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$PM_{2.5}$ and its components and respiratory disease healthcare encounters – Unanticipated increased exposure-response relationships in recent years after environmental policies

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A R T I C L E I N F O

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A B S T R A C T

Prior studies reported excess rates (ERs) of cardiorespiratory events associated with short-term increases in $PM_{2.5}$ concentrations, despite implementation of pollution-control policies. In 2017, Federal Tier 3 light-duty vehicle regulations began, and to-date there have been no assessments of population health effects of the policy. Using the NYS Statewide Planning and Research Cooperative System (SPARCS) database, we obtained hospitalizations and ED visits with a principal diagnosis of asthma or chronic obstructive pulmonary disease (COPD) for residents living within 15 miles of six urban $PM_{2.5}$ monitoring sites in NYS (2014–2019). We used a time-stratified case-crossover design and conditional logistic regression (adjusting for ambient temperature, relative humidity, and weekday) to estimate associations between $PM_{2.5}$, POC (primary organic carbon), SOC (secondary organic carbon), and rates of respiratory disease hospitalizations and emergency department (ED) visits from 2014 to 2019. We evaluated demographic disparities in these relative rates and compared changes in ERs before (2014–2016) and after Tier 3 implementation (2017–2019). Each interquartile range increase in $PM_{2.5}$ was associated with increased ERs of asthma or COPD hospitalizations and ED visits in the previous 7 days (ERs ranged from 1.1%–3.1%). Interquartile range increases in POC were associated with increased rates of asthma ED visits (lag days 0–6: ER = 2.1%, 95% CI = 0.7%, 3.6%). Unexpectedly, the ERs of asthma admission and ED visits associated with $PM_{2.5}$, POC, and SOC were higher during 2017–2019 (after Tier 3) than 2014–2016 (before Tier-3). Chronic obstructive pulmonary disease analyses showed similar patterns. Excess Rates were higher in children (<18 years; asthma) and seniors (≥65 years; COPD), and Black, Hispanic, and NYC residents. In summary, unanticipated increases in asthma and COPD ERs after Tier-3 implementation were observed, and demographic disparities in asthma/COPD and PM2.5, POC, and SOC associations were also observed. Future work should confirm findings and investigate triggering of respiratory events by source-specific PM.

1. Introduction

While air pollution's hazardous effects on respiratory health have been well recognized, few accountability studies evaluated whether the exposure-response relationship (i.e., rate of a health event associated with a standard increase in pollutant concentration) changed after

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implementation of one or more environmental policies, especially during recent years and among the most frequent and severe respiratory cases, i.e., asthma and chronic obstructive pulmonary diseases (COPD). Chronic obstructive pulmonary disease ranked as the fourth leading cause of death in the U.S. in 2018, affecting 6.4% of the population with 10.8% prevalence in those over 65, and incurring an economic cost of ~ $50 billion annually (American Lung Association (ALA), 2024a; American Lung Association, 2024b; Centers for Disease Control and Prevention CDC, 2023). Asthma affects over 27 million Americans (one in every twelve) and is especially common among children under the age of 18 years (4.5 million diagnosed cases). Bronx County in New York State (NYS) has the highest asthma rate in the nation. Across the U.S, asthma accounted for ten daily deaths on average and an economic burden surpassing $81.9 billion between 2008 and 2013 (Asthma & Allergy Foundation of America; Centers for Disease Control and Prevention, 2024a; Centers for Disease Control and Prevention, 2024b; Krall et al., 2017).

Our group and others have observed adverse effects of $PM_{2.5}$ on hospital admissions (Hopke et al., 2020; Jones et al., 2015; Renzi et al., 2022),emergency department (ED) visits (Krall et al., 2017; Li et al., 2021; Madani and Carpenter, 2023; Szyszkowicz et al., 2018; Villeneuve et al., 2007), and mortality (Atkinson et al., 2014; Janssen et al., 2013) for respiratory diseases, especially for COPD and asthma (Dominski et al., 2021; Hsieh et al., 2021; Li et al., 2016; Zhang et al., 2016). However, $PM_{2.5}$ consists of multiple chemical species including organic compounds including primary organic carbon (POC) and secondary organic carbon (SOC), elemental carbon, metals/metaloids, crustal elements, sulfate, and nitrate (Jones et al., 2015). Specifically, POC and SOC have different production mechanisms. POC is directly emitted to the atmosphere from sources such as vehicle exhaust and agricultural burning (Chen et al., 2023a; Yu et al., 2004). SOC is produced in the atmosphere through photochemical reactions involving oxidizing agents and volatile organic compounds (Hallquist et al., 2009; Salma et al., 2022). Limited studies have assessed the impact of specific PM components on respiratory health events. In NYS, Jones et al. (2015) reported 0.5%–2.0% increases in the risk of respiratory hospitalizations associated with increased concentrations of $PM_{2.5}$ total mass, sulfate, nitrate, and ammonium on respiratory hospitalizations at lags of 0–4 days (Jones et al., 2015). Croft et al. (2020) observed an excess rate (ER) of culture-negative pneumonia hospitalizations associated with interquartile range increases in secondary sulfate source-specific $PM_{2.5}$ on the same day. Similarly, in California, Ostro et al. (2009) reported 3.0%–5.4% increases in total respiratory admissions associated with increased $PM_{2.5}$, elemental carbon, organic carbon, nitrates, and sulfates in the previous 3 days.

Over the last decade, NYS's air quality initiatives included phasing out coal-fired power generation for natural gas and renewables. The United States and Canada established the North American Emissions Control Area. In addition, the economic downturn between late 2007 and early 2009 and changes in the relative costs of electricity generation by coal and gas have contributed to reductions in $PM_{2.5}$ concentrations (Chen et al., 2023b). Masiol et al. (2019) reported an increase in the proportion of PM attributable to SOC and spark-ignition vehicle $PM_{2.5}$ concentrations from 2006 to 2016. Previously, we reported a significant 8.9% excess rate of COPD hospitalization associated with an interquartile range increase in concentrations of $PM_{2.5}$ from spark-ignition vehicles on lag 0–6 days in 2014–2016, and 0.9%–3.1% increases in the risk of asthma ED visits associated with source-specific road dust on lag days 0, 0–3, and 0–6 in 2005–2007, 2008–2016, and 2014–2016, respectively (Hopke et al., 2020). Thus, although $PM_{2.5}$ decreased, the risk for influenza hospitalization and ED visits associated with increased $PM_{2.5}$ concentrations was higher in the 2014–2016 period compared to 2009–2013 (Croft et al., 2019). This work suggested that $PM_{2.5}$ toxicity per unit mass concentration may have increased after engine technology changed to improve fuel economy and gasoline was reformulated to reduce benzene exposures. In addition to limited accountability studies evaluating the changes in exposure-response relationships after policy implementations, there are limited studies assessing the adverse health effects of SOC, POC, and $PM_{2.5}$ and their temporal changes in their associations with respiratory health events.

Federal Tier 3 regulations require additional reductions in the emissions from light-duty vehicles to be phased in beginning in 2017 with full implementation by 2025. Prior work had shown that Tier 3 controls should reduce emissions that lead to the formation of secondary organic carbon compounds (Zhao et al., 2014, 2015, 2016, 2018). This regulation offers an opportunity to assess whether PM concentrations and their specific components will be reduced and whether the rates of COPD and asthma associated with increased $PM_{2.5}$ concentrations will change after the Tier 3 implementation.

This work 1) examined the association between $PM_{2.5}$, POC, SOC, and excess rates (ER) of COPD and asthma hospitalizations and ED visits from 2014 to 2019 in NYS; 2) compared the ERs in 2014–2016 (before Tier 3 implementation) to the ERs in 2017–2019 (after Tier-3 implementation); and 3) evaluated whether disparities in these associations regarding demographic characteristics existed.

2. Methods

Study population and hospital admissions data: Hospitalizations and emergency department (ED) visits were obtained from the Statewide Planning and Research Cooperative System (SPARCS) database. SPARCS includes patient information with the confirmed principal diagnoses and up to 24 additional diagnoses at the time of hospitalization or ED visit, as well as age, gender, race, ethnicity, street address, admission date, source of payment, and length of hospital stay. Data reported by hospitals are reviewed by SPARCS staff for accuracy and completeness. We geocoded the residential address for each case using the Street and Address Maintenance Program in ArcGIS 10.3.1.

The study population included all hospital admissions and ED visits (1/1/2014-12/31/2019) from patients with a principal diagnosis of asthma (ICD9 = 493; ICD10 = J45) or COPD (ICD9 = 491, 492, 496; ICD10 = J41, J42, J43, J44) for all New York State residents of any age, who resided within 15 miles of the monitoring sites in Buffalo, Rochester, Albany, Bronx, Manhattan, or Queens County (N = 1,355,436 respiratory visits available for analysis). This study was reviewed and approved by the NYS SPARCS Data Protection Board and Institutional Review Board at the State University of New York at Albany.

$PM_{2.5}$ mass/composition and meteorology: $PM_{2.5}$ concentrations (1/1/2014-12/31/2019) for the six sites (Albany, Buffalo, Rochester, Bronx, Manhattan, and Queens), were collected from the USEPA Air Quality System (https://aqs.epa.gov/api). Hourly $PM_{2.5}$ concentrations were measured at each site with Federal Equivalent Methods (FEM). Missing FEM data were replaced with FRM concentrations if available. $PM_{2.5}$ compositional data including organic (OC) and elemental carbon (EC) was retrieved from the EPA Chemical Speciation Network (CSN; AQS, www.epa.gov/aqs). The OC and EC data were used to estimate the POC and SOC using the approach described in the supplemental material file of Zhang et al. (2018). We retrieved hourly temperature and relative humidity data from the National Weather Service (National Climate Data Center, https://www.ncdc.noaa.gov/cdo-web/datatools/lcd) for the major airports of Buffalo, Rochester, Albany, Bronx, and Queens, or the closest weather station for Manhattan (Central Park). If a patient lived <15 miles from more than one monitoring site, we assigned that case the concentrations/values of the closest monitor. For each site, we then calculated 24-h daily average pollutant concentrations, temperature, and relative humidity averages if a day had ≥75% of hourly measurements for that day.

2.1. Study design and statistical analyses

$PM_{2.5}$: To estimate the rate of asthma or COPD hospitalization or ED visit associated with each interquartile range increase in $PM_{2.5}$ concentration, we used a time-stratified, case-crossover design and conditional logistic regression (Levy et al., 2001; Maclure, 1991). Case-crossover designs examine associations between acute environmental triggers and transient health outcomes. It is analogous to a matched case-control study design where cases serve as their own control. The hazard/case period is the day of the event (admission or visit) while control periods are the same day of the week in the same calendar month and year as the hazard period. Therefore, factors that do not vary within a month, including demographic and non-time-varying variables and any interactions between them, are controlled by design.

Using conditional logistic regression, we regressed case-control status (i.e., 1 = case, 0 = control) against the $PM_{2.5}$ concentration on lag day 0. The interquartile range (IQR) is a useful and common metric with multiple advantages in air pollution epidemiology research, such as being robust to outliers and effectively reflecting typical variability in air pollutant concentrations (Frery, 2023; Larson, 2006). The IQR has been used in many air pollution studies (e.g., Huang et al., 2019; Wu et al., 2016) as well as our prior studies (e.g., Croft et al., 2024; Lin et al., 2022; Rich et al., 2019) investigating the relationship between air pollutants and health outcomes. Temperature and relative humidity (time-varying factors, using the same lag day), as well as indicator variables for holidays, days of the week, and seasons, were included in the model as well. Temperature and relative humidity were modeled using natural splines with 4 degrees of freedom [df]), determined using Akaike's information criterion (Aho et al., 2014). From this model, we estimated the excess rate of asthma and COPD hospitalizations and ED visits associated with each interquartile range increase in $PM_{2.5}$ concentration (i.e. [rate ratio - 1.0] * 100%). Additionally, we examined if the associations between asthma or COPD and each interquartile range increase in $PM_{2.5}$ concentration differed between periods (2014–2016 versus 2017–2019) by adding an interaction term (2017–2019 * $PM_{2.5}$) to the model. We then reran these models for $PM_{2.5}$ on lag days 0–1, 0–2, 0–3, 0–4, 0–5, and 0–6 for asthma and COPD hospitalizations and emergency department visits separately. Since we examined 7 lag times for $PM_{2.5}$, statistical significance was defined as $p < 0.007$ (0.05/7). Stratified analyses by gender, age (0–5, 6–17, 18–64, and 65+), race (White, Black, Native American/Alaskan, Asian, and Native Hawaiian), ethnicity (Hispanic and non-Hispanic), and urbanicity (Upstate and New York) were conducted to examine whether there were disparities in these associations within these categories.

SOC and POC: For SOC and POC, which were only available every 3rd day, there would be very few complete sets of case and control days for analyses using this standard time-stratified design (where hazard and control days are 7 days apart). Therefore, we used a modified time-stratified design, where the day of hospitalization/ED visits was again the case day, but control days were now at 6-day intervals before and after the case day within the same calendar month. Using a conditional logistic regression model, we regressed case-control status (i.e., case = 1; control = 0) against the mean SOC/POC concentration on lag day 0, adjusting for the mean residual $PM_{2.5}$ concentration (i.e., residual $PM_{2.5}$ = $PM_{2.5}$ – SOC or POC), indicator variables for weekday or weekend, holidays, and season, and temperature (natural spline with 4 degrees of freedom [df]), and relative humidity (4df) on the same case and control days). We also re-ran this set of models for the mean SOC and POC concentration on lag days 0, 0–3, and 0–6 respectively in the same manner. As we did for $PM_{2.5}$, we examined whether the rates of asthma and COPD hospitalizations and ED visits associated with each interquartile range increase in POC or SOC concentration differed between the 2014–2016 and 2017–2019 periods by adding an interaction term (e.g., SOC * 2017–2019) to the model. Since we examined 3 lag times for each pollutant, statistical significance was defined as $p < 0.017$ (0.05/3). Last, stratified analyses by demographics (sex, age, race/ethnicity, and urbanicity) were conducted to examine POC or SOC-health association disparities. All statistical analyses were performed using R version 4.0.1 (R Core Team, 2021) (https://www.r-project.org/). The major analysis, conditional logistic regression, was conducted using the "clogit (k)" function from the R package, "survival" (Therneau, 2023).

3. Results

From 2014 to 2016, a total of 707,804 patients required hospitalization or ED visits for COPD or asthma in NYS (Supplemental Table S1). Subsequently, from 2017 to 2019, the number of hospitalizations decreased to 647,632 patients. All COPD admission and ED visit cases (100%) were adults, and 64% of the COPD admission cases were adults over 65 years of age. Alternatively, 36%–40% of the asthma cases were children (0–17 years old) and very few (5%–18%) older adults (above 64 years old) were treated for asthma.

As shown in Table 1, interquartile range increases in $PM_{2.5}$ concentration in the previous lag days (0, 0–1, 0–2, 0–3, 0–4, 0–5, and 0–6) were associated with increased excess rates of both asthma and COPD healthcare encounters (i.e., hospital admissions and ED visits). While the $PM_{2.5}$-rate ratios for these lag times were larger for asthma ED visits (ER range: 1.8%–2.4%) than COPD ED visits (ERs ranged from 1.1% to 2.4%), the ERs of COPD hospitalizations (range: 1.5%–3.1%) were higher than the ERs of asthma hospitalizations (range: 1.5%–2.1%). For each analysis, we observed increased ER's at all lag times examined, with the largest excess rates for asthma hospitalizations with $PM_{2.5}$ on lag days 0–2 (ER = 2.1%; 95% CI = 1.2%, 3.0%), for asthma ED visits at lag days 0–5 (ER = 2.4%; 95% CI = 2.0%, 2.8%), COPD hospitalizations at lag days 0–5 (ER = 3.1%; 95% CI = 2.1%, 4.2%), and for COPD ED visits at lag days 0–6 (ER = 2.4%; 95% CI = 1.2%, 3.6%).

Additionally, the ERs of both asthma and COPD admissions and ED visits associated with increased $PM_{2.5}$ concentrations across most lag times in the 2017–2019 period were slightly higher than those in the 2014–2016 period (Table 2). For example, the ERs of asthma ED visits associated with each interquartile range increase in $PM_{2.5}$ concentration on lag days 0–5 were larger in 2017–2019 (ER = 3.7%; 95% CI = 3.1%, 4.4%) than in 2014–2016 (ER = 1.7%; 95% CI = 1.2%, 2.1%). Similarly, ERs of asthma hospitalizations associated with interquartile range increases in $PM_{2.5}$ concentration on lag days 0–6 were also higher in 2017–2019 (ER = 3.9%; 95% CI = 2.0%, 5.8%) than in 2014–2016 (ER = 1.4%; 95% CI = 0.2%, 2.7%). Consistently, the ERs of both COPD hospitalization (ERs ranged: 1.0%–3.4%) and ED visits (ERs ranged: 1.2%–3.3%) in 2017–2019 were also higher than those ERs in

Table 1
Excess rates (ER) [a] of asthma and COPD admissions and ED visits associated with each IQR[b] increase in $PM_{2.5}$ concentrations in the previous 7 days during 2014–2019.

Lags	Admissions			ED Visits		
	IQR	Cases	Excess Rate (95% CI)	IQR	Cases	Excess Rate (95% CI)
Asthma						
0	5.10	101,953	1.7 (0.8, 2.7)	4.88	599,339	2.1 (1.7, 2.4)
0–1	4.40	101,124	1.5 (0.7, 2.3)	4.25	594,143	1.8 (1.5, 2.1)
0–2	4.09	100,332	2.1 (1.2, 3.0)	3.96	588,994	1.9 (1.5, 2.2)
0–3	3.71	99,539	2.1 (1.1, 3.0)	3.64	584,113	2.1 (1.7, 2.5)
0–4	3.56	98,798	2.0 (1.0, 3.0)	3.46	579,347	2.3 (2.0, 2.7)
0–5	3.40	98,152	2.0 (0.9, 3.0)	3.20	575,230	2.4 (2.0, 2.8)
0–6	3.28	97,559	2.1 (1.1, 3.2)	3.05	571,486	2.4 (2.0, 2.8)
COPD						
0	4.99	98,240	1.5 (0.5, 2.4)	4.84	75,576	1.2 (0.2, 2.4)
0–1	4.35	97,233	1.3 (0.4, 2.1)	4.22	74,834	1.1 (0.1, 2.0)
0–2	3.97	96,321	1.9 (1.0, 2.8)	3.91	74,137	1.3 (0.2, 2.3)
0–3	3.64	95,422	2.6 (1.6, 3.6)	3.61	73,478	1.8 (0.8, 2.9)
0–4	3.46	94,586	3.0 (2.0, 4.1)	3.48	72,826	1.9 (0.8, 3.1)
0–5	3.22	93,849	3.1 (2.1, 4.2)	3.22	72,291	2.1 (1.0, 3.3)
0–6	3.11	93,176	3.1 (2.0, 4.2)	3.06	71,773	2.4 (1.2, 3.6)

[a] When Excess rate was computed, temperature, relative humidity, holidays, date of the week and long-term trends were controlled in the logistic regression model.
[b] IQR: Interquartile Range ($\mu g/m^3$).

Table 2
Excess rates (ER) [a] of asthma and COPD admissions and ED visits associated with each IQR[b] increase in $PM_{2.5}$ concentrations in the previous 7 days, by period.

Admissions/ED visits	Lags	$PM_{2.5}$ IQR	2014–2016		2017–2019		*p*-value[c]
			Cases	ER (95% CI)	Cases	ER (95% CI)	
Asthma admissions	0	5.1	64,920	1.9 (0.8, 3.0)	37,033	1.4 (−0.1, 3.0)	0.632
	0–1	4.40	64,710	1.6 (0.7, 2.6)	36,414	1.2 (−0.1, 2.6)	0.632
	0–2	4.09	64,514	2.1 (1.0, 3.1)	35,818	2.0 (0.6, 3.5)	0.982
	0–3	3.71	64,290	1.8 (0.7, 2.8)	35,249	2.7 (1.2, 4.3)	0.295
	0–4	3.56	64,063	1.5 (0.4, 2.7)	34,735	3.0 (1.3, 4.8)	0.135
	0–5	3.40	63,861	1.3 (0.1, 2.5)	34,291	3.5 (1.7, 5.4)	0.042
	0–6	3.28	63,693	1.4 (0.2, 2.7)	33,866	3.9 (2.0, 5.8)	0.030
COPD admissions	0	4.99	49,052	1.7 (0.4, 2.9)	49,188	1.2 (−0.2, 2.6)	0.585
	0–1	4.35	48,829	1.5 (0.4, 2.6)	48,404	1.0 (−0.2, 2.3)	0.585
	0–2	3.97	48,637	2.3 (1.1, 3.5)	47,684	1.3 (−0.0, 2.6)	0.226
	0–3	3.64	48,428	2.7 (1.5, 3.9)	46,994	2.4 (1.0, 3.9)	0.756
	0–4	3.46	48,254	3.0 (1.7, 4.3)	46,332	3.1 (1.6, 4.6)	0.914
	0–5	3.22	48,073	3.0 (1.7, 4.3)	45,776	3.4 (1.8, 5.0)	0.697
	0–6	3.11	47,915	2.9 (1.5, 4.2)	45,261	3.4 (1.7, 5.0)	0.640
Asthma ED visits	0	4.88	343,378	2.0 (1.6, 2.5)	255,961	2.1 (1.5, 2.7)	0.818
	0–1	4.25	342,127	1.8 (1.4, 2.2)	252,016	1.8 (1.3, 2.3)	0.818
	0–2	3.96	340,890	1.7 (1.3, 2.2)	248,104	2.1 (1.6, 2.7)	0.287
	0–3	3.64	339,666	1.8 (1.3, 2.2)	244,447	2.7 (2.1, 3.3)	0.009
	0–4	3.46	338,486	1.7 (1.3, 2.2)	240,861	3.5 (2.8, 4.1)	<0.001
	0–5	3.20	337,336	1.7 (1.2, 2.1)	237,894	3.7 (3.1, 4.4)	<0.001
	0–6	3.05	336,354	1.7 (1.2, 2.2)	235,132	3.9 (3.2, 4.6)	<0.001
COPD ED visits	0	4.84	35,423	1.0 (−0.4, 2.5)	40,153	1.5 (−0.0, 3.1)	0.633
	0–1	4.22	35,216	0.9 (−0.3, 2.1)	39,618	1.3 (−0.0, 2.7)	0.633
	0–2	3.91	35,084	1.3 (−0.0, 2.7)	39,053	1.2 (−0.2, 2.7)	0.933
	0–3	3.61	34,922	1.7 (0.3, 3.1)	38,556	2.0 (0.4, 3.6)	0.778
	0–4	3.48	34,790	1.5 (0.0, 3.0)	38,036	2.5 (0.8, 4.2)	0.354
	0–5	3.22	34,656	1.5 (0.1, 3.0)	37,635	3.0 (1.3, 4.8)	0.185
	0–6	3.06	34,536	1.8 (0.3, 3.3)	37,237	3.3 (1.5, 5.1)	0.193

[a] When Excess rate was computed, temperature, relative humidity, holidays, date of the week and long-term trends were controlled in the logistic regression model.
[b] IQR: Interquartile Range ($\mu g/m^3$).
[c] *p*-values for the interaction term.

2014–2016. Notably, the differences in ERs of asthma admissions or ED visits between the two periods were statistically significant (interaction terms <0.007) for lag days 0–4, 0–5, and 0–6 days.

Supplemental Fig. S1 showed the temporal trends in the numbers of hospitalizations or ED visits due to asthma/COPD from 2014 to 2019. In general, both asthma hospitalization and ED visits decreased during 2014–2019, and the case numbers were much smaller during the 2017–2019 period compared to the 2014–2016 period. For COPD, the number of hospitalizations increased from 2014, reached a peak in 2017, and then declined until the end of 2019. The total number of COPD admissions was generally higher than asthma admissions, but ED visits for COPD were much lower than ED visits for asthma. The frequency of COPD ED visits increased gradually from 2014 to 2019.

Supplement Fig. S2 provides the annual changes of $PM_{2.5}$, SOC, and POC concentrations in NYS. The overall temporal trend in $PM_{2.5}$ concentrations generally decreased from 2014, and then reached the lowest concentrations in 2017 and 2019. $PM_{2.5}$ concentrations in the 2017–2019 period were substantially lower than those in the 2014–2016 period (Supplement Fig. S2). In addition, the overall trend of SOC concentration increased from 2015 to 2016, but has continuously decreased since 2016, while the overall trend of POC concentrations has increased over the study period. The median POC increased from 0.47 $\mu g/m^3$ in 2014–2016 to 0.83 $\mu g/m^3$ in 2017–2019. Using the Mann-Whitney Rank Sum Test (Mann and Whitney, 1947), the probability that the medians of these distributions were less than 0.001. However, SOC concentrations in 2017–2019 were not significantly different ($p = 0.344$) from the concentrations in 2014–2016 (Fig. S2 and Supplemental Table S2). The median values were 0.78 $\mu g/m^3$ and 0.77 $\mu g/m^3$ in 2014–2016 and 2017–2019, respectively.

As shown in Table 3 for the entire study period of 2014–2019, the associations between SOC and asthma and COPD hospitalizations and ED visits were not consistently greater than 0.0%. Specifically, the only significantly positive association found between SOC concentration and COPD hospitalization was in lag days 0–6 (ER: 4.2%, 95% CI: 1.1%, 7.4%). Similarly, a positive association was also found between increased POC concentration and asthma ED visits on lag days 0–6 (ER: 2.1%; 95% CI: 0.7%, 3.6%).

Table 4 and Table S2 show that the interquartile range increases in both SOC and POC concentrations were associated with larger ERs for asthma and COPD ED visits in the 2017–2019 period (ERs ranged from −1.9% to 4.4%) compared to the 2014–2016 period (ERs ranged from −3.4% to 0.9%). However, these increases were not observed for asthma and COPD hospitalizations. Specifically, the ERs of asthma ED visits associated with increased SOC concentrations were larger in 2017–2019 (ERs ranged from 0.4% to 1.8% for all three lags) than in 2014–2016 (ERs ranged from −0.7% to −1.3% for all lags). Similarly, ERs of COPD ED visits associated with increased SOC concentrations were generally larger in 2017–2019 (ERs ranged from 0.6% to 4.4% for all three lag times) than 2014–2016 (ERs ranged from −0.8% to 0.8%). ERs of asthma and COPD ED visits associated with increased POC concentrations consistently increased from 2014 to 2016 to 20-17-2019. Notably, the ER of COPD ED visits associated with increased POC concentration was larger in 2017–2019 (ER: 2.8%; 95% CI: 1.8%, 7.5%, 0–6 lag) than in 2014–2016 (ER: -3.4%; 95% CI: -8.7%, 2.2%). Similarly, the ER of asthma ED visits related to POC also increased from 0.9% (95% CI: -1.0%, 2.7%) in 2014–2016 to 3.2% (95%CI: 1.4%, 5.0%) in 2017–2019.

The disparities in the associations between $PM_{2.5}$, POC, and SOC concentration and asthma and COPD healthcare encounters by demographic characteristics (sex, age groups, race, ethnicity, and urbanicity) are described in Fig. 1 for hospitalizations (see also Table S4) and Fig. 2 for ED visits (see also in Table S5). $PM_{2.5}$ was associated with increased ERs of asthma and COPD hospitalizations and ED visits among both sexes. However, there were no differences by sex. The association between COPD hospitalizations and SOC concentration was larger in females compared to males. The association between asthma hospitalizations and ED visits and POC concentration was larger in males

Table 3
Excess rates (ER) [a] of asthma and COPD admissions and ED visits associated with each IQR[b] increase in SOC and POC concentrations in the previous 7 days, 2014–2019.

Chemicals/ Lags	Admissions			ED Visits		
	IQR	Cases	Excess Rate (95% CI)	IQR	Cases	Excess Rate (95% CI)
SOC						
Asthma						
0	0.82	30,765	−1.0 (−3.0, 1.0)	0.78	181,916	−0.4 (−1.1, 0.4)
0–3	0.61	27,943	−2.3 (−4.4, −0.1)	0.63	164,904	−0.4 (−1.3, 0.6)
0–6	0.67	29,877	−1.5 (−4.5, 1.6)	0.60	176,646	−0.5 (−1.6, 0.6)
COPD						
0	0.81	28,405	1.3 (−0.8, 3.5)	0.81	20,988	0.7 (−1.6, 3.1)
0–3	0.70	24,302	2.3 (−0.4, 5.0)	0.74	16,901	−0.3 (−3.5, 3.1)
0–6	0.65	27,585	4.2 (1.1, 7.4)	0.67	20,347	1.7 (−1.8, 5.3)
POC						
Asthma						
0	0.55	30,765	−1.4 (−3.5, 0.9)	0.54	181,916	−0.2 (−1.1, 0.7)
0–3	0.43	27,943	−0.2 (−2.7, 2.5)	0.41	164,904	1.1 (0.1, 2.2)
0–6	0.45	29,877	2.5 (−0.9, 6.1)	0.46	176,646	2.1 (0.7, 3.6)
COPD						
0	0.55	28,405	−0.5 (−2.5, 1.7)	0.54	20,988	−2.1 (−4.5, 0.4)
0–3	0.38	24,302	−1.8 (−4.0, 0.4)	0.38	16,901	−0.9 (−3.6, 2.0)
0–6	0.47	27,585	−1.9 (−5.0, 1.3)	0.47	20,347	0.5 (−3.4, 4.4)

[a] When Excess rate was computed, temperature, relative humidity, holidays, date of the week and long-term trends were controlled in the logistic regression model.
[b] IQR: Interquartile Range (μg/m^3).

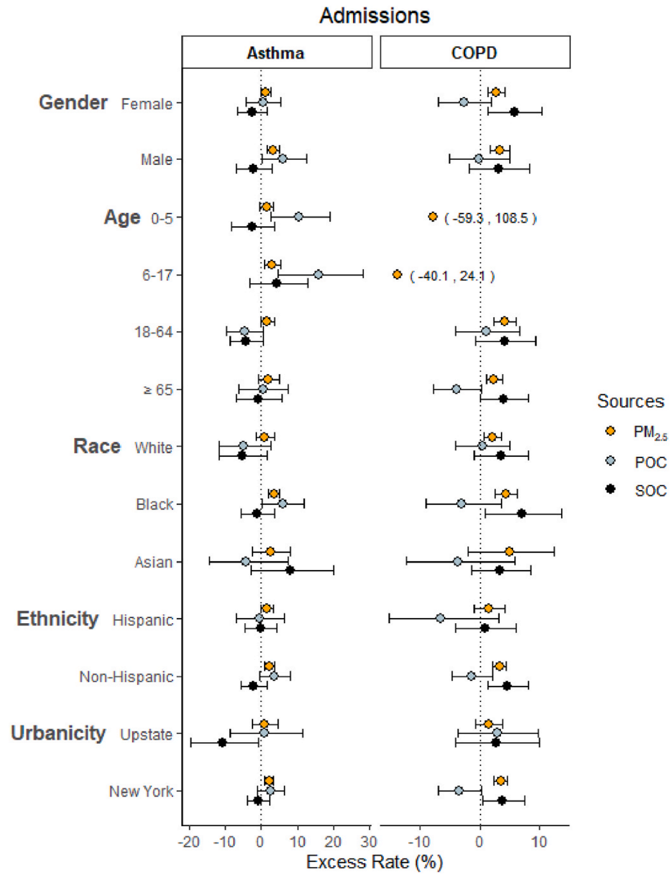

Fig. 1. Excess rate of asthma and COPD admissions associated with interquartile range (IQR)[21] increases in PM2.5, SOC, POC concentrations on lag days 0–6, stratified by demographic variables in NYS, 2014–2019.

compared to females. Additionally, we found higher ERs of asthma hospitalizations and ED visits associated with increased interquartile range increases in $PM_{2.5}$ or POC concentrations among children (0–5 and 6–17 yrs old) than in the other age groups. However, the increased associations between $PM_{2.5}$ or SOC concentrations and COPD hospitalizations and ED visits were only observed among adults, especially older adults. Additionally, the ERs for asthma hospitalizations and ED visits associated with increased $PM_{2.5}$ and POC concentrations were larger among Black, Asian, and Hispanic residents than White residents. Further, ER of COPD hospitalizations associated with increased SOC

Table 4
Excess rates (ER) [a] of asthma and COPD admissions and ED visits associated with each IQR[b] increase in SOC and POC concentrations in the previous 7 days, by period.

Admissions/ED visits	SOC			POC		
	2014–2016 ER (95% CI)	2017–2019 ER (95% CI)	*p*-value[$]	2014–2016 ER (95% CI)	2017–2019 ER (95% CI)	*p*-value[c]
Admissions						
Asthma						
0	−1.0 (−3.1, 1.2)	−1.0 (−4.0, 2.1)	0.995	0.1 (−2.8, 3.2)	−2.5 (−5.2, 0.2)	0.139
0–3	−2.7 (−4.9, 0.3)	−0.9 (−4.3, 2.6)	0.314	0.4 (−3.0, 3.8)	−0.7 (−3.8, 2.6)	0.629
0–6	−2.0 (−5.2, 1.2)	0.5 (−4.3, 5.5)	0.307	2.9 (−1.6, 7.5)	2.2 (−2.2, 6.7)	0.805
COPD						
0	1.4 (−0.9, 3.8)	1.2 (−1.6, 4.2)	0.907	−0.5 (−3.5, 2.7)	−0.5 (−2.9, 2.0)	0.994
0–3	2.3 (−0.6, 5.4)	2.1 (−1.6, 6.0)	0.916	−1.1 (−4.1, 2.0)	−2.2 (−4.8, 0.4)	0.531
0–6	5.2 (1.7, 8.7)	2.0 (−2.2, 6.5)	0.185	−0.7 (−5.1, 3.9)	−2.7 (−6.4, 1.2)	0.464
ED visits						
Asthma						
0	−0.7 (−1.5, 0.2)	0.4 (−0.7, 1.6)	0.049	−0.5 (−1.7, 0.7)	−0.0 (−1.1, 1.0)	0.499
0–3	−1.1 (−2.1, −0.1)	1.7 (0.3, 3.0)	<0.001	0.4 (−1.0, 1.7)	1.7 (0.5, 3.0)	0.091
0–6	−1.3 (−2.5, −0.1)	1.8 (0.1, 3.5)	<0.001	0.9 (−1.0, 2.7)	3.2 (1.4, 5.0)	0.044
COPD						
0	0.8 (−1.9, 3.5)	0.6 (−2.5, 3.8)	0.918	−2.5 (−6.0, 1.2)	−1.9 (−4.6, 1.0)	0.763
0–3	−0.8 (−4.4, 2.9)	0.8 (−3.6, 5.4)	0.491	−1.7 (−5.6, 2.3)	−0.4 (−3.6, 2.9)	0.557
0–6	0.4 (−3.5, 4.4)	4.4 (−0.6, 9.6)	0.140	−3.4 (−8.7, 2.2)	2.8 (−1.8, 7.5)	0.057

[a] When Excess rate was computed, temperature, relative humidity, holidays, date of the week and long-term trends were controlled in the logistic regression model.
[b] IQR: Interquartile Range (μg/m^3).
[c] p-values for the interaction term.

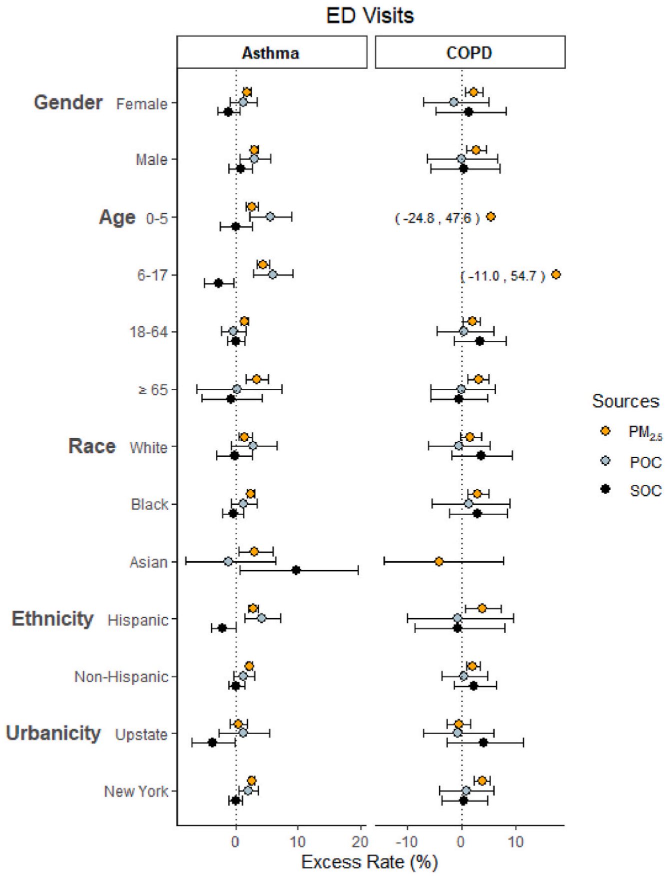

Fig. 2. Excess rate of asthma and COPD ED visits associated with each interquartile range (IQR)[31] increase in $PM_{2.5}$, SOC, POC concentrations on lag days 0–6, stratified by demographic variables in NYS (2014–2019).

concentrations were higher among Black residents than residents of other race/ethnicity groups. Patients with asthma or COPD hospitalizations and ED visits living in New York City (Bronx, Manhattan, Queens) had larger ERs associated with increased $PM_{2.5,}$ POC, and SOC concentration than upstate residents (Buffalo, Albany, Rochester).

4. Discussion

4.1. $PM_{2.5}$ and respiratory diseases

The current study found that increases in $PM_{2.5}$ concentration were associated with increased rates of both asthma and COPD hospitalizations and ED visits across all lag days (0 to 0–6). Consistent with our findings, almost all prior studies consistently demonstrated positive associations between acute increases in concentrations of $PM_{2.5}$ and respiratory ED visits or admissions across the nation, including the studies in St. Louis and Missouri-Illinois metropolitan area (Sarnat et al., 2015), 110 US counties (Powell et al., 2015), California (Ebisu et al., 2019), Denver (Kim et al., 2015), New York State (Hopke et al., 2019), and in 108 US Cities (Blomberg et al., 2019). Yu et al.'s (2023) literature review reported excess rates of prior studies ranged from 0.67% to 2.59%, which may not be directly comparable to each other since they were scaled to different pollutant concentration increases and covered different time periods since changes over time in toxicity per unit mass have been reported (Croft et al., 2019; Hopke et al., 2019). Multiple international studies also found positive associations between $PM_{2.5}$ and respiratory diseases, such as the study by Renzi et al. (2022) in Italy (whole country) that showed the excess rate of total respiratory diseases associated with increased $PM_{2.5}$ concentrations was 1.22% (0.76, 1.68). In a case-crossover study by Szyszkowicz et al. (2018), ED visits for COPD among males were found to be positively associated with increased $PM_{2.5}$ concentrations on lag days 1–8 in Ontario, Canada.

We found both immediately occurred (lag 0) and week-long (0–6 lag days) respiratory effects of $PM_{2.5}$ on both asthma and COPD hospitalizations and ED visits in the current study. While most prior studies only evaluated the $PM_{2.5}$-respiratory healthcare encounter association using $PM_{2.5}$ concentrations in lag days 1–2 or 1–3 and found increased odds or risk ratios immediately during the same day of high concentration of $PM_{2.5}$ exposure.

4.2. POC and SOC on respiratory health

In the current study, we found that increased concentrations of SOC were associated with increased rates of COPD hospitalization (lag days 0–6) and high POC concentrations were associated with increased rates of asthma ED visits (both lag days 0–3 and 0–6). As reported in our prior studies (Croft et al., 2019; Rich et al., 2019), the measured organic carbon (OC) is a component of $PM_{2.5}$ and was divided into primary organic carbon (POC) and secondary organic carbon (SOC). Consistent with our findings, Delfino et al. (2010) stated that $PM_{2.5}$ components may generate reactive-oxygen-species and induce oxidative stress, including POC from combustion sources and SOC from photochemically oxidized volatile organic compounds that could affect human health through systemic inflammation and oxidative stress (Delfino et al., 2010). Specifically, Delfino et al. (2010) found that SOC markers, fine particles ($PM_{0.25–2.5}$), and O_3 were positively correlated with increased exhaled NO, while POC, $PM_{0.25}$, CO, and nitrogen dioxide (NO_x) were positively associated with IL-6. Reactive oxygen species (ROCs) were associated with both outcomes. In addition, McConnell et al. (2003) examined the association between bronchitis symptoms and increased $PM_{2.5}$ concentrations, particulate organic and elemental carbon, NO_2, and other gaseous pollutants in a cohort of asthmatic children living in southern California. They found that increased respiratory symptoms, assessed yearly by questionnaire, were associated with increases in annual $PM_{2.5}$ concentrations. The biological mechanism(s) by which $PM_{2.5}$ or other pollutants contribute to asthma and COPD exacerbations and healthcare encounters is not completely understood. Zhang et al. (2018) suggested that due to the recent increase in SOC and POC as well as the increased toxicity of $PM_{2.5}$, additional oxidant exposures and subsequent inflammation and oxidative stress may result in increased rates of asthma or COPD. Different exposure concentrations of air pollution may have different health effects and may affect different biological processes in humans (Villeneuve et al., 2007). In low and middle-income countries with regularly high $PM_{2.5}$ concentrations (over 35 $\mu g/m^3$) (World Health Organization, 2021), such as those in megacities in India, Pakistan, and China, air pollutant exposure may result in irritant and inflammatory effects on airway neuroreceptors and epithelium. However, such exposures are rare in high-income countries (North America or Europe), in which there are more typically lower concentrations of $PM_{2.5}$ (below 15 $\mu g/m^3$) (World Health Organization, 2021).

Other mechanisms may be in operation via two characteristic features of asthma (i.e., pollutants can induce airway hyper-responsiveness or airway inflammation (Guarnieri and Balmes, 2014). Gowers et al. (2012) suggested four main mechanisms by which air pollution may contribute to the development of asthma and exacerbation of it. These include: 1) oxidative stress and damage; 2) airway remodeling; 3) immunological and inflammatory responses; and 4) enhancement of respiratory sensitization to aeroallergens. For COPD, one of the main mechanisms is likely mediated by oxidative stress (MacNee and Donaldson, 2000). Oxidative stress could injure the airway epithelium, making the airways of COPD patients more sensitive to further damage,

[2] See Supplement Table S4 for the IQRs.

and impairing the resistance capability of the immune system (Li et al., 1996). Another possible mechanism is that air pollution exposure can cause respiratory inflammation and subsequent parenchymal damage, thereby worsening pulmonary function in patients with COPD (Abbey et al., 1998).

4.3. Increased effects of $PM_{2.5}$ on asthma and COPD in recent years

We found that the $PM_{2.5}$ concentrations have declined over time since 2014 in NYS, with significantly lower concentrations from 2017 to 2019 than in 2014–2016. However, there were large fluctuations in SOC levels over time, and POC started to increase in 2016 with the highest concentrations in 2018–2019. Consistently, Squizzato et al. (2018a) found large reductions in all criteria pollutant concentrations, except ozone, in NYS, in 2005–2016. Similar findings extended these analyses to 2019 (Chen et al., 2023b). The reductions in $PM_{2.5}$ were largely reductions in the concentrations of sulfate, nitrate, and elemental and organic carbon. Chen et al. (2023) also observed large reductions in the $PM_{2.5}$ concentrations, primarily driven by reductions in particulate sulfate, although the rate of decrease has slowed in recent years due to relatively stable or increasing levels of particulate nitrate and secondary organic aerosol. Similar to what Squizzato et al. found, ozone concentrations increased at most monitoring sites, indicating a transition to VOC-limited conditions. The huge reductions in $PM_{2.5}$ and other air pollutant concentrations in NYS after 2016 could be due to the effects of multiple environmental policies implemented from 2005 to 2016, including those related to improved fuel quality and required emissions controls on new heavy-duty diesel on-road vehicles; upwind pollution source emissions controls to eliminate fossil fuel use for electricity generation through actions of the Ontario government; and U.S. actions such as the Cross-States Air Pollution Rule and lawsuit settlements with electricity generators to reduce their emissions. The 2008 economic recession also resulted in less demand for electricity and goods transport. Changes in coal and natural gas prices used to generate electricity resulted in a switch from coal to natural gas as electricity demand increased following the 2008 recession (Squizzato et al., 2018b).

However, an unexpected trend of higher ERs of asthma hospitalizations and ED visits associated with increased $PM_{2.5}$, POC, and SOC concentrations was found in the recent period (2017–2019) compared to the prior period (2014–2016). COPD showed similar trends with larger excess rates in the recent period (2017–2019) than in 20014-2016. It is surprising to find the increased ERs of both asthma and COPD urgent care utilization in the recent period given the multiple environmental emission control policies that have been implemented during the recent decade. For instance, Tier 3 light-duty vehicles and their reduced emissions were introduced in New York State in 2017, with all new vehicles being Tier 3 by 2025. This was expected to result in reduced tailpipe and evaporative emissions. We, therefore, hypothesized that improved air quality during the early implementation of Tier 3 (2017–2019) would result in reduced rates of respiratory disease hospitalization and ED visits associated with ambient $PM_{2.5}$ concentrations compared to 2014–2016 (pre-Tier 3 periods).

However, despite the implementation of many environmental policies and reductions in average $PM_{2.5}$ concentration during 2017–2019, the $PM_{2.5}$ - asthma/COPD ERs did not decrease, but actually increased suggesting that either toxic $PM_{2.5}$ components might have increased, or non-toxic species decreased during 2017–2019 leading to greater toxicity per unit mass. Hopke et al. (2020) found increased toxicity per unit mass over 2005 to 2016 for COPD and asthma. SOC concentrations across NYS decreased from 2005 to 2007 and 2008 to 2013. In contrast, SOC concentrations increased from 2014 to 2016 (Masiol et al., 2019). POC increased in 2017–2019 while SOC remained relatively constant. Thus, the remaining SOC appears to have become more toxic. The changes in SOC formation rates related to light-duty vehicle emissions have been discussed in our prior respiratory disease studies (Hopke et al., 2019, 2020).

Another plausible reason for these findings is that the proportion of particles smaller than 100 nm (ultrafine particles; UFP) increased from the 2014–2016 period to the 2017–2019 period, particularly in 10–20 nm and 20–50 nm particles (Chen et al., 2022). Increases in smaller particle formation (<50 nm) may be due to reduced accumulation mode particles (100–500 nm) concentrations, which serve as a condensation sink for condensable substances (McMurry and Friedlander, 1979). Increases in particles directly attributable to gasoline vehicles have also been observed in the most recent period (Hopke et al., 2024). Prior studies have found significant adverse effects of UFP on cardiovascular hospitalization (Lin et al., 2022).

The changes in demographic composition or hospital admission policy over time may also have affected our exposure-health associations. However, we have checked whether age, race/ethnicity, and admission policies in NYS changed from 2014 to 2019, and found no substantial changes in these variables between the two periods (i.e., 2014–2016 vs. 2017–2019). Finally, to evaluate whether asthma and COPD have become more severe in recent years, therefore requiring more use of urgent care, we examined temporal trends in asthma and COPD healthcare encounters in NYS. We found that the asthma and COPD hospitalizations and ED visits have not increased substantially since 2014, and the length of stay and number of procedures used have also not increased during 2017–2019. These details suggest that an increase in the baseline severity of respiratory diseases in 2017–2019 is less likely an explanation of the increase in asthma and COPD healthcare encounters in 2017–2019 compared to 2014–2016 and earlier periods. Furthermore, the recent environmental control policies were largely focused on sulfate and nitrate reduction and these constituents may have little direct health effects.

4.4. Demographic disparities

Our findings of higher rates of asthma hospitalizations and ED visits associated with increased $PM_{2.5}$ and POC concentrations for asthmatic children, but higher rates of COPD hospitalizations and ED visits associated with increased $PM_{2.5}$ and SOC concentrations among older. Consistent with our findings, most prior studies found the strongest effects of PM on risk or rate of asthma and COPD compared to other respiratory diseases (Croft et al., 2020; Lin et al., 2018; Renzi et al., 2022; Zhang et al., 2016), but few studies examined the respiratory effects of POC and SOC, and whether these associations are different across demographic characteristics.

Zhang et al. (2016) found generally stronger air pollution-asthma associations in children compared to adults 18–64 years of age. Children are thought to be more susceptible to PM related health effects because they are outdoors more than adults and thus are exposed to pollutant concentrations that are higher than those indoors. Children also generally inhale more air per unit of body weight and have physical activities that result in higher respiratory rates than adults, thereby increasing the total volume of inhaled air (and the accompanying pollution) (Hopke, 2015). In addition, the respiratory physiology of children facilitates deeper lung deposition of particles and interaction with the pulmonary capillary (Chen et al., 2022). Older adults (>65 years) may be more vulnerable to PM-related COPD. Older adults may also be more susceptible to air pollutants' adverse effects due to their reduced immune function and medical comorbidities (Medina-Ramón & Schwartz, 2008; Tibuakuu et al., 2018). The current study also < grant-highlight > supports</grant-highlight > prior findings (Ou et al., 2008; Pratt et al., 2015) that individuals from lower socio-economic backgrounds, such as Black and Hispanic adults and children, and those living in urban areas are more vulnerable to the adverse effects of $PM_{2.5}$ and its components.

[3] See Supplement Table S5 for the IQRs.

4.5. Strengths and limitations

This accountability study examined whether fine particles-health response relationships changed after new Tier 3 light-duty vehicles were introduced in NYS in 2017. The impacts of $PM_{2.5}$, POC and SOC on respiratory diseases were evaluated to help identify important $PM_{2.5}$ components recently increased in toxicity with respect to asthma and COPD medical events. This work may represent the largest study evaluating the effects of $PM_{2.5}$, POC, and SOC on both asthma and COPD. We evaluated 707,804 Asthma and COPD hospital admission records and ED visit cases in NYS. Another strength of this study is the use of objective SPARCS health data that reduces reporting bias, a common limitation encountered by studies based on survey data. In addition, we studied both asthma and COPD that represent the two population groups, i.e., children and older adults respectively who are most susceptible to the adverse effects of exposure to $PM_{2.5}$ and other air pollutants.

Alternatively, several potential limitations should be considered. First, we only included asthma and COPD hospital admission/ED visit cases (i.e., more severe patients) but not visits to doctor's offices (i.e., less severe cases). Therefore, the generalizability of study findings may be limited. However, asthma and COPD exacerbations usually require immediate medical attention. Therefore, hospitalization and ED visits are good measures of urgent/severe respiratory events. Another limitation is that our study was only focused on episodes of COPD and asthma, but we could not distinguish between new incident cases and an exacerbation of an existing case. Although residual confounding should be considered, the case-crossover study controls for non-time-varying factors (age, sex, race/ethnicity, health history, smoking history, and any interaction between them by design, minimizing such concerns.

While further studies should validate our findings, this accountability study may provide an important but unexpected warning message. The toxicity of some components of $PM_{2.5}$ have been increasing since 2015, and the effects of $PM_{2.5}$ on respiratory health were higher with 2–4 folds increases even after multiple prior and ongoing environmental policies were implemented. Researchers and environmental agencies may need to identify and mitigate the sources of POC and SOC as well as other $PM_{2.5}$ source-specific constituents. Furthermore, it may be important for clinical facilities and public health agencies to be aware of the burden and demands of these excess respiratory cases affected by $PM_{2.5}$, POC, and SOC, which could be used to prevent and intervene in those severe cases.

5. Conclusions

Our study found an effect of $PM_{2.5}$ in the prior week on both asthma and COPD admission and ED visits while the concentrations of $PM_{2.5}$ declined and POC and SOC concentrations rose in recent years. We also found significant 2-4-fold increases in excess rates of asthma and COPD in relation to these $PM_{2.5}$ components and significant demographic disparities during 2017–2019 compared to 2014–2016 despite the implementation of multiple environmental policies. These unanticipated increases in exposure-health response relationship in recent years could be due to exposure to SOC and POC with increased toxicity per unit mass.

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CRediT authorship contribution statement

Shao Lin: Writing – review & editing, Writing – original draft, Investigation, Funding acquisition, Formal analysis. **Yukang Xue:** Writing – original draft. **Sathvik Thandra:** Writing – original draft, Formal analysis. **Quan Qi:** Writing – original draft. **Philip K. Hopke:** Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Sally W. Thurston:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Daniel P. Croft:** Writing – review & editing, Funding acquisition, Conceptualization. **Mark J. Utell:** Writing – review & editing, Funding acquisition, Conceptualization. **David Q. Rich:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2024.124585.

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