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Lifetime Exposure to Traffic-related Pollution and Lung Function in Early Adolescence

To the Editor:

Long-term ambient air pollution exposure has been associated with reduced child lung function (1). Although some studies have demonstrated that early-life exposure has a persistent effect on child lung function, others have shown that more recent exposures have a greater impact, and improvements in air quality may reverse or attenuate these effects (2–6). We previously found that living close to a major roadway and past-year and lifetime exposure to particulate matter ⩽2.5 μm in aerodynamic diameter ($PM_{2.5}$) were associated with lower lung function among elementary school–aged children in the Boston area (2). In this follow-up study, we evaluate pollution exposures at different time points and associations with adolescent lung function. As $PM_{2.5}$ concentrations have been reduced, we also examined if change in $PM_{2.5}$ concentration during follow-up was associated with lung function growth.

Project Viva is a prospective prebirth cohort study of mother–child pairs followed from pregnancy to adolescence. We recruited 2,128 women in early pregnancy between 1999 and 2003 from Atrius Harvard Vanguard Medical Associates, a group practice in eastern Massachusetts. Children completed spirometry at a midchildhood visit (median age, 7.7 years; $n = 510$) and an early adolescent visit completed between 2013 and 2016 (median age, 12.8 years; $n = 844$). Details of the exposures, spirometry measurements, and study design have been described elsewhere (2, 7, 8). Participants' home addresses were collected at each visit, and any changes in address were estimated to have occurred halfway between the two visits. On the basis of published findings that traffic-related pollutants decay to background concentrations exponentially with distance from a freeway (9), we calculated the natural logarithm of the distance from each participant's home to the nearest major roadway. Annual and lifetime $PM_{2.5}$ exposures were estimated using a satellite model, as previously described (2). We analyzed associations of residential proximity to a major roadway (at birth, midchildhood, and adolescence) and $PM_{2.5}$ exposure (for the first year of life, the year before spirometry, average from birth to midchildhood, average since midchildhood, and lifetime at adolescence) with adolescent lung function (forced expiratory volume in 1 second [FEV_1], forced vital capacity [FVC], and FEV_1/FVC ratio) and lung function growth between visits. Finally, we examined if change in $PM_{2.5}$ between visits was associated with change in FEV_1 and FVC between visits.

All associations were analyzed using linear regression. We adjusted for child age, race or ethnicity, sex, height, household income, household smoking status, date of visit, season (as the sine and cosine of visit date), temperature and humidity the day before spirometry, and census tract medium income and education. As in our previous analysis in this cohort (2), participants with missing covariate data ($n = 41$ [4.9%]) were excluded. We tested for effect modification by sex, race (White vs. non-White), household income (⩽$70,000 vs. >$70,000), and current asthma.

Among participants with exposure and outcome data, 50.7% were female, 64.9% identified as White and 16.1% as Black, and 15.3% had asthma. Seventy-seven percent of households had annual incomes greater than $70,000, and 6.5% included at least one smoker. Mean FEV_1 was 2.7 L (97.9% predicted; standard deviation [SD], 12.9%), and mean FVC was 3.2 L (100.9% predicted; SD, 11.9%). Mean annual increases in FEV_1 and FVC between visits were 246 ml/yr (SD, 76.8 ml/yr) and 287 ml/yr (SD, 84.3 ml/yr), respectively. Median distance to a major roadway in adolescence was 1,350 m (interquartile range [IQR], 2,459 m). Median annual $PM_{2.5}$ exposure was 11.2 $\mu g/m^3$ (IQR, 1.5 $\mu g/m^3$) for the first year of life, 9.9 $\mu g/m^3$ (IQR, 1.3 $\mu g/m^3$) for the year before the midchildhood visit, 7.8 $\mu g/m^3$ (IQR, 0.8 $\mu g/m^3$) for the year before the adolescent visit, 8.0 $\mu g/m^3$ (IQR, 1.2 $\mu g/m^3$) for the years between visits, and 9.3 $\mu g/m^3$ (IQR, 1.1 $\mu g/m^3$) for lifetime exposure up to the adolescent visit. The logarithms of distance to a major roadway and annual average $PM_{2.5}$ preceding the adolescent visit were not correlated (Pearson $r = -0.18$).

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Author Contributions: S.A.M. developed the data analysis plan under the supervision of M.B.R., conducted the data analysis with assistance of M.B.R. and L.N., and wrote the first version of the manuscript. J.E.S., S.L.R.-S., H.L.-G., E.O., and D.R.G. advised on the data analysis. S.L.R.-S. assisted with creating variables for the study. E.O. and D.R.G. supervised the collection and quality control of data in the Viva Cohort study and obtained funding. All authors contributed to the interpretation of the data, revised the manuscript, and approved the final manuscript.

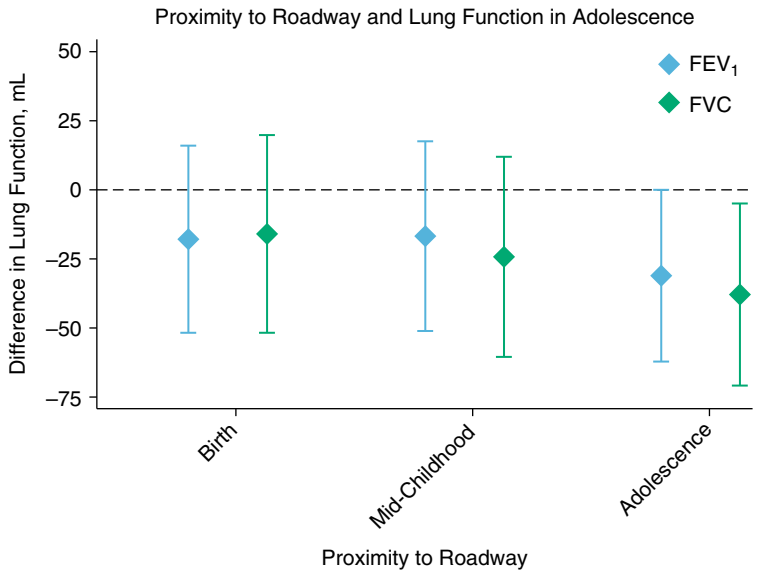

Figure 1. Associations of proximity to a major roadway and lung function in early adolescence. Results are scaled from the 75th to the 25th percentile of the log-transformed distance to a major roadway. All models are adjusted for child age, sex, race/ethnicity, and height; household income; household smoking; season (as sine and cosine terms); temperature and humidity the day before the spirometry examination; and census tract median household income and education. FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

Living closer to a major roadway at the adolescent visit was associated with lower adolescent FEV_1 (−31.2 ml; 95% confidence interval [CI], −62.5 to −0.01 ml) and FVC (−38.2 ml; 95% CI, −71.3 to −5.1 ml) per IQR difference in distance (log scale) (Figure 1). Lifetime $PM_{2.5}$ exposure was associated with lower FEV_1 (−34.2 ml; 95% CI, −67.9 to −0.5 ml), and average $PM_{2.5}$ since midchildhood was associated with lower FEV_1 (−42.5 ml; 95% CI, −76.4 to −8.5 ml) and FVC (−47.6 ml; 95% CI, −83.4 to −11.8 ml) per 1 μg/m^3 (Figure 2). There were no associations of proximity to a roadway at birth or midchildhood, $PM_{2.5}$ exposure during the first year of life, or $PM_{2.5}$ exposure in the prior year with adolescent lung function. There were no associations of these exposures with

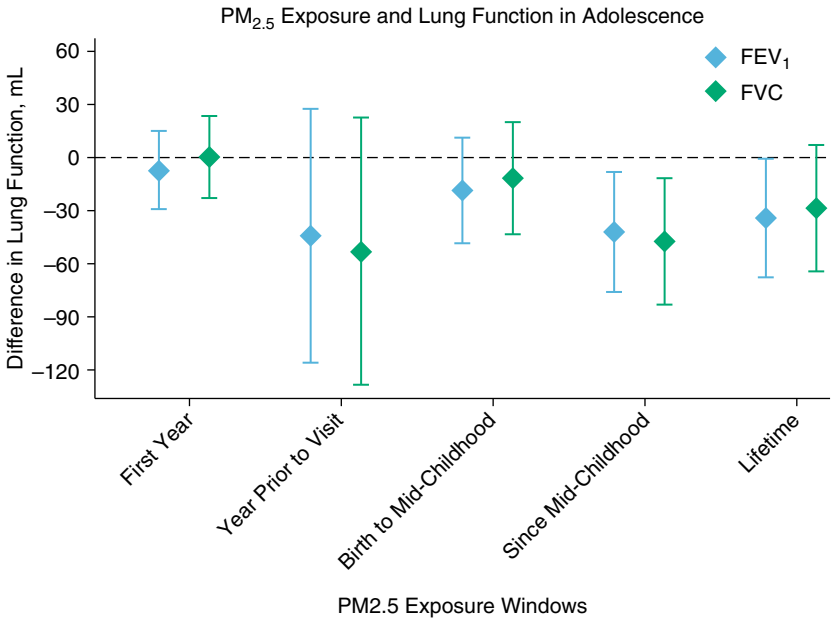

Figure 2. $PM_{2.5}$ exposure and lung function in adolescence. Results are scaled per 1 μg/m^3. All models are adjusted for child age, sex, race/ethnicity, height; household income; household smoking; season (as sine and cosine terms); temperature and humidity the day before the spirometry examination; and census tract median household income and education. FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; $PM_{2.5}$ = particulate matter ≤2.5 μm in aerodynamic diameter.

subsequent change in lung function between the two visits. Reduction in average annual $PM_{2.5}$ exposure between the midchildhood and early adolescent visits was associated with faster lung function growth: the mean difference in annual $PM_{2.5}$ between the visits of 0.4 $\mu g/m^3$ was associated with a 17.5 ml/yr (95% CI, 6.5 to 28.4 ml/yr) faster growth in FEV_1 and a 14.5 ml/yr (95% CI, 2.7 to 26.3 ml/yr) faster growth in FVC.

Associations between pollution and adolescent lung function differed by sex. Living closer to a roadway and $PM_{2.5}$ exposure in the prior year, since midchildhood, and lifetime were negatively associated with lung function for boys but were null among girls ($P_{interaction} < 0.05$). Among non-White participants, living closer to a road at birth was associated with lower FEV_1 in adolescence ($P_{interaction} < 0.05$). Associations did not differ by household income or asthma.

In this follow-up study, we found that lifetime $PM_{2.5}$ exposure and traffic-related pollution in adolescence were associated with lower adolescent lung function. Recent reduction in $PM_{2.5}$ exposure was also associated with more rapid lung function growth during adolescence.

Consistent with our prior findings regarding midchildhood lung function, exposures occurring closer to spirometry completion were more consistently associated with lower lung function compared with exposures in early life around the time of birth. Exposures in midchildhood had similar effect estimates as adolescent exposures, indicating a possible issue with power rather than a lack of association. In our study and the Children's Health Study in southern California, improvements in air quality were associated with greater lung function growth, suggesting at least a partial reversibility of the harmful effects of pollution and the importance of more recent exposures on adolescent lung function (3, 10). A study in the Netherlands and the Children's Health Study both revealed decrements in FEV_1 in adolescence and slower FEV_1 growth in association with greater long-term $PM_{2.5}$ exposure (5, 11, 12). Notably, these studies were conducted in areas with higher $PM_{2.5}$ concentrations than our study. Our findings suggest that respiratory health benefits of improved air quality can be realized with small changes in $PM_{2.5}$ at even lower pollution concentrations within current U.S. Environmental Protection Agency standards.

Several of the exposures in our study were associated with reduced lung function in boys, with no effect in girls. Similar effect modification for boys has been reported in other studies (3, 6), though results have been mixed and there is yet to be conclusive evidence of differing susceptibility to the detrimental effects of pollution on the basis of sex (1). There was no consistent difference in associations on the basis of race in our study.

There are several limitations to our study. Proximity to a roadway may not reflect actual pollution exposures and may incorporate nonpollution exposures such as noise and social stress. In addition, our analyses evaluating changes in lung function used only two time points for each child, and we were unable to assess trajectories in early childhood.

In conclusion, we found that more recent air pollution exposures may have a greater effect on adolescent lung function than early-life exposure, and improving air quality, even at already low air pollution concentrations, appears to be beneficial to adolescent respiratory health. ■

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Chronic Human Immunodeficiency Virus Infection Is Associated with Accelerated Decline of Forced Expiratory Volume in 1 Second among Women but Not among Men: A Longitudinal Cohort Study in Uganda

To the Editor:

People living with human immunodeficiency virus (PLWH) are at increased risk of chronic lung disease and mortality (1–3). Most studies of human immunodeficiency virus (HIV)-associated lung dysfunction are focused on PLWH in North America and Europe (1), yet two-thirds of the estimated 38 million PLWH globally reside in sub-Saharan Africa. In addition, HIV is more prevalent among men in the United States (4, 5) and Europe (6), resulting in predominantly male research cohorts, yet women comprise more than half of the global population living with HIV and incur nearly two-thirds of new HIV diagnoses in sub-Saharan Africa (7). Sex-specific differences in disease risk, severity, and outcomes have been demonstrated for many chronic lung diseases (8–10) but are not characterized for HIV-associated lung dysfunction. Therefore, we estimated the association between HIV serostatus and lung function trajectory in a longitudinal cohort of men and women with and without HIV in Uganda.

Methods

The Uganda Non-Communicable Diseases and Aging Cohort is a longitudinal, observational cohort of PLWH and age- (by decade) and sex-matched HIV-uninfected adults in southwestern Uganda. PLWH were at least 40 years of age, on antiretroviral therapy for at least 3 years, and in care at Mbarara Regional Referral Hospital's HIV clinic. HIV-uninfected participants were recruited from their homes from a census-based study in a nearby cluster of villages based on their age and sex. Sex was identified based on clinical documentation in participants' records or census tract data. Participants completed annual spirometry from 2015 through 2018. Post-bronchodilator forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were quantified (nDD Medical Technologies) per American Thoracic Society guidelines (11). Approval was obtained from Ugandan and U.S. research ethics committees, and participants provided informed consent.

We compared participant demographics by HIV serostatus and fit generalized mixed-effects linear regression models with random intercepts and slopes, and an HIV × time product term, to characterize the association between HIV serostatus and FEV_1 and FVC trajectories. We adjusted models for age, sex, height, smoking, socioeconomic status, and prior tuberculosis/pneumonia. We did not adjust models for biomass smoke exposure because nearly all study participants live in homes where biomass fuels are burned for cooking and/or heating, so there is no unexposed comparator population. We conducted preplanned analyses stratified by sex (Stata 16; StataCorp).

Results

A total of 278 (97%) participants completed 613 spirometry tests over a median of two visits (interquartile range [IQR], 1–2 visits) and 1.5 years of follow-up (IQR, 1.0–2.0 yr). Most spirometry (91%) met American Thoracic Society criteria. Among participants, 52% were PLWH, 47% were women, and median age was 52 years (IQR, 48–55 yr) (Table 1). Few (6%) had prior pulmonary tuberculosis, all of whom were PLWH and most of whom (16/17) were men. There were no substantive demographic differences between women with versus without HIV. Among PLWH, most (82%) had a CD4 (cluster of differentiation 4) ⩾ 350 cells/mm^3, and 94% had undetectable viral loads. Baseline lung function did not differ by HIV serostatus, either among the entire cohort or among women specifically.

In adjusted main effects models, FEV_1 and FVC declined by −24.4 (95% confidence interval [CI], −51.1 to 2.3; $P = 0.07$) and −34.5 (95% CI, −64.2 to −4.7; $P = 0.02$) ml/yr, respectively, neither of which differed by HIV serostatus. In sex-stratified models, women with HIV (WWH) had more accelerated FEV_1 decline than women without HIV (additional −46.3 ml/yr; 95% CI, −91.3 to −1.4; P for interaction = 0.04) (Figure 1). There was no HIV-associated difference in FEV_1 decline among men or in FVC decline among women or men (Table 2). The three-way interaction term between HIV serostatus, time, and sex was not statistically significant.

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