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Triggering of ST-elevation myocardial infarction by ultrafine particles in New York: Changes following Tier 3 vehicle introduction

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ABSTRACT

Background: Previously, we found increased rates of ST-elevation myocardial infarction (STEMI) associated with increased ultrafine particle (UFP; <100 nm) concentrations in the previous few hours in Rochester, New York. Relative rates were higher after air quality policies and a recession reduced pollutant concentrations (2014–2016 versus 2005–2013), suggesting PM composition had changed and the same PM mass concentration had become more toxic. Tier 3 light duty vehicles, which should produce less primary organic aerosols and oxidizable gaseous compounds, likely making PM less toxic, were introduced in 2017. Thus, we hypothesized we would observe a lower relative STEMI rate in 2017–2019 than 2014–2016.

Methods: Using STEMI events treated at the University of Rochester Medical Center (2014–2019), UFP and other pollutants measured in Rochester, a case-crossover design, and conditional logistic regression models, we estimated the rate of STEMI associated with increased UFP and other pollutants in the previous hours and days in the 2014–2016 and 2017–2019 periods.

Results: An increased rate of STEMI was associated with each 3111 particles/cm^3 increase in UFP concentration in the previous hour in 2014–2016 (lag hour 0: OR = 1.22; 95% CI = 1.06, 1.39), but not in 2017–2019 (OR = 0.94; 95% CI = 0.80, 1.10). There were similar patterns for black carbon, $UFP_{11–50nm}$, and $UFP_{51–100nm}$. In contrast, increased rates of STEMI were associated with each 0.6 ppb increase in SO_2 concentration in the previous 120 h in both periods (2014–2016: OR = 1.26, 95% CI = 1.03, 1.55; 2017–2019: OR = 1.21, 95% CI = 0.87, 1.68).

Conclusions: Greater rates of STEMI were associated with short term increases in concentrations of UFP and other motor vehicle related pollutants before Tier 3 introduction (2014–2016), but not afterwards (2017–2019). This change may be due to changes in PM composition after Tier 3 introduction, as well as to increased exposure misclassification and greater underestimation of effects from 2017 to 2019.

1. Introduction

Since the early 2000s, policy initiatives to improve air quality have been implemented nationally and across New York State (NYS), including reductions in sulfur concentrations in multiple fuels begun in October 2006 with on-road diesel fuel, emissions controls on heavy-duty diesel on-road trucks and buses (July 1, 2007 and January 1, 2010), reduced SO_2 and NOx emissions from power plants upwind of NYS in response to the planned Cross-State Air Pollution Rule, electricity policy changes in Ontario, and closure of coal-fired power plants in NYS. Major economic drivers, such as the 2008 recession and the change in the price of natural gas compared to coal and oil, also had effects on air quality

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(Squizzato et al., 2018). Previously, we reported that $PM_{2.5}$ and its major constituents decreased across NYS from 2005 to 2016 following implementation of these air quality policies and the co-occurring economic changes. However, these reductions also came with a change in PM composition that included decreased sulfate, nitrate, elemental carbon, and primary organic carbon [POC], and increased secondary organic carbon [SOC] concentrations and contributions from spark-ignition vehicles (Masiol et al., 2019). Increases in SOC were consistent with increased ozone concentrations and projected increases in SOC formation due to the reduced NOx emissions in New York State and the transition to gasoline direct-injection engine (GDI) light-duty vehicles during this time (Squizzato et al., 2018). Further, in the Buffalo, Rochester, Albany, and New York City metropolitan areas, we reported that interquartile range increases in $PM_{2.5}$ concentration (lag days 0–2) were associated with higher rates of respiratory, respiratory infectious disease, and cardiovascular hospital admissions and emergency department visits (e.g., ischemic heart disease) in adult NYS residents, after these policy and market changes (2014–2016) compared to before (2005–2007) and during this period of change (2008–2013). (Croft et al., 2019; Hopke et al., 2019; Zhang et al., 2018).

We similarly reported an increased rate of ST-elevation myocardial infarction (STEMI) associated with increased ultrafine particle (<100 nm; UFP) concentrations in the previous hour among adults treated at the University of Rochester Medical Center in Rochester, NY from 2005 to 2016 (Wang et al., 2019). Further, we similarly reported that this relative rate was substantially higher in the 2014–2016 period, than in 2005–2007 or 2008–2013 (Wang et al., 2019), even though particle number count (PNC) concentrations had been decreasing (Masiol et al., 2018). Together, these studies suggested that although the concentrations of $PM_{2.5}$ and particle number count/UFP decreased from 2005 to 2016 in New York State and Rochester, the composition of $PM_{2.5}$ and UFP also changed after these policies and market changes, and the toxicity of the PM may have increased.

On January 1, 2017, the sale of new Tier 3 light-duty vehicles began, with Tier 3 regulations requiring fleet average emissions for each manufacturer to decrease steadily until 2025, when the full set of emission limits must be met by all new vehicles and the sulfur content of gasoline must be reduced to less than 10 ppm from the previous 30 ppm limit. (Final Rule for Control ofa) This approach parallels that in the Tier 2 regulations that required full compliance with the emission standards by 2010. (Final Rule for Control ofb) Thus, work is needed to determine if these changes in particulate emissions and concentrations from 2017 to 2019 altered the rate of STEMI associated with increased UFP concentrations.

Using STEMI events from patients treated at the University of Rochester Medical Center from 2014 to 2019, and hourly ultrafine and other pollutant concentrations from the Rochester monitoring site, we estimated the rate of STEMI associated with increased UFP concentrations in the previous few hours and days in both the 2014–2016 and 2017–2019 periods. We hypothesized that the rate of STEMI associated with the same sized increase in UFP concentration in the previous hour would be lower in the 2017–2019 period compared to 2014–2016.

2. Methods

2.1. Study population and outcome definition

All patients treated at the University of Rochester Medical Center Cardiac Catheterization Laboratory (Cath Lab) for ST-elevation myocardial infarction (STEMI) between January 1, 2014, and December 31, 2019, who lived within 15 miles of the monitoring station (described below), were included in this study. Based on the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines, we diagnosed STEMI at the time of patient admission. A STEMI was defined as a myocardial infarction with an ST segment elevation on the presenting electrocardiogram of larger than 1 mm in 2 or more contiguous precordial leads, in 2 or more adjacent limb leads, or new or presumed new left bundle branch block in the presence of angina or angina equivalent (O'Gara et al., 2013). Symptom onset time (date and hour of first symptoms) was collected via self-report from each patient upon arrival at the Cath lab. If the patient was unable to provide this information, it was obtained from the patient's kin.

STEMI events within a single patient during the study period were only counted as additional events if the subsequent STEMI was ≥72 h after their previous STEMI. Demographic and clinical characteristics were obtained from the Cath Lab for all patients, from medical history and chart review. Patients were enrolled from throughout the University of Rochester's Health Care System, which includes six hospitals and their associated emergency rooms, and fifteen urgent care centers that referred patients to the University's academic center for evaluation and advanced treatment. This study was approved by the University of Rochester Medical Center Research Subjects Review Board. Informed consent was not required since data were past events and the research could not affect treatment. There was no contact with study subjects, and all results are presented in aggregate only.

2.2. Air pollution and meteorology measurements

Hourly air pollution concentrations were obtained from the air quality monitoring site in Rochester, New York operated by the New York State Department of Environmental Conservation, where $PM_{2.5}$ concentrations, SO_2, O_3, and CO were measured continuously throughout the study period (2014–2019). This site operates a two-wavelength (370 and 880 nm) aethalometer (Magee Scientific, Berkeley, CA, USA) to measure black carbon (BC) and UV black carbon (UVBC). Particle number size distributions were measured using a Scanning Mobility Particle Sizer (SMPS, TSI, Inc., Shoreview, MN), with concentrations aggregated into several size groups including UFP (≤100 nm) and accumulation mode particles (AMP; 100–500 nm). The UFP were further divided into $UFP_{11\text{-}50}$ (11–50 nm; marker for nucleation and spark ignition vehicle emissions) (Kittelson et al., 2006a) and $UFP_{50\text{-}100}$ (50–100 nm; marker of diesel vehicle emissions and residential wood burning; Aitken mode) (Kasumba et al., 2009; Kittelson, 1998; Kittelson et al., 2006b). These data have been presented and their trends analyzed in several recent studies (Masiol et al., 2019; Masiol et al., 2018; Chen et al., 2022). Masiol et al. (2018) reported small upward trends in particle number concentrations between 2013 and 2016 for most size bins. However, Chen et al. (2022) saw a sharper rise in particle number concentrations particularly in the 11–20 nm size range after 2018, as shown in Fig. S1.

2.3. Study design and statistical analyses

We used a time-stratified case-crossover design (Levy et al., 2001; Maclure, 1991) to estimate the rate of STEMI associated with air pollutant concentrations in the previous few hours and days. Control periods were matched to each case period by hour of the day, weekday, month, and year, resulting in 3–4 controls per case. Because case and control periods were from the same patient, time-invariant confounders such as age, gender, and comorbidities were controlled by design. Factors that varied between the case and control periods (e.g., temperature and relative humidity) were potential confounders and were included in the analytic models described below. Associations with each pollutant were examined in single pollutant models that included data from both time periods (2014–16 and 2017–19) using an interaction term for period*pollutant.

We calculated the average concentrations of each pollutant (UFP, $UFP_{11\text{-}50}$, $UFP_{50\text{-}100}$, $PM_{2.5}$, AMP, BC, SO_2, O_3, and CO) in the 1 h before the STEMI symptom onset time (i.e. start of the case period) and its matched control times. If the time of symptom onset of a STEMI event was in the first 29 min of the hour (e.g., 10:24), then lag hour 0 was defined as the previous hour (i.e. 09:00–09:59). If the STEMI symptom

onset time was reported to be in the 30th minute or after (e.g. 10:31 or 10:59), then lag hour 0 was defined as that same hour (i.e. 10:00–10:59). We then calculated average pollutant concentrations for the 3 h (lag hours 0–2), 12 h (lag hours 0–11), 24 h (lag hours 0–23), 48 h (lag hours 0–47), 72 h (lag hours 0–71), 96 h (lag hours 0–95) and 120 h (lag hours 0–119) before each case and control period.

Next, we used a conditional logistic regression, stratified by matched case/control set, to regress case-control status (case = 1, control = 0) against the mean UFP concentration in the previous 1 h (lag hour 0). In this model, we also included the mean temperature (as a linear term) and relative humidity (using a natural spline with 4 degrees of freedom [df]) during the same lag hours, as well as an indicator variable for holidays (i.e., New Year's Day, Memorial Day, July 4th, Labor Day, Thanksgiving Day, day after Thanksgiving, Christmas). We used Akaike's information criterion to select the optimal functional form (natural spline with 2, 3, 4, or 5 df versus 1 df/linear) for temperature and relative humidity. We also included an interaction term (UFP * 2017–2019) in this model to examine whether the relative rate was different in the 2014–2016 and 2017–2019 periods. From this interaction model, we present the odds ratio (OR), equivalent to the rate ratio in a case-crossover study, and its 95% confidence interval separately in the 2014–2016 and 2017–2019 periods. We then re-ran this interaction model to estimate the rate of STEMI associated with each interquartile (IQR) increase in the mean UFP and other pollutant concentrations at all lag times, in both the 2014–2016 and 2017–2019 periods.

Next, we stratified the sample by residential distance to the monitoring station (≤median distance from residence to monitoring station versus > median distance), and re-ran this same interaction model in each strata. We also stratified the sample by season and re-ran the same interaction model in each strata. Additionally, we separately re-ran the same interaction model while controlling for a second pollutant ($PM_{2.5}$, CO, SO_2, AMP, BC, and O_3), and compared results with those from the main analysis.

Last, we examined whether our estimates of period-specific relative rates and any difference between them were robust to inclusion of interaction terms between the lag hour 0 UFP concentration and subject demographic or clinical characteristics in the model. In separate models, we added interaction terms between each characteristic (i.e., age, sex, race, prior myocardial infarction, prior percutaneous coronary intervention, smoking, hypertension, dyslipidemia, diabetes, family history of coronary artery disease, chronic lung disease, body mass index, and health insurance) and UFP lag hour 0 to the interaction model described above examining effect modification by period. Body mass index and health insurance each had three categories and thus each had two interaction terms included in this model. All data management was performed using SAS (version 9.4; SAS institute Inc., Cary, NC), and all statistical analyses were completed using R (version 4.1.2 R foundation for statistical computing, Vienna, Austria, splines package). Statistical significance was defined as $p < 0.05$.

3. Results

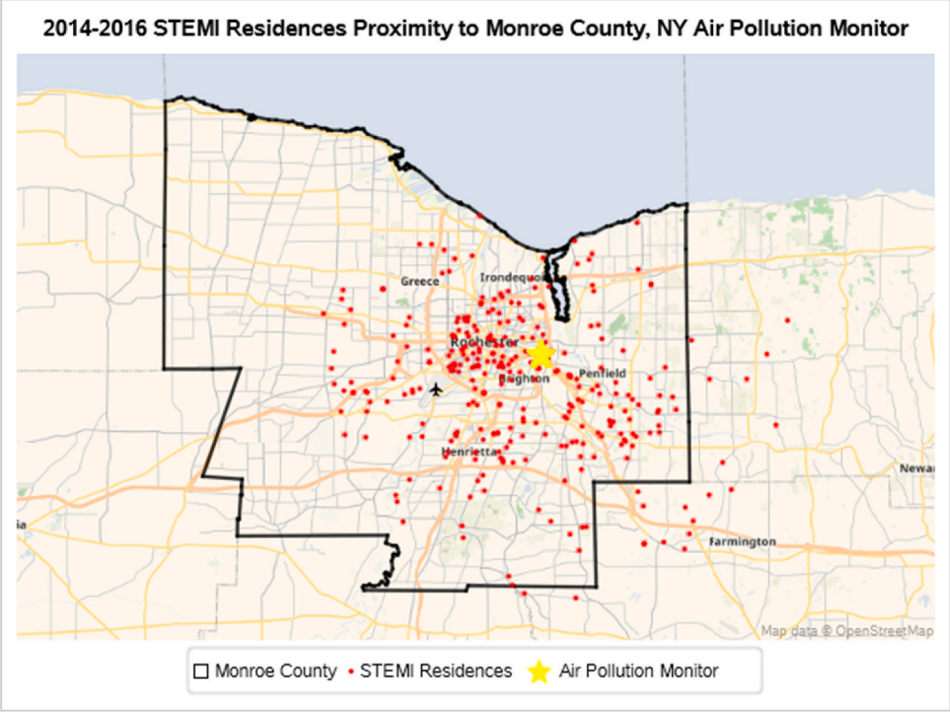
Demographic characteristics of STEMI patients were generally similar in the 2014–2016 and 2017–2019 periods (Table 1). However, when compared to the 2014–2016 period, STEMI patients in the 2017–2019 period were slightly more likely to have had a prior MI (22% compared to 14%) and to be a smoker (46% compared to 36%), while they were less likely to have a family history of coronary artery disease (19% compared to 29%). Further, in the 2017–2019 period, STEMI patients were less likely to have private health insurance (62%) and more likely to have Medicare (27%) and Medicaid (10%), than STEMI patients in the 2014–2016 period (86%, 7%, and 4%, respectively). The mean length of patient stay was similar for patients in both periods (2014–2016: 4.6 ± 8.9 days; 2017–2019: 4.3 ± 6.1 days). As shown in Fig. 1, there were similar spatial distributions of STEMI patient residences between both periods, but the average distance between the monitoring station and a subject's residence was slightly greater in the 2017–2019 period.

Table 1
Characteristics of STEMI patients in the 2014–2016 and 2017–2019 periods.

Characteristic	2014–2016 (N = 304) n (%)	2017–2019 (N = 360) n (%)
Age (years)		
<50	60 (20)	53 (15)
50-59	76 (25)	93 (26)
60-69	88 (28)	118 (33)
70-79	50 (17)	64 (18)
>80	30 (10)	32 (9)
Mean ± SD	62 ± 13	63 ± 12
Sex		
Female	74 (24)	111 (31)
Male	230 (76)	249 (69)
Race		
Missing	3 (1)	5 (1)
Caucasian	261 (87)	309 (87)
African American	30 (10)	38 (11)
Asian	9 (3)	8 (2)
Other Race	1 (0)	0 (0)
Ethnicity		
Missing	3 (1)	1 (0)
Hispanic/Latino	11 (4)	13 (4)
Clinical Presentation (*Each subject may have more than one*)		
Prior Myocardial Infarction	42 (14)	80 (22)
Prior Percutaneous Coronary Intervention	48 (16)	59 (16)
Prior Coronary Artery Bypass Graft	13 (4)	10 (3)
Cardiovascular Disease	17 (6)	20 (6)
Smoking	108 (36)	165 (46)
Hypertension	200 (66)	227 (63)
Dyslipidemia	167 (55)	191 (53)
Diabetes	74 (24)	84 (23)
Prior Heart Failure	8 (3)	17 (5)
Family History Coronary Artery Disease	88 (29)	68 (19)
Prior Peripheral Arterial Disease	14 (5)	8 (2)
Current Dialysis	2 (1)	0 (0)
Chronic Lung Disease	25 (8)	21 (6)
Length of Stay (Days) Mean ± SD[a]	4.6 ± 8.9	4.3 ± 6.1
Body Mass Index		
Missing	2 (1)	1 (0)
Normal (<25 kg/m^2)	67 (22)	92 (26)
Overweight (25 kg/m^2 ≤ BMI <30 kg/m^2)	129 (43)	136 (38)
Obesity (30 kg/m^2 ≤ BMI <35 kg/m^2)	65 (22)	84 (23)
Severe Obesity (BMI ≥35 kg/m^2)	41 (14)	48 (13)
Mean ± SD	29 ± 5	29 ± 6
Health Insurance		
Missing	31 (10)	9 (2)
Private	234 (86)	218 (62)
Medicare	19 (7)	96 (27)
Medicaid	11 (4)	34 (10)
No Insurance	5 (2)	0 (0)
Other (military, state, non-US)	4 (2)	3 (1)

[a] One outlier (length of stay = 347 days) removed from 2014 to 2016 period.

Period-specific summary statistics of pollutant concentrations are shown in Table 2. From the 2014–2016 period to the 2017–2019 period, there was small reductions in the median concentration of $PM_{2.5}$ (−7.3%), UFP (−5.7%), $UFP_{11\text{-}50}$ (−5.5%), and $UFP_{51\text{-}100}$ (−5.7%), CO (−5.6%), and BC (−3.8%), and increases in median concentrations of SO_2 (8.7%) and RH (1.5%), but little to no change in AMP, O_3, or temperature. During the study period, hourly concentrations of UFP were highly correlated with $UFP_{11\text{-}50}$ (r = 0.96) and moderately correlated with $UFP_{50\text{-}100}$ (r = 0.66), but not correlated with other pollutants (Table 3). AMP was moderately correlated with $PM_{2.5}$ (r = 0.61), $UFP_{50\text{-}100}$ (r = 0.68), and BC (r = 0.67), while BC was also moderately



Period	Minimum	25th Percentile	50th Percentile	75th Percentile	Maximum	Mean	Standard Deviation
2014-2016	0.25	3.83	5.53	8.27	14.97	6.28	3.48
2017-2019	0.42	4.21	6.63	9.01	14.97	6.92	3.64

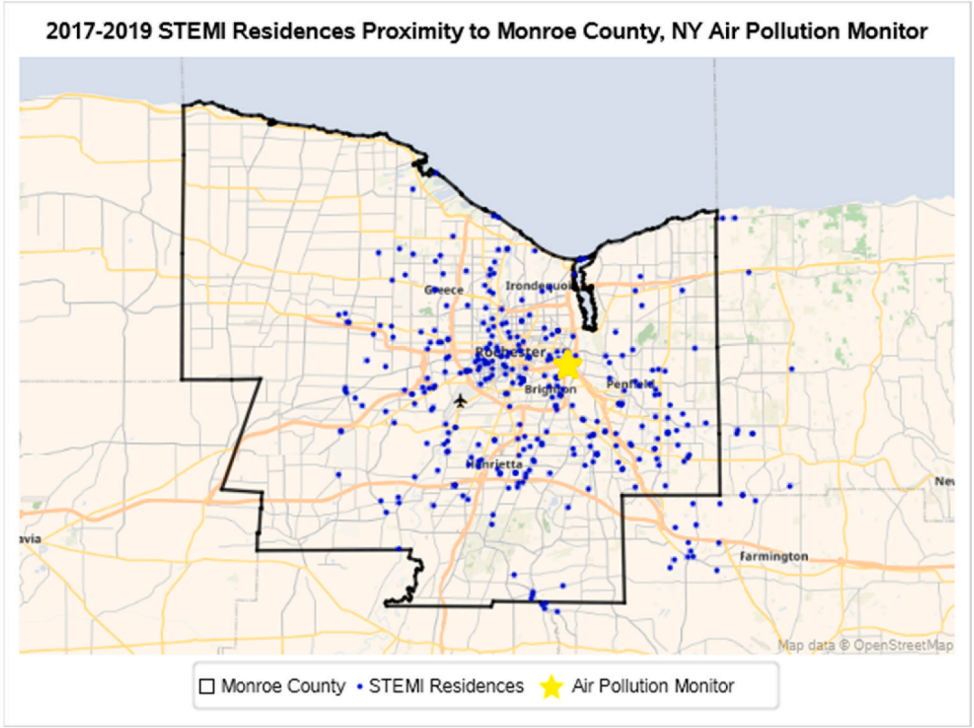


Fig. 1. STEMI patient residential locations relative to NYS DEC air pollution monitoring station, and distribution of distances (miles) between residential locations and monitoring station, by year period.

Table 2
Distribution of hourly pollutant concentration and weather characteristics[a].

	N	Mean	Minimum	5th Percentile	25th Percentile	Median	75th Percentile	95th Percentile	Maximum	Inter Quartile Range
UFP (particles/cm^3)										
2014–2016	921	3783	0	586	1845	2947	5005	9292	31,417	3160
2017–2019	1217	3580	0	531	1628	2780	4658	9279	20,764	3030
UFP (11–50 nm) (particles/cm^3)										
2014–2016	921	2667	0	344	1099	1895	3436	7134	29,559	2337
2017–2019	1217	2530	0	288	996	1791	3338	7415	19,670	2342
UFP (51–100 nm) (particles/cm^3)										
2014–2016	921	1116	0	138	497	900	1495	2781	7270	998
2017–2019	1217	1049	0	146	442	849	1432	2665	6309	990
AMP (particles/cm^3)										
2014–2016	921	608	0	101	280	511	847	1414	2150	567
2017–2019	1217	588	0	91	258	507	815	1398	2926	557
$PM_{2.5}$ (μg/m^3)										
2014–2016	913	6.3	−2.7	0.5	3.2	5.5	8.6	15.0	26.9	5.4
2017–2019	1211	6.0	−4.6	0.3	2.9	5.1	8.2	14.8	44.9	5.3
CO (ppm)										
2014–2016	923	0.16	0.00	0.00	0.09	0.18	0.22	0.33	2.08	0.14
2017–2019	1212	0.16	−0.01	0.00	0.00	0.17	0.22	0.32	1.02	0.22
SO_2 (ppb)										
2014–2016	942	0.54	−0.10	0.00	0.10	0.21	0.48	1.89	12.66	0.38
2017–2019	1246	0.53	0.00	0.00	0.10	0.23	0.50	1.81	16.35	0.40
O3 (ppb)										
2014–2016	927	28.5	0.0	5.0	20.0	29.0	37.0	49.0	71.0	17.0
2017–2019	1219	29.2	0.0	7.0	21.0	29.0	37.0	51.0	75.0	16.0
BC (μg/m^3)										
2014–2016	972	0.33	−0.04	0.04	0.14	0.26	0.43	0.87	1.91	0.29
2017–2019	1274	0.32	−0.12	0.05	0.14	0.25	0.43	0.87	2.13	0.30
Temperature (°C)										
2014–2016	967	12	−18	−6	3	13	21	28	34	17
2017–2019	1275	12	−21	−8	3	12	21	28	34	18
Relative Humidity (%)										
2014–2016	967	65	14	30	50	64	81	94	100	31
2017–2019	1276	64	16	31	49	65	79	95	100	30

[a] Hourly concentrations in control periods.

Table 3
Pearson correlation coefficients between hourly pollutant concentrations and weather measurements 2014–2019[a].

	UFP	UFP_{11-50}	UFP_{50-100}	AMP	$PM_{2.5}$	CO	SO_2	O_3	BC	Temperature	Relative Humidity
UFP	1.00	0.96	0.66	0.38	0.17	0.18	0.19	−0.22	0.47	−0.02	−0.04
UFP_{11-50}		1.00	0.44	0.22	0.09	0.17	0.20	−0.20	0.35	−0.06	−0.07
UFP_{50-100}			1.00	0.68	0.32	0.14	0.08	−0.20	0.60	0.09	0.05
AMP				1.00	0.61	0.13	0.02	−0.01	0.67	0.21	0.08
$PM_{2.5}$					1.00	0.22	0.02	−0.01	0.57	0.14	0.12
CO						1.00	0.00	−0.26	0.31	−0.06	0.05
SO_2							1.00	0.01	−0.04	−0.09	−0.08
O_3								1.00	−0.35	0.29	−0.61
BC									1.00	0.13	0.25
Temperature										1.00	−0.26
Relative Humidity											1.00

[a] Hourly concentrations in control periods.

correlated with UFP_{50-100} (r = 0.60) and $PM_{2.5}$ (r = 0.57). O_3 was negatively correlated with relative humidity (r = −0.61) during the study period (Table 3). The changes in particle size distributions for the morning rush hour (07:00–09:00) are presented in Fig. S2, and for midday (10:00–15:00; photochemical new particle formation events) in Fig. S3.

In the 2014–2016 period, an increased rate of STEMI was associated with each interquartile range (IQR) increase in UFP concentration in the previous 1 h (lag hour 0) (OR = 1.22; 95% CI = 1.06, 1.39), but not during the 2017–2019 period (OR = 0.94; 95% CI = 0.80, 1.10) (Table 4; Fig. 2). There were similar patterns across the 2014–2016 and 2017–2019 periods for UFP in the previous 3, 48, 72, 96, and 120 h. Similarly, increased rates of STEMI were associated with IQR increases in concentrations (in the previous hour) of UFP_{11-50} (OR = 1.20; 95% CI = 1.06, 1.35) and BC (OR = 1.16; 95% CI = 0.99, 1.34) in the 2014–2016 period, but not the 2017–2019 period ($UFP_{11-50;}$ OR = 0.95; 95% CI = 0.82, 1.10; BC: OR = 0.85; 95% CI = 0.72, 1.01; Fig. 2). In contrast, increased rates of STEMI were associated with IQR increases in SO_2 concentrations in the previous 120 h in both the 2014–2016 period (OR = 1.26; 95% CI = 1.03, 1.55) and the 2017–2019 period (OR = 1.21; 95% CI = 0.87, 1.68), with similar patterns for other lag times. Although imprecise, increased rates of STEMI were associated with increased UFP_{51-100} concentrations at most lags in the 2014–2016 period, but not the 2017–2019 period (Table 4; Fig. 2). There were no associations with any other pollutant in either period (Table 4).

As shown in Table 5, the relative rates of STEMI associated with each 3111 particles/cm^3 increase in UFP in the previous hour in the 2014–2016 and 2017–2019 periods were relatively unchanged when including an interaction term between an individual patient characteristic and UFP in the model. When including these interaction terms, the OR for STEMI associated with each IQR increase in UFP in the previous hour in the 2014–2016 period ranged from 1.11 to 1.27 (similar to the

Table 4
Period-specific rates of STEMI associated with each interquartile range (IQR) increase in pollutant concentration, from a model including the interaction between pollutant concentration and period (2014–2016 versus 2017–2019).

Lag hour	Inter Quartile Range	2014–2016				2017–2019				Period Interaction P-Value
		N	Odds Ratio	95% Confidence Interval	P-value	N	Odds Ratio	95% Confidence Interval	P-value	
UFP (particles/cm^3)										
0	3111	286	1.22	1.06, 1.39	<0.01	333	0.94	0.80, 1.10	0.42	0.01
0-2	2952	285	1.19	1.03, 1.38	0.02	326	0.94	0.80, 1.11	0.47	0.04
0-11	2574	288	1.01	0.83, 1.22	0.96	328	0.96	0.80, 1.14	0.62	0.71
0-23	2324	285	1.04	0.84, 1.27	0.73	327	0.86	0.71, 1.04	0.13	0.19
0-47	1875	285	1.11	0.91, 1.35	0.32	325	0.82	0.68, 0.99	0.04	0.03
0-71	1616	284	1.16	0.95, 1.41	0.15	326	0.87	0.72, 1.05	0.16	0.04
0-95	1536	281	1.24	1.01, 1.53	0.04	324	0.89	0.73, 1.09	0.26	0.02
0-119	1341	278	1.22	1.00, 1.49	0.06	326	0.93	0.77, 1.12	0.45	0.05
UFP_{11-50} (particles/cm^3)										
0	2361	286	1.20	1.06, 1.35	<0.01	333	0.95	0.82, 1.10	0.46	0.01
0-2	2237	285	1.18	1.03, 1.35	0.02	326	0.94	0.80, 1.10	0.42	0.03
0-11	1944	288	1.00	0.82, 1.21	0.98	328	0.99	0.84, 1.17	0.90	0.95
0-23	1712	285	1.00	0.81, 1.23	0.97	327	0.89	0.75, 1.07	0.22	0.44
0-47	1404	285	1.05	0.84, 1.30	0.68	325	0.84	0.70, 1.01	0.06	0.11
0-71	1231	284	1.13	0.91, 1.41	0.26	326	0.87	0.72, 1.04	0.13	0.06
0-95	1168	281	1.26	1.01, 1.58	0.04	324	0.88	0.72, 1.07	0.20	0.02
0-119	1078	278	1.28	1.01, 1.61	0.04	326	0.91	0.75, 1.11	0.34	0.03
UFP_{51-100} (particles/cm^3)										
0	1004	286	1.12	0.95, 1.32	0.16	333	0.94	0.79, 1.12	0.49	0.14
0-2	981	285	1.10	0.93, 1.31	0.27	326	0.98	0.82, 1.17	0.81	0.34
0-11	903	288	1.02	0.85, 1.22	0.84	328	0.88	0.72, 1.08	0.22	0.28
0-23	869	285	1.10	0.91, 1.34	0.33	327	0.82	0.66, 1.02	0.07	0.04
0-47	732	285	1.22	0.99, 1.49	0.06	325	0.81	0.65, 1.02	0.08	0.01
0-71	692	284	1.22	0.97, 1.53	0.08	326	0.92	0.72, 1.16	0.47	0.08
0-95	641	281	1.22	0.97, 1.54	0.10	324	0.95	0.74, 1.21	0.67	0.13
0-119	599	278	1.18	0.92, 1.50	0.19	326	0.99	0.77, 1.27	0.92	0.31
AMP (particles/cm^3)										
0	559	286	1.03	0.84, 1.26	0.77	333	0.81	0.66, 0.99	0.04	0.09
0-2	543	285	1.01	0.83, 1.24	0.90	326	0.8	0.65, 0.99	0.04	0.10
0-11	503	288	0.96	0.79, 1.18	0.71	328	0.82	0.66, 1.01	0.07	0.25
0-23	485	285	1.00	0.82, 1.23	0.98	327	0.85	0.68, 1.06	0.15	0.25
0-47	437	285	1.02	0.82, 1.27	0.85	325	0.92	0.73, 1.16	0.50	0.51
0-71	387	284	0.99	0.79, 1.24	0.94	326	1.00	0.79, 1.25	0.99	0.96
0-95	371	281	0.98	0.78, 1.23	0.85	324	1.01	0.79, 1.30	0.92	0.83
0-119	360	278	0.96	0.75, 1.22	0.72	326	1.03	0.80, 1.32	0.83	0.66
$PM_{2.5}$ (μg/m^3)										
0	5.4	290	0.94	0.79, 1.12	0.51	335	1.01	0.86, 1.19	0.91	0.56
0-2	5.3	288	1.01	0.84, 1.23	0.88	328	0.97	0.82, 1.16	0.75	0.73
0-11	4.8	291	1.00	0.83, 1.21	0.99	323	1.08	0.91, 1.28	0.40	0.54
0-23	4.5	290	1.03	0.86, 1.25	0.73	323	1.11	0.94, 1.32	0.23	0.55
0-47	3.6	289	1.05	0.88, 1.24	0.60	329	1.11	0.95, 1.31	0.20	0.58
0-71	3.4	285	1.08	0.90, 1.28	0.41	330	1.15	0.97, 1.35	0.10	0.59
0-95	3.1	287	1.07	0.90, 1.28	0.42	331	1.14	0.96, 1.34	0.13	0.63
0-119	3.0	290	1.04	0.87, 1.26	0.65	330	1.14	0.96, 1.36	0.14	0.46
CO (ppm)										
0	0.22	294	1.26	0.84, 1.88	0.26	323	0.95	0.63, 1.45	0.82	0.34
0-2	0.22	290	1.1	0.69, 1.74	0.70	315	0.92	0.58, 1.46	0.72	0.59
0-11	0.19	299	1.01	0.65, 1.57	0.96	325	0.88	0.57, 1.36	0.57	0.66
0-23	0.16	301	1.12	0.75, 1.67	0.57	324	0.9	0.59, 1.37	0.63	0.46
0-47	0.12	300	1.06	0.75, 1.50	0.75	329	1.13	0.87, 1.46	0.37	0.78
0-71	0.11	300	1.03	0.70, 1.52	0.86	328	1.16	0.82, 1.63	0.40	0.66
0-95	0.10	303	1.05	0.72, 1.53	0.81	332	1.19	0.82, 1.72	0.37	0.64
0-119	0.10	303	0.97	0.65, 1.45	0.90	334	1.08	0.71, 1.64	0.72	0.73
SO_2 (ppb)										
0	0.40	297	1.04	1.00, 1.07	0.04	342	1.02	0.98, 1.06	0.39	0.50
0-2	0.43	297	1.06	1.01, 1.10	0.01	331	1.04	0.97, 1.11	0.30	0.64
0-11	0.49	300	1.07	1.00, 1.16	0.06	339	1.06	0.95, 1.20	0.30	0.90
0-23	0.54	301	1.12	1.02, 1.23	0.01	343	1.1	0.95, 1.28	0.20	0.85
0-47	0.58	300	1.16	1.02, 1.32	0.03	344	1.21	1.00, 1.46	0.05	0.73
0-71	0.59	301	1.16	0.99, 1.36	0.07	345	1.22	0.97, 1.55	0.09	0.72
0-95	0.58	303	1.22	1.02, 1.47	0.03	346	1.26	0.95, 1.66	0.11	0.86
0-119	0.59	302	1.26	1.03, 1.55	0.03	346	1.21	0.87, 1.68	0.25	0.83
O_3 (ppb)										
0	17.0	293	0.91	0.70, 1.19	0.50	332	1.05	0.82, 1.34	0.68	0.38
0-2	16.3	290	0.96	0.74, 1.26	0.79	323	1.06	0.83, 1.35	0.67	0.58
0-11	14.3	300	0.99	0.77, 1.29	0.96	331	1.01	0.79, 1.29	0.94	0.91
0-23	12.5	300	0.96	0.74, 1.26	0.78	331	0.98	0.77, 1.26	0.89	0.90
0-47	11.3	300	1.03	0.77, 1.37	0.84	331	1.22	0.93, 1.60	0.14	0.33
0-71	10.4	301	0.97	0.72, 1.30	0.82	328	1.15	0.85, 1.56	0.35	0.35
0-95	10.0	304	0.92	0.67, 1.27	0.62	325	1.10	0.79, 1.53	0.57	0.39

(*continued on next page*)

Table 4 (*continued*)

Lag hour	Inter Quartile Range	2014–2016				2017–2019				Period Interaction P-Value
		N	Odds Ratio	95% Confidence Interval	P-value	N	Odds Ratio	95% Confidence Interval	P-value	
0-119	9.5	304	0.98	0.70, 1.38	0.91	322	1.04	0.74, 1.47	0.82	0.78
BC (μg/m^3)										
0	0.30	301	1.15	0.99, 1.34	0.06	344	0.85	0.72, 1.01	0.06	0.01
0-2	0.29	301	1.09	0.93, 1.28	0.30	339	0.85	0.71, 1.01	0.06	0.03
0-11	0.27	302	1.03	0.87, 1.22	0.69	341	0.86	0.71, 1.04	0.13	0.14
0-23	0.24	303	1.09	0.92, 1.28	0.32	342	0.91	0.76, 1.10	0.33	0.15
0-47	0.20	303	1.11	0.94, 1.31	0.22	346	0.90	0.75, 1.08	0.25	0.08
0-71	0.17	304	1.11	0.95, 1.31	0.19	346	0.95	0.80, 1.13	0.56	0.16
0-95	0.15	304	1.10	0.94, 1.29	0.22	348	0.95	0.80, 1.14	0.61	0.20
0-119	0.14	304	1.05	0.90, 1.22	0.52	348	0.92	0.77, 1.09	0.35	0.23

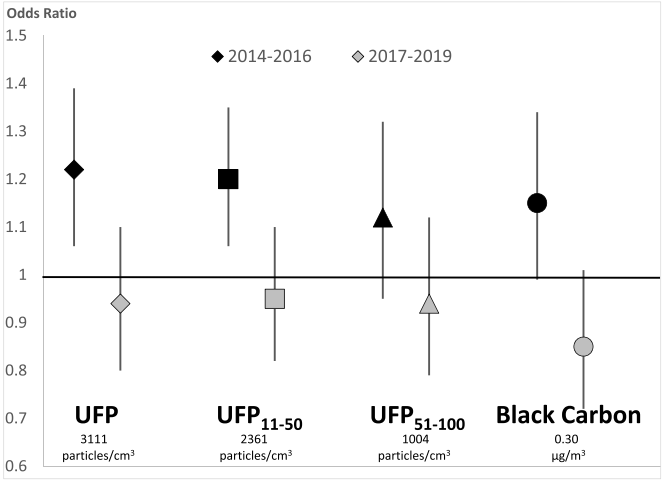


Fig. 2. Rate of STEMI associated with each interquartile range increase in mean pollutant concentration in lag hour 0, by period.

OR = 1.22 from the main analysis), and in the 2017–2019 period from 0.60 to 0.97 (similar to the OR = 0.94 from the main analysis). These period-specific UFP/STEMI relative rates were significantly different from each other in all Table 5 models (all $p \leq 0.03$) as well.

Among subjects living closer to the monitoring station (≤5.96 miles), each 3111 particles/cm^3 increase in UFP concentration in the previous hour was associated with a 26% increased rate of STEMI in 2014–2016 (95% CI = 5%, 50%), but not in 2017–2019 (OR = 0.97; 95% CI = 0.75, 1.25). Among subjects living further from the monitor, the results were similar but somewhat attenuated (2014–2016: OR = 1.17; 95% CI = 0.94, 1.45; 2017–2019: OR = 0.92; 95% CI = 0.75, 1.13).

For those STEMI that occurred in summer, each 3111 particles/cm^3 particle increase in UFP in the previous hour was associated with an increased rate of STEMI in both the 2014–2016 period (OR = 1.26; 95% CI = 0.99, 1.60) and 2017–2019 period (OR = 1.27; 95% CI = 0.91, 1.77) (Supplementary Table 1). However, for STEMI that occurred in the winter, spring, and autumn, each 3111 particles/cm^3 particle increase in UFP in the previous hour was associated with increased rates of STEMI in 2014–2016, but not in 2017–2019.

Similar to the period-specific relative rates from the single pollutant UFP model (2014–2016: OR = 1.22; 95% CI = 1.06, 1.39; 2017–2019: OR = 0.94, 95% CI = 0.80, 1.10), each 3111 particles/cm^3 particle increase in UFP in the previous hour was associated with an increased rate of STEMI in the 2014–2016 period (OR = 1.27; 95% CI = 1.10, 1.46), but not in 2017–2019 period (OR = 0.99; 95% CI = 0.84, 1.17) (Supplementary Table 2) when adjusting for AMP at the same lag time. This pattern was consistent across all two-pollutant models (i.e., when controlling for AMP, $PM_{2.5}$, CO, SO_2, O_3, and BC separately).

4. Discussion

In Rochester, New York from 2014 to 2016, increased rates of STEMI were associated with increased concentrations of UFP, $UFP_{11\text{-}50}$, $UFP_{51\text{-}100}$, and BC (markers of traffic and diesel pollution) in the previous 1 h, but were not associated with these pollutants from 2017 to 2019. These

Table 5
Rate of STEMI associated with each 3111 particles/cm^3 increase in UFP in the previous hour (lag hour 0), separately by period (2014–2016 and 2017–2019), when including interaction terms between individual patient characteristics and UFP.

Characteristic in Interaction Term with UFP lag hour 0	2014–2016				2017–2019				Period [a] UFP Interaction term p-value	Characteristic [a] UFP Interaction term p-value
	N	Odds Ratio	95% Confidence Interval	P-value	N	Odds Ratio	95% Confidence Interval	P-value		
None–Main Analysis Table 4	286	1.22	1.06, 1.39	<0.01	333	0.94	0.80, 1.10	0.42	0.01	–
Age: 70+	286	1.11	0.88, 1.40	0.39	333	0.85	0.67, 1.09	0.21	0.01	0.33
Sex: Male	286	1.23	1.07, 1.42	<0.01	333	0.95	0.8, 1.14	0.59	0.02	0.65
Race: White	283	1.25	1.08, 1.44	<0.01	328	0.95	0.81, 1.12	0.52	0.01	0.29
Prior MI: Yes	286	1.27	0.96, 1.69	0.10	333	0.97	0.75, 1.25	0.81	0.01	0.74
Prior PCI: Yes	286	1.27	0.96, 1.69	0.10	333	0.97	0.75, 1.25	0.81	0.01	0.74
Smoking: Yes	286	1.21	0.99, 1.47	0.06	305	0.89	0.74, 1.09	0.27	0.01	0.91
Hypertension: Yes	286	1.26	1.07, 1.48	<0.01	264	0.94	0.78, 1.12	0.49	0.01	0.40
Dyslipidemia: Yes	284	1.22	1.03, 1.44	0.02	333	0.94	0.78, 1.13	0.49	0.01	0.99
Diabetes: Yes	286	1.12	0.88, 1.42	0.36	333	0.87	0.68, 1.11	0.25	0.02	0.41
Family History CAD: Yes	286	1.15	0.92, 1.44	0.23	331	0.88	0.68, 1.15	0.34	0.01	0.52
Chronic Lung Disease: Yes	284	1.24	0.91, 1.69	0.17	333	0.96	0.67, 1.37	0.82	0.02	0.88
Body Mass Index[a]	284	1.18	0.96, 1.45	0.11	333	0.78	0.54, 1.12	0.17	<0.01	0.37, 0.29
Health Insurance[b]	257	1.22	0.47, 3.12	0.69	325	0.60	0.21, 1.70	0.34	0.03	0.83, 0.39

[a] Body Mass Index had three categories (Normal, Overweight, Obese) with two interaction terms included in the model.
[b] Health Insurance had three categories (Private, Public, Other [non-public]) with two interaction terms included in the model.

differences in relative rates between periods were independent of any differences in subject characteristics between periods, any interaction between subject characteristics and UFP concentrations, and other pollutant concentrations at the same lag time. In contrast, increased rates of STEMI were associated with increased concentrations of SO_2 at multiple lag times within 120 h in both periods, likely reflecting no change in the composition of non-traffic air pollutants or no effect on the rate of STEMI by such changes. Vehicles sold beginning in 2017 had to meet stricter emission standards. Thus, these changes in UFP, $UFP_{11\text{-}50}$, $UFP_{51\text{-}100}$, and BC relative rates from 2014 to 2016 to 2017–2019 may reflect changes in UFP and PM composition resulting from lower emissions of precursors to the formation of secondary organic carbon in Tier 3 vehicles (Zhao et al., 2018). However, in 2020, only 36% of vehicles registered in NYS were Tier 3 (i.e., manufactured in 2017 or later), suggesting there was only limited penetration of these Tier 3 vehicles into the fleet during 2017–2019. Further discussion of this and other explanations for these findings are presented below.

We and others have previously reported increased rates of STEMI associated with increased $PM_{2.5}$ and other pollutant concentrations in the previous hours and days (Evans et al., 2017; Gardner et al., 2014; Akbarzadeh et al., 2018; Argacha et al., 2016; Lozano-Sabido et al., 2021; Pope et al., 2015; Sahlen et al., 2019; Wang et al., 2015). In a study of STEMI patients treated at the same Cath Lab as our study from 2005 to 2016, we previously reported increased rates of STEMI were associated with increased concentrations of UFP, $UFP_{11\text{-}50}$, BC, and CO in the previous hour, as well as SO_2 at multiple lag times, with the largest relative rates from 2014 to 2016 (Wang et al., 2019). In other work, we similarly reported increased rates of cardiovascular hospitalizations, including ischemic heart disease and myocardial infarction, associated with increased $PM_{2.5}$ concentrations in the previous few days among adult residents of Rochester and other cities in New York State from 2005 to 2016 (Zhang et al., 2018). Further, relative rates were greatest in 2014–2016, after a series of air quality regulations and actions were implemented, and an economic recession occurred, suggesting the PM may have become more toxic with increased rates of hospitalizations or emergency department visits for specific cardiovascular (Zhang et al., 2018), respiratory infections (Croft et al., 2019), and respiratory diseases/events (Hopke et al., 2019). Further, these increased rates of cardiovascular hospitalizations were most strongly associated with increased concentrations of $PM_{2.5}$ from spark-ignition and diesel vehicles, suggesting that any increased PM toxicity may have been due to changes in the relative contribution to PM of motor vehicle and traffic sources and increases in secondary organic carbon (Rich et al., 2019). This is consistent with previous studies reporting associations between cardiovascular events/hospitalizations and traffic pollution (Ito et al., 2011; Samoli et al., 2016; Ye et al., 2017, 2018).

Although numerous studies have conducted accountability studies to assess health benefits of air quality actions in a population, and have been reviewed and summarized previously (Boogaard et al., 2017; Burns et al., 2019, 2020; Henneman et al., 2017; Rich, 2017), only a few have similarly examined whether the toxicity of PM changed over time (Bi et al., 2020; Henneman et al., 2019). In Atlanta, Henneman et al. (2019) reported that the air pollution mixture became less toxic from 1999 to 2013, with smaller rates of cardiovascular and respiratory emergency department visits associated with increased $PM_{2.5}$ concentrations in the previous 3 days during the second half of the study period. In Los Angeles, Bi et al. (2020) reported that the relative rate of cardiovascular emergency department (ED) visits (i.e., rate of cardiovascular ED visits associated with each 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations in the previous 4 days) was larger in 2013–2016 (RR = 1.03, 95% CI = 1.010, 1.030) than in 2005–2008 (RR = 1.003, 95% CI = 0.996, 1.010), but the relative rate of asthma emergency department visits was smaller in 2013–2016 compared to 2005–2008. Although Bi et al. (2020) is consistent with our previous work (Zhang et al., 2018; Wang et al., 2019; Rich et al., 2019), neither study examined whether there were any further changes in relative rates from 2017 to 2019.

Major influences on ambient UFP and BC concentrations have likely included the requirement of particle traps on all new heavy-duty diesel trucks sold after July 1, 2007, combined with reductions in the sulfur content of on-road diesel fuel that began in 2006. Reductions of sulfur in non-road diesel and home heating fuels that occurred between 2010 and 2014 would also reduce ambient UFP and BC concentrations. These changes in traffic related UFP are reflected in the changing particle size distributions for morning rush hour times (07:00 to 09:00; Fig. S2) and midday photochemical new particle formation events that affect the 10:00 to 15:00 periods (Fig. S3), which showed consistent particle number count decreases from 2005 to 2007 to 2011–2013. The size distributions also provide more detail about the increased counts of $UFP_{11\text{–}20nm}$ in the 2017–2019 period seen in Fig. S1. Compared to 2014–2016, $UFP_{11\text{–}20nm}$ concentrations increased during the morning rush hour, which is especially noticeable in the summer and autumn of 2017–2019. (Fig. S2). The upward trend suggests changes in either emissions or chemical processes leading to increased numbers of these smallest sized particles (11–20 nm). It is likely that the reductions in accumulation mode particles (100–500 nm), that provide the surface area onto which condensable organic material would condense, has led to increased new particle formation in this small size range that contribute negligible mass to the measured $PM_{2.5}$ value. These sized particles will likely deposit earlier in the tracheobronchial tree and less in the alveolar region (Asgharian et al., 2001, 2004, 2006). Such deposition may result in better mucosal clearance, and thus may result in lower PM doses in the critical tissues of the respiratory tract. Thus, the same concentration of UFP in 2017–2019 (3111 particles/cm^3) may have triggered a lower rate of STEMI as that same UFP concentration in 2014–2016.

The summer UFP/STEMI relative rates were similar in the 2014–2016 period and 2017–2019 period, but the period-specific relative rates in the winter, spring, and autumn were different and had the same pattern as the main analysis. In the summer, the higher photoperiod, temperatures, and faster chemical reactions may produce more new particles with different compositions than the other seasons. Gasoline direct-injection (GDI) engines produce sub-10 nm particles (Yi et al., 2022) that, under colder ambient temperatures, can serve as the nuclei in the plume of the tailpipe emissions for heterogeneous nucleation of the co-emitted semi-volatile organic compounds that would be in the 11–20 nm size range. In the summer, the temperatures would inhibit nucleation. However, the higher photochemical activity would lead to secondary organic aerosol that could homogeneously nucleate into the smallest measured size range. These summer particles would have different compositions than particles in the other seasons. This difference may be why the period-specific relative rates were similar in the summer, but different in the other seasons.

There are several other potential explanations for the substantial decrease in the relative rate of STEMI associated with each 3111 particles/cm^3 in UFP (and other pollutants) in the previous hour from the 2014–2016 period (e.g., UFP: OR = 1.22) to the 2017–2019 period (e.g., UFP: OR = 0.94). First, this decreased relative rate could have been due to differences in subject characteristic between periods (e.g., changes in the age, underlying co-morbidities, and/or other factors of STEMI patients from 2014 to 2019), and differences in the response to UFP exposure due to those different characteristics. Although there were small differences in a few subject characteristics between the 2014–2016 and 2017–2019 periods (i.e., history of a prior MI, family history of coronary artery disease, smoking, and insurance type), these differences were likely random, as other important characteristics such as age, race, coronary interventions, obesity, and mean length of stay were similar between periods. There were some differences in the referring physicians and their respective patient populations, but there was no evidence of a systematic difference among the referred patients between periods. Further, there was little difference in period specific UFP/STEMI relative rates when including interactions between these characteristics and UFP in the model. Further, due to the matching on

non-time varying characteristics by the case-crossover design, thereby controlling for these factors and any interactions between them by design, the significant difference in 2014–2016 and 2017–2019 period relative rates is independent of any differences in subject characteristics between periods.

Second, all subjects were assigned the same UFP and other pollutant concentrations from the single monitoring site of the study, no matter how far they lived from it. As shown in our analyses stratified by residential distance to the monitoring station, this appears to have resulted in non-differential exposure misclassification and underestimation of the relative rates. Further, since the distance between STEMI patient residences and the pollutant monitoring site was slightly greater in the 2017–2019 period (median = 6.63 miles) than in the 2014–2016 period (median = 5.53 miles; Fig. 1), there could be more underestimation of the relative rate in the 2017–2019 period than in the 2014–2016 period. However, since this difference in distances between periods is small, it does not seem likely that this would completely explain the null findings in the 2017–2019 period.

Third, therapeutic and preventive approaches have changed over this same time period as well. Early studies reported evidence of small-to-modest cardiovascular benefit in high risk patients with low dose aspirin, and low dose aspirin was frequently recommended for healthy elderly adults as well (Ridker et al., 2005). However, 3 clinical trials published in 2018 revealed little efficacy of aspirin in preventing adverse cardiovascular events in older patients (Gaziano et al., 2018; Group, 2018; McNeil et al., 2018; Ridker, 2018). For example, the ASPREE (ASPirin in Reducing Events in the Elderly) trial did not demonstrate reduced cardiovascular events in adults over 70 years old and reported increased risk for major hemorrhagic events (McNeil et al., 2018). Subsequently, the American College of Cardiology/American Heart Association modified prevention guidelines in 2019, recommending that low-dose aspirin not be routinely administered for primary prevention of atherosclerotic cardiovascular disease among adults >70 years of age (Arnett et al., 2019). Nelson et al. (2022) raised the question regarding safety of stopping aspirin therapy without a clinical indication in patients over age 70 (Nelson et al., 2022). Murphy and McEvoy (2022) suggested that there was a potential signal for harm among those who stopped aspirin, particularly for cardiovascular events including STEMI, and questioned whether rebound platelet reactivity could occur on aspirin cessation (Murphy and McEvoy, 2022). Presumably, this increased platelet reactivity in the population could increase the rate of STEMI associated with short-term UFP exposures. However, in the 2017–2019 period, when low-dose aspirin use was reduced and this increased platelet activity may have occurred, we instead observed a reduced rate of STEMI per 3111 particles/cm^3 increase in UFP concentration, suggesting this is not a likely explanation for our findings.

In addition to the study limitation discussed above (i.e., non-differential exposure misclassification and underestimation of relative rates resulting from use of pollutant concentrations from a central monitoring station for all study subjects), there are several study strengths that should be considered when making inference. These strengths include the use of a well-defined study population of STEMI events/patients all seen at the same Cath Lab/medical center in Rochester, measurement of particle count concentrations that allowed measurement of ultrafine particle and accumulation mode particle concentrations during the study period, and use of a case-crossover study design that controlled for all non-time varying factors by design, and any interactions between them, thereby minimizing confounding by these factors.

5. Conclusions

In a study of STEMI events treated at the University of Rochester Medical Center from 2014 to 2019, and UFP and other pollutant concentrations measured in Rochester, NY, increased rates of STEMI were associated with short term increases in concentrations of UFP and other motor vehicle related pollutants before Tier 3 light-duty vehicle introduction (2014–2016), but not afterwards (2017–2019). These changes in relative rates over this time period may, in part, be due to changes in UFP/PM composition after these vehicles entered the vehicle fleet, and to increased exposure misclassification and greater underestimation of effects from 2017 to 2019. Future work will examine whether other cardiorespiratory health events responded to UFP and other pollutant concentration changes similarly.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: David Rich reports financial support was provided by New York State Energy Research Development Authority. David Rich reports financial support was provided by National Institute of Environmental Health Sciences. David Rich reports a relationship with US Environmental Protection Agency that includes: consulting or advisory.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114445.

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