

# Impact of environmental pollution and weather changes on the incidence of ST-elevation myocardial infarction

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**Giuseppe Biondi-Zoccai<sup>1,2</sup>, Giacomo Frati<sup>1,3</sup>,  
Achille Gaspardone<sup>4</sup>, Enrica Mariano<sup>5</sup>, Alessandro D Di Giosa<sup>6</sup>,  
Andrea Bolignano<sup>6</sup>, Angela Dei Giudici<sup>7</sup>, Simone Calcagno<sup>7</sup>,  
Massimiliano Scappaticci<sup>7</sup>, Sebastiano Sciarretta<sup>1,3</sup>,  
Valentina Valenti<sup>7</sup>, Rebecca Casati<sup>7</sup>, Giuseppe Visconti<sup>8</sup>,  
Maria Penco<sup>9</sup>, Maria B Giannico<sup>4</sup>, Mariangela Peruzzi<sup>1,2</sup>,  
Elena Cavarretta<sup>1,2</sup>, Simone Budassi<sup>5</sup>, Joseph Cosma<sup>5</sup>,  
Massimo Federici<sup>10</sup>, Leonardo Roever<sup>11</sup>, Francesco Romeo<sup>5</sup>  
and Francesco Versaci<sup>7</sup>**

## Abstract

**Background:** Environmental pollution and weather changes unfavorably impact on cardiovascular disease. However, limited research has focused on ST-elevation myocardial infarction (STEMI), the most severe yet distinctive form of acute coronary syndrome.

**Methods and results:** We appraised the impact of environmental and weather changes on the incidence of STEMI, analysing the bivariate and multivariable association between several environmental and atmospheric parameters and the daily incidence of STEMI in two large Italian urban areas. Specifically, we appraised: carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), nitric oxide (NO<sub>x</sub>), ozone, particulate matter smaller than 10 µm (PM<sub>10</sub>) and than 2.5 µm (PM<sub>2.5</sub>), temperature, atmospheric pressure, humidity and rainfall. A total of 4285 days at risk were appraised, with 3473 cases of STEMI. Specifically, no STEMI occurred in 1920 (44.8%) days, whereas one or more occurred in the remaining 2365 (55.2%) days. Multilevel modelling identified several pollution and weather predictors of STEMI. In particular, concentrations of CO ( $p=0.024$ ), NO<sub>x</sub> ( $p=0.039$ ), ozone ( $p=0.003$ ), PM<sub>10</sub> ( $p=0.033$ ) and PM<sub>2.5</sub> ( $p=0.042$ ) predicted STEMI as early as three days before the event, as well as subsequently, and NO predicted STEMI one day before ( $p=0.010$ ), as well as on the same day. A similar predictive role was evident for temperature and atmospheric pressure (all  $p < 0.05$ ).

**Conclusions:** The risk of STEMI is strongly associated with pollution and weather features. While causation cannot yet be proven, environmental and weather changes could be exploited to predict STEMI risk in the following days.

## Keywords

Acute myocardial infarction, environment, pollution, ST-elevation myocardial infarction, weather

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<sup>1</sup>Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Italy

<sup>2</sup>Mediterranea Cardiocentro, Italy

<sup>3</sup>IRCCS NEUROMED, Italy

<sup>4</sup>Division of Cardiology, Ospedale S. Eugenio, Italy

<sup>5</sup>Division of Cardiology, Tor Vergata University, Italy

<sup>6</sup>ARPA Lazio, Italy

<sup>7</sup>Division of Cardiology, Santa Maria Goretti Hospital, Italy

<sup>8</sup>ASL Latina, Italy

<sup>9</sup>Division of Cardiology, University of L'Aquila, Italy

<sup>10</sup>Department of Systems Medicine, Tor Vergata University, Italy

<sup>11</sup>Department of Clinical Research, Federal University of Uberlandia, Brazil

## Corresponding author:

Giuseppe Biondi-Zoccai, Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Corso della Repubblica 79, 04100 Latina, Italy.

Email: giuseppe.biondizoccai@uniroma1.it

## Introduction

Weather and environmental pollution represent two atherothrombotic risk factors which impact individuals at large by means of population effect.<sup>1–8</sup> Indeed, several studies have highlighted, for instance, how lower temperatures are associated with an increased risk of acute cardiovascular events, ranging from sudden death to unstable angina.<sup>9–12</sup> Similarly, it is well established how the outdoor concentration of several pollutants, such as fine particulate matter, is associated with cardiovascular morbidity and mortality.<sup>13</sup> Moreover, it is increasingly clear that the consequences of anthropogenic activities, particularly atmospheric emissions, have both direct and indirect adverse impacts upon cardiovascular health.<sup>11,12,14,15</sup> The public health relevance of a trigger is dependent not only on the individual relative risk but also on the prevalence of this risk factor within the population. Some risk factors, such as cocaine use, have a high individual acute myocardial infarction (AMI) risk. In contrast, environmental triggers expose the entire population and have a considerable public health impact despite a small individual relative risk.

Several recent research efforts have aimed at disentangling the mechanistic impact of pollution and weather features on atherothrombosis, but few reports have focused explicitly on the interplay between these two separate yet interactive factors.<sup>6</sup> Of note, there is conflicting evidence on the role of different pollutants, given the interaction between the concentration of many of them.<sup>16,17</sup> On top of this, the independent and multiplicative impact of ambient weather features on pollution and the ensuing risk of the most severe form of atherothrombosis, that is, acute ST-elevation myocardial infarction (STEMI), remains hitherto debated.<sup>7,18</sup>

We aimed at appraising the impact of pollution and weather on the risk of STEMI in contemporary practice, focusing on STEMI risk acutely and in the days following specific exposures to pollutants and weather changes.

## Methods

This is a retrospective analysis of anonymized data on the incidence of STEMI between 2017 and 2019 in three high-volume centres with 24/7 primary percutaneous coronary intervention (PCI) services in Lazio, Italy.<sup>19</sup> Specifically, the number of daily STEMI cases was systematically collected per centre, and matched with data on local weather provided by Italian Air Force, Rome, Italy, and data on local pollution provided by Agenzia Regionale per la Protezione dell'Ambiente (ARPA) of Lazio, also in Rome, Italy.

While our data collection did not include all patients at risk in the Lazio region, all cases treated in the three high-volume centres participating in the study were included, without any exclusion. Accordingly, changes in population at risk could not be accounted for directly.

In terms of environment, the following pollutants were systematically collected, with several daily measurements: carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), nitric oxide (NO<sub>x</sub>), ozone (O<sub>3</sub>), fine particulate matter (i.e. with mean aerodynamic diameter < 2.5 µm in diameter (PM<sub>2.5</sub>)) and particulate matter with mean aerodynamic diameter < 10 µm in diameter (inclusive of PM<sub>2.5</sub> (PM<sub>10</sub>)), and all expressed as µm/m<sup>3</sup>, with the exception of CO, which was measured in mg/m<sup>3</sup>.<sup>20</sup>

Accordingly, per-centre and per-day minimum, maximum, mean and change estimates for all the above pollutants were collected. In terms of weather, the following features were systematically collected as previously specified: temperature (°C), atmospheric pressure, humidity (%) and rainfall (mm).<sup>18</sup> Similarly, per-centre and per-day minimum, maximum, mean and change estimates for all the above weather features were collected, with the exception of rainfall. We explicitly aimed at appraising the impact of pollution and weather features on same day STEMI, as well as STEMI occurring one, two or three days afterwards. Additional exploratory analyses focused on the impact of environmental pollution and weather features on the risk of STEMI four, five, six, seven, 14 and 30 days later, as well as subgroup analyses focusing on per-centre and per-season effects.

Descriptive analysis was based on computing mean ± standard deviation, as well as coefficient of variation (i.e. standard deviation/mean). After appraising between-variable correlations by visual inspection of heatmaps and dendrograms,<sup>21</sup> inferential analysis was based first on bivariate analysis using a mixed effect model with Poisson likelihood and log link, to account for centre-wise clustering.<sup>18</sup> Models with and without quadratic terms were tested separately, to appraise the impact of non-linear effects. Computations were performed with Stata 13 (StataCorp, College Station, Texas, USA) and R 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

A total of 4285 days at risk were appraised with 3473 cases of STEMI (Table 1). Specifically, no STEMI occurred in 1920 (44.8%) days, whereas one case occurred in 1526 (35.6%) days, two cases in 618 (14.4%) days, and three or more in 221 (5.2%). Descriptive analysis highlighted significant variability in pollution and weather features, as shown by

**Table 1.** Descriptive analysis.

Feature	n (%) or mean $\pm$ standard deviation	Coefficient of variation
Daily PCI		
0	1920 (44.8)	–
1	1526 (35.6)	–
2	618 (14.4)	–
3 or more	221 (5.2)	–
Carbon monoxide, $\mu\text{m}^3$	0.61 $\pm$ 0.34	55.7%
Nitrogen dioxide, $\mu\text{m}^3$	35.57 $\pm$ 15.73	44.1%
Nitric oxide, $\mu\text{m}^3$	63.22 $\pm$ 44.08	69.8%
Ozone, $\mu\text{m}^3$	52.02 $\pm$ 20.73	39.8%
PM10, $\mu\text{m}^3$	26.92 $\pm$ 12.69	47.2%
PM2.5, $\mu\text{m}^3$	17.41 $\pm$ 11.17	64.4%
Temperature, $^{\circ}\text{C}$	14.29 $\pm$ 6.96	47.9%
Atmospheric pressure, ATM	1014.94 $\pm$ 6.96	46.4% <sup>a</sup>
Humidity, %	70.87 $\pm$ 12.78	18.0%
Rainfall, mm	2.32 $\pm$ 6.96	300.0%

<sup>a</sup>Computed using mean – 1000.

ATM: atmospheric pressure; PCI: percutaneous coronary intervention;

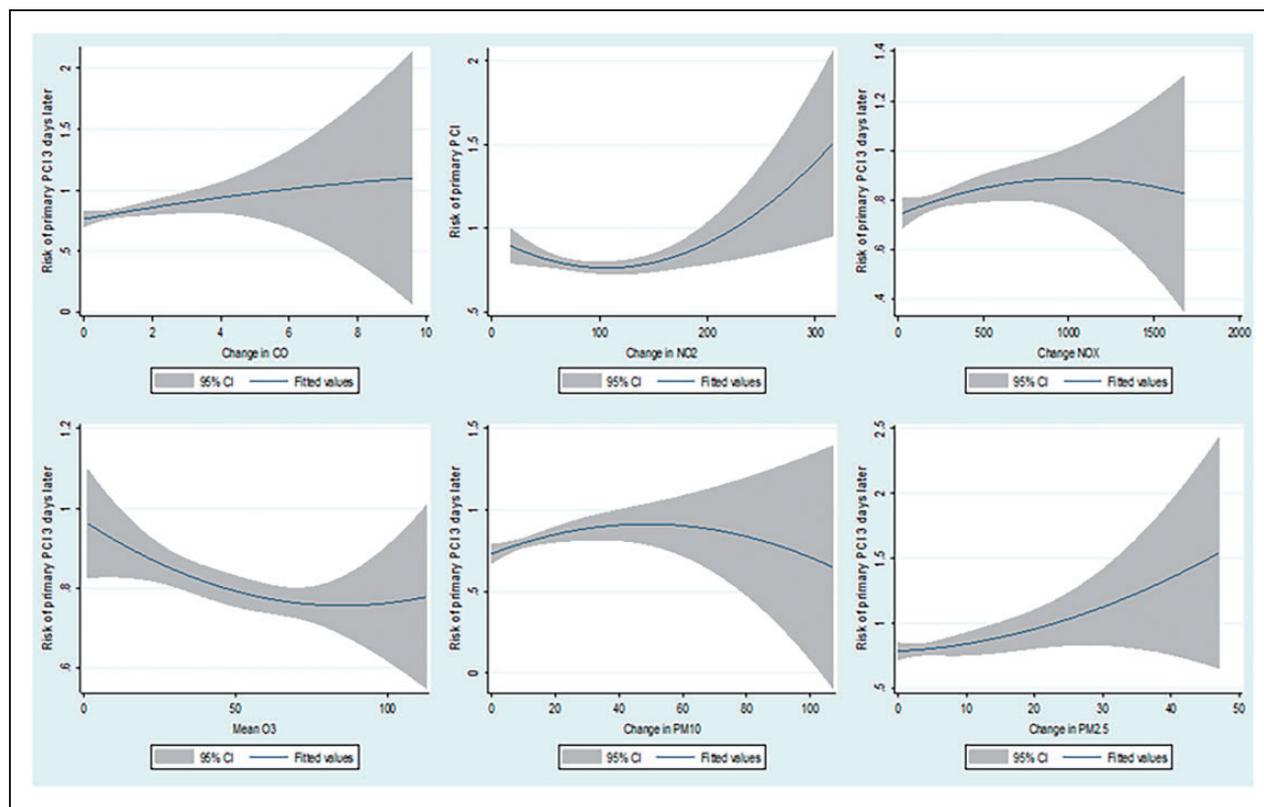
PM10: particulate matter with a diameter between 2.5  $\mu\text{m}$  and 10  $\mu\text{m}$ ;

PM2.5: particulate matter with a diameter less than 2.5  $\mu\text{m}$

coefficient of variations ranging from 18% to 300%. Most interestingly, weather and pollution features were significantly correlated (Supplementary Material Figures 1S and Figure 2S online). In particular, O3 was significantly and positively associated with temperature.

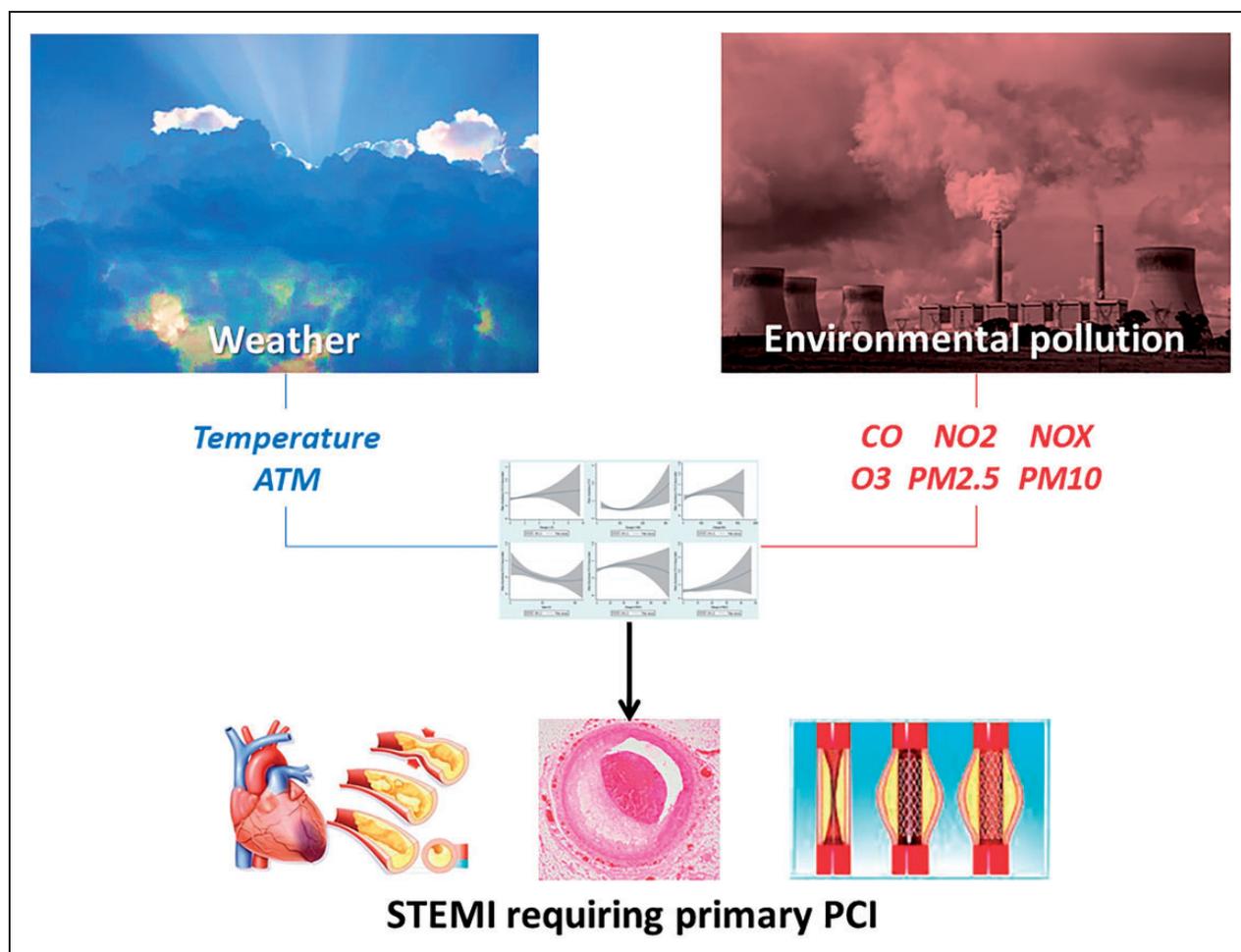
Multilevel modelling identified several pollution and weather predictors of STEMI, occurring either on the same day or on the following ones (Tables 2 and 3; Figure 1). Concentrations of CO ( $p=0.024$ ), NOX ( $p=0.039$ ), O3 ( $p=0.003$ ), PM10 ( $p=0.033$ ) and PM2.5 ( $p=0.042$ ) predicted STEMI as early as three days before the event, as well subsequently, and NO predicted STEMI one day before ( $p=0.010$ ), as well as on the same day. A similar significant role was evident for temperature and atmospheric pressure (all  $p<0.05$ ). Notably, O3, as well as temperature and atmospheric pressure, was inversely associated with the risk of STEMI, as days with high O3 concentration, high temperature and high atmospheric pressure were associated with a lower risk of STEMI on the same day or on the following ones (Figure 2).

Associations were not linear in most cases, but curvilinear instead, as demonstrated by the presence of



**Figure 1.** Association between environmental pollution and weather features on the risk of ST-elevation myocardial infarction treated with primary percutaneous coronary intervention.

CI: confidence interval; CO: carbon monoxide; NO2: nitric dioxide; NOX: nitric oxide; O3: ozone; PM10: particulate matter with a diameter between 2.5  $\mu\text{m}$  and 10  $\mu\text{m}$ ; PM2.5: particulate matter with a diameter less than 2.5  $\mu\text{m}$



**Figure 2.** Graphical illustration summarizing the main study findings.

ATM: atmospheric pressure; CO: carbon monoxide; NO<sub>2</sub>: nitric dioxide; NO<sub>X</sub>: nitric oxide; O<sub>3</sub>: ozone; PCI: percutaneous coronary intervention; PM<sub>10</sub>: particulate matter with a diameter between 2.5  $\mu\text{m}$  and 10  $\mu\text{m}$ ; PM<sub>2.5</sub>: particulate matter with a diameter less than 2.5  $\mu\text{m}$ ; STEMI: ST-elevation myocardial infarction

significant quadratic terms and also shown by visual inspection of quadratic prediction plots. This held true for the association between CO, NO<sub>2</sub> and NO<sub>X</sub> with same-day STEMI, as well as for the association between NO<sub>2</sub> with STEMI occurring one day later, and for the association between temperature and atmospheric pressure with STEMI occurring two days later.

When exploring the impact of weather and environmental features on the risk of STEMI four, five, six, seven, 14 and 30 days later, we found that several of the features already impacting at short-term were also impactful subsequently (Supplementary Table 1S), and this held true for all of them, from CO to NO<sub>2</sub>, NO<sub>X</sub>, O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub>. Conversely, pollutants were not homogeneously impactful in all participating centres (Supplementary Table 2S), suggesting that additional geographic factors (e.g. proximity to

the sea, altitude, crowding and traffic) may be mechanically related to STEMI risk. Finally, season-specific analyses suggested that most of the biologic effect of pollution and climate was evident in spring, summer and fall.

## Discussion

Despite ongoing developments in the diagnosis, prevention, treatment and rehabilitation of AMI, several unmet needs remain. Accordingly, the overall impact of weather change on cardiovascular disease and particularly incident AMI is still unclear and will be the net result of several, sometimes divergent, effects and developments.<sup>22</sup> Due to a decrease in cold days, there may be a drop in cold-related AMI, but this effect may be mitigated because AMI risk is mainly related to short-term major temperature changes, whereas

**Table 2.** Exploratory inferential analysis.

Daily environmental or weather feature	Incidence			
	Same day	Day +1	Day +2	Day +3
<b>Carbon monoxide</b>				
Minimum	$p = 0.021^a$	$p = 0.434$	$p = 0.575$	$p = 0.432$
Maximum	$p = 0.012^a$	$p = 0.179$	$p = 0.632$	$p = 0.029$
Mean	$p = 0.016$	$p = 0.060$	$p = 0.388$	$p = 0.107$
Change	$p = 0.008^a$	$p = 0.139$	$p = 0.288$	$p = 0.024$
<b>Nitrogen dioxide</b>				
Minimum	$p = 0.048^a$	$p = 0.065$	$p = 0.295$	$p = 0.760$
Maximum	$p = 0.027$	$p = 0.010^a$	$p = 0.509$	$p = 0.163$
Mean	$p = 0.107$	$p = 0.021^a$	$p = 0.524$	$p = 0.098$
Change	$p = 0.020$	$p = 0.016^a$	$p = 0.416$	$p = 0.178$
<b>Nitric oxide</b>				
Minimum	$p = 0.011^a$	$p = 0.207$	$p = 0.206$	$p = 0.156$
Maximum	$p = 0.125$	$p = 0.290$	$p = 0.263$	$p = 0.042$
Mean	$p = 0.063$	$p = 0.196$	$p = 0.354$	$p = 0.039$
Change	$p = 0.124$	$p = 0.309$	$p = 0.243$	$p = 0.043$
<b>Ozone</b>				
Minimum	$p = 0.126$	$p = 0.325$	$p = 0.360$	$p = 0.068$
Maximum	$p = 0.002$	$p = 0.001$	$p = 0.002$	$p = 0.003$
Mean	$p = 0.028$	$p = 0.011$	$p = 0.019$	$p = 0.003$
Change	$p = 0.003$	$p = 0.004$	$p = 0.007$	$p = 0.031$
<b>PM10</b>				
Minimum	$p = 0.578$	$p = 0.366$	$p = 0.435$	$p = 0.183$
Maximum	$p = 0.261$	$p = 0.751$	$p = 0.075$	$p = 0.033$
Mean	$p = 0.339$	$p = 0.735$	$p = 0.251$	$p = 0.104$
Change	$p = 0.012$	$p = 0.228$	$p = 0.059$	$p = 0.018$
<b>PM2.5</b>				
Minimum	$p = 0.175$	$p = 0.552$	$p = 0.205$	$p = 0.136$
Maximum	$p = 0.387$	$p = 0.654$	$p = 0.673$	$p = 0.281$
Mean	$p = 0.179$	$p = 0.438$	$p = 0.328$	$p = 0.079$
Change	$p = 0.267$	$p = 0.240$	$p = 0.667$	$p = 0.042$
<b>Temperature</b>				
Minimum	$p = 0.055$	$p = 0.234$	$p = 0.222$	$p = 0.294$
Maximum	$p = 0.008$	$p = 0.012$	$p = 0.007$	$p = 0.031$
Mean	$p = 0.001$	$p = 0.006$	$p = 0.003$	$p = 0.004$
Change	$p = 0.012$	$p = 0.004$	$p = 0.002^a$	$p = 0.015$
<b>Atmospheric pressure</b>				
Minimum	$p = 0.578$	$p = 0.788$	$p = 0.417$	$p = 0.095$
Maximum	$p = 0.707$	$p = 0.264$	$p = 0.218$	$p = 0.030$
Mean	$p = 0.389$	$p = 0.620$	$p = 0.869$	$p = 0.056$
Change	$p = 0.192$	$p = 0.088$	$p = 0.023^a$	$p = 0.410$
<b>Humidity</b>				
Minimum	$p = 0.604$	$p = 0.287$	$p = 0.096$	$p = 0.130$
Maximum	$p = 0.111$	$p = 0.384$	$p = 0.225$	$p = 0.206$
Mean	$p = 0.201$	$p = 0.169$	$p = 0.109$	$p = 0.420$
Change	$p = 0.806$	$p = 0.228$	$p = 0.071$	$p = 0.451$
Rainfall	$p = 0.480$	$p = 0.798$	$p = 0.169$	$p = 0.413$

<sup>a</sup>Including significant quadratic term.

PM10: particulate matter with a diameter between 2.5  $\mu\text{m}$  and 10  $\mu\text{m}$ ; PM2.5: particulate matter with a diameter less than 2.5  $\mu\text{m}$

global warming is characterized by a small, long-term temperature increase.

It is now evident that weather and pollution can also impact on the risk of atherothrombosis in apparently

healthy subjects who are, however, prone to coronary instability, by modulating inflammation, thrombosis, vasoreactivity and many other pathophysiologic pathways.<sup>11,12,14,15,23</sup> Several studies have focused on the

**Table 3.** Detailed inferential analysis.<sup>a</sup>

Timing	Daily environmental or weather feature	Specifics	Point estimate	95% confidence interval	p	
Same day	Carbon monoxide	Minimum	2.486 <sup>b</sup>	1.150–5.376 <sup>b</sup>	0.021	
		Maximum	1.170 <sup>b</sup>	1.036–1.322 <sup>b</sup>	0.012	
		Mean	1.187	1.033–1.365	0.016	
		Change	1.184 <sup>b</sup>	1.044–1.343 <sup>b</sup>	0.008	
	Nitrogen dioxide	Minimum	1.001 <sup>b</sup>	1.000–1.002 <sup>b</sup>	0.048	
		Maximum	1.001	1.000–1.003	0.027	
		Change	1.002	1.000–1.003	0.020	
	Nitric oxide	Minimum	1.001 <sup>b</sup>	1.000–1.001 <sup>b</sup>	0.011	
		Ozone	Maximum	0.998	0.996–0.999	0.002
	One day before	Ozone	Mean	0.998	0.996–1.000	0.028
			Change	0.998	0.996–0.999	0.003
			Change	1.005	1.001–1.009	0.012
PM10		Change	1.001 <sup>b</sup>	1.000–1.001 <sup>b</sup>	0.010	
		Change	1.001 <sup>b</sup>	1.000–1.001 <sup>b</sup>	0.021	
		Change	1.001 <sup>b</sup>	1.000–1.001 <sup>b</sup>	0.016	
Ozone		Maximum	0.998	0.996–0.999	0.001	
		Mean	0.998	0.996–0.999	0.011	
		Change	0.998	0.997–0.999	0.004	
Two days before		Ozone	Maximum	0.998	0.997–0.999	0.002
			Mean	0.998	0.996–1.000	0.019
			Change	0.998	0.997–0.999	0.007
Three days before	Carbon monoxide	Maximum	1.047	1.005–1.091	0.029	
		Change	1.053	1.007–1.102	0.024	
	Nitric oxide	Maximum	1.001	1.000–1.001	0.042	
		Medium	1.001	1.000–1.002	0.039	
		Change	1.001	1.000–1.001	0.043	
	Ozone	Maximum	0.998	0.997–0.999	0.003	
		Mean	0.997	0.996–0.999	0.003	
		Change	0.999	0.997–1.000	0.031	
	PM10	Maximum	1.007	1.001–1.013 <sup>b</sup>	0.033	
		Change	1.004	1.001–1.008	0.022	
	PM2.5	Change	1.011	1.000–1.021	0.042	

<sup>a</sup>Mixed effect model with Poisson likelihood and log link, to account for centre-wise clustering.<sup>18</sup> Models with and without quadratic terms were tested separately, to appraise the impact of non-linear effects (with the latter presented in the case of nominally significant ( $p < 0.05$ ) results).

<sup>b</sup>Quadratic term.

PM10: particulate matter with a diameter between 2.5  $\mu\text{m}$  and 10  $\mu\text{m}$ ; PM2.5: particulate matter with a diameter less than 2.5  $\mu\text{m}$

impact of weather and pollutants on the risk of AMI in general, and some already on the risk of STEMI in particular, such that improvements in environment and pollution may directly lead to reductions in age-adjusted rates of coronary artery disease events.<sup>10,24–26</sup> Indeed, CO, PM10 and PM2.5, among others, have already been linked to the risk of coronary events in several works.<sup>10,17,27,28</sup> However, uncertainty persists on the real impact of such environmental features on cardiovascular risk, given the competing effects of different variables, the non-linear associations and the typical time lag between exposure and disease. We thus aimed at disentangling this complex scenario by appraising the impact of several pollutants and weather features on the risk of STEMI in two large urban Italian areas.

Briefly, we found that the risk of STEMI was strongly associated with several pollution and weather features. While causation cannot be directly inferred from our work, concentrations of CO, NOX, PM10, O3 and PM2.5 were all individually capable of predicting STEMI risk well before the adverse event. In particular, these features changed significantly as early as three days before the event, with increasing values being associated with an increased risk (with the notable exclusion of O3). Pollutant concentrations also predicted STEMI risk on a shorter term (i.e. two days later, one day later, or on the same day). In addition, NO also proved capable of significantly predicting STEMI risk, in a concordant fashion, albeit only one day before the event (yet also on the same day). On top of pollutants, temperature and atmospheric pressure

were significantly associated with STEMI risk, even days before the adverse event. Yet, temperature, atmospheric pressure and, as stated above, O<sub>3</sub>, were inversely related to STEMI risk. Thus, colder days were the days of higher risk of STEMI, with concomitant lower pressures, lower O<sub>3</sub> concentrations and worse pollution. The interplay with sun exposure remains a focus of intense research, whereas rainfall, albeit not proving as a significant and independent predictor in our study, is important given its role in impacting on pollution.<sup>29</sup>

Overall, these findings have major population and clinical implications. First, they confirm and expand prior works on the same topic, including detailed reports from the extensive data gathered by the United States Environmental Protection Agency.<sup>8,16,30</sup> Most importantly, they challenge decision-makers and stakeholders working on population interventions and infrastructure planning on one hand, and clinicians and patients aiming at individualized care on the other hand. Interventions for environmental safety and weather improvement are direly needed to protect frail patients and populations at large.<sup>6,7</sup> Focusing on a shorter term, adverse changes in environmental pollutants and weather features need to raise the alert and the responsiveness of emergency services, while cautioning patients in terms of pharmacologic therapy and avoidance of unnecessary untoward exposures.<sup>31–33</sup>

Strengths of our work are several, and include the carefully selected population, featuring only patients with STEMI admitted for primary PCI. Accordingly, case definition was based on both clinical and angiographic criteria, and not on discharge diagnoses, as done in the vast majority of prior studies on this topic. Indeed, STEMI is almost invariably due to occlusive or subocclusive atherothrombosis, defining a quite homogenous and high-risk clinical condition, at odds with the clinical category of non-STEMI, characterized by substantial clinical and pathophysiological heterogeneity.

Weaknesses of this work include the retrospective design, lack of direct estimates for catchment area and patients at risk, limited adjustment for confounders (e.g. per-patient ones such as comorbidities or socio-economic status), lack of penalization for multiple testing, and impossibility to focus on patient features thus enabling subgrouping of STEMI risk strata. As we did not rely on a universally inclusive population at risk, only independent association was appraised with statistical modelling, refraining from computing population attributable fraction. In addition, the link between STEMI occurrence and exposure can only be inferred by admission to one of the participating centres, as AMI leading to sudden cardiac death without hospital admission was not included in the data

capturing system. Accordingly, only indirect validity for our results can be purported for sudden cardiac death or AMI not leading to emergency hospital admission. The apparent protective effect of O<sub>3</sub> should be viewed in light of the correlation between this agent and other weather and environment features, as well as the heterogeneity and threshold effects already demonstrated for O<sub>3</sub>.<sup>34</sup> Thus, we look forward to formally confirming or disproving the present findings in an external validation cohort, possibly also testing the impact of other interacting features such as traffic blocks and mitigation efforts. Another useful analytical approach would be to appraise (as control or adjustment tool), an outcome which should not per se be associated with weather or pollution (for instance elective coronary procedures).

### Author contribution

GB-Z and GF contributed equally to this work. GB-Z, GF and FV designed the study, handled data analysis and interpretation and drafted the manuscript. AG, EM, ADDG, AB, ADG, SC, MS, SS, VV, RC, GV, MBG, MPer, EC, SB, JC, MF, LR and FR participated in data collection, data analysis and interpretation and critically reviewed the manuscript for important intellectual content. All authors finally approved the manuscript.

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