Short-term impact of $PM_{2.5}$ on contemporaneous asthma medication use: Behavior and the value of pollution reductions

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Asthma ranks among the most costly of chronic diseases, accounting for over $50 billion annually in direct medical expenditures in the United States. At the same time, evidence has accumulated that fine particulate matter pollution can exacerbate asthma symptoms and generate substantial economic costs. To measure these costs, we use a unique nationwide panel dataset tracking asthmatic individuals' use of rescue medication and their exposure to $PM_{2.5}$ (particulate matter with an aerodynamic diameter of <2.5 μm) concentration between 2012 and 2017, to estimate the causal relationship between pollution and inhaler use. Our sample consists of individuals using an asthma digital health platform, which relies on a wireless sensor to track the place and time of inhaler use events, as well as regular nonevent location and time indicators. These data provide an accurate measurement of inhaler use and allow spatially and temporally resolute assignment of pollution exposure. Using a high-frequency research design and individual fixed effects, we find that a 1 μg/m^3 (12%) increase in weekly exposure to $PM_{2.5}$ increases weekly inhaler use by 0.82%. We also show that there is seasonal, regional, and income-based heterogeneity in this response. Using our response prediction, and an estimate from the literature on the willingness to pay to avoid asthma symptoms, we show that a nationwide 1 μg/m^3 reduction in particulate matter concentration would generate nearly $350 million annually in economic benefits.

particulate matter | asthma | rescue inhaler | economic value

There is a large literature, spanning many disciplines, that focuses on the relationship between health outcomes and environmental conditions. For air pollution and outcomes such as asthma morbidity, researchers have documented physiological and epidemiological linkages (1–6). Specific examples include subacute (symptomatic) linkages (7–9) and studies relating pollution to hospital admissions or clinic visits (10–14). Researchers have also identified behavioral responses such as exposure avoidance (12), school absences (15), and defensive expenditures (16). The latter is of particular interest to economists, because responses to changes in environmental conditions provide one vehicle for understanding the external costs of pollution (17–19).

One important strand of economic research on pollution and morbidity focuses on using observational data to estimate a causal relationship between pollution and a health or productivity outcome. Recent examples include the effect of conventional pollutants [ground-level ozone, carbon monoxide, and particulate matter (PM)] on hospital admissions (20–23), lead exposure on student test scores (24), and studies linking pollution to labor productivity in physically and cognitively demanding tasks (25–27). In this pollution/morbidity literature there is a large emphasis on minimizing threats to causal inference by using narrowly defined sources of variation to mimic a controlled experiment. For example, hospital admissions for respiratory and cardiovascular symptoms are determined by a large number of factors besides pollution, including the socioeconomic and general health profiles of local populations. Characteristics of local populations are at the same time correlated with environmental outcomes, since economic activity—and hence income, population, transportation use, and so on—and pollution emissions are codetermined. As a result, observing an association between hospital admissions and average pollution over a long time scale does not provide evidence of a causal relationship. To circumvent this, economists have sought variation in pollution that is independent from other determinants of health outcomes, which can be used to mimic a controlled experiment relating health and pollution. For example, researchers have used day-over-day variation in local pollution concentrations and hospital visits to isolate the relationship. The identifying assumption is that other drivers of hospital visits vary at longer time scales, or do not vary systematically with pollution at short time scales, and are therefore plausibly independent from short-term variation in pollution.

This type of high-frequency research design has convincingly demonstrated the existence of a number of pathways through which pollution can impact human health and productivity (28–31). Despite this progress, however, gaps remain—particularly in the relationship between pollution and morbidity, where high-frequency designs have focused almost exclusively on hospitalizations as the health outcome. Causal impacts on subacute events, such as asthma symptoms that may not require medical attention, have been less well examined, due mainly to a lack of suitable data (8). Many of the studies that do exist are small in sample or geographical area, or focus on establishing associations rather than causality (7–9, 32–34). This is an important omission: If pollution exacerbates the symptoms of illnesses in a way that impacts day-over-day quality of life but does not rise to a level requiring medical attention, the cost of pollution may be substantially underestimated.

In this paper we address this omission by examining the relationship between asthma symptoms and fine PM pollution. Using a unique nationwide panel dataset spanning several years, we estimate the relationship between asthmatic individuals' daily

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use of rescue inhalers and the daily concentration of $PM_{2.5}$ (PM with an aerodynamic diameter of <2.5 μm) to which they are exposed. We estimate models that show an average relationship, as well as effects that vary over season, climate region, and income level. After finding statistically and economically significant relationships using contemporary reduced-form econometric methods, we use our nationwide sample coverage and overall size of the US population with asthma to infer that the economic benefits of a 12% nationwide reduction in $PM_{2.5}$ concentrations are nearly $350 million annually.

Background and Data

In 2015 there were 24.6 million people in the United States with asthma, representing nearly 8% of the population (35). Between 2008 and 2013, the annual per-asthmatic incremental medical cost of treatment was $3,266, and aggregate annual medical costs attributable to asthma were over $50 billion in 2015 dollars (36). Additional burdens of the disease operating through mortality and indirect avenues such as lost work and school days contribute an additional $32 billion in costs (36), with impaired quality of life adding additional nonmarket costs. The high incidence of asthma, spending on treatment, and disruptive nature of the disease imply asthma is one of the most costly chronic health conditions in the country (37).

There is strong evidence that air pollution exacerbates asthma morbidity and mortality among people with the disease, and some evidence that air pollution may affect asthma prevalence (5). This suggests a substantial component of the costs of air pollution may operate through the asthma mechanism; however, these outcomes represent rare, sentinel asthma events. Here we describe a unique data source, collected by digital health sensors, which we use to study the interaction among PM pollution, asthma symptoms, and treatment behavior at the individual level. These data provide a proximal assessment of the lived experience of a person with asthma.

The use of digital health technologies to support self-management and clinical care for asthma is becoming increasingly common and has demonstrated positive clinical outcomes (38–42). Previous digital health studies have leveraged the inhaler use data collected by sensors in clinical applications and in environmental health studies (4), but these studies have only focused on a single region and were limited by smaller sample sizes. This study examines nationwide temporal and geographic trends in the impact of $PM_{2.5}$ on asthma medication use across the United States, with a sample of over 2,800 participants over 6 y (2012–2017). Further, this paper uniquely addresses the more subtle nuances of the impact of air pollution exposure across climate regions, seasons, and socioeconomic levels.

Asthma Medication Use Data. Participants were eligible if they had a self-reported or a physician diagnosis of asthma, a prescription for a compatible asthma medication, and were greater than 3 y of age. Inclusion and exclusion criteria were kept as simple as possible to achieve real-world data collection. As such, children and pregnant women were included in the study.

Participants were enrolled through a variety of recruitment channels, including in-clinic enrollment, employer wellness fairs and programs, health plan programs, local community events, and self-enrollment through social media campaigns on Facebook and local print and digital media. All participants consented to the Propeller User Agreement, which explicitly enables the use of deidentified data for public health analyses, and the protocol was approved by the Copernicus Independent Review Board (PRH1-18-132).

After enrollment, participants received a kit that included digital sensor(s) to attach to their inhaler(s), as well as a hub (syncing device) if the participant did not have a smartphone. Medications included short-acting beta agonist (SABA), or "rescue," medications, taken to relieve acute symptoms, as well as controller medications, taken daily to prevent symptoms. The sensor and platform (Propeller Health) comprise a Food and Drug Administration-cleared digital health intervention that combines inhaler sensors, patient-facing mobile applicatins, web-based clinical dashboards, and predictive analytics, designed to promote adherence, predict exacerbations, and reduce the severity and cost of symptoms (38–40, 43, 44). See *SI Appendix*, Fig. S4 for an image of the platform.

The sensor objectively monitors the use of medications, capturing the date, time, and number of puffs, and wirelessly transmits these data in an encrypted fashion to secure servers through a smartphone application or hub base station. Sensors may also transmit a signal called a "heartbeat," which marks the time and confirms no actuations have occurred since the last sync, and reports sensor battery life. The heartbeat occurs approximately every 3 h, depending on usage and battery life. The latest version of the sensor has a battery life of up to 2 y and does not require charging. Among those participants transmitting data via a smartphone, Global Positioning System location data were assigned to all medication use events and sensor heartbeats when available. Following American Thoracic Society and European Respiratory Society guidance, SABA actuations occurring within a time period can be considered a single medication use "event," although the individual puffs were maintained as discrete records in the database for validation purposes (45). We utilized a 2-min time period to define an event. Controller medications are prescribed to be taken on a daily basis, so this variable was measured as daily puffs capped at the prescribed number of puffs. Adherence was calculated as the total number of puffs taken over the number of puffs prescribed per day according to each individual's self-reported medication regimen.

Environmental and Income Data. Each rescue use or sensor heartbeat event was assigned weather condition data acquired from the National Oceanic and Atmospheric Administration (NOAA) Quality Controlled Local Climatological Data Repository. Assignments include hourly measures for air temperature, relative humidity, pressure, and wind speed. An event was assigned weather data on the same date, and from a station within the same state, at the closest of possible sequential time-period steps: at the same time as the event, within 2 h of the event, or within 3 h of the event. If no such data existed after the above three steps, that event was not assigned any weather data; 99.6% of observations were matched to weather data using this procedure.

$PM_{2.5}$ data were acquired from the EPA's Air Quality System for the entire contiguous United States. Pollution data were assigned to an event based on the closest air-quality monitoring station within the same state or climate region on the event date. If no data were assigned using these criteria, pollution was assigned based on the closest air-quality monitoring station within the same state or climate region within 24 h of the event. If no such data existed after the above steps, that event was not assigned any air-quality data. Using this method, we were able to assign $PM_{2.5}$ data to 95.4% of the total rescue and heartbeat events. Climate regions were used to bound assignments because climatic conditions and dispersion of air pollutants can differ significantly across different climate regions, as determined by NOAA longitudinal data (46).

After assigning environmental measures to each recorded event, data were aggregated into a daily individual panel by summing inhaler use and averaging pollution exposure and weather characteristics by individual and date. Since the effect of pollution exposure accumulates over time (47), a 4-d moving average was used to estimate the cumulative impact of $PM_{2.5}$ on inhaler use (3- and 5-d averages led to similar results). Since the moving averages of $PM_{2.5}$ incorporate many location observations

throughout the previous few days, these measures provide accurate exposure histories, implicitly taking advantage of the fine temporal variation in the data. For our baseline estimates, the sample was restricted to person-days in which a heartbeat location was observed. This ensured that missing person-days were essentially random and did not bias our results. Alternative sample criteria, including filling in missing days based on home address, led to similar results (*SI Appendix*, Table S2). To operationalize our preferred estimator, the fixed-effects Poisson model, individuals with only one recorded location or with no variation in daily rescue events were omitted from the estimation sample. This left 2,874 individuals and 226,182 total person-day observations spanning the years 2012–2017. Between 2012 and 2017, the number of participants represented in the data grew from 166 to 1,722. This growth in participation has also expanded the geographic coverage of the dataset. Data on income, obtained from the American Community Survey 5-y estimates (2012–2016), were assigned to each individual using their self-reported home address. Income was measured as the census tract average household income-to-poverty threshold ratio (see *SI Appendix* for more details).

Summary Statistics. Table 1 presents summary statistics for the study population. Mean rescue events per day were 0.45 per person. To put this usage in context, we examined data from the 2016 Medical Expenditure Panel Survey and found that users of albuterol, a common SABA medication, fill on average 2.8 prescriptions annually. If these inhalers average enough medication for 100 rescue events, then an upper bound on mean daily events for a nationally representative user would be 0.77. This is an upper bound since filled prescriptions need not imply full usage. Nonetheless, our mean of 0.45 suggests that the intensity of inhaler use among participants in our study is not abnormally high. Mean $PM_{2.5}$ exposure was 8.7 $\mu g/m^3$, and median distance of a heartbeat or rescue event to a $PM_{2.5}$ monitor was 16 km. Participants in the sample who were prescribed controller medications ($n = 1{,}275$) took on average 1.3 daily puffs, representing 41% of the number of daily puffs prescribed.

Modeling

We are interested in understanding the relationship between Y_{it}, a random variable recording the number of times person i uses an inhaler on day t, and PM_{it}, which is a measure of level of exposure to $PM_{2.5}$ that the person experienced on day t. The conditional mean of the relationship is

$$E(Y_{it}) = \exp\left(\beta \ln PM_{it} + \gamma X_{it} + \theta_i + \tau_{t(j)}\right), \quad [1]$$

where X_{it} is a vector of controls, θ_i is a person fixed effect that captures characteristics about the person that are constant over time and may influence daily inhaler use, and $\tau_{t(j)}$ is a set of flexible day-of-week, month, and year time dummies. Year dummies are differentiated across the $j = 1,\ldots,9$ climate regions in the continental United States. The person and time fixed effects imply that the coefficients are estimated using within-person/year/month variation in inhaler events, which limits the extent to which unobserved factors may threaten causal inference. Observable factors X_{it} include copollutants (ground-level ozone and carbon monoxide), weather controls, and the length of time a participant has been enrolled in the program. Temperature and humidity variables enter into the model as 10° bins to allow for a more flexible relationship between weather and asthma medication use (25). The main coefficient of interest is β, the elasticity of rescue inhaler use with respect to PM. This measures the average percentage change in inhaler use from a 1% change in PM exposure. The pollution data are often heavily skewed to the right, so taking the natural log of PM reduces the influence of outliers. This transformation also improves the interpretability of marginal changes in pollution, and recent literature has found evidence supporting this specification (48, 49). In what follows we consider this basic specification, as well as more general specifications designed to illustrate heterogeneity in the inhaler use response.

We assume that Y_{it} is distributed Poisson and estimate the parameters in Eq. **1** using the Poisson fixed-effects model, also known as the conditional maximum likelihood Poisson model (50). Use of fixed effects, rather than random effects, is common in economic research, since the distributional assumptions on the individual effects are considered more realistic in the former. In particular, fixed effects models do not require that θ_i in Eq. **1** be independent of other covariates included in the model. This feature is crucial in causal analyses since some individual characteristics, such as experience with managing asthma symptoms, may be related to surrounding environmental characteristics. The θ_i parameters flexibly control for individual-level characteristics that are not changing over time, so this eliminates the need to include person-specific controls, such as gender or socioeconomic status, in the model. The fixed-effects Poisson model has some limitations, in that the effects of time-invariant covariates cannot be estimated, and individuals with no temporal variation in the outcome measure drop out of the estimation sample. These are not, however, concerns for our objectives in this study, and heterogeneous effects over time-invariant characteristics can be explored through the inclusion of interaction terms.

The assumptions that are needed to interpret an estimate of β as causal are similar to those used in other high-frequency research designs (e.g., refs. 22, 23, and 25). Specifically, we assume that daily fluctuations in $PM_{2.5}$ are uncorrelated with short-term variation in the determinants of rescue inhaler use that are not included among the variables in X_{it}. This assumption is plausible in our context, given the use of person, day-of-week, month, and year fixed effects, along with our accounting for weather and copollutants among the covariates. Furthermore, focusing on the impact of $PM_{2.5}$ exposure, rather than ozone exposure, reduces

Table 1. Estimation sample summary statistics

Variable	No. of people	Observations	Median	Mean	SD	Minimum	Maximum
Rescue events per day	2,874	226,182	0	0.45	1.75	0.00	217
Controller puffs per day	1,275	99,433	0	1.30	1.60	0.00	13
Adherence	1,203	88,999	0.38	0.41	0.43	0.00	1
Income-to-poverty ratio	1,167	1,167	1.65	1.59	0.28	0.29	2
Days in sample	2,874	2,874	39	78.70	112.42	2	1,117
$PM_{2.5}$, $\mu g/m^3$	2,874	226,182	7.85	8.71	4.93	0.06	190.8
Distance to $PM_{2.5}$ monitor, km	2,874	225,218	16.09	44.84	86.42	0.02	1,143.3

Observations are individual daily averages. Income-to-poverty ratio was measured at the census-tract level based on address matching. Days in sample refers to the number of daily observations per individual. $PM_{2.5}$ was measured as a 4-d moving average. Not all individuals were prescribed controller medication, and for a subset we were not able to match address to census tract.

worry of bias from a common avoidance behavior: staying indoors on poor air-quality days. $PM_{2.5}$ permeates indoors to a greater degree than other pollutants, so avoidance behaviors will have less of an effect on estimated exposure–response relationships (51).

Results

Average Effect of $PM_{2.5}$ Exposure on Asthma Medication Use. We first estimate the average impact of $PM_{2.5}$ exposure on the use of asthma medications, including both rescue and controller medications. We find a strongly significant response in rescue events, indicating a 0.07% increase in events associated with a 1% increase in average daily $PM_{2.5}$ exposure ($P < 0.05$; Table 2). Scaling pollution coefficients by the interquartile range (IQR) is common in epidemiologic studies to demonstrate clinically relevant impacts. Our results suggest an IQR increase in pollution (4.5 $\mu g/m^3$) would be associated with a 3.6% increase in rescue medication use. Controller medication puffs and adherence, however, are not significantly associated with $PM_{2.5}$. Results are similar when using alternative model specifications (*SI Appendix*, Table S3). The absence of response in the adherence outcome suggests that individuals' decisions on general disease control strategies may not vary sharply with short-term fluctuations in pollution; however, previous studies have demonstrated a significant association between perceptions of illness and adherence (52). It is important to note that adherence also varies with perceptions of the necessity and possible risk of controller medication therapy (53). Nonetheless, based on the rescue and controller use regression results, we conclude that rescue inhaler use is a useful response margin to examine, and that an increase in PM exposure does causally affect asthma symptoms, as marked by a significant increase in rescue inhaler use.

Seasonal Heterogeneity. Rescue inhaler use exhibits seasonality, so we document how the impact of $PM_{2.5}$ on recue events varies by time of year. Table 3 presents mean $PM_{2.5}$ exposure, average daily rescue events, and average daily controller medication use for each season. Average $PM_{2.5}$ levels are lowest in spring and highest in the winter, but the second-highest frequency of rescue events occurs during spring. This is perhaps because other asthma-exacerbating factors, such as allergens like pollen, are more prevalent during spring. To examine seasonal heterogeneity in the marginal response to pollution, we estimate a regression that allows the effect of $PM_{2.5}$ to vary by season and include the results in the final column of Table 3. The season-specific coefficients measure the percent change in daily rescue events associated with a 1% increase in $PM_{2.5}$, conditional on being in a particular season. We find significant ($P < 0.1$) and positive impacts of $PM_{2.5}$ on rescue events in each season, with the exception of fall, which shows a negative but only marginally significant association. The strongest response occurs during summer and the weakest response occurs during fall. To assess whether our log-log model specification is driving this result, we also estimated a linear model with untransformed rescue events and $PM_{2.5}$. This exercise results in the same ordering of the interaction effects, with spring and fall having the largest and smallest effects, respectively (*SI Appendix*).

Table 2. Impact of $PM_{2.5}$ on daily rescue events and controller medication use

	1	2	3
Variable	Rescue events	Controller puffs	Adherence
Log($PM_{2.5}$)	0.0680**	0.00855	0.00759
	(0.0277)	(0.0142)	(0.0139)
Observations	226,182	89,614	86,183
No. of ID	2,874	1,171	1,170

Models were estimated using Poisson fixed-effects models with log-log specifications. Dependent variable is daily inhaler use (columns 1 and 2) and ratio of controller puffs used over puffs prescribed (adherence). Time controls include day of week, year, and climate region-by-month fixed effects. Climate regions are defined according to NOAA (https://www.ncdc.noaa.gov/monitoring-references/maps/us-climate-regions.php) to include nine regions: Northeast, Southeast, Upper Midwest, Ohio Valley, Northern Rockies and Plains, South, Northwest, West, and Southwest. Controls, measured as 4-d moving averages, include copollutants, 10° temperature and humidity bins, air pressure, wind speed, and days enrolled in program. Robust SEs, clustered by ID, are shown in parentheses. $^{**}P < 0.05$.

Climate Region Heterogeneity. Asthma rescue use and $PM_{2.5}$ concentrations also exhibit spatial heterogeneity. To examine this variation, we stratify summary statistics and $PM_{2.5}$ effects by climate region. Climate region statistics and results were generated using the full sample with missing days filled in for participants without heartbeat locations. This sample provides nationwide coverage except for two climate regions, the Northwest and the Northern Rockies and Plains, due to the small number of individuals represented in those regions. For all remaining regions, Table 4 presents the number of individuals, mean daily $PM_{2.5}$ exposure for individuals in the regions, mean rescue events, and the average income-to-poverty ratio for an individual's assigned census tract. Column 5 displays results from a regression that allowed the impact of $PM_{2.5}$ on rescue events to vary by climate region. Coefficients are statistically significant ($P < 0.1$) for five of the seven regions shown. Interestingly, regions with lower mean $PM_{2.5}$ exposure tend to exhibit a larger rescue medication use response than regions with relatively high mean exposure. A notable exception to this is the South, which has the third-largest response to $PM_{2.5}$ and the third-highest mean $PM_{2.5}$ level.

Income Heterogeneity. As reflected in high direct medical spending for asthma annually (36, 54), properly managing asthma symptoms can require purchasing costly medications and other care. Our data allow us to explore how average income in an individual's neighborhood is related to asthma medication use and pollution responsiveness. For this we first assign participants into four income quartiles, as defined by the average household income-to-poverty ratio, where a higher ratio indicates higher income. Summary statistics by quartile show an inverse relationship between neighborhood income and both rescue events and $PM_{2.5}$ exposure, demonstrating that neighborhoods with lower income experience higher mean $PM_{2.5}$ exposure and higher mean rescue medication use (Table 5). An exception to this is the third income quartile, which has the highest average $PM_{2.5}$ exposure. Controller medication use and adherence have more complex relationships with income. The highest number of prescribed controller medication puffs occurred within the poorest quartile, which could reflect greater asthma severity, but the highest adherence level occurred within the highest income quartile. The final rows in Table 5 show results of four regressions on each income quartile of the data. The association between $PM_{2.5}$ and rescue use increases from the poorest to the third-highest income quartile but decreases in the highest income quartile. The effects in the first and fourth income quartiles are not statistically different from zero.

Fig. 1 plots differences in $PM_{2.5}$ responsiveness across income groups as reflected in the use of rescue inhalers. The lowest income group experiences the highest mean rescue event rate overall, but has lower relative responsiveness across varying levels of pollution exposure. At the same time, individuals in income quartile 3 show much higher responsiveness to $PM_{2.5}$, as seen in the steeper slope, but have fewer predicted mean rescue events except at very high levels of pollution. These results indicate that although chronic, long-term $PM_{2.5}$ exposure may be associated with higher rescue medication use on average, as seen in the poorest quartile, rescue medication responsiveness may be

Table 3. Mean $PM_{2.5}$, rescue events, and controller puffs by season, as well as the model estimates for the impact of PM2.5 on rescue events, varying by season

Season	Mean $PM_{2.5}$	Mean rescue events	Mean controller puffs	Log($PM_{2.5}$) interaction
Spring	7.32	0.56	1.32	0.0876**
	(3.10)	(1.56)	(1.58)	(0.0409)
Summer	8.60	0.21	0.40	0.324***
	(4.38)	(1.30)	(1.65)	(0.117)
Fall	9.52	0.35	1.23	−0.157*
	(5.31)	(2.25)	(1.63)	(0.0872)
Winter	9.96	0.57	0.41	0.0767*
	(6.31)	(1.60)	(1.57)	(0.0446)

SDs/errors are given in parentheses. Model coefficients were estimated using Poisson fixed-effects models with log-log specifications. Estimates are based on 226,182 person-day observations. Time controls include day of week, year, and climate region-by-month fixed effects. Controls, measured as 4-d moving averages, include copollutants, 10° temperature and humidity bins, air pressure, wind speed, and days enrolled in program. Robust SEs, clustered by ID, are shown in parentheses. ***$P < 0.01$, **$P < 0.05$, *$P < 0.1$.

highest among higher-income groups that experience lower chronic pollution exposure over prolonged periods of time.

There are multiple reasons why income might be related to $PM_{2.5}$ exposure responsiveness. First, income is related to the level of ambient air pollution an individual faces on a daily basis (55, 56). If the effect of pollution on rescue use is nonlinear, then this will also be reflected in heterogeneous income responses. Next, income may impact one's ability to optimally manage asthma symptoms. Higher incomes may allow more frequent visits to asthma specialists and better adherence to expensive controller medications. It also may impact the probability that an individual invests in remediation of home-based triggers through the use of air purifiers or filtration systems. Furthermore, higher income may also be associated with improved indoor air quality, with lower likelihood of the presence of cockroaches, rodents, and second-hand smoke exposure (57). Those with typically lower exposure levels may not be acclimated to high-exposure environments and therefore may have greater responsiveness at high levels of air pollution. Alternatively, better-managed symptoms may reduce marginal responsiveness to pollution if it decreases vulnerability to long-term pollution damages. Finally, income is related to other socioeconomic factors, like education, that may lead to differential responsiveness through more acute awareness of symptom causes and appropriate medication responses, or the ability to make behavioral changes to mitigate the impact of pollution.

Discussion

Our finding that PM exposure affects rescue inhaler use among people with asthma contributes to the literature demonstrating how pollution can affect health and productivity outcomes. Further, our evidence of heterogeneous effects provides insights into how pollution responsiveness varies across individuals and seasons. For instance, the most intensive inhaler users often exhibit less responsiveness to marginal changes in $PM_{2.5}$. Since rescue inhalers are the first line of defense against asthma exacerbations, those who already frequently utilize inhalers may be forced to seek out other modes of defense during periods of increased pollution.

Previous studies have demonstrated strong relationships with acute asthma outcomes such as emergency department visits, hospitalizations, and mortality, but it has been challenging to demonstrate a relationship with a proximal and subacute outcome such as medication use or symptoms (8, 34). Seen in this light, our estimates provide evidence of the existence of an effect at even subacute levels and, similar to other studies using a high-frequency research resign, our reduced-form approach generates estimates that are plausibly causal. While this is useful, it does not help us understand the extent to which the asthma mechanism is an important component of the economy-wide costs of particulate pollution. For this, we need to extrapolate beyond our marginal findings to predict the aggregate welfare consequences of a wide-scale change in pollution concentration.

Our nationwide dataset and focus on a common and widespread response provide a useful platform for this. To take advantage, we extrapolate predictions on the asthmatic population's response to changes in $PM_{2.5}$ exposure and use these predictions

Table 4. Number of individuals and mean PM2.5, rescue events, and income by climate region, as well as the model coefficients for the impact of $PM_{2.5}$ on rescue events as varying by climate region

	1	2	3	4	5
Climate region	Individuals	Mean $PM_{2.5}$	Mean rescue events	Mean income	Log($PM_{2.5}$) interaction
Southwest	319	6.70	0.50	1.57	0.274***
		(2.23)	(0.73)	(0.27)	(0.0345)
Upper Midwest	309	6.80	0.57	1.57	0.165***
		(2.28)	(1.03)	(0.29)	(0.0619)
Northeast	674	7.26	0.50	1.66	0.0636*
		(2.66)	(0.84)	(0.27)	(0.0369)
Southeast	446	8.19	0.45	1.57	0.0464
		(3.00)	(0.89)	(0.26)	(0.0565)
South	389	8.50	0.70	1.59	0.141***
		(2.50)	(1.13)	(0.28)	(0.0545)
Ohio Valley	1,795	8.58	0.42	1.53	0.0161
		(1.89)	(0.82)	(0.33)	(0.0281)
West	1,312	8.67	0.64	1.57	0.0542***
		(2.68)	(0.94)	(0.26)	(0.0205)

Climate regions ordered by low to high mean $PM_{2.5}$ exposure. SDs/errors are given in parentheses. Northern Rockies and Plains and Northwest regions were omitted due to a small number of represented individuals. The model was estimated on 959,257 person-day observations. Individual, climate region, climate region-by-year and climate region-by-month fixed effects are included in the column 5 regression. Controls, measured as 4-d moving averages, include copollutants, 10° temperature and humidity bins, air pressure, wind speed, and days enrolled in program. Robust SEs, clustered by ID, are shown in parentheses. ***$P < 0.01$, *$P < 0.1$.

Table 5. Summary statistics by income quartiles, poorest (1) to wealthiest (4)

	Income quartile			
Variable	1	2	3	4
Daily rescue events	0.56	0.51	0.45	0.43
Adherence	0.40	0.36	0.40	0.44
Prescribed controller puffs	3.80	2.96	3.13	3.15
Taken controller puffs	1.47	1.05	1.35	1.37
Median distance to monitor, km	11.93	26.67	26.73	20.05
Mean $PM_{2.5}$	8.73	8.72	8.80	8.65
Log($PM_{2.5}$) regression coefficients	−0.0836	0.0948**	0.193***	−0.0172
	(0.0606)	(0.0403)	(0.0598)	(0.0467)

Prescribed and taken controller puffs are conditional on having been prescribed a controller medication. Their units are in average daily puffs. Each regression coefficient comes from a separate regression on a subset of the data, divided into four quartiles based on household income. Individual, climate region, climate region-by-year, and climate region-by-month fixed effects are included in each regression. Controls, measured as 4-d moving averages, include copollutants, 10° temperature and humidity bins, air pressure, wind speed, and days enrolled in program. Robust SEs, clustered by ID, are shown in parentheses. ***$P < 0.01$, **$P < 0.05$.

to compute an important component of the aggregate welfare consequences of changes in pollution. As a baseline, consider a uniform 1 μg/m^3 decrease in $PM_{2.5}$ concentrations nationwide, which corresponds to ∼12% of the daily mean exposure level shown in Table 1. Note that our simplest model in column 1 of Table 2 implies that this change in pollution leads to a 0.82% reduction in daily average rescue inhaler use. Given an average of 0.45 rescue events per day, this suggests that a 12% reduction in $PM_{2.5}$ concentration causes an expected reduction of 0.0037 events per day, or 1.35 events per year per person. While we focus on this marginal change in what follows, we also note that a 50% reduction (based approximately on the IQR value of 4.5 μg/m^3 noted above) would lead to a 3.4% reduction in daily rescue events. This corresponds to an expected reduction of 0.015 events per day, or 5.6 fewer rescue events per year. The magnitude of this effect is largely consistent with previous studies that estimated associations between pollution and subacute asthma outcomes. For example, ref. 7 finds increases of 0.32–1.39% in lower respiratory symptoms from a 1 μg/m^3 increase in PM_{10}, and ref. 33 finds that lung functioning decreases by 0.24% from a 1 μg/m^3 increase in $PM_{2.5}$. As a comparison with our elasticity estimate, ref. 19 finds that a 1% increase in average ozone, and a 1% increase in high ozone days, leads to 0.27 and 0.036% increases in medication expenditures, respectively.

There are several conceptual possibilities for translating this medication-use response into an estimate of the economic benefits from the pollution reduction. One example relies on the averting expenditures framework (17, 19), which relates changes in expenditures on a private good arising from an environmental change—rescue inhaler use in our case—to the willingness to pay for the change. A second approach seeks to directly measure the willingness to pay to avoid the actual disease symptoms that the inhaler-use response seeks to mitigate (17). In these studies, the estimated willingness to pay reflects direct costs, such as medication purchases and medical care costs, as well as hard-to-measure costs such as personal suffering and lowered work productivity. Thus, willingness to pay captures the broad economic costs of a disease. Here, we consider a line of logic based on the second approach.

Environmental and health economists have long been interested in measuring the willingness to pay to avoid symptoms of illnesses associated with environmental conditions. A common approach is to use stated preference methods, whereby a sample of individuals express their willingness to exchange money for symptom relief via hypothetical scenarios presented in a survey. Examples of studies focused on asthma or related respiratory conditions, include refs. 58–60. For our purposes ref. 60 is the most useful. For a population of asthmatic children, the authors estimate that households are willing to pay approximately $2.36 per day (2018 dollars) for a 50% reduction in a child's asthma symptoms. For our data, a 50% reduction in symptoms corresponds to an average of 0.225 fewer rescue events per day, which implies people are willing to pay $10.48 per avoided rescue event. Based on this, we predict that asthmatics in our sample would be willing to pay on average $14.16 per year for a decrease of 1.35 rescue events that is provided by the 12% reduction in $PM_{2.5}$. Extrapolating to the 24.6 million people in the country with asthma, a first-order approximation based on our results is that a 1 μg/m^3 uniform reduction in $PM_{2.5}$ pollution would generate nearly $350 million annually in economic benefits, operating through the asthma mechanism. In *SI Appendix*, Table S6 we examine how regional heterogeneity in pollution responsiveness and the asthmatic population impacts our prediction of the economic benefits.

This prediction is subject to a number of caveats and uncertainties, and it hinges on several assumptions. First, although we have nationwide coverage, our data reflect a convenience sample that may not be representative of the general asthmatic population. Second, the pollution change must be small enough that it does not induce extensive margin adjustments, including migration. For this reason, we examine a comparatively small

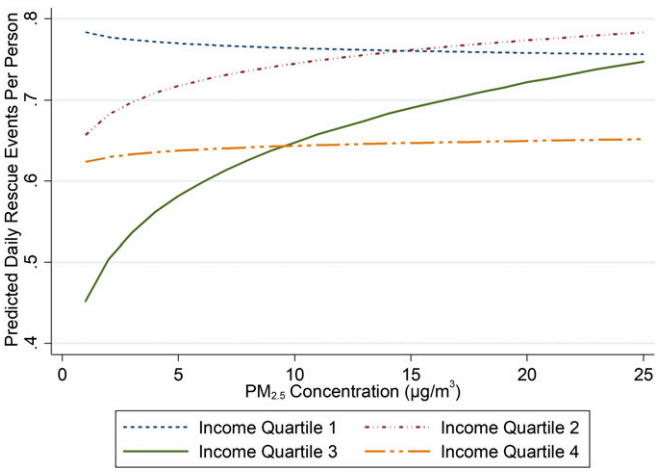

Fig. 1. Predicted rescue events per day by income quartile and $PM_{2.5}$ concentration. Income quartile 1 is the poorest and income quartile 4 is the wealthiest.

change in pollution. Most importantly, the prediction relies on the extent to which the value estimated in ref. 60 is an accurate representation of general population preferences. For example, the authors use surveys of parents to elicit values for reductions in asthma symptoms in children, but this may not fully internalize infrequent, high-cost events such as hospitalizations. On the positive side, the authors in ref. 60 elicit their willingness to pay by describing a hypothetical digital device that would provide information useful for managing, and therefore reducing, symptoms—a product remarkably similar to that used by people in our sample. Thus, these caveats notwithstanding, our sense is that our study provides a useful example of how the reduced-form paradigm, focused on identifying the existence of pathways through which pollution affects health and productivity outcomes, can be expanded to include the measurement of economy-wide effects that are relevant for policy. For this it is necessary to study a widespread response to pollution over a large spatial and temporal scale—rescue inhaler use in our case—that marks symptoms with welfare effects that can be quantified using willingness to pay or defensive expenditure methods.

There are also potential limitations to note regarding our overall research design. We rely on high-frequency variation and assert that potential economic confounders operate on a longer time scale, but short-run idiosyncratic economic shocks may still occur. Furthermore, certain types of avoidance behavior, such as changing activity patterns in response to pollution levels, may lead to underestimates of the true dose–response effect. Addressing this would require an instrumental variables strategy, similar to what has been used in the hospital admissions literature (20, 21). Finally, our analyses focus on contemporaneous effects of pollution, although intermediate- and longer-term exposure may also impact daily use of rescue medications.

Research in this area can be expanded in several ways that are relevant for the theme of this Sackler Colloquium. Our analysis here is only one step toward using this unique dataset to understand the costs of air pollution as it operates through the asthma mechanism. A logical next step is to better understand how heterogeneity measured at the individual (as opposed to census-tract) level affects the pollution/asthma symptom relationship and use this to predict the distributional consequences of changes in pollution concentrations. Also, our measure of the willingness to pay to avoid a symptom day is a first-order approximation. Despite asthma's wide prevalence, there are relatively few studies examining the welfare benefits of eliminating an asthma symptom day among the general asthmatic population. An original study differentiating the willingness to pay across observable individual heterogeneity would provide a more accurate measure of the welfare impacts of the changes in symptoms, as marked by changes in rescue inhaler use conditional on the same heterogeneity. Combining a more complete understanding of individuals' behavioral response and willingness to pay, conditional on observable characteristics, would provide a strong platform for predicting the efficiency and distributional consequences of spatially differentiated pollution changes.

More generally, researchers working on the health, productivity, and pollution nexus should look for opportunities to expand the agenda to consider important response margins, such as broader categories of spending on medical service spanning longer timeframes, that may be of first-order importance for understanding the magnitude of economy-wide external costs. Recent examples of this type of research include ref. 19, whose authors consider seasonal expenditures on medications and other medical services related to chronic respiratory conditions. Studies like these, which move beyond high-frequency designs, increase identification challenges but provide a broader understanding of the size of pollution externalities.

Finally, research seeking to measure the costs of health- and productivity-related pollution externalities can contribute to the challenges identified in the colloquium and this special issue related to sustainable development. The recently published *Lancet* Commission on pollution and health (3) identifies environmental degradation as a major, albeit heretofore underappreciated, driver of premature mortality, disease burden, and lost productivity worldwide—particularly in low- and middle-income countries. Our understanding of these costs is likely to grow as additional pathways linking pollution and disease are investigated. Initiatives that seek health and productivity improvements via pollution reductions are likely to generate ecological benefits simultaneously, while also pushing human capital and wealth toward levels where environmental sustainability becomes important for broader sets of reasons. In this regard, environmental improvements that provide local and private improvements in health and productivity may be important steps toward global sustainability.

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