sup>1</sup> Prior studies have identified outdoor air pollution as a trigger of COPD exacerbations, with a higher risk of COPD hospitalizations and COPD mortality during periods of higher outdoor air pollution levels.<sup>2-4</sup> Recent studies utilizing personal air monitoring have determined that changes in air quality, even at relatively low levels, are associated with worse lung function and symptoms among adults with COPD.<sup>5,6</sup>

COPD patients often have low levels of physical activity, even early in the disease. Lower levels of physical activity are associated with poor outcomes, including COPD exacerbations, worse health-related quality of life, and mortality in COPD.<sup>7,8</sup> Even though COPD patients often have respiratory limitations to exercise, physical activity is encouraged as it has been demonstrated to improve outcomes in COPD, including a lower risk of hospitalization, all-cause mortality, and respiratory mortality.<sup>9-12</sup> However, exercise in outdoor settings may lead to greater exposure to air pollution and, therefore, may have potentially harmful effects on respiratory health. Higher minute ventilation during physical activity, whether it occurs indoors or outdoors, may also increase the effective dose of air pollution delivered to the lungs by increasing deposition to the lungs and thereby may augment short-term harmful effects of air pollutants.<sup>13</sup> It is unknown if higher routine daily physical activity increases personal daily exposure to ambient air pollutants [such as fine particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), and ozone (O<sub>3</sub>)], and whether physical activity attenuates or exacerbates the known effect of pollutants on lung function in patients with COPD.

In our Study of Pollution and COPD Exacerbation (SPACE), we recruited 30 former smokers with COPD living in an urban environment in the greater Boston area.<sup>6</sup> We followed each participant for 4 non-consecutive months in different seasons over a year, during which participants measured their daily step count by Fitbit, daily personal exposure to pollutants (PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>) by a portable personal air quality monitor (PAM), and daily lung function by office-grade spirometers. We hypothesized that a higher daily step count would be associated with higher exposure

to personal pollutants, and that physical activity would exacerbate the previously reported association between personal exposure to NO<sub>2</sub> and lung function in this small study population.<sup>6</sup>

**Methods****Study Population**

The study population consists of 30 former smokers with COPD who were recruited as part of SPACE at Beth Israel Deaconess Medical Center in Boston, Massachusetts. To be eligible, study participants were required to be former smokers without any active smoking for at least 6 months prior to enrollment, have a  $\geq 10$  pack-year smoking history, and have a home address within 50km of the Harvard air pollution supersite in Boston, Massachusetts, and a clinical diagnosis of COPD with at least moderate (Global Initiative for Chronic Obstructive Lung Disease stage 2)<sup>14</sup> airflow obstruction, defined as forced expiratory volume in 1 second (FEV<sub>1</sub>)/forced vital capacity (FVC) ratio of  $<0.70$  and FEV<sub>1</sub> $<80\%$  predicted, using National Health and Nutrition Examination Survey III prediction equations. Participants with a history of lung cancer, interstitial lung diseases, or bronchiectasis were ineligible to participate. The study was approved by the authorized institutional review board of the Beth Israel Deaconess Medical Center (Protocol # 2015P000336/03). Written informed consent was obtained from all study participants.

**Data Collection**

Participants entered the study between February 24, 2017, and January 17, 2019. At study entry, demographic information, height, weight, past medical history, medication history, and baseline measures of lung function were obtained, and participants were instructed on the use of the Fitbit, portable spirometer, and PAM to be used for subsequent data collection in the home. Participants were directly observed successfully completing lung function testing using the portable EasyOne™ spirometer at the entry visit and then used the same device at home. They were then observed for up to 4 non-consecutive 30-day periods in different seasons over 12 months. Participants measured their lung function daily in the morning before taking any medications, using the portable EasyOne™ Plus Diagnostic Spirometer, a device that meets American Thoracic Society guidelines<sup>15</sup> and has built-in quality assurance and incentive software. EasyOne™ incorporates an automatic quality control function, where at least 3 acceptable reproducible maneuvers must be performed before a participant is able to complete a session. At the end of the follow-up, the 30 participants had contributed a total of 3314 observation days.

## Exposure Assessment

We measured personal 24-hour step counts using the portable Fitbit® Charge 2 worn by participants each day for all hours, except during bathing (during which the participants were instructed to charge the device). We excluded observation days with a recorded total step count of zero. We measured personal pollutant exposures using PAMs (Atmospheric Sensors Ltd., model 520). Details about the PAM technology, reproducibility of pollutant measurements, and agreement with stationary monitors in diverse settings have been reported previously.<sup>16</sup> All personal 24-hour exposure measures for PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> collected during our study were calibrated against reference monitors prior to data analysis, as previously described.<sup>6</sup>

## Statistical Analyses

### Associations with Same-Day Pollutant Exposure and Daily Step Count:

To assess the association of daily step count with daily personal exposure to each pollutant, we constructed unadjusted multilevel linear mixed-effects models with random intercepts for person and person-observation month and an autoregressive correlation structure. We also constructed multivariable models with adjustments for age, sex, body mass index, season, humidity, and temperature.

### Interaction Between Step Count and Previous-Day Pollutant Exposure on Daily Lung Function:

We have previously reported that personal exposure to NO<sub>2</sub> is associated with lower lung function in this study population.<sup>6</sup> To determine whether the relationship between prior-day personal exposure to pollutants (PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>) and daily lung function (FEV<sub>1</sub> and FVC) differs by prior-day total step count, we included a cross-product term in our adjusted models and evaluated the *p*-value for the statistical test for interaction with step count. We classified step count per tertile: low (<1998 steps), medium (1988–4169 steps), and high (>4169 steps). If we found evidence of effect modification (*p*<sub>interaction</sub><0.05), we performed stratified analyses to determine associations of pollution and lung function within each tertile of step count. All models were adjusted for age, sex, race, height, weight, pack years of cigarette use, education, income, season, temperature, and humidity.

## Results

### Study Participants

Baseline participant characteristics are reported in Table 1. Participants were on average 71.1±8.4 years of age and

were 80% non-Hispanic White and 20% non-Hispanic Black or African American, with a slight majority of females. Baseline lung function was impaired, with a mean FEV<sub>1</sub> of 54% predicted, FVC of 80% predicted, and FEV<sub>1</sub>/FVC ratio of 51%.

### Exposure Distributions and Associations

Table 2 displays the distribution of personal exposure to pollutants and daily total step count. Median previous-day 24-hour personal exposure to PM<sub>2.5</sub> (8.8μg/m<sup>3</sup>) was within the EPA 24-hour PM<sub>2.5</sub> standard<sup>17</sup> of 35μg/m<sup>3</sup> and the annual standard of 12μg/m<sup>3</sup>. Median previous-day personal exposure to both NO<sub>2</sub> and O<sub>3</sub> were also relatively low (6.8 parts per billion [ppb] and 9.6 ppb, respectively). The median daily total step count was 2930 steps, which is a low level of physical activity (4000 steps or less) and falls below the recommended Centers for Disease Control and Prevention physical activity guideline of 10,000 daily steps.<sup>18</sup>

### Associations with Same-Day Pollutant Exposure and Daily Step Count:

Adjusted associations between daily step count and personal exposure to each pollutant are presented in Figure 1. In adjusted models, higher daily physical activity was associated with higher same-day personal exposure to PM<sub>2.5</sub>, and O<sub>3</sub>, but not NO<sub>2</sub>. Each interquartile range (IQR) increment in daily step count was associated with a 0.97μg/m<sup>3</sup> (95% CI: 0.30, 1.64) higher exposure to PM<sub>2.5</sub> and a 0.15 ppb (95% CI: -0.05, 0.35) higher personal exposure to O<sub>3</sub>. A similar pattern was seen in unadjusted models. For example, per IQR higher daily step count, daily PM<sub>2.5</sub> was 0.98μg/m<sup>3</sup> higher (95% CI: 0.31, 1.65).

### Interaction Between Step Count and Previous-Day Pollutant Exposure on Daily Lung Function:

A total of 2689 participant days with exposure and lung function data were included for the analysis of effect modification by physical activity. Step count modified the relationship between prior-day NO<sub>2</sub> and FEV<sub>1</sub> (*p*<sub>interaction</sub>=0.004) and FVC (*p*<sub>interaction</sub>=0.045). We did not find evidence of effect modification by physical activity for the associations of PM<sub>2.5</sub> or O<sub>3</sub> with lung function.

We then examined associations of previous-day NO<sub>2</sub> exposure and lung function within tertiles of prior-day total step count. The negative associations between NO<sub>2</sub> and lung function were greatest in magnitude on participant days with the lowest level of physical activity and absent on participant days with the highest activity levels (Figure 2). For example, in the lowest tertile of physical activity (prior-day step count <1988 steps), each IQR increment in NO<sub>2</sub>

**Table 1. Baseline Characteristics of Participants<sup>a</sup>**

Demographics	Mean (SD) or n(%)
Age, years	71.1 (8.4)
Height, cm	165.1 (10.2)
Weight, kg	85.3 (17.7)
Total Pack-Year Smoking History	54.4 (30.7)
<b>Sex</b>	
Male	14 (46.7)
Female	16 (53.3)
<b>Race</b>	
White, non-Hispanic	24 (80.0)
Black or African American, non-Hispanic	6 (20.0)
<b>Income</b>	
< \$25,000	10 (33.3)
\$25,000 - \$49,999	10 (33.3)
> \$50,000	9 (30.0)
Other/Missing	1 (3.3)
<b>Education</b>	
Up to grades 12 or GED	8 (26.7)
Some college – Associates' degree	13 (43.3)
Bachelor's degree and above	9 (30.0)
<b>Baseline Lung Function</b>	Mean (SD)
FEV <sub>1</sub> (absolute, L)	1.3 (0.5)
FEV <sub>1</sub> (% predicted)	54.3 (14.5)
FVC (absolute, L)	2.6 (0.8)
FVC (% predicted)	79.9 (15.7)
FEV <sub>1</sub> /FVC	51.1 (11.5)

<sup>a</sup>n=30SD=standard deviation; GED=high school diploma equivalency; FEV<sub>1</sub>=forced expiratory volume in 1 second; FVC=forced vital capacity**Table 2. Same-Day Personal Exposure to Air Pollutants and Total Step Count**

Exposure	n, obs	Median	IQR
PM <sub>2.5</sub> , µg/m <sup>3</sup>	3026	8.8	4.0
NO <sub>2</sub> , ppb	3026	6.8	5.4
O <sub>3</sub> , ppb	3026	9.6	5.1
<b>Daily Total Step Count</b>	3606	2930	3637

IQR=interquartile ranger; PM<sub>2.5</sub>=fine particulate matter; NO<sub>2</sub>=nitrogen dioxide; O<sub>3</sub>=ozone

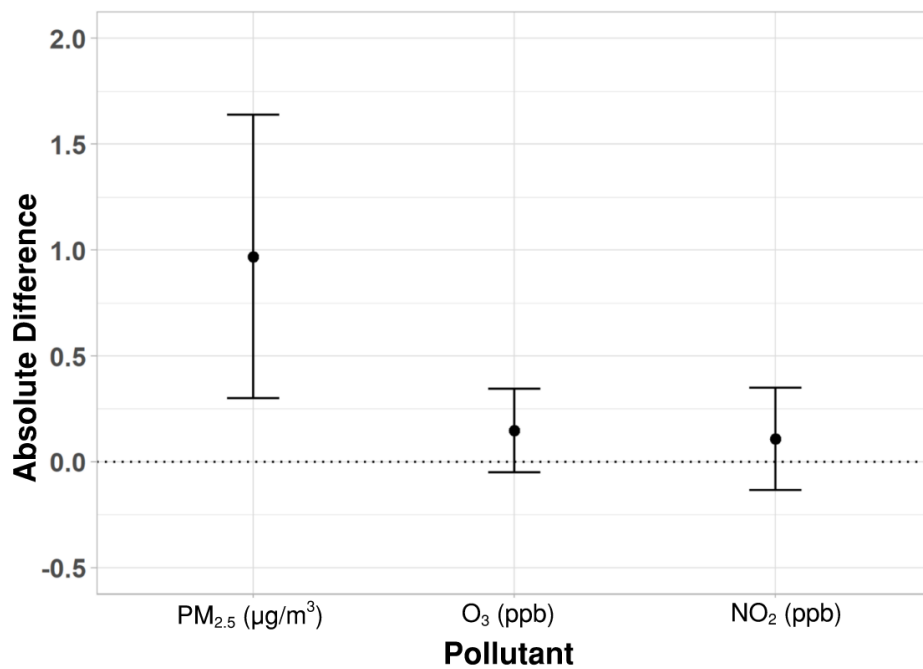
was associated with a 28.5mL (95% CI: -41.0, -15.9) lower FEV<sub>1</sub>. On days when the prior-day step count was between 1988 and 4168 steps, we observed a 13.3mL (95% CI: -25.5, -1.0) lower FEV<sub>1</sub>. In the highest tertile of physical activity (prior-day step count ≥4169 steps), there was no association between NO<sub>2</sub> exposure and FEV<sub>1</sub> (-1.6 mL, 95% CI: -18.4, 15.2).

## Discussion

In this urban setting, routine physical activity resulted in a modest increase in pollution exposure compared to sedentary behavior for some pollutants. Higher daily step count was associated with a small increase in personal exposure to PM<sub>2.5</sub>, a small, borderline significant increase

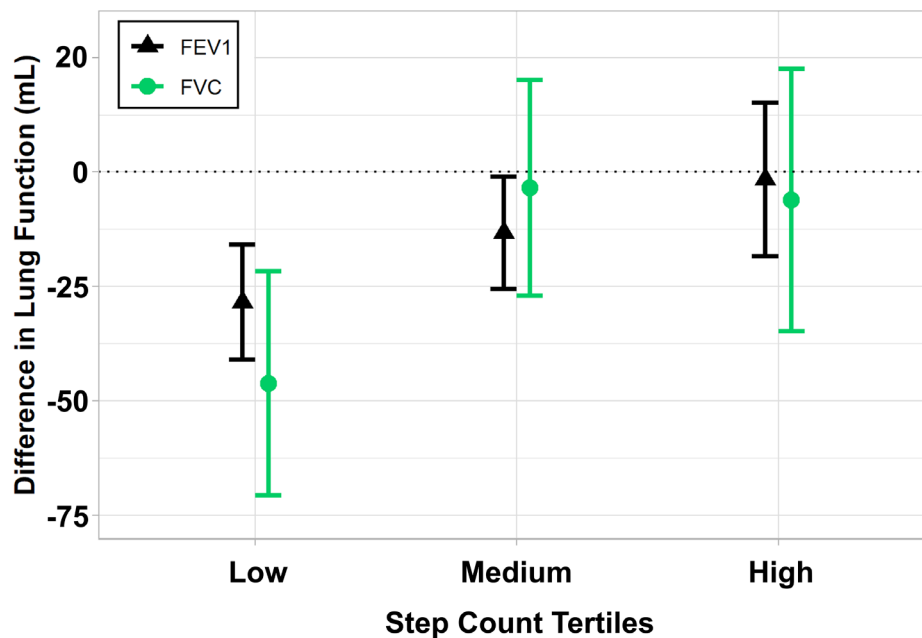
in exposure to O<sub>3</sub>, and no difference in exposure to NO<sub>2</sub> among COPD patients living in the Boston area. We also found that physical activity, when examined continuously, attenuated the association between NO<sub>2</sub> and lung function. When examining tertiles of physical activity, personal NO<sub>2</sub> exposure was negatively associated with FEV<sub>1</sub> and FVC on more sedentary days (in the lower tertiles of physical activity), but not on more active days (in the highest tertile of physical activity). These findings suggest that, within the relatively low pollution levels of the Boston area where our study population resided, higher daily physical activity appears to mitigate, not exacerbate, the harmful effects of NO<sub>2</sub> on lung function in COPD. However, we did not find evidence of physical activity modifying associations of PM<sub>2.5</sub> or O<sub>3</sub> with lung function.

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**Figure 1. Associations of Daily Step Count with Personal Exposure to Air Pollutants<sup>a</sup>**

<sup>a</sup>All associations scaled per IQR-increment in same-day total step count (3637 steps).

PM<sub>2.5</sub>=fine particulate matter; O<sub>3</sub>=ozone; NO<sub>2</sub>=nitrogen dioxide; IQR=interquartile range

**Figure 2: Associations of Previous-Day Nitrogen Dioxide Exposure and Lung Function Within Tertiles of Prior-Day Total Step Count<sup>a</sup>**

<sup>a</sup>All associations are scaled per IQR difference (5.4 ppb) in previous-day personal NO<sub>2</sub> exposure. Step counts per tertile: <1988 steps (low), 1988 to 4169 steps (medium), >4,169 steps (high).

FEV<sub>1</sub>=forced expiratory volume in 1 second; FVC=forced vital capacity; IQR=interquartile range; NO<sub>2</sub>=nitrogen dioxide

A limited number of studies have examined interactions between short-term exposure to pollution and physical activity on cardiopulmonary health, and few have focused on COPD.<sup>19,20</sup> One case crossover study in London involving former smokers with COPD found a lung function benefit

from walking for 2 hours in the relatively less polluted Hyde Park in London, but that walking along the more polluted Oxford street attenuated the lung function benefit of exercise.<sup>21</sup> Estimated and/or measured exposure to NO<sub>2</sub>, PM<sub>2.5</sub>, black carbon, and fine particles was higher during the

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walk along the urban street compared to the park. Although not a primary aim of our study, we did not find that daily physical activity (as quantified by step count) improved lung function the next morning, and we did not measure lung function immediately after exercise. However, as reported in the London experiment, we did find an interaction between physical activity and pollution exposure on lung function, with a higher step count attenuating the harms of NO<sub>2</sub> exposure on FEV<sub>1</sub> and FVC. Notably, the London study also found, as in our Boston population, that higher exposure to NO<sub>2</sub> was associated with lower lung function. In contrast, the London study did not directly test if the amount of physical activity mitigated or exacerbated the effect of a given level of pollution. Many patients, especially those limited by severe COPD, may not have a lot of choice about where they are physically active in their daily lives. Overall, the findings of our study in Boston are reassuring, as we found that while routine physical activity modestly increased exposure to select pollutants, it did not increase the harms of daily pollution exposure and in fact, reduced the apparent effects of NO<sub>2</sub> on lung function.

A few studies have examined if long-term exercise habits modify the harmful effects of long-term exposure to pollution on cardiopulmonary health, based on the concern that exercise enhances the uptake of pollutants into the lung. These studies, largely conducted in Western Europe at relatively low pollution levels, have generally found that the benefits of exercise outweigh the harms of higher pollution exposure attributable to exercise.<sup>20,22</sup> The Danish Diet, Cancer, and Health cohort of more than 50,000 adults with 16 years of follow-up examined whether baseline participation in sports and cycling moderated associations between pollution exposure and incident asthma and COPD.<sup>13</sup> The authors found that while long-term NO<sub>2</sub> exposure was associated with incident asthma and COPD hospitalization, physical activity reduced the risk of these outcomes, and there was no evidence of an interaction between physical activity and pollution exposure on COPD (or asthma) incidence. The authors concluded that the long-term benefits of exercise for respiratory health were not reversed by the harms of pollution exposure during exercise. Although this large population-level study in Denmark and our study favor physical activity despite the risks of pollution exposure, there are some key differences in methodology between the studies. The Danish Diet, Cancer and Health cohort study investigated long-term exposure over many years in the general population compared to our short-term study of daily exposure among COPD patients, as well as investigating the outcome of incident COPD hospitalizations rather than lung function. Taken together, our collective findings provide evidence in favor of greater physical activity for COPD patients, and for exercising in less polluted areas when possible.

Our study has several limitations. While we collected a

large number of repeated measures (3314 observation days in total), our study only included 30 unique individuals in the Boston area. Therefore, our findings should be interpreted with caution given our small sample size and will require replication in larger cohorts with COPD. Our findings are limited in their generalizability to other patients with COPD, including those with milder diseases, those with and without asthma/COPD overlap, those with more vigorous exercise habits, or those living or exercising in more polluted urban environments or rural settings. Our study population consists only of former smokers and may not be generalizable to current smokers with COPD. While we were able to assess for personal exposures to air pollutants with the use of PAM and Fitbit devices, we did not measure device adherence (e.g., whether a participant left the home without the PAM or did not wear the Fitbit for part of the day), which may result in some misclassification of the personal pollutant exposure and step count estimates. However, such misclassification would likely result in a bias towards the null.

Our study also has several strengths. Our unique longitudinal study design with daily exposure and health measures allowed us to evaluate how day-to-day variability in step count and personal exposure to air pollutants is associated with daily lung function in an older population with COPD. We accounted for within-person correlation of measurements and adjusted for a robust list of potential individual-level and seasonal confounders. We used lightweight portable exposure monitors, calibrated to gold standard stationary monitors, to measure exposure at the individual level for a prolonged period (a total of 4 months) across different seasons. Our study demonstrates that measuring physical activity and personal pollution exposure using portable monitors is feasible for extended durations in a high-risk older population with COPD in order to address research questions about how typical exposures and activity levels affect respiratory health in the outpatient setting at an individual patient level. A recent American Thoracic Society workshop called for this type of research on the trade-offs of exercise and avoiding outdoor air pollution, especially for chronic medical conditions such as COPD that have known long-term health benefits of physical activity.<sup>23</sup>

In this study of former smokers with COPD living in an urban environment, routine physical activity resulted in only a modest difference in pollution exposure compared to sedentary behavior. Further, physical activity attenuated the negative association between personal exposure to NO<sub>2</sub> and lung function in COPD. Our study did not find evidence to suggest that COPD patients should forego physical activity in order to avoid pollution exposure at typical daily exposure levels within current EPA standards.

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**Author contributions:** MBR, KC, MA, AJS, LN, PK, and BAC planned the quantitative analyses for the study, which were carried out by KC and AJS. KC interpreted the findings, and KC, MA, and AP wrote the first manuscript draft. MBR supervised all aspects of the study, including data collection, analysis, interpretation, and manuscript preparation. All authors contributed to the critical revision of the manuscript and approved the final submitted version.

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**Declaration of Interest**

The authors have no potential conflicts of interest to declare.

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