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Impact of Personal, Subhourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents with Asthma

Ashley L. Turner[1], Cole Brokamp[2,3], Chris Wolfe[3], Tiina Reponen[1], and Patrick H. Ryan[2,3]

[1]Department of Environmental and Public Health Sciences and [2]Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, Ohio; and [3]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

ORCID ID: 0000-0001-7741-228X (A.L.T.).

Abstract

Rationale: Ultrafine particle (UFP; particles <0.1 μm in diameter) concentrations exhibit high spatiotemporal variability; thus, individual-level exposures and health risks are difficult to estimate.

Objectives: To determine the effects of recent UFP exposures on respiratory health outcomes in children and to determine if children with asthma are at increased risk.

Methods: Personal sampling of UFPs was completed by adolescents in combination with repeated personal spirometry measurements and ecological momentary assessment of respiratory symptoms (wheeze, cough, and/or shortness of breath). We assessed the association between UFP exposures every 30 minutes up to 150 minutes before measuring forced expiratory volume in 1 second (FEV_1), peak expiratory flow, and respiratory symptoms using mixed-effects models and interaction with asthma diagnosis.

Results: Participants ($N = 105$; 43% with asthma) completed an average of 11 spirometry measurements and 16 symptom responses throughout sampling. After adjustments (maternal education, physical activity, season, and distance to nearest roadway), a 10-fold increase in UFP exposure was significantly associated with a 0.04-L decrease (95% confidence interval [CI], −0.07 to −0.001) in FEV_1 90 minutes later. Asthma status modified this association in which participants with asthma had significantly lower FEV_1 values in response to UFP exposures 30 minutes earlier than participants without asthma. We found a significant increase in the odds of reporting a respiratory symptom 30 minutes after increased UFP exposure (odds ratio, 1.8; 95% CI, 1.00 to 3.00).

Conclusions: Greater UFP exposure conferred deleterious effects on lung function and respiratory symptoms within 90 minutes of exposure and was more pronounced among participants with asthma.

Keywords: ambient particulate matter; environmental epidemiology; exposure monitoring; acute exposure; pediatric asthma

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Correspondence and requests for reprints should be addressed to Ashley L. Turner, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229. E-mail: okonal@mail.uc.edu.

This article has a data supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

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Much of the research on particulate matter (PM) exposure is devoted to fine particulate matter, whereas the health impacts of ultrafine particles (UFPs; <0.1 μm in diameter) are less understood. UFPs dominate ambient particle number concentration, accounting for up to 90% of total particle number (1) but contribute little to the mass of PM in ambient air (2). Toxicological evidence suggests that UFPs may be more toxic than larger particles because of proinflammatory properties and oxidative stress potential (3). UFPs also have increased surface area-to-mass ratios (4) and can deposit into alveolar regions of the lungs at an increased deposition rate in comparison with larger particles (5, 6). Within the lungs, UFPs can evade macrophage clearance, can cross epithelial barriers into the circulation and the central nervous system, and can be retained in airways for upward of 48 hours after exposure (6–8). Children may be at heightened risk for UFP-related health effects because deposition rates for inhaled UFPs are 50% higher for children than for adults (9). During lung development *in utero* and in childhood, UFPs can alter distal airway architecture (10) and generate oxidative DNA damage (11).

To date, epidemiologic studies examining UFPs have reported adverse associations with respiratory outcomes, including forced expiratory volume in 1 second (FEV_1) (12, 13); forced vital capacity (FVC) (13, 14); peak expiratory flow (PEF) (15); average expiratory flow of FVC between 25% and 75% ($FEF_{25–75}$) (12); current asthma (16); and wheezing (17). Studies in adults exposed to diesel exhaust particles on a busy street reported greater deficits in FEV_1 and FVC values when compared with lung function changes in low-exposure routes, and this effect was more pronounced in participants with asthma (13). In children with asthma, exposure estimates of UFPs through personal sampling showed that higher daily alveolar deposited surface area doses were significantly associated with decreases in FEV_1 and $FEF_{25–75}$ (12). Because UFPs are highly variable both spatially and temporally, measurements from central site monitors are only a surrogate for personal exposure and lack the spatial resolution to account for individual exposure variability, potentially resulting in measurement error and inaccurate health effect estimates (18).

Although new modeling techniques in exposure assessment have allowed prediction of ambient air pollution at higher spatial resolutions than central site monitoring networks, these models are limited by the available data that support them and are unable to characterize the high but short exposures that children and adults receive in specific microenvironments, during transit, or within homes (19). In contrast, personal and real-time monitoring offers the potential to characterize the contribution of short peaks in individual PM exposure at the spatiotemporal resolution required to study their health effects. Recent advances in sensor technology have resulted in UFP monitors that enable researchers to characterize variability in children's exposure across individually based microenvironments and time-varying activities (20). In this analysis, we sought to identify subhourly, personal exposure windows associated with adverse respiratory health effects. We hypothesized that acute personal exposures to elevated concentrations of UFPs are associated with subsequent decreases in lung function and increased respiratory symptoms among adolescents. In addition, we hypothesized that adolescents with asthma may be at heightened risk for adverse respiratory health outcomes associated with acute UFP exposures.

Methods

Study Population

Adolescents between the ages of 13 and 17, with and without asthma, participating in the EcoMAPPE (Ecological Momentary Assessment of Personal Particle Exposure) study were included in this analysis as previously described (21). Caregivers provided written informed consent, and adolescents gave their assent to participate. Study protocols were approved by the Cincinnati Children's Hospital Institutional Review Board (2017-1068).

Personal UFP Exposure Assessment

Participants wore personal UFP counters (PUFP C200, Enmont LLC) (20, 22) for a total of 3 hours each day for 7 consecutive days to record UFP concentrations (particles/cm^3 [p/cm^3]) at one measurement per second.

Health Outcomes

Participants recorded their own FEV_1 (L) and PEF (L/min) about five times per day using a portable spirometer (Spirobank Smart, Medical International Research). Additional training and validation protocol information of personal spirometry testing can be found in the online data supplement, Section 2.3. Ecological momentary assessment (EMA) questionnaires were administered to participants on a mobile phone (PiLR Health; https://pilrhealth.com/pilr-ema-product-features/) to ascertain the prevalence of respiratory symptoms (i.e., wheeze, cough, shortness of breath) throughout their day (yes or no).

On the basis of the time when each health outcome event occurred (i.e., lung function measurement or EMA response), we calculated 30-minute retrospective averages of UFP exposure as p/cm^3 in which at least 1 minute of UFPs was sampled. We considered UFP exposures within 150 minutes before each outcome event in our analyses based upon available data (*see* Figure E1 in the data supplement) and evidence from a similar study (13).

Covariates and Statistical Analysis

Distributions of demographic covariates and health outcomes for the entire sample and by asthma status were characterized using summary statistics. Distributions of the variability in UFP exposure between and within participants were explored using a random set of 12 participants from the original dataset. All outcome events (lung function and respiratory symptoms) for these participants were considered, and the average UFP exposure for every time window was calculated. UFP concentrations were then logarithmically transformed before analysis to ensure normality of model residuals.

Associations between mean UFP exposure within each 30-minute time window (up to 150 min) before each lung function measurement and FEV_1 and PEF were estimated using mixed-effects models with individual-specific intercepts to account for the correlation of within-individual measurements. Initial models were fitted and then adjusted for maternal education, season, distance to nearest roadway, and number of steps per day identified via a directed acyclic graph (21) (*see* the description of covariates in Section 2.4 of the data supplement). Similarly, we fitted mixed-effects logistic regression models to estimate the association between UFP exposure and the prevalence of respiratory symptoms. We also examined the confounding effect of cumulative UFP exposure over the entire 150 minutes by fitting adjusted models additionally for

cumulative exposure. We did so with the addition of a separate term for each time window model denoting the mean exposure from the time of the outcome event until 150 minutes prior, not including the exposure that occurred within the time window. We also examined the effect of the average UFP exposure over the entire 150-minute window preceding each of the lung function outcomes and respiratory symptom responses using similar mixed-effects models explained above. We then conducted a sensitivity analysis on FEV_1 and PEF adjusted models by adding a term for the time of day (A.M. and/or P.M.) in which lung function measurements were conducted because spirometry measures can fluctuate daily within persons (23). Finally, effect modification by asthma status was tested on each of the models by including an interaction term between UFP exposure and asthma status. Interaction terms that produced changes in outcome below a significance level of 0.05 were considered for further analyses in stratified models. We interpreted all regression coefficients of models as the change in FEV_1 or PEF values (L) or the presence of a respiratory symptom per 10-fold increase in personal UFP concentrations. Because exposure is on the logarithmic scale, the increment between each increase in exposure is 10 times that of the previous one.

All data analyses were conducted using R version 3.6.1 (R Foundation for Statistical Computing). For more details on our methods and statistical analysis approach, refer to the data supplement.

Results

Study Population

In total, 117 participants completed a 7-day sampling period, and of these, sampling and covariate data were available for 105 for inclusion in the analyses. The average age of participants was 15.4 years, and the majority (55.6%) were female (Table 1). Participants with caregiver-reported, physician-diagnosed asthma did not differ from participants without asthma with respect to age, sex, race, and proximity to busy roads, but they reported significantly lower household income ($P = 0.02$) and maternal education ($P < 0.01$) (Table 1). The numbers of available lung function and symptom response events were 2,464 and 3,520, respectively. The average number of outcome events per exposure window can be found in Table E2 in the data supplement.

UFP Exposure

Average UFP concentrations recorded within 30-minute windows within and between a randomly selected 10% subset of participants' exposure measurements are depicted in Figure 1. Among this subset, the range of UFP concentrations per participant varied from 3,651 p/cm^3 to 82,358 p/cm^3. UFP concentrations of adjacent time windows were significantly correlated for both lung function outcomes (Spearman correlation $\rho > 0.7$; range, 0.75–0.83) and symptom outcomes ($\rho > 0.7$; range, 0.7–0.76) (Table E1 of the online data supplement).

Lung Function

During their sampling week, participants completed an average of 11 lung function measurements and 16 EMA responses. Overall, the mean ± standard deviation (SD)

Table 1. Sample population characteristics for entire sample and by asthma status

Characteristic	All Participants ($N = 105$)	Asthma ($n = 45$)	Nonasthma ($n = 60$)	P Value
Age, yr, mean (SD)	15.5 (1.27)	15.7 (1.34)	15.3 (1.21)	0.15
Sex, *n* (%)				0.29
Female	58.0 (55.2)	28.0 (62.2)	30.0 (50.0)	
Male	47.0 (45.8)	17.0 (37.8)	30.0 (50.0)	
Race, *n* (%)				0.04*
Black	17.0 (16.2)	12.0 (26.7)	5.0 (8.33)	
Mixed	8.0 (7.62)	3.0 (6.67)	5.0 (8.33)	
White	80.0 (76.2)	30.0 (66.7)	50.0 (83.3)	
Maternal education, *n* (%)				0.007*
Less than high school, high school, some college	29.0 (27.6)	19.0 (42.2)	10.0 (16.7)	
College graduate, graduate school	76.0 (72.4)	26.0 (57.8)	50.0 (83.3)	
Distance to nearest roadway, *n* (%)				0.95
⩽400 m	8.0 (7.62)	4.0 (8.89)	4.0 (6.67)	
>400 m	97.0 (92.4)	41.0 (91.1)	56.0 (93.3)	
Season of sampling, *n* (%)				0.54
Winter	17.0 (16.2)	8.0 (17.8)	9.0 (15.0)	
Spring	22.0 (21.0)	7.0 (15.6)	15.0 (25.0)	
Summer	39.0 (37.1)	16.0 (35.6)	23.0 (38.3)	
Fall	27.0 (25.6)	14.0 (31.1)	13.0 (21.7)	
Average steps per day, mean (SD)	7,150 (2,660)	6,800 (2,630)	7,410 (2,680)	0.25
Lung function, mean (SD)				
FEV_1, L	3.51 (0.79)	3.28 (0.64)	3.65 (0.84)	<0.001*
PEF, L/min	466 (122)	449 (116)	477 (124)	<0.001*
Symptom responses, *n* (%)				<0.001*
Yes	176 (5.44)	112 (9.6)	64 (3.1)	
No	3,062 (94.6)	1,050 (90.4)	2,010 (96.9)	

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second; PEF = peak expiratory flow; SD = standard deviation.
Values are mean (SD), count (percent), and age in years. *P* values represent significant differences between asthma and non asthma groups determined by two-sample *t* test.
*$P < 0.05$.

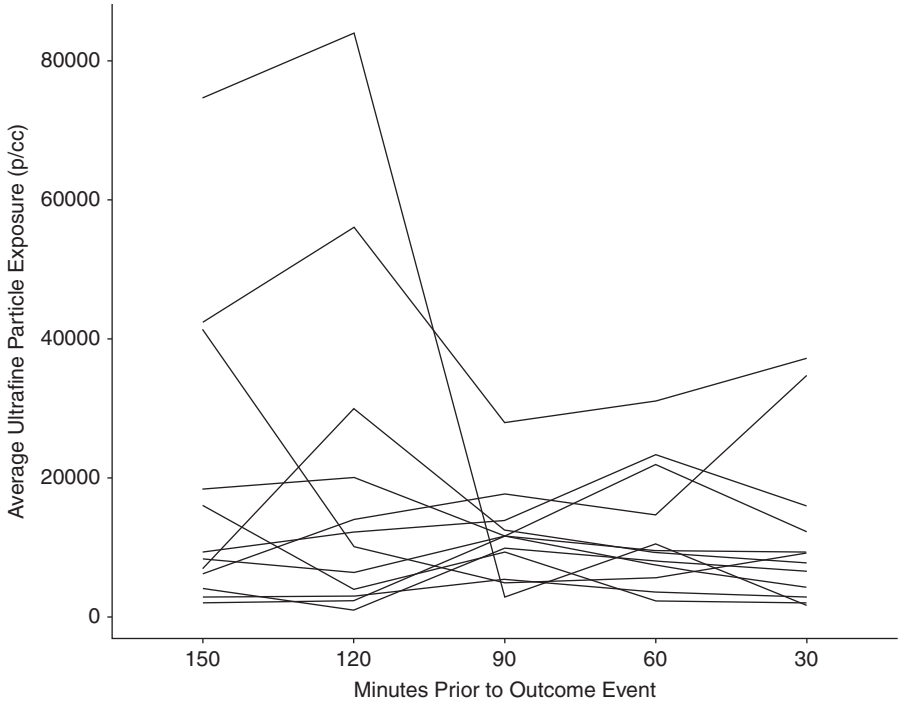

Figure 1. Distribution of the average ultrafine particle exposures (particles/cm^3) before all outcome events (i.e., lung function or symptom response) at each time window. A random sample of 12 participants is shown for simplicity, with each line representing a different participant.

FEV_1 and PEF were 3.5 ± 0.8 L and 463 ± 121 L/min, respectively, and both were lower among participants with asthma (Table 1). FEV_1 measurements recorded by the participants using the Spirobank were significantly correlated with spirometry results conducted by technicians at clinic visits ($R = 0.95$; $P < 0.001$) (*see* Figure E1 of the online data supplement), published previously (21). Roughly 30% of Spirobank tests were measured in the A.M.

Figure 2A presents the association between mean UFP exposures within 30-minute time windows 0 to 150 minutes before lung function outcomes after adjustment for covariates. Decreased FEV_1 values were significantly associated with 10-fold increases in personal UFP concentrations in the 90 minutes before the Spirobank measurement (−0.04 L; 95% confidence interval [CI], −0.07 to −0.004), and this association remained significant after adjusting for covariates (−0.04 L; 95% CI, −0.07 to −0.001). Similar negative but nonsignificant associations were observed for all other time windows. Figure 2B presents the results of the associations between UFP exposure and PEF; estimated adjusted associations between 10-fold increases in UFP exposure and PEF were mostly positive, showing a significant association at time 30 minutes (11.6 L/min; 95% CI, 0.1 to 23.1). Coefficient values and CIs for all FEV_1 and PEF models are detailed in Tables E3 and E4 of the online data supplement, respectively. Results of unadjusted models examining the effect of the average UFP exposure over the entire 150 minutes preceding the outcomes showed no significant associations for FEV_1, PEF, or respiratory symptom response events (results not shown).

We observed a significant effect modification of UFP exposure on lung function by asthma status ($P < 0.05$). As shown in Figure 3, the association between UFP exposure and FEV_1 was greater in participants with asthma at the time of the outcome (−0.02 L; 95% CI, −0.05 to 0.009), 30 minutes before (−0.03 L; 95% CI, −0.07 to 0.02), and 150 minutes before (−0.03 L; 95% CI, −0.09 to 0.009). After adjusting for the time of day when outcomes were measured (A.M. and/or P.M.), we observed no change in original effect estimates, and time of day was therefore not included in final models (*see* Table E6 of the online data supplement).

Respiratory Symptoms

The distributions of respiratory symptom responses for study participants and by asthma status are summarized in Table 1. Overall, respiratory symptoms were reported in 5.5% of the EMA responses (184 of 3,336); among participants with asthma, this frequency was 9% compared with only 3% among those without asthma ($P < 0.001$). Collectively, 45% ($n = 53$) of the 117 participants reported a respiratory symptom on at least one EMA response, with 53% of the participants with asthma reporting a symptom at least once compared with 39% of those without asthma ($P = 0.04$).

Results of mixed-effects logistic regression models are shown in Figure 4 and are detailed in Table E5 of the online data supplement. In the unadjusted model, we observed an 80% increase in the odds of reporting a symptom 30 minutes after a 10-fold increase in UFP exposure (odds ratio [OR], 1.8; 95% CI, 1.00–3.00; $P = 0.04$). The significant association with UFPs at 30 minutes was attenuated after adjustment for covariates (OR, 1.5; 95% CI, 0.89–2.6) and prior exposure (OR, 1.7; 95% CI, 0.77–3.9). A negative relationship was observed at 150 minutes in both the unadjusted and adjusted models.

We found significant effect modification between UFP exposure and symptom responses by asthma status at 0, 30, and 60 minutes before the outcome ($P < 0.05$) (Figure 5). After adjustment for covariates, asthma-specific model coefficients showed greater odds of reporting respiratory symptoms at 0, 30, and 60 minutes in participants with asthma than those without asthma. However, participants with asthma were less likely than those without asthma to report respiratory symptoms at time windows 90, 120, and 150 minutes.

Discussion

There is emerging but limited evidence that short-term exposure to UFPs has deleterious effects on respiratory health, especially among adults with asthma (13, 17, 24–26). Here, we examined lung function and respiratory symptoms associated with personal exposure to UFPs and whether children with asthma were at increased risk. To our knowledge, this is the first study to use repeated clinical measures of respiratory health among a pediatric population to study subhourly personal UFP exposure across multiple time windows and microenvironments. Our findings indicate that UFPs are associated

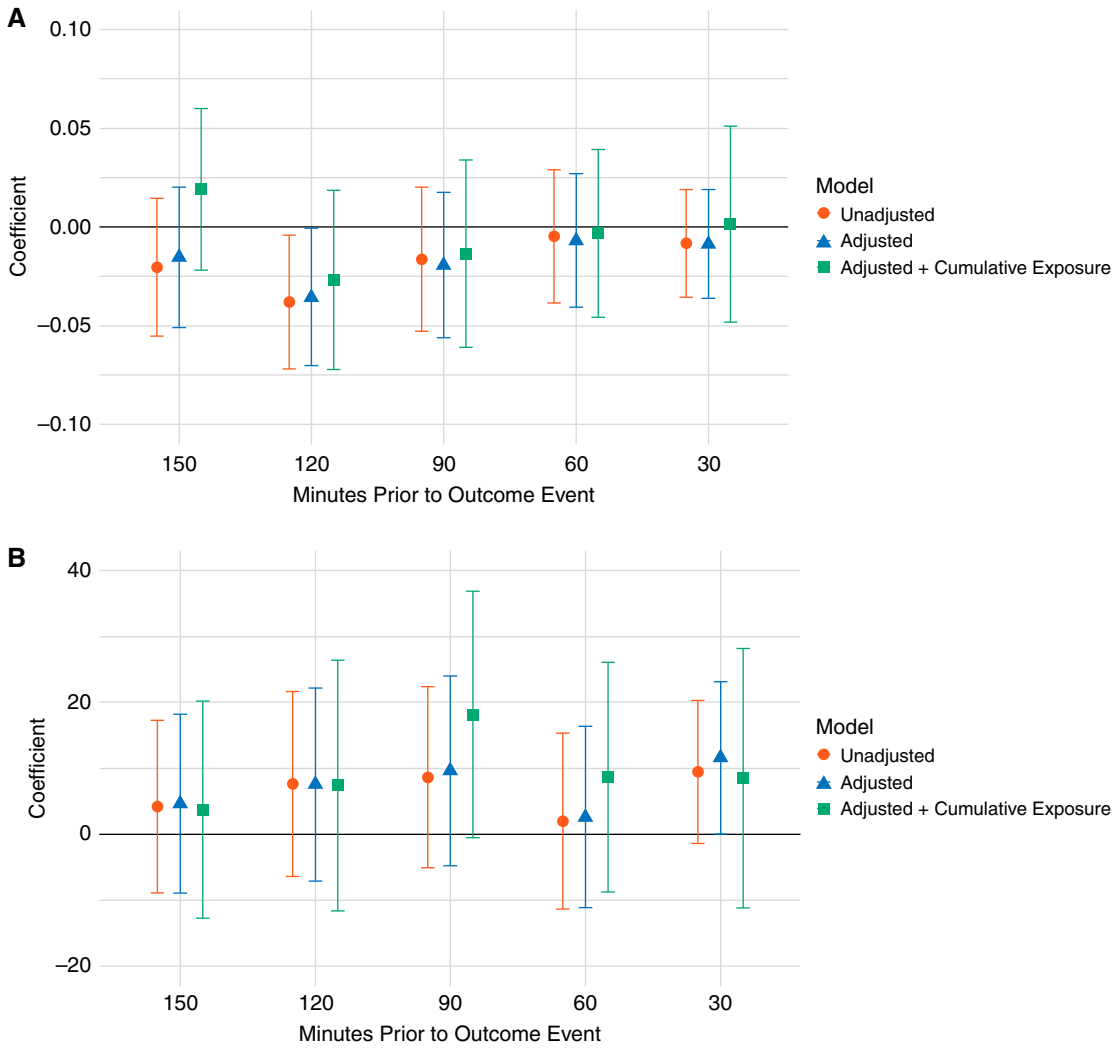

Figure 2. (*A* and *B*) Association between short-term, mean ultrafine particles (UFPs; particles/cm^3) and forced expiratory volume in 1 second (FEV_1) (L) (*A*) and peak expiratory flow (PEF) (L/min) (*B*). Each time window represents average 30-minute exposure 0–150 minutes before the outcome. Red circles represent unadjusted estimates; blue triangles represent adjusted estimates for model covariates (mother's education, season, distance to nearest roadway, and average total steps per day); and green squares represent estimates adjusted for covariates and previous UFP exposure.

with deficits in respiratory health within 60–90 minutes after exposure and that this association was more pronounced among adolescents with asthma.

The negative association we observed between FEV_1 and UFPs is consistent with several epidemiologic (12–14, 27–31) and experimental studies (25). However, the majority of prior studies characterized UFP exposure using average daily or longer time periods. Given the high temporal variation in UFPs and potential for very high but short exposures to occur near UFP sources, we examined windows of exposure at much smaller temporal resolutions. Our findings suggest that these short-term exposures, which may occur during transit periods, when near school buses, and other sources of UFPs, are associated with changes in lung function and elevated risk for respiratory symptoms. We also observed that children with asthma had greater decreases in FEV_1 after UFP exposure. This is consistent with prior studies that found children (12, 14) and adults (13, 27) with asthma are at a higher risk for UFP-associated decreases in lung function. Significant decreases in $FEF_{25–75}$ (12, 32, 33) and FEV_1/FVC ratio (34) have also been observed, suggesting future analyses of other lung function outcome measurements are warranted.

We identified a significant increase in PEF 30 minutes after an increase in UFP exposure, suggesting that a UFP exposure resulted in a protective effect. However, in one European study, increased UFP exposure 1 day before was associated with significant decreases in evening PEF ($\beta = -1.00 \pm 0.60$ L/min) (15). The same study also observed that increased exposure to particles in the size range 0.032 to 0.010 μm 2 days before was associated with significant decreases in morning PEF ($\beta = -0.97 \pm 0.58$ L/min) (35). It is possible that this outcome measurement may be more susceptible to the accumulation of UFPs over time, which would explain why we did not find any observable associations in the expected direction between exposure and PEF within the first 150 minutes.

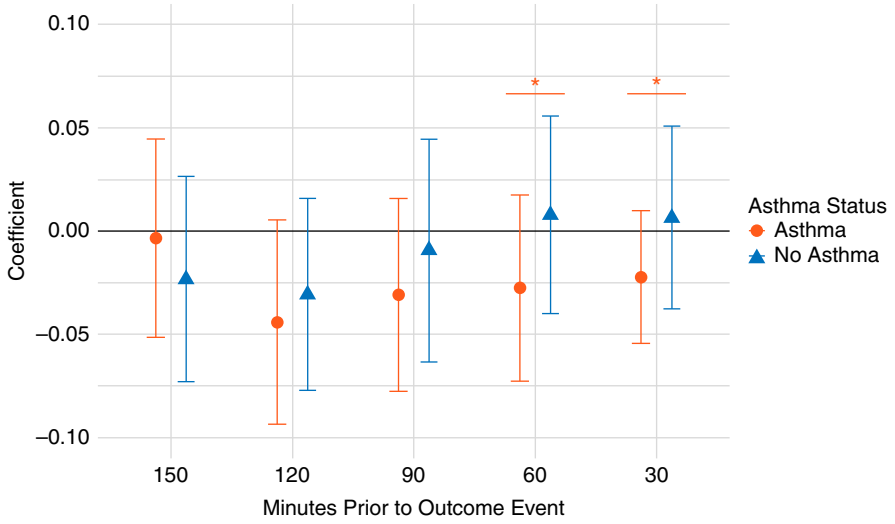

Figure 3. Effect modification of asthma status on the adjusted association between ultrafine particles (UFPs; particles/cm^3) and forced expiratory volume in 1 second (FEV_1) (L) and 95% confidence intervals. Separate models were built for asthma and nonasthma groups and adjusted for covariates. Each time window represents average 30-minute exposures 0–150 minutes before the outcome. *Significant interaction of asthma status and UFPs on outcome.

In addition, we did not see similar responses of PEF and FEV_1 to increased UFP exposure. We and others have observed only moderate correlations between FEV_1 and PEF predicted values in adults with respiratory disease (36, 37) and in a population of healthy adolescents (38), suggesting they are not equivalent in the assessment of airway obstruction and in fact may measure different aspects of lung flow. For example, PEF is a measure of large-caliber airway function (39), whereas FEV_1 mirrors functioning of peripheral small airways (40, 41). Therefore, our results make sense because UFPs tend to deposit at high efficiency in the alveolar and smaller airway regions because of their small size (42), creating acute inflammatory responses in the regions that are more indicative of changes in FEV_1.

One important strength of our study was the use of EMA to ascertain respiratory symptoms among study participants. Using this approach, we observed increased UFP exposure to be associated with elevated risk for respiratory symptoms 30 minutes later with increased likelihood of experiencing respiratory symptoms until 120 minutes after the exposure occurred. Positive associations have been shown in an Australian study in which children with atopy were 21% and 8% more likely to experience wheeze and cough, respectively, in response to increases in UFPs than students without atopy (43). However, participants' exposure in this prior study was quantified over an entire year through land-use regression models. In contrast, other studies did not observe an association between long-term exposure to UFPs and wheeze symptoms (16). Studies examining shorter-term UFP exposures generally report positive associations with respiratory symptoms. For example, in a panel study of adults with asthma in Germany, mean UFPs over the previous 5 days were positively associated with feeling ill and cough, whereas only cough remained significant after adjusting for different measures of particle exposure in different size fractions

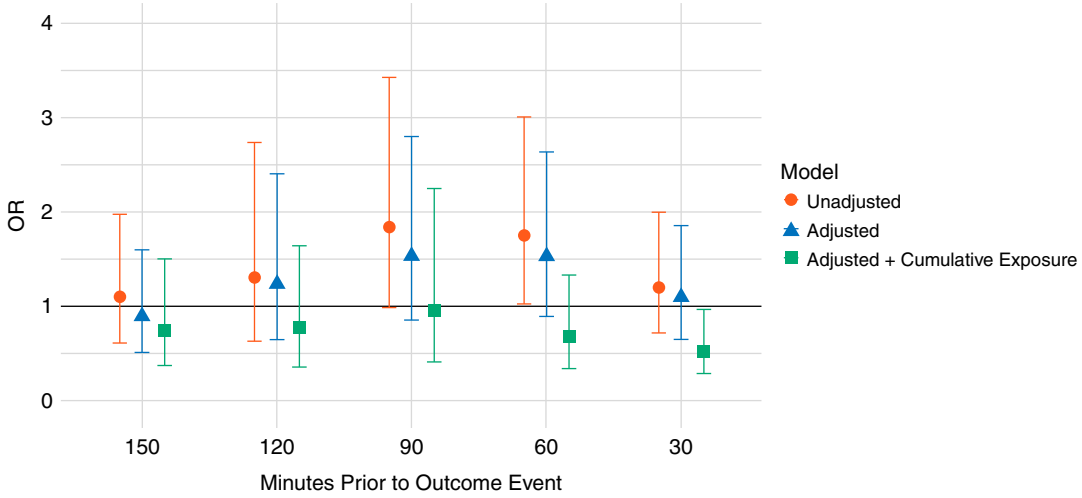

Figure 4. Mixed-effects logistic regression summary plots of association between mean ultrafine particles (UFPs; particles/cm^3) and positive symptom responses. Effects are displayed as odds ratios (ORs) and 95% confidence intervals. Each time window represents average 30-minute exposures 0–150 minutes before the outcome. Red circles represent unadjusted estimates; blue triangles represent adjusted estimates for model covariates (mother's education, season, distance to nearest roadway, and average total steps per day); and green squares represent estimates adjusted for covariates and previous exposure. The adjusted plus prior exposure model at 150 minutes was left out intentionally because of model deconstruction.

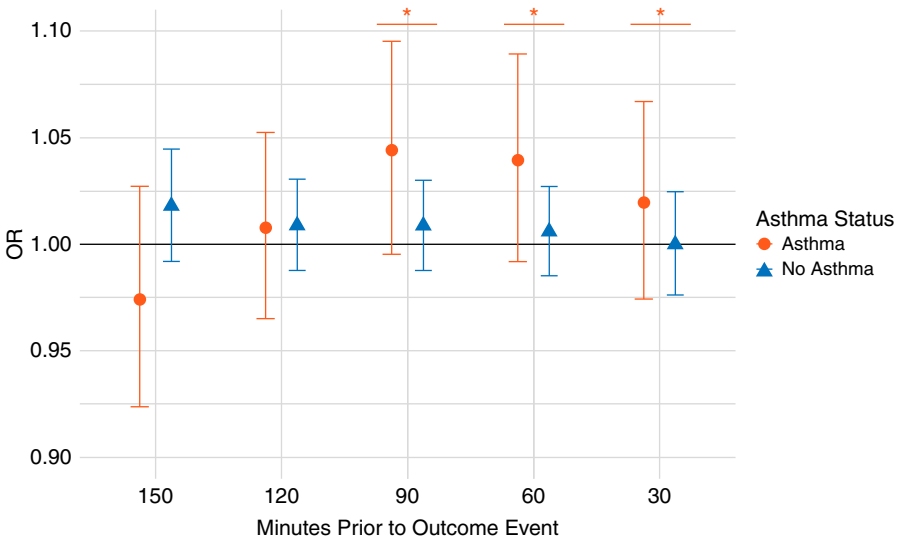

Figure 5. Effect modification of asthma status on the adjusted association between ultrafine particles (UFPs; particles/cm^3) and respiratory symptom responses. Estimates are reported as odds ratios (ORs) and 95% confidence intervals. Separate models were built for asthma and nonasthma groups and adjusted for covariates. Each time window represents average 30-minute exposures 0–150 minutes before the outcome. *Significant interaction of asthma status and UFPs on outcome.

(OR, 1.36; 95% CI, 1.10–1.67) (44). Increase in respiratory symptoms was associated with UFP exposure 1, 2, and 6 days before (45), immediately and 5 hours after exposure (13), over a 4-day average (15), and 2–4 days before the exposure in infants aged 0–1 years (17), though none of these effects were significant.

Among our participants, especially those with asthma, the risk for respiratory health effects in response to increased UFP exposure rose immediately after exposure up to 90 minutes after the exposure, then decreased. A similar trend was observed in the McCreanor and colleagues study: Participants experienced their lowest lung function values 2 hours after exposure, followed by a decrease in effects, and this effect was more pronounced in participants with asthma (13). The source of UFPs in the McCreanor and colleagues study, however, was predominantly diesel exhaust, which may differ in composition from the UFPs we measured because sampling occurred most often indoors and away from traffic sources. Similarly, in a series of randomized, double-blind experimental studies, healthy adults and adults with asthma were exposed to carbon UFPs and filtered air, followed by pulmonary function tests and symptom questionnaires (33). The authors observed greater changes from baseline FEV_1 values in participants with asthma 3.5 hours after exposure than values observed at 21 hours and 45 hours after exposure, suggesting that UFP effects occur shortly after exposure (33). One potential explanation for the trend observed in our study is the use of medication by participants with asthma with resulting improved lung function or resolution of respiratory symptoms. Prior studies have noted increased asthma medication use associated with UFP exposure, though we did not ascertain this information from EcoMAPPE study participants (46).

Strengths and Limitations

Our study had multiple strengths, including the use of personal sampling, enabling exposures to be captured across time, behavior, and location. In addition to personal sampling, our study measured health outcomes repeatedly using handheld spirometers and an EMA-based mobile application platform to log respiratory symptoms. EMA has been shown to have greater validity than traditional questionnaires (47) and to aid in reducing recall bias in assessing psychosocial risk as a predictor of cardiovascular disease progression (47). Aside from these strengths, our approach to identifying susceptible time windows of exposure is a novel contribution to understanding the health risks associated with short-term exposures to UFPs. To our knowledge, our study is the first to characterize short-term exposures during activities of daily living and to examine the effects of these on respiratory outcomes in adolescents. The combination of personal real-time sampling and time windows of exposure at smaller resolutions may be more effective at capturing acute but small deficits in health outcomes.

There are also some limitations to our study that should be considered. First, because of battery limitations in the PUFP C200, participants completed only 3 hours of personal sampling per day. Thus, the exposure assessment presented here may not capture the overall variability of daily UFP exposure. We attempted to minimize this limitation by instructing participants to wear the PUFP C200 at various times and during activities throughout the 1-week sampling period. In addition, participants of the EcoMAPPE cohort were primarily White and of higher socioeconomic status. The study population is therefore not representative of a general sample of adolescents, and health effects associated with UFP exposure may be greater among disadvantaged and minority populations, so we suggest that future larger studies be conducted in a generalizable sample. Finally, it is possible that unmeasured pollutants, including PM of $\leqslant$2.5 μm in aerodynamic diameter, may contribute to the health effects observed in our study. However, UFPs have been shown to dominate particle number concentration and are poorly correlated with PM $\leqslant$2.5 μm in aerodynamic diameter and PM $\leqslant$10 μm in aerodynamic diameter (48, 49) because of differences in distribution, seasonal variability, and source factors, suggesting our results were most likely not affected by other particulate pollutants.

In conclusion, we identified significant associations between recent UFP exposures and decreased lung

function and increased respiratory symptoms. Consistent with prior air pollution studies, the effects of UFP exposure were greater among adolescents with asthma. Although future research is needed to rule out other causative pollutants, our results suggest that relatively short but high exposures to UFPs may have deleterious respiratory effects. Given the frequency with which adolescents and others are likely to experience high exposures to UFPs, including during transit periods, walking near roads, from school buses, and other sources, research into reducing these exposures and subsequent improvements in respiratory health outcomes are warranted. ■

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References

1 Stanier CO, Khlystov AY, Pandis SN. Ambient aerosol size distributions and number concentrations measured during the Pittsburgh Air Quality Study (PAQS). *Atmos Environ* 2004;38:3275–3284.
2 Morawska L, Thomas S, Jamriska M, Johnson G. The modality of particle size distributions of environmental aerosols. *Atmos Environ* 1999;33: 4401–4411.
3 Leikauf GD, Kim S, Jang A. Mechanisms of ultrafine particle-induced respiratory health effects. *Exp Mol Med* 2020;52:329–337.
4 Oberdörster G. Pulmonary effects of inhaled ultrafine particles. *Int Arch Occup Environ Health* 2001;74:1–8.
5 Geiser M, Kreyling WG. Deposition and biokinetics of inhaled nanoparticles. *Part Fibre Toxicol* 2010;7:2.
6 Möller W, Felten K, Sommerer K, Scheuch G, Meyer G, Meyer P, *et al.* Deposition, retention, and translocation of ultrafine particles from the central airways and lung periphery. *Am J Respir Crit Care Med* 2008; 177:426–432.
7 Elder A, Gelein R, Silva V, Feikert T, Opanashuk L, Carter J, *et al.* Translocation of inhaled ultrafine manganese oxide particles to the central nervous system. *Environ Health Perspect* 2006;114:1172–1178.
8 Geiser M, Casaulta M, Kupferschmid B, Schulz H, Semmler-Behnke M, Kreyling W. The role of macrophages in the clearance of inhaled ultrafine titanium dioxide particles. *Am J Respir Cell Mol Biol* 2008;38:371–376.
9 Olvera HA, Perez D, Clague JW, Cheng Y, Li W, Amaya MA, *et al.* The effect of ventilation, age, and asthmatic condition on ultrafine particle deposition in children. *Pulm Med* 2012;2012:736290.
10 Lee D, Wallis C, Wexler AS, Schelegle ES, Van Winkle LS, Plopper CG, *et al.* Small particles disrupt postnatal airway development. *J Appl Physiol* 2010;109:1115–1124.
11 Vriens A, Nawrot TS, Saenen ND, Provost EB, Kicinski M, Lefebvre W, *et al.* Recent exposure to ultrafine particles in school children alters miR-222 expression in the extracellular fraction of saliva. *Environ Health* 2016;15:80.
12 Buonanno G, Marks GB, Morawska L. Health effects of daily airborne particle dose in children: direct association between personal dose and respiratory health effects. *Environ Pollut* 2013;180:246–250.
13 McCreanor J, Cullinan P, Nieuwenhuijsen MJ, Stewart-Evans J, Malliarou E, Jarup L, *et al.* Respiratory effects of exposure to diesel traffic in persons with asthma. *N Engl J Med* 2007;357:2348–2358.
14 Li YR, Feng LT, Chen BY, Kim H, Yi SM, Guo YL, *et al.* Association of urban particle numbers and sources with lung function among children with asthma or allergies. *Sci Total Environ* 2016;542:841–844.
15 Tiittanen P, Timonen KL, Ruuskanen J, Mirme A, Pekkanen J. Fine particulate air pollution, resuspended road dust and respiratory health among symptomatic children. *Eur Respir J* 1999;13:266–273.
16 Kim JL, Elfman L, Wieslander G, Ferm M, Torén K, Norbäck D. Respiratory health among Korean pupils in relation to home, school and outdoor environment. *J Korean Med Sci* 2011;26:166–173.
17 Andersen ZJ, Loft S, Ketzel M, Stage M, Scheike T, Hermansen MN, *et al.* Ambient air pollution triggers wheezing symptoms in infants. *Thorax* 2008;63:710–716.
18 Özkaynak H, Baxter LK, Dionisio KL, Burke J. Air pollution exposure prediction approaches used in air pollution epidemiology studies. *J Expo Sci Environ Epidemiol* 2013;23:566–572.
19 Brokamp C, Brandt EB, Ryan PH. Assessing exposure to outdoor air pollution for epidemiological studies: model-based and personal sampling strategies. *J Allergy Clin Immunol* 2019;143: 2002–2006.
20 Ryan PH, Son SY, Wolfe C, Lockey J, Brokamp C, LeMasters G. A field application of a personal sensor for ultrafine particle exposure in children. *Sci Total Environ* 2015;508:366–373.
21 Turner A, Brokamp C, Wolfe C, Reponen T, Ryan P. Personal exposure to average weekly ultrafine particles, lung function, and respiratory symptoms in asthmatic and non-asthmatic adolescents. *Environ Int* 2021;156:106740.
22 Asbach C, Schmitz A, Schmidt F, Monz C, Todea A. Intercomparison of a personal CPC and different conventional CPCs. *Aerosol Air Qual Res* 2017;17:1132–1141.
23 Medarov BI, Pavlov VA, Rossoff L. Diurnal variations in human pulmonary function. *Int J Clin Exp Med* 2008;1:267–273.
24 Evans KA, Halterman JS, Hopke PK, Fagnano M, Rich DQ. Increased ultrafine particles and carbon monoxide concentrations are associated with asthma exacerbation among urban children. *Environ Res* 2014; 129:11–19.
25 Gong H Jr, Linn WS, Clark KW, Anderson KR, Sioutas C, Alexis NE, *et al.* Exposures of healthy and asthmatic volunteers to concentrated ambient ultrafine particles in Los Angeles. *Inhal Toxicol* 2008;20: 533–545.
26 Iskandar A, Andersen ZJ, Bønnelykke K, Ellermann T, Andersen KK, Bisgaard H. Coarse and fine particles but not ultrafine particles in urban air trigger hospital admission for asthma in children. *Thorax* 2012;67: 252–257.
27 Habre R, Zhou H, Eckel SP, Enebish T, Fruin S, Bastain T, *et al.* Short-term effects of airport-associated ultrafine particle exposure on lung function and inflammation in adults with asthma. *Environ Int* 2018; 118:48–59.
28 Liu JY, Hsiao TC, Lee KY, Chuang HC, Cheng TJ, Chuang KJ. Association of ultrafine particles with cardiopulmonary health among adult subjects in the urban areas of northern Taiwan. *Sci Total Environ* 2018;627:211–215.
29 Park HY, Gilbreath S, Barakatt E. Respiratory outcomes of ultrafine particulate matter (UFPM) as a surrogate measure of near-roadway exposures among bicyclists. *Environ Health* 2017;16: 1–7.
30 Paunescu A, Casas M, Ferrero A, Pañella P, Bougas N, Beydon N, *et al.* Associations of black carbon with lung function and airway inflammation in schoolchildren. *Environ Int* 2019;131: 104984.
31 Strak M, Boogaard H, Meliefste K, Oldenwening M, Zuurbier M, Brunekreef B, *et al.* Respiratory health effects of ultrafine and fine particle exposure in cyclists. *Occup Environ Med* 2010;67: 118–124.
32 Newcomb P, Hunt A, Rast P, Cauble D, Rowe N, Li J. Acute effects of walking environment and GSTM1 variants in children with asthma. *Biol Res Nurs* 2012;14:55–64.
33 Pietropaoli AP, Frampton MW, Hyde RW, Morrow PE, Oberdorster G, Cox C, *et al.* Pulmonary function, diffusing capacity, and inflammation in healthy and asthmatic subjects exposed to ultrafine particles. *Inhal Toxicol* 2004;16:59–72.
34 Karottki DG, Bekö G, Clausen G, Madsen AM, Andersen ZJ, Massling A, *et al.* Cardiovascular and lung function in relation to outdoor and indoor exposure to fine and ultrafine particulate matter in middle-aged subjects. *Environ Int* 2014;73:372–381.
35 Pekkanen J, Timonen KL, Ruuskanen J, Reponen A, Mirme A. Effects of ultrafine and fine particles in urban air on peak expiratory flow among children with asthmatic symptoms. *Environ Res* 1997;74: 24–33.

36 Aggarwal AN, Gupta D, Jindal SK. The relationship between Fev1 and peak expiratory flow in patients with airways obstruction is poor. *Chest* 2006;130:1454–1461.
37 Llewellin P, Sawyer G, Lewis S, Cheng S, Weatherall M, Fitzharris P, *et al.* The relationship between Fev1 and Pef in the assessment of the severity of airways obstruction. *Respirology* 2002;7: 333–337.
38 Mehta B, Bhandari B, Singhal A, Mavai M, Dutt N, Raghav P. Screening asymptomatic school children for early asthma by determining airway narrowing through peak expiratory flow rate measurement. *J Educ Health Promot* 2020;9:72–72.
39 Shakeri J, Paknejad O, Moghadam KG, Taherzadeh M. Logistic regression model for prediction of airway reversibility using peak expiratory flow. *Tanaffos* 2012;11:49–54.
40 Hegewald MJ, Lefor MJ, Jensen RL, Crapo RO, Kritchevsky SB, Haggerty CL, *et al.* Peak expiratory flow Is not a quality indicator for spirometry. *Chest* 2007;131:1494–1499.
41 Usmani OS, Dhand R, Lavorini F, Price D. Why we should target small airways disease in our management of chronic obstructive pulmonary disease. *Mayo Clin Proc* 96;2021:2448–2463.
42 Oberdörster G. Pulmonary effects of inhaled ultrafine particles. *Int Arch Occup Environ Health* 2001;74:1–8.
43 Clifford S, Mazaheri M, Salimi F, Ezz WN, Yeganeh B, Low-Choy S, *et al.* Effects of exposure to ambient ultrafine particles on respiratory health and systemic inflammation in children. *Environ Int* 2018;114: 167–180.
44 Peters A, Wichmann HE, Tuch T, Heinrich J, Heyder J. Respiratory effects are associated with the number of ultrafine particles. *Am J Respir Crit Care Med* 1997;155:1376–1383.
45 Karakatsani A, Analitis A, Perifanou D, Ayres JG, Harrison RM, Kotronarou A, *et al.* Particulate matter air pollution and respiratory symptoms in individuals having either asthma or chronic obstructive pulmonary disease: a European multicentre panel study. *Environ Health* 2012;11:75.
46 von Klot S, Wölke G, Tuch T, Heinrich J, Dockery DW, Schwartz J, *et al.* Increased asthma medication use in association with ambient fine and ultrafine particles. *Eur Respir J* 2002;20:691–702.
47 Kamarck TW, Muldoon MF, Shiffman SS, Sutton-Tyrrell K. Experiences of demand and control during daily life are predictors of carotid atherosclerotic progression among healthy men. *Health Psychol* 2007; 26:324–332.
48 de Jesus AL, Rahman MM, Mazaheri M, Thompson H, Knibbs LD, Jeong C, *et al.* Ultrafine particles and PM2.5 in the air of cities around the world: are they representative of each other? *Environ Int* 2019;129: 118–135.
49 Desai U, Watson A. Associations between ultrafine particles and co-pollutant concentrations in the Tampa bay area. *J Environ Health* 2016;78:14–21.

Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in a Population of Adolescent Asthmatics

Ashley L Turner[1*], Cole Brokamp[2,3], Chris Wolfe[3], Tiina Reponen[1], Patrick H. Ryan[2,3]

ONLINE DATA SUPPLEMENT

ADDITIONAL METHODS

2.1 Study Population

Children with and without asthma participating in the Ecological Momentary Assessment of Personal Particle Exposure (EcoMAPPE) study were included in this analysis as previously described [1]. Briefly, adolescents between the ages of 13 and 17 were recruited via emails and advertisements distributed to employees of Cincinnati Children's Hospital Medical Center (CCHMC). In addition, participants in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) cohort with asthma were contacted by email and invited to enroll. We attempted to enroll one-half of the study population with asthma, (caregiver report of doctor-diagnosis). Caregivers provided written informed consent and adolescents gave their assent to participate.

2.2 Ultrafine Particle Assessment

Personal UFP exposure was measured using the Personal Ultrafine Particle Counter (PUFP C200, Enmont LLC, Cincinnati, OH USA) [2, 3], described elsewhere [1]. Participants were instructed to wear the PUFP for seven days, a total of 3 hours each day at their discretion. UFP concentrations (particles / cm^3, p/cc) were recorded at a temporal resolution of one measurement per second. On school days, participants conducted sampling before and after school hours and during transit, with the option to choose when to sample on the weekend. For participants whose sampling sessions occurred

during summer, they were asked to sample two of the seven days in the morning, two at night and two in the afternoon, with the option to sample at any time on the seventh day.

2.3 Health Outcomes

Participants monitored their lung function throughout sampling using a portable, Bluetooth-enabled spirometer (Spirobank® Smart, Medical International Research, New Berlin, WI, USA). The iSpirometry application was downloaded to smartphones to record values and initiate testing procedures. Each participant was instructed to complete at least five tests or 'events' per day. FEV_1 (liters, L) and PEF (liters/minute, L/min) raw values were recorded in the app and included in the analyses. Participants were trained on spirometer procedures and recording prior to the start of the study by a trained spirometry technician who had completed a NIOSH-approved training course. To ensure Spirobank data was valid, participants completed three trials per test and the highest of the three values was recorded and used in our analysis. Additionally, extreme outliers (> 150% or < 50% of predicted values) were excluded from analyses (12/2470). In comparing personal Spirobank measures to clinic spirometry testing, we found raw FEV_1 values were highly correlated ($r = 0.95$, see Supplemental Figure 1) and this correlation was similar for those with asthma and those without.

Participants also monitored their respiratory symptoms through the use of Ecological momentary assessment (EMA), collected on smartphones using a survey-based mobile application (PiLR Health, https://pilrhealth.com/pilr-ema-product-features/). EMA questionnaires were triggered by time of day, entry and departure from homes and

schools, and motion detected by the accelerometer sensor in the phone and included the question “Have you experienced any of the following respiratory symptoms in the previous 30 mins: wheezing, cough, and/or shortness of breath?”. The prevalence of respiratory symptoms was used in our analysis as binary outcome ‘events’ (yes/no).

Health outcome ‘events’ (i.e., personal Spirobank measures/EMA respiratory symptom responses) were collected repeatedly by participants during the sampling period. Using the time at which the outcome event occurred (i.e., lung function measurement or EMA response = time 0), we calculated the average UFP exposure [particles/cm^3 (p/cc)] every 30-minutes, up to 150 minutes before the outcome event. We considered UFP exposures within 150 minutes prior to each outcome event in our analyses based upon available data and evidence from a similar study [4]. The average UFP concentration was calculated for all 30-minute time windows of each event in which at least one minute of UFPs was sampled.

2.4 Covariates

Information on demographic characteristics including age, gender, race, and maternal education were obtained by participants through questionnaires prior to sampling.

Participants were provided Fitbit activity monitors (Fitbit, Inc., San Francisco, CA) and instructed to wear them during the entirety of their sampling session. Data was retrieved from the Fitbit web API at the conclusion of the 7-day sampling period, and the average

steps per day calculated for each participant as a measure of participants' physical activity.

In urban settings, traffic is a major contributor to various air pollutants other than, and correlated with, UFPs, which can be individually associated with respiratory health effects in humans. Therefore, to estimate the direct effect of UFP exposure coming from sources other than traffic-related (TRAP), we adjusted for distance to roadway as a surrogate to TRAP other than UFPs (e.g., NO_2, elemental carbon) that may be correlated. We used a distance of 400 m as a proxy of TRAP exposure based on previous research showing the decay of these pollutants as a function of distance from the roadway edge [5,6]. Therefore, residential locations of study participants were geocoded[7] and their proximity to the nearest primary (S1100) roadways was calculated[7] (degauss-org.github.io) and categorized as either near (≤ 400 m) or far (> 400 m) from major traffic sources.

2.5 Statistical Analysis

UFP concentrations recorded by the PUFP above 250,000 p/cc were replaced with 250,000 p/cc in order to eliminate readings outside the particle range capacity of the device. This resulted in truncation of 1% of the total dataset.

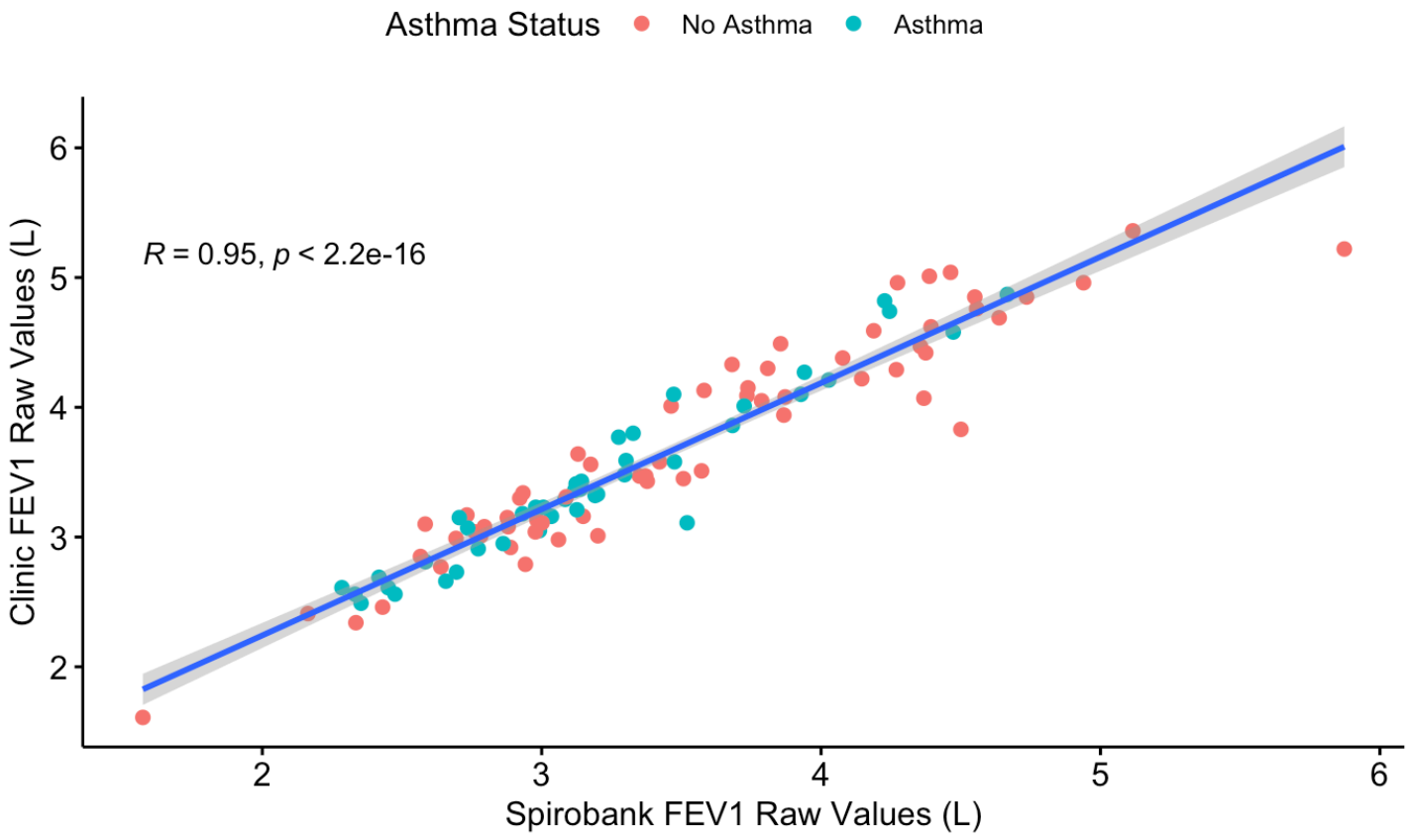
Associations between the mean UFP exposure within each 30-minute time window prior to each lung function measurement were estimated using a mixed-effects model with individual-specific intercepts to account for the correlation of within-individual

measurements. Initial models included UFP exposure and were then adjusted for maternal education (< high school, high school, and some college, or college and graduate school graduates), season (winter, spring, summer, or fall), distance to nearest roadway (near ≤ 400 m or far > 400 m), and average number of steps taken by participants per day identified via a directed acyclic graph (DAG) [1]. Similarly, we developed mixed-effects logistic regression models to estimate the association between UFP exposure and the presence / absence of respiratory symptoms as recorded by the participant using the EMA app. Effect estimates for each time window were reported as odds ratios (ORs) per 10-fold increase in mean UFP exposure.

The influence of UFP exposure during the entire 150 minutes was assessed in our final models to determine confounding by cumulative exposure on each 30-minute time window. Therefore, a 150-min mean was used to summarize the cumulative impact of UFPs by calculating the average UFP concentration over all time windows from 0 – 150 minutes and included as an additional term to adjusted models.

Effect modification by asthma status was examined for lung function and respiratory symptom models. We considered effect modification to be present if the interaction term between asthma diagnosis and UFP exposure had a corresponding p-value of < 0.05. Models in which at least one time window revealed a significant effect modification of asthma status on UFP were used to generate asthma-specific model coefficients (per

10-fold increase in UFP concentrations). All data analyses were conducted using R version 3.6.1.



Supplemental Figure E1: Correlations between clinic FEV_1 measurements and weekly average of personal Spirobank FEV_1 measurements

Supplemental Table E1: Correlation Matrix of Exposure Windows

Spirobank events					
Time Window of Exposure (mins)	30	60	90	120	150
30	-				
60	0.83*	-			
90	0.68*	0.82*	-		
120	0.44*	0.6*	0.75*	-	
150	0.31*	0.43*	0.55*	0.78*	-

EMA symptom events					
Time Window of Exposure (mins)	30	60	90	120	150
30	-				
60	0.72*	-			
90	0.48*	0.68*	-		
120	0.38*	0.51*	0.76*	-	
150	0.29*	0.39*	0.52*	0.72*	-

Spearman's correlation coefficients; * denotes $p < 0.05$

Supplemental Table E2: Sample size and available data of outcome events per 30-minute time window of UFP exposure

Time window (mins)	Lung Function events (N)	Symptom events (N)	Average available exposure data (mins)
0-30	537	894	21.1
31-60	384	641	23.7
61-90	306	478	25.2
91-120	249	344	24.4
121-150	187	229	23.9

Values represent total number of events and exposure data available for analysis for each exposure time window

Supplemental Table E3: Regression coefficients of associations between short-term UFPs and FEV_1 up to 150 minutes

Time window (mins)	β (95% CI)[1]	β (95% CI)[2]	β (95% CI)[3]
0-30	-0.008 (-0.035, 0.019)	-0.009 (-0.036, 0.019)	0.001 (-0.048, 0.051)
31-60	-0.005 (-0.038, 0.029)	-0.007 (-0.04, 0.027)	-0.003 (-0.046, 0.039)
61-90	-0.016 (-0.053, 0.02)	-0.019 (-0.056, 0.017)	-0.013 (-0.061, 0.034)
91-120	-0.038 (-0.072, -0.004)	-0.036 (-0.07, -0.001)	-0.027 (-0.072, 0.019)
121-150	-0.02 (-0.055, 0.014)	-0.015 (-0.051, 0.02)	0.019 (-0.022, 0.06)

β expressed as change in estimate per 10-fold increase in UFPs. FEV_1, forced expiratory volume in 1 s; [1]Unadjusted model; [2]Adjusted for distance to nearest roadway, average total steps per day, maternal education, and season; [3]Adjusted for covariates and cumulative average exposure up to 150 mins

Supplemental Table E4: Regression coefficients of associations between short-term UFPs and PEF up to 150 minutes

Time window (mins)	β (95% CI)[1]	β (95% CI)[2]	β (95% CI)[3]
0-30	9.5 (-1.3, 20.3)	11.6 (0.1, 23.1)	8.5 (-11.1, 28.2)
31-60	2.0 (-11.3, 15.2)	2.6 (-11.1, 16.3)	8.7 (-8.7, 26.1)
61-90	8.6 (-5.0, 22.3)	9.6 (-4.7, 24.0)	18.2 (-0.5, 36.8)
91-120	7.6 (-6.3, 21.6)	7.6 (-7.0, 22.1)	7.4 (-11.6, 26.4)
121-150	4.2 (-8.8, 17.2)	4.7 (-8.9, 18.2)	3.7 (-12.7, 20.1)

β expressed as change in estimate per 10-fold increase in UFPs. PEF, peak expiratory flow; [1]Unadjusted model; [2]Adjusted for distance to nearest roadway, average total steps per day, maternal education, and season; [3]Adjusted for covariates and cumulative average exposure up to 150 mins

Supplemental Table E5: Odds of reporting positively to EMA symptoms questionnaires

Time window (mins)	OR (95% CI)[1]	OR (95% CI)[2]	OR (95% CI)[3]
0-30	1.2 (0.72, 2.0)	1.1 (0.65, 1.9)	0.52 (0.28, 0.96)
31-60	1.8 (1.0, 3.0)	1.5 (0.89, 2.6)	0.67 (0.34, 1.3)
61-90	1.8 (0.98, 3.4)	1.5 (0.85, 2.8)	0.96 (0.41, 2.2)
91-120	1.3 (0.63, 2.7)	1.2 (0.65, 2.4)	0.77 (0.36, 1.6)
121-150	1.1 (0.61, 2.0)	0.9 (0.51, 1.6)	0.75 (0.37, 1.5)

OR expressed as change in the odds of reporting a symptom per 10-fold increase in mean UFPs; [1]Unadjusted model; [2]Adjusted for distance to nearest roadway, average total steps per day, maternal education, and season; [3]Adjusted for covariates and cumulative average exposure up to 150 mins

Supplemental Table E6: Sensitivity analysis on the effect of outcome event time period (AM/PM) on mixed-effects models

	FEV_1	
	Adjusted	Adjusted + time of day
Time window (mins)	β (95% CI)	β (95% CI)
0-30	-0.009 (-0.036, 0.019)	-0.012 (-0.039, 0.015)
31-60	-0.007 (-0.04, 0.027)	-0.007 (-0.041, 0.026)
61-90	-0.019 (-0.056, 0.017)	-0.022 (-0.059, 0.015
91-120	-0.036 (-0.07, -0.001)	-0.036 (-0.071, -0.002)
121-150	-0.015 (-0.051, 0.02)	-0.016 (-0.052, 0.019)
	PEF	
	Adjusted	Adjusted + time of day
Time window (mins)	β (95% CI)	β (95% CI)
0-30	11.6 (0.1, 23.1)	10.8 (-0.65, 22.4)
31-60	2.6 (-11.1, 16.3)	2.4 (-0.11, 16.2)
61-90	9.6 (-4.7, 24.0)	9.6 (-4.7, 24.1)
91-120	7.6 (-7.0, 22.1)	7.4 (-7.09, 22.0)
121-150	4.7 (-8.9, 18.2)	4.7 (-8.84, 18.2)
	Symptom Responses	
	Adjusted	Adjusted + time of day
Time window (mins)	OR (95% CI)	OR (95% CI)
0-30	1.1 (0.65, 1.9)	1.15
31-60	1.5 (0.89, 2.6)	1.56
61-90	1.5 (0.85, 2.8)	1.63
91-120	1.2 (0.65, 2.4)	1.23
121-150	0.9 (0.51, 1.6)	1.01

β expressed as change in estimate per 10 fold increase in UFPs (p/cc); OR, odds ratios per 10-fold increase in UFPs (p/cc); FEV_1 (L), forced expiratory volume in 1 sec; PEF (L/min), peak expiratory flow; Adjusted: distance to nearest roadway, average total steps per day, maternal education and season; Adjusted + time of day (AM/PM): distance to nearest roadway, average total steps per day, maternal education, season, and time period outcome event was measured (AM/PM).

REFERENCES (ONLINE DATA SUPPLEMENT)

1. Turner, A., Brokamp, C., Wolfe, C., Reponen, T., Ryan, P. (2021). Personal exposure to average weekly ultrafine particles, lung function, and respiratory symptoms in asthmatic and non-asthmatic adolescents. *Environment International, 156, 106740.*
2. Asbach, C., Schmitz, A., Schmidt, F., Monz, C., & Todea, A. (2017). Intercomparison of a personal CPC and different conventional CPCs. *Aerosol and Air Quality Research, 17*, 1132-1141.
3. Ryan, P. H., Son, S. Y., Wolfe, C., Lockey, J., Brokamp, C., & LeMasters, G. (2015). A field application of a personal sensor for ultrafine particle exposure in children. *Science of the Total Environment, 508*, 366-373. doi:https://doi.org/10.1016/j.scitotenv.2014.11.061
4. McCreanor, J., Cullinan, P., Nieuwenhuijsen, M. J., Stewart-Evans, J., Malliarou, E., Jarup, L., et al. (2007). Respiratory effects of exposure to diesel traffic in persons with asthma. *The New England Journal of Medicine, 357*(23), 2348-2358.
5. Reponen, Tiina, Sergey A. Grinshpun, Saulius Trakumas, Dainius Martuzevicius, Zhong-Min Wang, Grace Lemasters, James E. Lockey, and Pratim Biswas. "Concentration Gradient Patterns of Aerosol Particles near Interstate Highways in the Greater Cincinnati Airshed." *Journal of Environmental Monitoring* 5, no. 4 (2003-01-01 2003): 557. https://doi.org/10.1039/b303557c.
6. Karner, A. A., D. S. Eisinger, and D. A. Niemeier. "Near-Roadway Air Quality: Synthesizing the Findings from Real-World Data." [In eng]. *Environ Sci Technol* 44, no. 14 (Jul 15 2010): 5334-44. https://doi.org/10.1021/es100008x.
7. Brokamp, C., C. Wolfe, T. Lingren, J. Harley, and P. Ryan. "Decentralized and Reproducible Geocoding and Characterization of Community and Environmental Exposures for Multisite Studies." [In eng]. *J Am Med Inform Assoc* 25, no. 3 (Mar 1 2018): 309-14. https://doi.org/10.1093/jamia/ocx128.

ICMJE DISCLOSURE FORM

Date: 3/14/2022
Your Name: Patrick Ryan
Manuscript Title: Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents With Asthma
Manuscript number (if known): White-202108-947OC.R2

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13	Other financial or non-financial interests	_X___None	

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Date: 3/14/2022
Your Name: Ashley L Turner, Ph.D
Manuscript Title: Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents With Asthma
Manuscript number (if known): White-202108-947OC.R2

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ICMJE DISCLOSURE FORM

Date: 3/14/2022
Your Name:____Cole Brokamp_____
Manuscript Title: Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents With Asthma
Manuscript number (if known): White-202108-947OC.R2

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Date: 3/16/2022
Your Name: Christopher Lee Wolfe
Manuscript Title: Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents With Asthma
Manuscript number (if known): White-202108-947OC.R2

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Date: 3/14/2022
Your Name:_____Tiina Reponen_____
Manuscript Title: Impact of Personal, Sub-hourly Exposure to Ultrafine Particles on Respiratory Health in Adolescents With Asthma
Manuscript number (if known): White-202108-947OC.R2

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