Agricultural Burning Smoke Exposure and Health Effects Assessment in Eastern Washington

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Introduction

The prescribed burning of vegetation and crop residue under controlled conditions is a common agricultural practice in the United States (United States Environmental Protection Agency 2012), and has been shown to be capable of producing significant quantities of air pollutants including respirable particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) (Naeher et al., 2007). However, the health effects of agricultural field burning smoke exposure have been less extensively studied in comparison to other anthropogenic air pollutants such as fossil fuel combustion (Grigg 2002). This may partly be due to the relatively brief and intermittent nature of air pollution excursions in the setting of a sparser air quality monitoring infrastructure where agricultural field burning typically takes place (Wu et al., 2006). Nevertheless, there is an increasing body of evidence documenting its negative impacts on air quality (Cheng et al., 2009; Kakareka & Kukharchyk 2003; Oppenheimer et al., 2004; Radzi bin Abas et al., 2004).

It has been well established that children, the elderly, and individuals with pre-existing cardiopulmonary conditions have increased susceptibility to the effects ambient air pollution (Sacks et al., 2011). Given the relatively high prevalence of asthma in the general population (Centers for Disease Control 2010), the impacts of ambient air pollution on asthma has been extensively studied. Indeed, previous epidemiologic studies have demonstrated significant associations between exposure to biomass smoke, whether derived from agricultural field burning (Arbex et al., 2007; Cancado et al., 2006; Golshan et al., 2002; Long et al., 1998), wildfires (Johnston et al., 2007; Sutherland et al., 2005), or residential wood burning (Larson & Koenig 1994), and increased asthma morbidity (e.g. reporting of asthma related symptoms, medication use, emergency department visits, and hospitalizations). Limited data from controlled

exposure studies in humans have implicated several mediators of inflammation (Barregard et al., 2006; Sallsten et al., 2006) and oxidative stress (Sehlstedt et al., 2010). To that end, Koenig et al. (Koenig et al., 2003) reported small but significant associations between ambient $PM_{2.5}$ exposure and increases in nitric oxide concentrations in exhaled breath (FeNO), which is being used with increasing frequency in both research and clinical practice as a marker of lower airways inflammation (Dweik et al., 2011). Similarly, ambient $PM_{2.5}$ exposure has been associated with decrements in spirometric measures of lower airways patency [forced expiratory volume in 1 second (FEV_1) and forced expiratory flow 25-75% (FEF_{25-75})] in a cohort of children living in a wood smoke impacted area (Allen et al., 2008). Concurrent use of an anti-inflammatory medication modified the effects of ambient $PM_{2.5}$ exposure on health outcomes in these studies and others (Delfino et al., 2002). Finally, most epidemiologic studies have focused on exposure metrics averaged over a 24 hour period. However, there are limited data to support the rationale for this averaging time, and utilizing hourly peak measures may actually be a more realistic and informative way of understanding the health effects of air pollutants (Delfino et al., 1998).

The overall goal of the present study was to investigate the health effects of agricultural field burning smoke exposure among adults with intermittent to moderate persistent asthma. We hypothesized that increases in peak 1-hour central monitoring site $PM_{2.5}$ concentrations over the previous 24 hours would be positively associated with FeNO and negatively associated with FEV_1 and FEF_{25-75}. We further hypothesized that use of an asthma controller medication would modify these relationships by exerting a protective effect and attenuating the magnitude of these associations.

Methods

Study design and setting. The data utilized in the present analysis were collected as part of a longitudinal study characterizing air quality and personal exposure assessment conducted during the fall 2002 agricultural field burning season (9/3/02 – 11/1/02) in Pullman, Washington (Jimenez et al., 2006; Wu et al., 2006). Pullman was selected due to its relatively large population (approximately 25,000) among eastern Washington and northern Idaho cities impacted by agricultural field burning activities. These exposure data were linked to repeated measures of FeNO, FEV_1, and FEF_{25-75} obtained from 32 healthy non-smoking adults diagnosed with intermittent to moderate persistent asthma living and working in the area.

Subjects were equally randomized to start one of two concurrent 30-day monitoring sessions. Those in the "active" session underwent scheduled thrice weekly (Monday, Wednesday, and Friday) health outcomes assessments and were also called in during study-declared agricultural field burning episodes. Subjects in the "on-call" session only underwent health outcomes assessments during study-declared burning episodes. At the end of the first 30-day monitoring session, all subjects immediately crossed over to the alternate assignment to complete a second 30-day monitoring session.

Subjects. Thirty two healthy non-smoking adults 18 years of age and older living in non-smoking residences diagnosed with intermittent to moderate persistent asthma were enrolled. Exclusion criteria included a baseline FEV_1 less than 70% predicted, maintenance systemic corticosteroid requirement, and any of the following within 30 days prior to study enrollment: signs or symptoms of an acute upper or lower respiratory tract infection, increased use of asthma controller and/or rescue medications, or any systemic corticosteroid use. This study was approved by the Institutional Review Boards at the University of Washington and Washington State University.

Exposure assessment. Detailed methodology has been previously described (Jimenez et al., 2006). Briefly, air pollutant concentrations were measured at a central rooftop monitoring site (approximately 12 meters above street level) at the Washington State University campus (average elevation approximately 768 meters above sea level). $PM_{2.5}$ and PM_{10} concentrations were measured using a tapered element oscillating microbalance (TEOM) monitor (Series 1400a; Rupprecht & Patashnick Company, Inc.; Albany, NY) in 30-minute averages. $PM_{2.5}$ concentrations were also determined using a light scattering nephelometer (M903; Radiance Research; Seattle, WA) in 10-minute averages. Integrated 12-hour $PM_{2.5}$ samples (08:00 – 20:00 and 20:00 – 08:00) from three co-located single-stage 10 L/min Harvard Impactors (Air Diagnostics, Inc.; Naples, ME) were also obtained. The nephelometer was then calibrated against the Harvard Impactor measurements. TEOM $PM_{2.5}$ data were not available from 9/28/02 through 10/17/02 due to equipment malfunction. Due to the substantial amount of missing consecutive data, only nephelometer measurements (and therefore only $PM_{2.5}$ concentrations) were used in the present analyses. Temperature and relative humidity were measured with a small weather monitoring station (WeatherLink; Davis Instruments Corp.; Hayward, CA) in 30-minute averages.

Additional exposure measurements were utilized for sensitivity analyses. In-lab ambient NO concentrations were measured with a nitric oxide analyzer (NOA 280i; Sievers; Boulder, CO). Home indoor $PM_{2.5}$ concentrations were measured using the Radiance Research nephelometer or a personal aerosol monitor (personal DataRAM; Thermo-Andersen; Smyrna, GA). Personal exposure to agricultural burning-related $PM_{2.5}$ concentrations (E_b) was estimated using subjects' self-reported time-activity information and particle infiltration efficiency from central site to home indoor environments as previously described (Wu et al., 2006). Teflon filters

from one of the three Harvard Impactors were analyzed for levoglucosan (LG) concentrations via gas chromatography/mass spectrometry as previously described (Simpson et al., 2004) as a more specific marker of wood smoke.

Declaration of agricultural field burning episodes. For the secondary analyses, agricultural field burning episodes were crudely defined based on a combination of criteria including: direct observations of vegetative smoke plumes not upwind of the central monitoring site by the study team, regional burn calls from the Washington State Department of Ecology or Idaho Department of Environmental Quality, and/or when three or more 30-minute average TEOM $PM_{2.5}$ concentrations at the central monitoring site exceeded 40 $\mu g/m^3$ during any 24-hour period. The 40 $\mu g/m^3$ threshold was selected *a priori* based on previous work investigating agricultural field burning practices in this area (Jimenez et al., 2006). A "sham" burning episode blinded to subjects was also declared to allow assessment of the impacts of burn declarations on health outcomes independent of the environmental exposures of interest.

Health outcomes assessment. Testing was performed according to current American Thoracic Society guidelines (American Thoracic Society 1995) at the same time of day for each subject throughout the study. In addition to scheduled thrice weekly assessments for subjects in the "active" monitoring group, subjects in both monitoring groups ("active" and "on-call") were called in for three consecutive daily assessments at the start of each declared burning episode whenever possible. Online measurements of FeNO were obtained with the Sievers nitric oxide analyzer. Forced vital capacity (FVC), FEV_1, and FEF_{25-75} were subsequently measured with a portable spirometer (MicroDL; Micro Direct, Inc.; Lewiston, ME).

Statistical analysis. Prior to the study, repeated simulations (1000 iterations) determined that 32 participants would allow for 96% power to detect a 2 mL/μg/m^3 change in FEV_1 with a 50 μg/m^3 increase in $PM_{2.5}$ concentrations assuming a base probability of an agricultural field burning event of 0.1.

For the primary analyses, the marginal model was used to estimate the effect of peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours (X_{it}) on population average measures of FeNO, FEV_1, or FEF_{25-75} (Y_{it}). The marginal model specifies the basic form

$$E(Y_{it} \mid X_{it}) = \beta^0 + \beta^M \cdot X_{it}$$

or the expected value of Y_{it} as a function of X_{it} for subject *i* on day *t*. The marginal parameter β^M represents the estimated difference in mean FeNO, FEV_1, or FEF_{25-75} for two groups differing by a 1 μg/m^3 difference in $PM_{2.5}$. Age, gender, asthma severity, use of an asthma controller medication, body mass index (BMI), visit type, day of health assessment, temperature, relative humidity, and an interaction term between $PM_{2.5}$ concentrations and medication use were included in the model to increase precision. The parameters in the model were estimated using generalized estimating equations with *a priori* assumptions of a Gaussian family, identity link function, and an exchangeable working correlation matrix structure. Robust standard errors are reported.

For the secondary analyses, the same models were used to estimate differences in average FeNO, FEV_1, and FEF_{25-75} between burning versus non-burning episodes. To assess for confounding by burn declaration, these analyses were repeated after stratification within declaration status.

Several sensitivity analyses were performed. In an effort to identify individuals with greater detectable effects from agricultural field burning exposure, the primary analyses were repeated excluding subjects with a baseline FeNO greater than 100 ppb. In a separate set of analyses, in-lab ambient NO concentrations were accounted for by subtracting the value from the subject's FeNO. Ambient NO measurements were excluded if values were missing or exceeded the subject's FeNO. A final set of sensitivity analyses were carried out with more specific and proximate exposure metrics including average indoor $PM_{2.5}$ concentrations over the previous 12 hours, personal E_b concentrations over the previous 12 hours, and average central site LG concentrations over the previous 12 hours.

Descriptive statistics were used for baseline subject characteristics and time-varying data. All analyses were performed using Stata version 10.1 (StataCorp LP; College Station, TX).

Results

Twenty one of the 32 subjects were not on an asthma controller medication during the study. Demographic and baseline clinical characteristics of the two groups were comparable with the exception of the distribution of asthma severity; a greater proportion of subjects not on an asthma controller medication were diagnosed with intermittent asthma, consistent with general treatment guidelines (Table 1). Two of the 11 subjects on an asthma controller medication did not have an inhaled corticosteroid as part of their maintenance regimen. Three subjects in each group had a baseline FeNO greater than 100 ppb. Four agricultural field burning episodes occurred during the study period, two of which were retrospectively identified during data analysis and therefore not declared (Table 2).

Peak 1-hour central site $PM_{2.5}$ concentrations during the study ranged between 4.9 and 42.6 $\mu g/m^3$ (mean ± SD: 23.0 ± 9.0 $\mu g/m^3$). Concentrations of each of the exposure metrics on average tended to be higher during burning episodes compared to non-burning episodes (Table 3). There were no substantial differences in exposures between subjects taking and not taking an asthma controller medication. Out of 595 subject-days, 594 FeNO, 590 FEV_1, and 590 FEF_{25-75} measurements were obtained during the study period after excluding missing or technically unacceptable data. In contrast to exposure metrics, health outcomes measurements generally remained stable across burning and non-burning episodes.

For the primary analyses, there was no significant effect of a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours on FeNO, FEV_1, or FEF_{25-75} (Table 4). There was no evidence of a significant interaction between $PM_{2.5}$ concentrations and use of an asthma controller medication when evaluating FeNO (p=0.766), FEV_1 (p=0.482) or FEF_{25-75} (p=0.136). Nevertheless, contrary to our original hypothesis, the point estimates suggested that medication use was not protective with slightly greater increases in FeNO and slightly greater decreases in FEV_1 and FEF_{25-75} compared to measurements obtained from non-medication users.

For the secondary analyses, FeNO measurements on average were higher during burning compared to non-burning episodes, though this difference did not reach statistical significance (Table 5). FEV_1 and FEF_{25-75} measurements on average were unexpectedly higher during burning versus non-burning episodes, though again this difference was not statistically significant. When stratified within declaration status, average FEV_1 and FEF_{25-75} values were significantly higher during burning episodes that were not declared during the study (i.e. retrospectively identified during data analysis) compared to non-burning episodes.

For the sensitivity analyses, excluding subjects with a baseline FeNO greater than 100 ppb (Table 6) or accounting for in-lab ambient NO concentrations (Table 7) resulted in similarly null associations. Though analysis with indoor $PM_{2.5}$ (Table 8) and personal E_b (Table 9) also did not result in any significant associations, the potentially protective effects of an asthma controller medication on spirometric measures, but not FeNO, became apparent when utilizing these more refined and proximate exposure metrics. Finally, there were non-hypothesized increases in FEV_1 with a 1 $\mu g/m^3$ increase in LG concentrations (Table 10) but no significant associations with FeNO or FEF_{25-75}.

Discussion

In this cohort of healthy adults with intermittent to moderate persistent asthma, we did not find a significant effect of a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours on FeNO, an exhaled breath marker of lower airways inflammation. Our results slightly differ from findings reported by Koenig et al., who examined associations between central site $PM_{2.5}$ concentrations and FeNO measurements obtained during two 10-day monitoring sessions during a single winter/spring season from a cohort of 19 school-aged children with asthma (Koenig et al., 2003). Though the range of exposures in the Seattle study were modestly lower than those encountered in the present study, the investigators detected a comparably small but significant association between $PM_{2.5}$ exposure and FeNO among children specifically not on inhaled corticosteroid therapy. This discrepancy may be due to chance or to physicochemical differences in the ambient exposures as it relates to the geographic settings of the two studies (i.e. urban versus rural), intrinsic differences between the adult and pediatric subjects studied (e.g. age, presence of atopy or intercurrent viral respiratory infection), or differences in the distribution of asthma severity and level of control.

Nitric oxide is formed from the oxidation of L-arginine by nitric oxide synthase (Moncada & Higgs 1993), and has multiple functions influencing vascular and airway smooth muscle tone, inflammation, and innate immunity in the lung (Dweik et al., 2001). Though FeNO is a sensitive measure of lower airways inflammation, measured levels can be influenced by a number of factors including acute infections with respiratory syncytial virus (Gadish et al., 2010) or atopy (Payne 2003). Furthermore, FeNO is closely correlated with eosinophilic airway inflammation when analyzing sputum (Jatakanon et al., 1998) and bronchial biopsy (Payne et al., 2001) samples from asthmatics. However, controlled exposure to wood smoke has been shown to elicit a predominantly neutrophilic airway inflammatory response in humans (Ghio et al., 2012) and could explain the null associations we found between $PM_{2.5}$ exposure and FeNO in the present study. Future studies utilizing outcome measures focusing on neutrophilic inflammation in the airways are warranted to more precisely define the health effects of agricultural field burning.

We also did not find a significant effect of a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours on FEV_1 and FEF_{25-75}, both spirometric measures of airflow obstruction. These results generally agree with the point estimates (which also did not achieve statistical significance) reported by Allen et al., who analyzed spirometric data obtained from the same pediatric cohort studied by Koenig et al. (Allen et al., 2008), and those reported by Slaughter et al. (Slaughter et al., 2004), who analyzed differences in FEV_1 in relation to $PM_{3.5}$ exposures during an 8-hour shift among firefighters engaged in prescribed forest burns. While the present study lacked the precision to confirm a true decrement in our spirometric measures of lung function with exposure to agricultural field burning related $PM_{2.5}$, the bounds of the confidence intervals suggest that any true effects on FEV_1 and FEF_{25-75} are

likely modest at best. Whether these changes actually equate to clinically meaningful changes in spirometry remains unclear. In asthma clinical research trials, the minimal patient perceivable improvement value in FEV_1 was approximately 200 mL (Santanello et al., 1999). To our knowledge, there are no published studies evaluating minimal clinically important differences in FEV_1 related to agricultural or other biomass burning smoke exposure.

Contrary to our original hypothesis, use of an asthma controller medication did not significantly modify the relationship between $PM_{2.5}$ associated with agricultural field burning and lung function. Furthermore, we found conflicting evidence of its presumably protective effects. In our primary analyses, we found slightly larger increases in FeNO and slightly larger decreases in FEV_1 and FEF_{25-75} among controller medication users (Table 4). In contrast, the protective effects only became evident in sensitivity analyses utilizing indoor $PM_{2.5}$ and personal E_b concentrations (Tables 8 and 9). One possibility is that these specific and proximate assessments more accurately represent actual exposures compared to measurements obtained at centrally located monitoring sites (Wu et al., 2006). Future studies to further validate these sensitive measures are warranted.

The generalizability of our findings is limited by the exclusion of healthy controls and subjects with severe asthma. Indeed, it has become increasingly evident that there is substantial heterogeneity among asthma phenotypes (Nair et al., 2012). The retrospective nature of the present analysis however, prevented us from collecting additional phenotypic data for the subjects such as quantitative assays of the sputum to characterize the nature of airway inflammation, skin prick testing to assess for atopy, or obtaining additional historical elements such as occupational history and clinical responsiveness to corticosteroids. Practical limitations precluded concurrent intensive health outcomes assessments for all of the subjects for the

duration of the study. We have attempted to overcome this limitation with the randomly ordered "active" and "on-call" monitoring sessions. This limitation also required us to rely on a relatively crude index of defining an agricultural field burning event, as evidenced by two burning episodes retrospectively identified during data analysis. We included a "sham" burning episode to partially address this and to allow us to control for changes in health outcome measures not specifically related to agricultural field burning smoke exposure. Separate source apportionment analyses conducted by our group also indicate that the contribution of airborne soil to ambient $PM_{2.5}$ concentrations observed in this study was comparable to that by vegetative field burning (Jimenez et al., 2006). This in turn motivated sensitivity analyses utilizing alternative exposure metrics such as indoor $PM_{2.5}$, personal E_b, and LG concentrations. Though these more specific and proximate measures of agricultural field burning did not substantially alter the original point estimates, we did not have sufficient statistical power to exclude potentially subclinical effects.

Conclusion

At the observed range of exposures, episodic short-term exposure to $PM_{2.5}$ related to agricultural field burning does not exert detectable changes in exhaled breath measures of airway inflammation or spirometric measures of airflow obstruction among healthy adults with intermittent to moderate persistent asthma.

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Table 1. Subject characteristics

	Not on asthma controller (n=21)	On asthma controller (n=11)
Age, years		
Mean ± SD	27.1 ± 8.3	28.6 ± 10.8
Range	18 - 47	18 - 52
Caucasian, n (%)	19 (90)	10 (100)*
Men, n (%)	7 (33)	4 (36)
Asthma severity, n (%)		
Intermittent	11 (52)	1 (9)
Mild persistent	7 (33)	7 (64)
Moderate persistent	3 (14)	3 (27)
Type of controller medication, n (%)		
ICS only	-	5 (45)
ICS and LTRA	-	1 (9)
ICS+LABA only	-	2 (18)
ICS+LABA and LTRA	-	1 (9)
LTRA only	-	2 (18)
BMI, kg/m^2		
Mean ± SD	27.4 ± 7.9	28.3 ± 8.1
Range	18 - 55	19 - 44
FeNO, ppb		
Median (IQR)	35 (32, 64)†	52 (20, 122)$^{\#}$
Range	16 - 229†	10 - 196$^{\#}$
FVC, % predicted		
Mean ± SD	97 ± 8.1	103 ± 14.0
Range	80 - 115	73 - 121
FEV_1, % predicted		
Mean ± SD	93 ± 9.6	97 ± 12.7
Range	72 - 117	75 - 119
FEV_1/FVC ratio		
Mean ± SD	0.81 ± 0.075	0.80 ± 0.066
Range	0.67 - 0.95	0.70 - 0.92
FEF_{25-75}, % predicted		
Mean ± SD	84 ± 24.5	86 ± 23.7
Range	47 - 138	58 - 122

Data for: *n=10; †n=20; $^{\#}$n=9 subjects

ICS: inhaled corticosteroid; LTRA: leukotriene receptor antagonist; LABA: long acting β-agonist

Table 2. Summary of agricultural field burning episodes

Start date	Stop date	Burning episode?	Declared episode?
9/11/02	9/15/02	Yes	Yes
9/25/02	9/26/02	Yes*	No*
10/9/02	10/11/02	No†	Yes†
10/17/02	10/19/02	Yes	Yes
10/24/02	10/26/02	Yes*	No*

*Burning episodes retrospectively identified during data analysis
†Sham episode

Table 3. Summary statistics for exposure metrics and health outcomes

	Overall		Burning*		Non-burning†	
	Obs.	**Mean ± SD**	**Obs.**	**Mean ± SD**	**Obs.**	**Mean ± SD**
Not on asthma controller						
Peak 1-hour central site $PM_{2.5}$ over the previous 24 hours ($\mu g/m^3$)	381	23.2 ± 8.9	145	27.1 ± 6.8	236	20.8 ± 9.3
Average indoor $PM_{2.5}$ over the previous 12 hours ($\mu g/m^3$)	214	17.5 ± 18.8	65	27.1 ± 25.3	149	13.2 ± 13.1
Average personal E_b over the previous 12 hours ($\mu g/m^3$)	244	3.0 ± 2.6	101	4.1 ± 3.1	143	2.2 ± 1.7
Average central site LG over the previous 12 hours ($\mu g/m^3$)	363	0.08 ± 0.09	132	0.10 ± 0.11	231	0.07 ± 0.07
FeNO (ppb)	388	58.2 ± 73.3	145	56.9 ± 67.7	243	59.0 ± 76.6
FEV_1 (mL)	387	3377 ± 745	144	3350 ± 725	243	3392 ± 758
FEF_{25-75} (mL/s)	387	3000 ± 854	144	2925 ± 805	243	3045 ± 881
On asthma controller						
Peak 1-hour central site $PM_{2.5}$ over the previous 24 hours ($\mu g/m^3$)	200	22.7 ± 9.1	80	27.0 ± 7.1	120	19.9 ± 9.2
Average indoor $PM_{2.5}$ over the previous 12 hours ($\mu g/m^3$)	137	17.4 ± 15.3	46	22.3 ± 14.8	91	15.0 ± 15.1
Average personal E_b over the previous 12 hours ($\mu g/m^3$)	133	3.3 ± 3.7	53	5.3 ± 4.8	80	1.9 ± 1.7
Average central site LG over the previous 12 hours ($\mu g/m^3$)	187	0.08 ± 0.09	67	0.11 ± 0.11	120	0.06 ± 0.07
FeNO (ppb)	206	49.4 ± 36.7	80	53.1 ± 40.6	126	47.1 ± 34.0
FEV_1 (mL)	203	3529 ± 1030	80	3586 ± 1062	123	3491 ± 1011
FEF_{25-75} (mL/s)	203	3142 ± 1285	80	3243 ± 1335	123	3076 ± 1252

*Includes burning episodes retrospectively identified during data analysis

†Includes sham episode

Table 4. Associations between peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours and FeNO, FEV_1, and FEF_{25-75}*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	0.68	-2.64, 4.01
Not on controller	0.49	-3.56, 4.55
On controller	1.04	-2.04, 4.13
FEV_1 (mL)		
All subjects	-11.06	-27.90, 5.77
Not on controller	-6.19	-26.20, 13.81
On controller	-20.30	-52.66, 12.06
FEF_{25-75} (mL/s)		
All subjects	-22.82	-61.89, 16.23
Not on controller	-3.96	-42.30, 34.38
On controller	-58.59	-125.41, 8.24

*Coefficients relate to a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours. Model includes: use of an asthma controller medication, an interaction term between $PM_{2.5}$ concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between $PM_{2.5}$ concentrations and medication use when evaluating FeNO (p=0.766), FEV_1 (p=0.482) or FEF_{25-75} (p=0.136).

Table 5. Difference in average FeNO, FEV_1, and FEF_{25-75} between burning and non-burning episodes*

	Coefficient	95% CI
All[†]		
FeNO (ppb)	3.23	-1.16, 7.63
FEV_1 (mL)	8.09	-26.34, 42.51
FEF_{25-75} (mL/s)	29.65	-41.94, 101.24
Declared[#]		
FeNO (ppb)	4.06	-4.04, 12.16
FEV_1 (mL)	1.59	-45.51, 48.69
FEF_{25-75} (mL/s)	22.43	-62.84, 107.69
Non-declared[§]		
FeNO (ppb)	0.97	-3.75, 5.68
FEV_1 (mL)	40.99	2.16, 79.81
FEF_{25-75} (mL/s)	77.05	3.72, 150.38

*Coefficients relate to a difference in average FeNO, FEV_1, and FEF_{25-75} between the burning and non-burning episodes (i.e. burning – non-burning). Model includes: use of an asthma controller medication, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity.

[†]Regardless of declaration status; burning episodes include those retrospectively identified during data analysis; non-burning episodes includes sham episode

[#]Burning episodes only include those prospectively identified during data collection; non-burning episodes includes sham episode

[§]Burning episodes only include those retrospectively identified during data analysis

Table 6. Associations between peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours and FeNO, FEV_1, and FEF_{25-75} after excluding subjects with a baseline FeNO greater than 100 ppb*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	-1.07	-2.76, 0.61
Not on controller	-0.93	-2.90, 1.04
On controller	-1.49	-3.66, 0.68
FEV_1 (mL)		
All subjects	-0.12	-15.39, 15.14
Not on controller	4.65	-14.34, 23.65
On controller	-14.38	-35.41, 6.65
FEF_{25-75} (mL/s)		
All subjects	3.62	-28.29, 35.53
Not on controller	14.90	-23.01, 52.81
On controller	-30.07	-60.17, 0.03

*Coefficients relate to a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours after excluding subjects with a baseline FeNO greater than 100 ppb (n=3 in each group). Model includes: use of an asthma controller medication, an interaction term between $PM_{2.5}$ concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between $PM_{2.5}$ concentrations and medication use when evaluating FeNO (p=0.679), FEV_1 (p=0.199), or FEF_{25-75} (p=0.052).

Table 7. Associations between peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours and FeNO accounting for in-lab ambient NO*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	0.71	-2.64, 4.05
Not on controller	0.62	-3.46, 4.69
On controller	0.88	-2.52, 4.27

*Coefficients relate to a 10 $\mu g/m^3$ increase in peak 1-hour central site $PM_{2.5}$ concentrations over the previous 24 hours after accounting for in-lab ambient NO. Model includes: use of an asthma controller medication, an interaction term between $PM_{2.5}$ concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between $PM_{2.5}$ concentrations and medication use when evaluating adjusted FeNO (p=0.899).

Table 8. Associations between average indoor $PM_{2.5}$ concentrations over the previous 12 hours and FeNO, FEV_1, and FEF_{25-75}*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	-0.22	-1.38, 0.94
Not on controller	-0.12	-1.26, 1.01
On controller	-0.56	-2.97, 1.86
FEV_1 (mL)		
All subjects	0.66	-4.73, 6.05
Not on controller	-0.21	-6.02, 5.61
On controller	3.68	-12.52, 19.88
FEF_{25-75} (mL/s)		
All subjects	0.26	-19.07, 19.59
Not on controller	-9.57	-25.38, 6.24
On controller	34.24	-12.80, 81.29

*Coefficients relate to a 10 $\mu g/m^3$ increase in average indoor $PM_{2.5}$ concentrations over the previous 12 hours. Model includes: use of an asthma controller medication, an interaction term between indoor $PM_{2.5}$ concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between indoor $PM_{2.5}$ concentrations and medication use when evaluating FeNO (p=0.710), FEV_1 (p=0.660) or FEF_{25-75} (p=0.071).

Table 9. Associations between average personal E_b concentrations over the previous 12 hours and FeNO, FEV_1, and FEF_{25-75}*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	1.15	-1.22, 3.52
Not on controller	1.52	-1.82, 4.86
On controller	0.89	-0.81, 2.60
FEV_1 (mL)		
All subjects	-2.08	-8.61, 4.45
Not on controller	-6.97	-16.71, 2.78
On controller	1.32	-5.06, 7.70
FEF_{25-75} (mL/s)		
All subjects	1.95	-11.73, 15.63
Not on controller	-7.93	-27.86, 12.00
On controller	8.84	-10.92, 28.59

*Coefficients relate to a 1 $\mu g/m^3$ increase in average personal E_b concentrations over the previous 12 hours. Model includes: use of an asthma controller medication, an interaction term between E_b concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between E_b concentrations and medication use when evaluating FeNO (p=0.513), FEV_1 (p=0.122) or FEF_{25-75} (p=0.251).

Table 10. Associations between average central site LG concentrations over the previous 12 hours and FeNO, FEV_1, and FEF_{25-75}*

	Coefficient	95% CI
FeNO (ppb)		
All subjects	13.07	-21.56, 47.72
Not on controller	19.67	-25.16, 64.50
On controller	0.54	-33.36, 34.44
FEV_1 (mL)		
All subjects	134.31	24.46, 244.17
Not on controller	200.48	61.29, 339.67
On controller	8.02	-172.48, 188.52
FEF_{25-75} (mL/s)		
All subjects	231.79	-42.48, 506.06
Not on controller	213.87	-74.36, 502.09
On controller	265.99	-325.70, 857.68

*Coefficients relate to a 1 $\mu g/m^3$ increase in average central site LG concentrations over the previous 12 hours. Model includes: use of an asthma controller medication, an interaction term between LG concentrations and medication use, age, gender, asthma severity, BMI, visit type, day of health assessment, temperature, relative humidity. There was no evidence of a significant interaction between LG concentrations and medication use when evaluating FeNO (p=0.439), FEV_1 (p=0.114) or FEF_{25-75} (p=0.877).