

# Effect of air pollution exposure on risk of acute coronary syndromes in Poland: a nationwide population-based study (EP-PARTICLES study)



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## Summary

**Background** Air pollution (AP) is linked up to 20% of cardiovascular deaths. The aim of this nationwide study was to investigate subpopulations vulnerable to AP for non-ST- (NSTEMI) and ST-elevation myocardial infarction (STEMI) incidence.

**Methods** We analysed short- (lags up to seven days) and mid-term (0–30 days moving average) influence of particulate matter (PM<sub>2.5</sub>), sulphur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>) and benzo(a)pyrene (BaP) on hospitalizations due NSTEMI and STEMI in 2011–2020. Data on AP concentrations were derived using GEM-AQ model. Study included residents of five voivodeships in eastern Poland, inhabited by over 8,000,000 individuals.

**Findings** Higher NO<sub>2</sub> and PM<sub>2.5</sub> concentrations increased mid-term risk of NSTEMI in patients aged < 65 years by 1.3–5.7%. Increased SO<sub>2</sub> and PM<sub>2.5</sub> concentration triggered STEMI in the short- (SO<sub>2</sub>, PM<sub>2.5</sub>) and mid-term (PM<sub>2.5</sub>) amongst those aged ≥ 65 years. In the short- and mid-term, women were more susceptible to PM<sub>2.5</sub> and BaP influence resulting in increased STEMI incidence. In rural regions, STEMI risk was triggered by SO<sub>2</sub>, PM<sub>2.5</sub> and BaP. Income-based stratification showed disproportions regarding influence of BaP concentrations on NSTEMI incidence based on gross domestic product (up to 1.4%).

**Interpretation** There are significant disparities in the influence of air pollution depending on the demographic and socio-economic factors. AP exposure is associated with the threat of a higher risks of NSTEMI and STEMI, especially to younger people, women, residents of rural areas and those with lower income.

**Funding** National Science Center and Medical University of Białystok, Poland.

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**Keywords:** Air pollution; Cardiology; Public health; Acute coronary syndrome; Myocardial infarction

The Lancet Regional Health - Europe  
2024;41: 100910

Published Online xxx  
<https://doi.org/10.1016/j.lanepe.2024.100910>

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### Research in context

#### Evidence before this study

We searched databases for relevant studies up to March 29th 2024 through PubMed, EMBASE, the Web of Science, Clinical Key and Google Scholar registries, as well as published proceedings from major cardiac conferences. Search terms included (“air pollution” OR “benzo(a)pyrene” OR “particulate matter” OR “PM2.5” OR “nitrogen dioxide” OR “NO<sub>2</sub>” OR “sulphur dioxide” OR “SO<sub>2</sub>”) AND (“myocardial infarction” OR “STEMI” OR “NSTEMI”). No language, publication date, or publication status restriction was imposed. The most updated or inclusive data for each study were used for abstraction. The references of articles were cross-checked. The search revealed that air pollution was a significant yet underestimated, modifiable risk factor for cardiovascular diseases. However, despite numerous publications examining the association between exposure to air pollution and the occurrence of myocardial infarction, little attention has been given to particularly vulnerable groups and the differentiation between NSTEMI and STEMI. Additionally, a large proportion of these studies focused solely on the impact of long-term exposure to air pollution. Various pollutants, despite different physicochemical characteristics, may trigger acute coronary syndrome through common pathophysiological pathways, primarily by promoting oxidative stress, DNA methylation, systemic inflammation, and autonomic dysfunction, leading

to atherosclerotic plaque destabilization and thrombotic events.

#### Added value of this study

The current study, including 8,000,000 residents, investigated the effects of four main air pollutants on myocardial infarction incidence in eastern Poland, aiming to find the most vulnerable subgroups. Due to the adoption of the novel GEM-AQ model, we were able to perform analysis with high spatiotemporal resolution (community resolution grids with hourly outputs from the surface layer aggregated to annual averages) that facilitated precise statistical analysis. Moreover, our study was one of the first to investigate the detrimental effect of benzo(a)pyrene on acute coronary syndromes. We found that air pollution exposure was associated with an important threat of higher risk of NSTEMI and STEMI, especially to younger people, women, residents of rural areas and with lower income.

#### Implications of all the available evidence

Our study underlines that additional global efforts are insufficient to mitigate pollution-induced health outcomes, including CVD, necessitating better implementation strategies, funding for research, and novel solutions. Inclusion of environmental factors in CVD preventive measures should be considered in the future.

## Introduction

Cardiovascular diseases (CVD) confer major challenges globally in terms of public health, economic and social aspects. In the European Union, CVD accounted for 1.7 million deaths in 2021, as well as the loss of 1.3 million working years.<sup>1</sup> Among the various CVD, ischemic heart disease, most commonly caused by coronary artery disease (CAD), accounts for the highest percentage of mortality, being the cause of 34% of deaths in 2021.<sup>1</sup> During the course of CAD, exacerbations may occur in the form of acute coronary syndromes (ACS), which include a life-threatening ST-segment elevation myocardial infarction (STEMI), often induced by sudden coronary artery closure, and non-ST-segment elevation MI (NSTEMI), resulting from heterogeneous causes leading to an imbalance between myocardial oxygen demand and supply capabilities.<sup>51</sup> In this study, we examined the influence of air pollution exposure on the risk of the aforementioned diseases. Well-established MI risk factors encompass arterial hypertension, diabetes, obesity, chronic kidney disease, hyperlipidaemia, and smoking, but in recent decades, air pollution and its impact on human health has been the focus of numerous studies, demonstrating the harmful impact of this environmental risk factor in the case of ACS.<sup>2,3</sup>

Air pollution constitutes a dynamically changing mixture of various chemical compounds present in both gaseous and solid forms, which include particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>), sulphur dioxide (SO<sub>2</sub>), and polycyclic aromatic hydrocarbons (PAH) such as benzo(a)pyrene (BaP).<sup>4</sup> Different geographical areas are characterized by varying concentrations of these substances. For example, the occurrence of so-called London-type smog is associated with highly industrialized areas and is characterized by high levels of SO<sub>2</sub>, NO<sub>2</sub>, carbon monoxide (CO), carbon dioxide (CO<sub>2</sub>), and PM.<sup>5</sup> On the other hand, densely populated areas with heavy traffic are linked to the occurrence of photochemical smog, widely known as Los Angeles-type.<sup>6</sup> Polish smog represents a novel form of air pollution distinguished by a unique chemical composition, differing from previously characterized smog types. Its formation is influenced by distinct meteorological conditions and is localized to specific regions.<sup>52</sup> This unique type of smog is characterized by elevated concentrations of PM and PAH, coupled with comparatively lower levels of SO<sub>2</sub> and CO. Polish smog also distinguishes itself through its formation under conditions of high atmospheric pressure and negative air temperatures, setting it apart from the London and Los

Angeles-types of smog. Additionally, as the region of eastern Poland is one of the poorest parts of Europe,<sup>53</sup> it is primarily associated with non-optimal heating choices made by households during the winter months.<sup>5</sup> Similar composition of smog may also occur in other geographical areas with continental climate where (like in eastern Poland) have very low temperatures and high-pressure episodes in cold seasons, characterized by analogous heating choices by its residents.

The association between exposure to air pollution and the prevalence as well as mortality in CVD is the subject of extensive research.<sup>7–9</sup> Recent studies suggest that air pollution is linked to 20% of all deaths resulting from CVD.<sup>8</sup> This means that air pollution has a greater impact on CVD mortality compared to factors such as high LDL cholesterol levels, high BMI, lack of physical activity, and alcohol consumption.<sup>8</sup> It has been estimated that maintaining a consistent level of air pollution will result in an accumulated cost of caring for patients exceeding £5 billion pounds in the UK in years 2018–2035.<sup>10</sup>

In light of the health and socio-economic costs generated by smog, the purpose of this study was to analyse the relationship between exposure to air pollution characterizing the regions of Eastern Poland and the occurrence of NSTEMI and STEMI. Secondly, we aimed to identify subpopulations of individuals particularly vulnerable to the influence of air pollution on ACS. We therefore analysed a population of over 700 municipalities in Eastern Poland over a period of 10 years, filling the current gap in evidence regarding relationship between exposure to Polish smog and the occurrence of ACS.

## Methods

### Study region

The eastern part of Poland, the focus of this study, is often perceived as one of Europe's less economically advanced areas.<sup>53</sup> It is characterized by a lower GDP per capita compared to other regions, a relatively sparse population, and an extensive rural landscape. This region, home to over eight million inhabitants, comprises five voivodeships, 101 counties, and 709 communities.

### Hospitalizations data

Data on hospitalizations from 2011 to 2020 were obtained from Poland's National Health Fund. Analysed variables included demographics and ICD-10 codes of non-ST- and ST-elevation myocardial infarction (NSTEMI/STEMI) according to ICD-10: I21.4, and I21.X, respectively. The obtained data included individual patient code, therefore phenomenon of repeating patients did not occur in our analysis. Detailed list of catheterization labs in analysed region is presented in [Supplementary Table S15](#).

### Air pollution data

Initial data were collected from local environmental stations across the region. Subsequently, in collaboration with the Institute of Environmental Protection—National Research Institute, we used the GEM-AQ model for further calculations. The GEM-AQ (Global Environmental Multiscale–Air Quality) model is an advanced numerical tool for air quality modelling across various scales—from local to global.<sup>54,55</sup> It is an integrated chemical-transport model that combines detailed physical and chemical processes occurring in the atmosphere. The model is used for national air quality forecasting and assessment in Europe and operates as a partner model in the Copernicus Atmosphere Monitoring Service (CAMS), which is the European Union's Earth Observation Programme. Air pollution including PMs, BaP, SO<sub>2</sub> and NO<sub>2</sub> concentrations were computed using community resolution grids, with hourly outputs from the surface layer aggregated to annual averages.

### Meteorological data

Meteorological data, including temperature, relative humidity, and atmospheric pressure, were obtained from the Institute of Meteorology and Water Management in Poland. Measurements were conducted in a standardized meteorological enclosure and recorded automatically at specified intervals. Data accuracy was maintained, with temperature and pressure accurate to 0.1 [°C or hPa] and humidity to 1%. These measurements are representative of the counties studied. The list of measurement stations is presented in [Supplementary Table S14](#).

### Statistical analysis

The assessment of variable distribution was conducted through the Shapiro–Wilk test. For continuous variables, the presentation was in the form of mean values with standard deviation (SD) or median (Me) values with interquartile range (IQR), while categorical variables were presented as counts (N) and proportions (%). The two-tailed t-test and chi-square ( $\chi^2$ ) tests were utilized for the comparative analysis of data that followed a normal distribution. In instances where multiple subgroups with non-normally distributed variables were compared, the Kruskal–Wallis test was employed. For categorical variables comparison, the chi-square ( $\chi^2$ ) test was applied.

In the first stage, we estimated community-specific associations of air pollution concentration with incidence using quasi-Poisson generalized additive models, in accordance with the approaches used in previous studies. We included an indicator variable for the admission day of week to account for possible variations over weekends, an indicator variable for public holiday. We also controlled our models for epidemics by using

dummy variables and seasonal trends [STEMI—simple indicator variable (the time interval for the daily data was the elapsed month, which resulted in the creation of 120 strata); NSTEMI—natural spline (ns) with six degrees of freedom (df) per year]. To exclude potential nonlinear and delayed confounding effects of weather conditions we use ns with 6 df or 0–1-day moving average temperature and 0–6 moving average and three df for relative humidity and atmospheric pressure.

In the second stage we pooled community-specific estimates with a random-effects meta-analysis using the restricted maximum-likelihood estimator of the between-community variance.

The data from each community were analysed according to the same protocol and expressed as a change in the incidence of STEMI and NSTEMI per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  and  $\text{NO}_2$  concentration (in the case of  $\text{SO}_2$  1  $\mu\text{g}/\text{m}^3$  and BaP 1  $\text{ng}/\text{m}^3$ ), therefore we could compare the effect of pollution in the areas. To avoid the co-linearity effect, we separately modelled each air pollutant. Based on our previous experience,<sup>2,3,7,56</sup> we also conducted separate analyses for different lag: simple lags of 0–6 days (lag 0 to lag 6), 0–1 days moving average (lag 0–1), 0–6 days moving average (lag 0–6), and 0–30 days moving average (lag 0–30).

We also calculated country gross domestic product (GDP) per capita in USD at LAU-1 level as a mean of whole analysed period. The date of GDP we obtained from Institute of Development in Poland. For further analysis, all municipalities were divided into those with low (<2Q) and high ( $\geq$ 2Q) values of the above parameters. Summary at the NUTS2 level. The same strategy we used in municipality type, and all are assigned as rural or for urban areas.

Further subgroup analyses were performed for age and sex, consumption of tobacco hypertension, and diabetes prevalence. Data on were aggregated on county level (LAU-1) as standardized hospitalization rates and standardized death rates were aggregated on county level. We also tested the two-pollutant models—BaP with  $\text{PM}_{2.5}$  and gaseous pollutants with the different outcomes.

Data are presented as relative risks (RRs) and 95% confidence intervals (95% CI).

To determine the P for risk differences in relative ratio of air pollution, for example in male vs. females, are statistically we used calculation as follow:

$$Z_{\text{score}} = \frac{\beta_{\text{male}} - \beta_{\text{female}}}{\sqrt{se(\beta_{\text{male}})^2 + se(\beta_{\text{female}})^2}}$$

Where:

$\beta$ —is the pooled regression coefficient of admission per unit increment in air pollution concentration at given lag.

To calculate the attributable cases associated with  $\text{PM}_{2.5}$  exposure, we used the formula:

$$AC = N \times [1 - e^{-\beta \times (\text{Mean PM}_{2.5} \text{ concentration} - \text{threshold})}]$$

Where:

AC—attributable cases

$\beta$ —is the pooled regression coefficient of admission per unit increment in air pollution concentration at lag 0–1.

N—represents the number of hospital admissions on days with  $\text{PM}_{2.5}$  concentration above the threshold.

To plot concentration-response curves, we used the AirQ+ software.<sup>57</sup> The concentration-response function relates exposure levels to  $\text{PM}_{2.5}$  with the number of STEMI and NSTEMI cases across the study area and period. These functions represent the relative health risk associated with a change in exposure level at lag 0–1.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and the STROBE guidelines to ensure transparency and reproducibility of the results (Supplementary Table S15). Additionally, was approved by the Bioethics Committee of the Medical University of Bialystok (approval number APK.002.81.2022).

All analyses were performed using Stata Statistical Software, (StataCorp, 2023, version 18, TX, USA), MS Excel (Microsoft, 2023, version 16.78.3, Redmond, WA, USA), AirQ+ (WHO Regional Office for Europe, 2023, version 2.2, Copenhagen, Denmark, United Europe). The threshold of statistical significance was set at  $P < 0.05$  for all the tests.

### Role of the funding source

Study sponsors had no influence on any stages of the study course.

### Results

In the analysed period, we recorded 63,154 hospitalizations and 5921 in-hospital deaths (9.4%) due to STEMI; and 76,543 hospitalizations and 4079 (5%) in-hospital deaths due to NSTEMI (Fig. 1). The majority of patients admitted with STEMI were male (64.3%) and mean age was 67.5 (SD 12.5). In the NSTEMI group, 62% were male and mean age was 70.2 (SD 11.9). In the analysed period, overall median standardized hospitalization rate (SHR) was 88 (24–289) per 100,000 population/year for STEMI, with a significantly decreasing trend over time ( $P < 0.001$ ). In the same timeframe, the SHR for NSTEMI was 110 (37–341) per 100,000 population/year, with non-significantly increasing trend ( $P = 0.86$ ) (Supplementary Fig. S1).

In the analysed years we observed significantly decreasing concentrations of all air pollutants ( $P < 0.001$

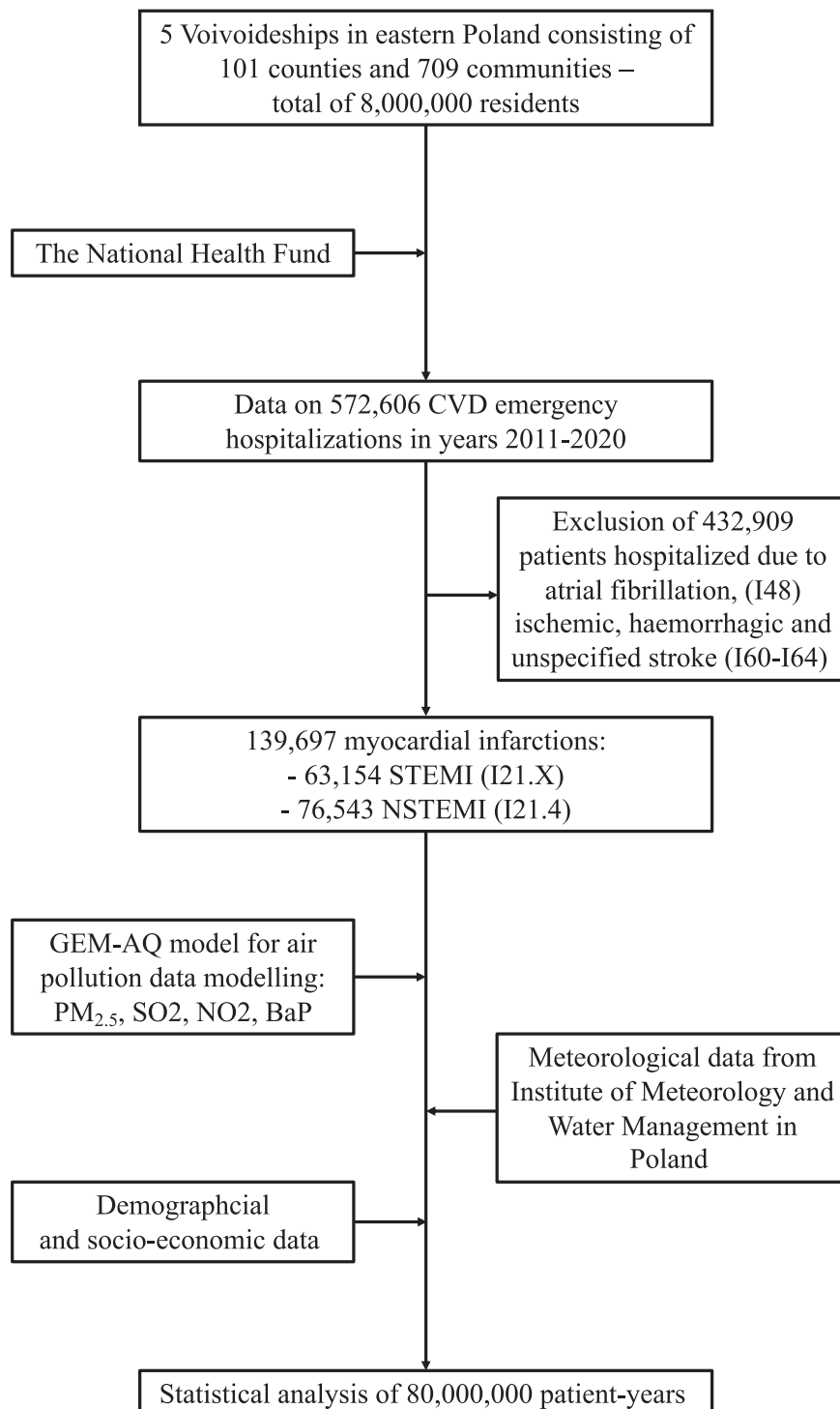


Fig. 1: Flowchart of the current EP-PARTICLES Study analysis.

for all) in both rural and urban areas. The concentrations still remained higher than thresholds recommended by WHO and European Environment Agency, with daily mean  $PM_{2.5}$ ,  $NO_2$ ,  $SO_2$  and BaP concentrations being 20.6 (SD 12.8)  $\mu g/m^3$ , 7.8 (SD 8.0)  $\mu g/m^3$ , 3.6 (SD 5.2)  $\mu g/m^3$ , 1.5 (SD 2.0)  $ng/m^3$ , respectively.

Correlation matrix of all air pollutants is presented in [Supplementary Table S10](#). The analysis including the local socio-economic status and type of the area showed consistent moderate correlation between BaP and  $PM_{2.5}$  (Spearman's  $\rho = 0.64$  and  $0.65$ ) across the regions. The highest correlation was found between  $PM_{2.5}$  and  $SO_2$  (Spearman's  $\rho = 0.79$  in the urban and Spearman's  $\rho = 0.83$  in rural and higher income areas), while the lowest was observed between BaP and  $SO_2$  (Spearman's  $\rho = 0.56$  and  $0.57$ ). P-value was  $<0.001$  for all of the performed tests.

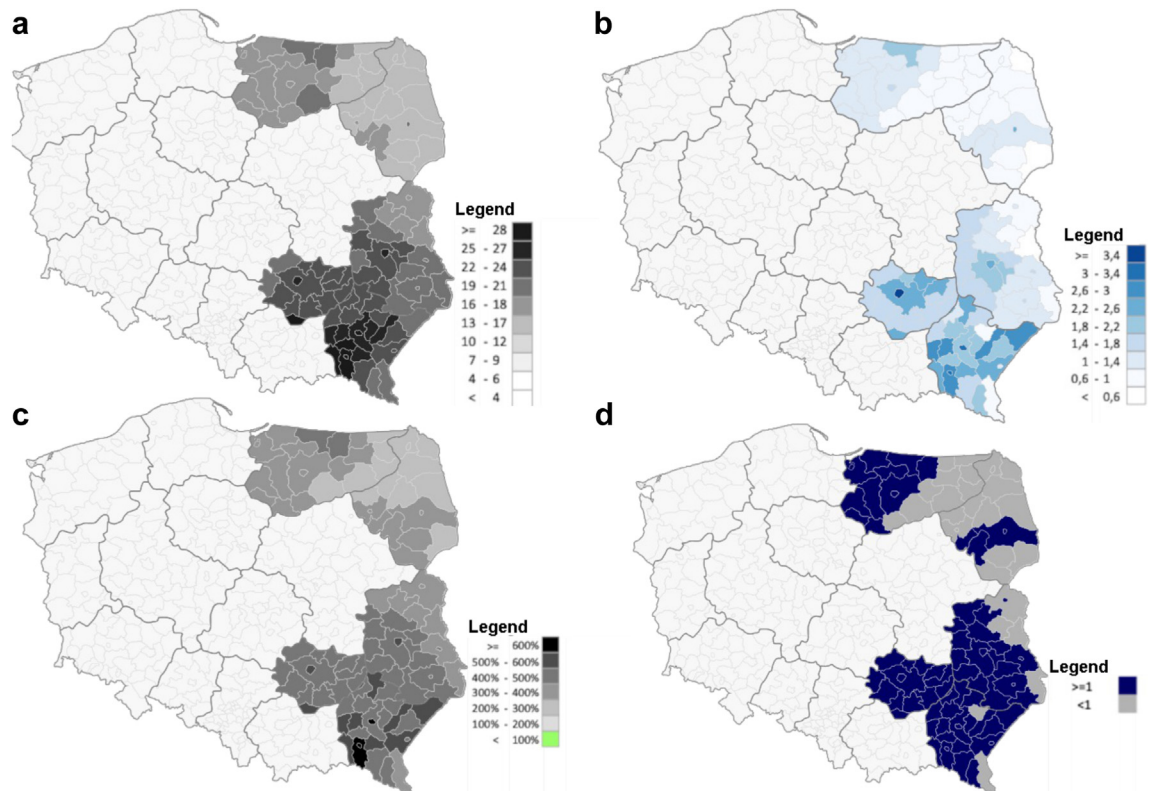
Detailed information regarding baseline characteristics of analysed population, SHR rates, air quality and meteorological conditions are presented in [Fig. 2](#), [Fig. 3](#), [Supplementary Fig. S1](#) and [Tables S1–S4](#).

In the overall population, a 10  $\mu g/m^3$  increase in  $PM_{2.5}$  and 1  $\mu g/m^3$  increase in BaP concentrations were associated with significantly higher risk of

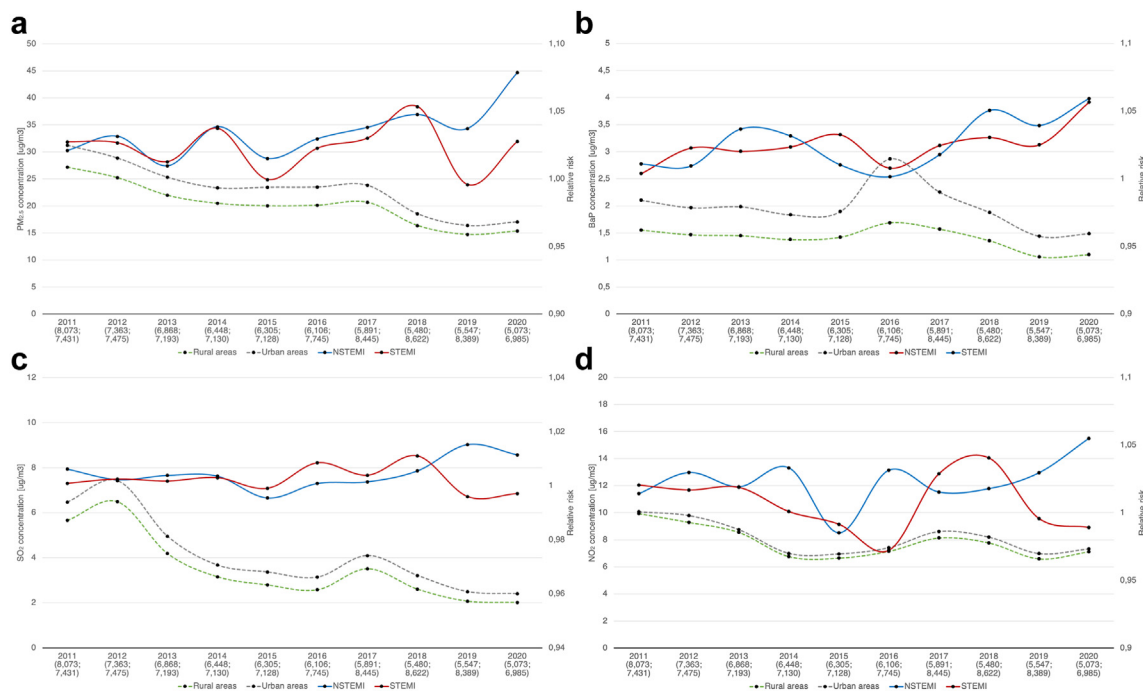
hospitalization due to STEMI and NSTEMI. Detailed results are presented in [Fig. 4](#), [Fig. 5](#) and [Supplementary Table S5](#). Increase in gaseous air pollutants— $NO_2$  and  $SO_2$ —had short- and mid-term detrimental effects in the STEMI group, while in the NSTEMI group only a mid-term effect was noticed. The results of two-pollutant models regarding influence of BaP on NSTEMI (RR 1.017, 95% CI 1.009–1.026,  $P < 0.001$  for model with adjustment for  $PM_{2.5}$ ) support single-pollutant models results that its impact may be more pronounced than on STEMI incidence. Influence of BaP on STEMI incidence, which we found to be significant in the one-pollutant model, loses its significance after adjustment for  $PM_{2.5}$  concentrations (RR 1.002, 95% CI 0.988–1.008,  $P = 0.65$  for model with adjustment for  $PM_{2.5}$ ). Detailed results on two-pollutant model are presented in [Supplementary Tables S11 and S12](#).

### Subgroup analyses

In the age-stratified analysis, increase in  $NO_2$  and  $PM_{2.5}$  concentrations significantly increased short and mid-term risk of hospitalization due to NSTEMI in patients aged  $<65$  years by 1.3–5.7%. Increases in  $SO_2$  and  $PM_{2.5}$



**Fig. 2: Air pollutants' concentrations in the studied region.** Panel a, mean yearly  $PM_{2.5}$  concentration; Panel b, mean yearly BaP concentration; Panel c, the rate of exceeded yearly WHO norm for  $PM_{2.5}$ ; Panel d, exceeded yearly WHO norm for BaP. Abbreviations: NSTEMI, Non-ST Elevation Myocardial Infarction; STEMI, ST-Elevation Myocardial Infarction.



**Fig. 3: Temporal trends in air pollutants' concentrations in urban and rural areas and relative risk of hospitalization due to STEMI and NSTEMI on lag 0.** Analysed air pollutants are presented as follows: panel a,  $PM_{2.5}$ ; panel b, BaP; panel c,  $SO_2$ ; panel d,  $NO_2$ . Numbers in parentheses state the exact number of STEMI and NSTEMI cases in each year, respectively. Abbreviations: BaP, Benzo(a)pyrene; CI, Confidence Interval;  $NO_2$ , Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction;  $PM_{2.5}$ , Particulate Matter with 2.5 Micrometers or Less; RR, Relative Risk;  $SO_2$ , Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction.

were associated with triggering effect on hospitalization due to STEMI in the short- and mid-term (lag 0–30 for  $PM_{2.5}$ ) observation in older patients.

In the short- and mid-term observation women were significantly more susceptible to hospitalization due to STEMI related with increases in  $PM_{2.5}$  and BaP, with no differences in influence of gaseous pollutants. In comparison to men, as a result of a  $10 \mu\text{g}/\text{m}^3$  increase in  $PM_{2.5}$  concentration, the risk of NSTEMI was 3.6% higher in the female group in the case of mid-term exposure. Detailed information regarding influence of air pollution stratified by age and sex are presented in [Supplementary Tables S6–S9](#) and [Fig. 6](#).

We performed subgroup analysis of based on socio-economic factors in 709 municipalities. There were differences in urbanization rates, ranging from 7.1% in the Świętokrzyskie to 23.5% in the Podlaskie Voivodeship, with the overall mean of 17.8%. Mean GDP was \$32,108 (SD 8192) USD, with the minimal and maximal mean GDPs of \$20,205 and \$66,031 in Podkarpackie. In our analysis, an increased BaP concentration in regions with  $\text{GDP} < 2\text{Q}$  was significantly associated with a higher risk of MI compared to areas with  $\text{GDP} \geq 2\text{Q}$ .

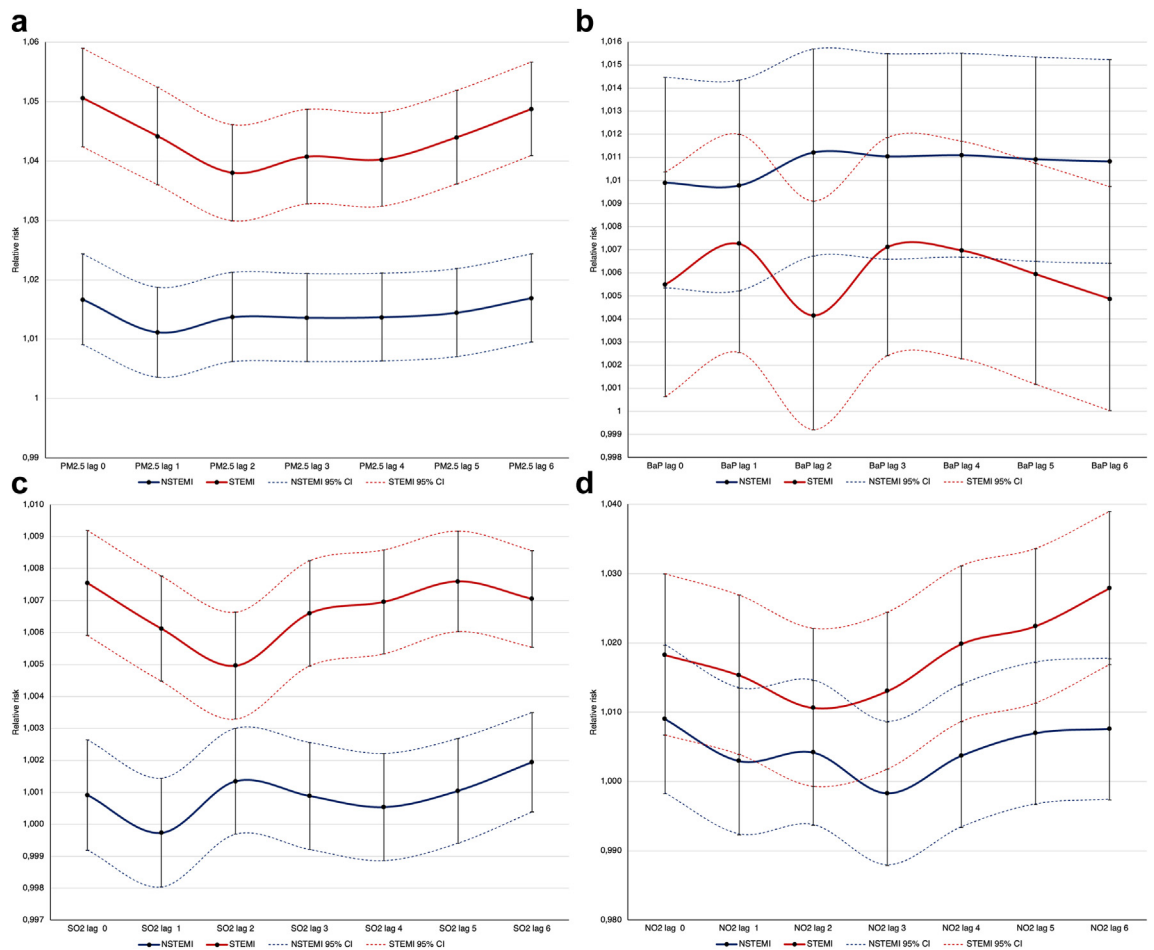
The remaining results were not statistically significant. The relationships between air pollution and

socio-economic factors are summarized in [Table 1](#), [Table 2](#) and [Fig. 6](#).

In the rural, as compared to urban regions, the risk of hospitalization due to STEMI was triggered by increases in  $SO_2$  (RRR 1.008, 95% CI 1.004–1.012,  $P < 0.001$ ),  $PM_{2.5}$  (RRR 1.03, 95% CI 1.012–1.049,  $P = 0.001$ ) and BaP (RRR 1.019, 95% CI 1.008–1.031,  $P = 0.001$ ).

GDP-based stratification showed in regions with lower mean income increase in  $1 \text{ ng}/\text{m}^3$  of BaP was associated with 1.4% higher risk of NSTEMI hospitalization. No differences regarding STEMI incidence were found between two groups.

In the sub-analysis including classical risk factors, in the overall population the mean smoking population was 27% (min 23%–max 31%), the mean standardized morbidity rate was 315 (min 291–max 342) for hypertension and 86 (min 79–max 91) for diabetes. For STEMI, impact of  $PM_{2.5}$ ,  $SO_2$  and  $NO_2$  was higher in populations with the higher prevalence of classical risk factors. In the case of assessing the impact of BaP concentrations, an inverse relationship was observed, with greater negative effects of air pollution in areas with a lower percentage of tobacco user. For NSTEMI, there were no differences noted for significant impact results by subpopulation for



**Fig. 4: Short-term effect of air pollution on overall population.** Analysed air pollutants are presented as follows: panel a, PM<sub>2.5</sub>; panel b, BaP; panel c, SO<sub>2</sub>; panel d, NO<sub>2</sub>. Abbreviations: BaP, Benzo(a)pyrene; CI, Confidence Interval; NO<sub>2</sub>, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; PM<sub>2.5</sub>, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Risk; SO<sub>2</sub>, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction.

hypertension prevalence and smoking. Detailed results of analyses are presented in [Supplementary Table S13](#).

**Impact of reduction to WHO recommendations**

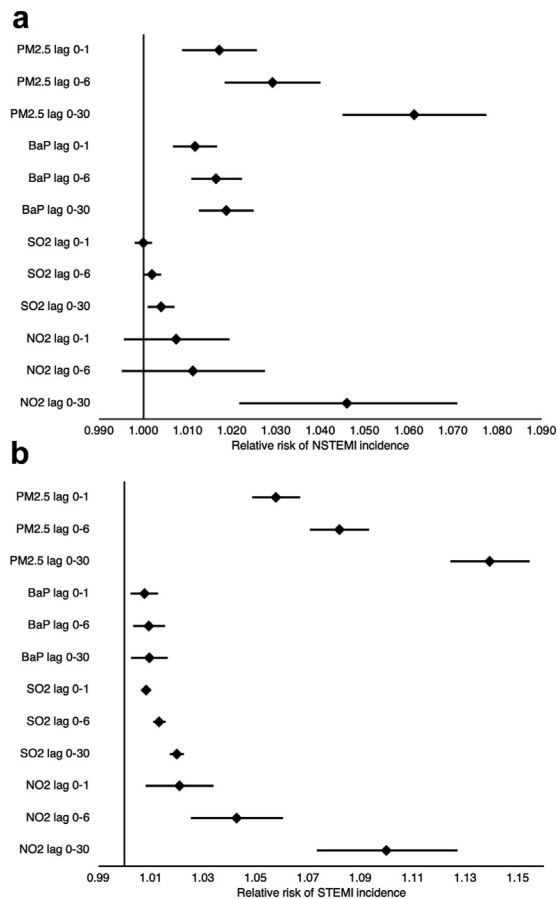
Total population attributable fraction related with exposure to PM<sub>2.5</sub> was estimated to be 2693 (95% CI 1387–3977) NSTEMI and 7029 (5997–8042) STEMI cases. Reduction to recommended by WHO daily concentrations threshold in the analysed period would result in avoidance of NSTEMI and STEMI hospitalizations by 641 (95% CI 325–953) and 1159 (95% CI 1349–1831), respectively. Maintaining yearly WHO norms would have resulted in reduction of NSTEMI and STEMI cases by 2033 (95% CI 1045–3099) and 5634 (4566–6150), respectively. Detailed analysis is presented in [Table 3](#) and [Supplementary Fig. S2](#).

**Discussion**

The principal findings of this study reveal the negative impact of both short-term and mid-term exposure to air pollution on the risk of hospitalization due to MI and secondly, we specify the most vulnerable subgroups, based on demographic and socio-economic data. We show that women are the most susceptible group to the adverse effects of short- and mid-term exposure to air pollution, although these effects vary across age groups depending on STEMI and NSTEMI. Third, the risks of air pollution were greater in rural as compared to urban settings, as well as socio-economic factors, with higher risks in communities with lower mean income. However, worth noting is also that different pollutants have been observed to have varying effects, with some cases also showing no significant impact.

This study provides novel data on Polish smog, as well as providing a unique and comprehensive





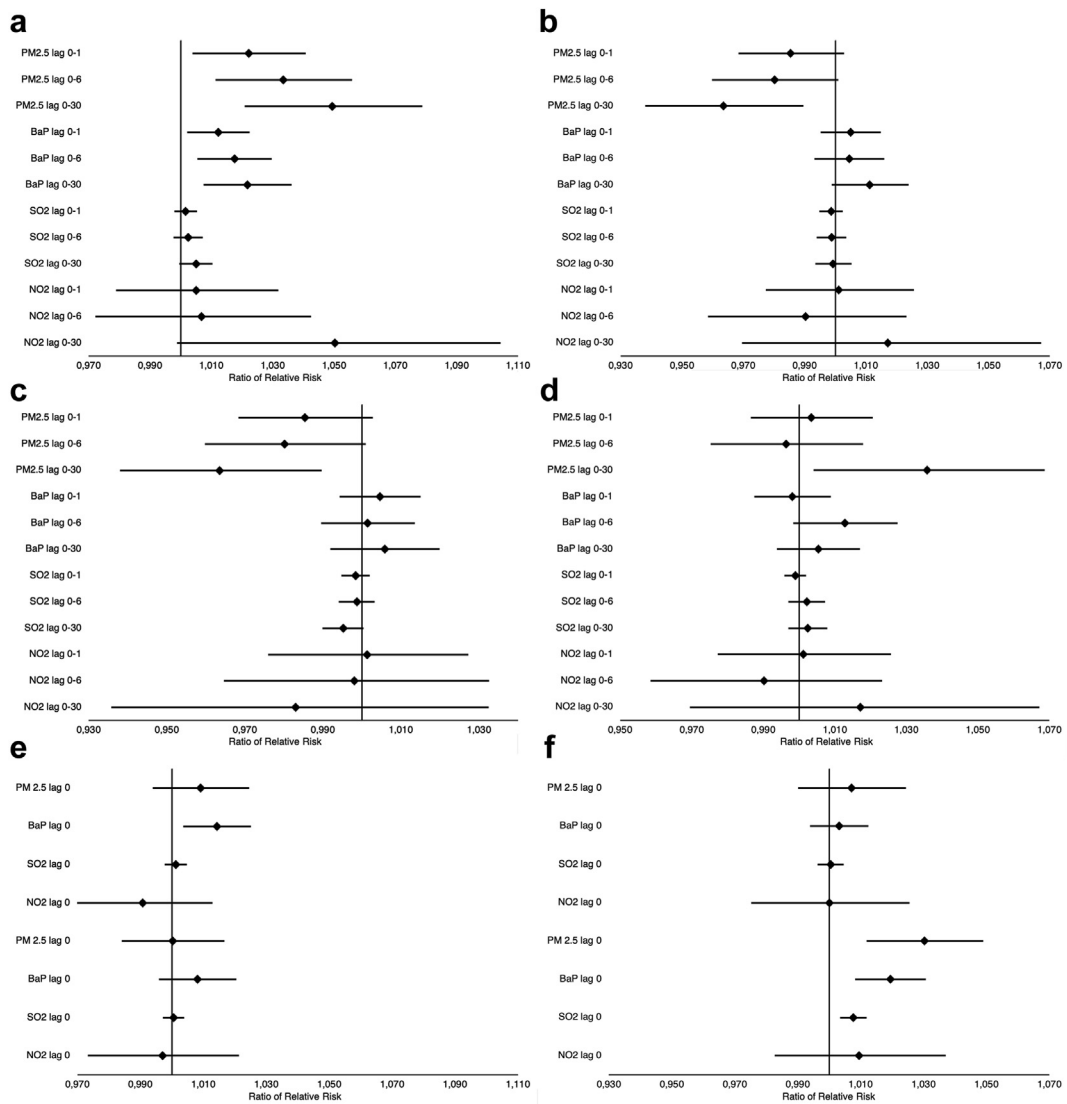
**Fig. 5: Short- and mid-term effects of air pollution on overall population.** Panel a, influence of air pollution on NSTEMI incidence. Panel b, influence of air pollution on STEMI incidence. Abbreviations: BaP, Benzo(a)pyrene; CI, Confidence Interval; NO<sub>2</sub>, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; PM<sub>2.5</sub>, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Risk; SO<sub>2</sub>, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction.

assessment of the impact of exposure to BaP on the occurrence of MI. Despite the well-established carcinogenic properties of PAH, including BaP,<sup>11</sup> its influence on cardiovascular risk has not been extensively explored until now. This addresses an important gap in existing evidence. Our overall results generally align with findings from various studies on air pollution and ACS<sup>2,12,58</sup>. However, there are some limitations in the current evidence regarding the relationship between short-term exposure to air pollution and the occurrence of NSTEMI and STEMI events separately, as the majority of studies, such as those included in the systematic review and meta-analysis conducted by Wu et al.<sup>59</sup> did not consider the subdivision of MI into NSTEMI and STEMI events. In some studies incorporating this separation, such as the one conducted by Buszman et al.<sup>58</sup> there was a significant association between short-term exposure to PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and the incidence of

NSTEMI observed, while for STEMI, significant associations were found for exposure to PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and SO<sub>2</sub>. These findings are mostly consistent with data obtained from our study. Another study by Gardner et al.,<sup>510</sup> found short-term exposure to PM<sub>2.5</sub> was significantly associated with the increased risk of STEMI, but no significant association was found in the case of NSTEMI. On the other hand, Chen et al.,<sup>12</sup> which focused on Chinese population where air pollution concentrations are particularly high, an association between short-term exposure to PM<sub>2.5</sub>, NO<sub>2</sub>, and SO<sub>2</sub> and the incidence of both NSTEMI and STEMI was demonstrated.

There are also contradictory studies, such as the one conducted by Vaudrey et al.<sup>13</sup> which demonstrated a lack of short-term effects of exposure to PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub> on the incidence of MI without considering STEMI and NSTEMI separately. Finally, as regards to influence of BaP on NSTEMI incidence (which we found to be significant in all models), this suggests that BaP itself may have negative influence on human health, and the loss of statistical significance in STEMI group after adjustment for PM<sub>2.5</sub> in two-pollutant model may require a more experimental approach.

To emphasize the value of this study, the large study population and comprehensive statistical analysis are strengths. Not only did the study investigate the triggering effects of specific pollutants, but also considered the mid-term effects, reflecting impact of cumulative doses. Additionally, we conducted an analysis of the impact of BaP, which was a factor not considered in previous studies, which was found to be important for NSTEMI incidence. Another important aspect of this work demonstrates an increased risk of NSTEMI among young individuals, a group not commonly perceived as being at high risk, both from the general public awareness and among health professionals. This may provide a potential explanation for epidemiological data indicating an increase in the number of NSTEMI cases and stabilization of post-hospital discharge mortality rates in recent years.<sup>511,512</sup> Simultaneously, due to improvements in preventive and treatment methods, there has been a decrease in the number of STEMI cases and post-hospital discharge mortality rates.<sup>511,512</sup> These global trends align with our observations as depicted in [Supplementary Fig. S1 and Tables S1 and S2](#). However, in-hospital mortality remains higher in STEMI than in NSTEMI cases,<sup>513</sup> and as evidenced, there is a significant disparity in STEMI risk between females and males. Highlighting that females are particularly vulnerable is potentially explained by prolonged retention and accumulation of fat-soluble contaminants.<sup>514</sup> We believe that the outcomes of the current and our forthcoming studies may contribute to modifying the classification and recommendation levels concerning individual exposure to air pollution, focusing on specific components of smog and highlighting particularly



**Fig. 6: Forest plots visualizing impact of air pollution on myocardial infarction risk among studies subgroups in selected lag patterns.** Analysed subgroups are as follows: panel a and b—ratio of relative risk of STEMI and NSTEMI in women as compared to men; panel c and d—ratio of relative risk of STEMI and NSTEMI in patients aged <65 as compared to ≥65 y.o.; panel e—ratio of relative risk of STEMI (upper part) and NSTEMI (lower part) in regions with GDP < 2 as compared to GDP ≥ 2; panel f—ratio of relative risk of STEMI (upper part) and NSTEMI (lower part) in rural regions as compared to urban regions. Abbreviations: BaP, Benzo(a)pyrene; CI, Confidence Interval; GDP, gross domestic product; NO<sub>2</sub>, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; PM<sub>2.5</sub>, Particulate Matter with 2.5 Micrometers or Less; SO<sub>2</sub>, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction.

vulnerable groups, allowing better and more personalized preventive strategies.

**Underlying pathophysiology**

The mechanisms of the harmful impact of air pollution on the cardiovascular system are complex and include promotion of inflammation, intracellular oxidative stress, endothelial dysfunction, and genetic alternations such as disrupted DNA-methylation, leading to dysfunction of the cardiovascular system.<sup>14</sup> The

detrimental impact of air pollution on the occurrence of CAD also varies depending on the duration of exposure, whereby long and mid-term exposure generally leads to the progressive development of atherosclerotic plaques, while both short- and long-term exposure has been associated with a higher risk of plaque rupture.<sup>15-17</sup>

Of note, the influence of air pollution on the frequency of ACS occurrence is greater in individuals previously diagnosed with CAD compared to those without such a diagnosis.<sup>17</sup> In the group of individuals

	Air pollutant	Rural			Urban			Ratio		
		RR	95% CI	P-value	RR	95% CI	P-value	RRR	95% CI	P-value
NSTEMI	SO <sub>2</sub>	1.001	0.999–1.003	0.28	1.001	0.997–1.004	0.75	1.000	0.996–1.005	0.82
	PM <sub>2.5</sub>	1.019	1.01–1.028	<0.001	1.012	0.997–1.027	0.11	1.007	0.99–1.024	0.41
	BaP	1.012	1.005–1.018	<0.001	1.008	1.002–1.015	0.02	1.003	0.994–1.013	0.50
	NO <sub>2</sub>	1.010	0.997–1.022	0.12	1.009	0.988–1.032	0.40	1.000	0.975–1.026	0.99
STEMI	SO <sub>2</sub>	1.009	1.007–1.011	<0.001	1.002	0.998–1.005	0.40	1.008	1.004–1.012	<0.001
	PM <sub>2.5</sub>	1.060	1.05–1.07	<0.001	1.029	1.013–1.045	<0.001	1.03	1.012–1.049	0.001
	BaP	1.014	1.007–1.021	<0.001	0.995	0.986–1.004	0.25	1.019	1.008–1.031	0.001
	NO <sub>2</sub>	1.022	1.008–1.035	0.001	1.012	0.988–1.036	0.33	1.010	0.983–1.037	0.49

BaP, Benzo(a)pyrene; CI, Confidence Interval; GDP, Gross domestic product per capita; NO<sub>2</sub>, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; PM<sub>2.5</sub>, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Ratio; SO<sub>2</sub>, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction; RRR, Ratio of Relative Risk; SO<sub>2</sub>, Sulphur Dioxide.

**Table 1: Impact of increased air pollution concentrations on the risk of hospitalization due to myocardial infraction in different types of areas.**

with initially more advanced atherosclerotic changes and coexisting diseases, short-term exposure to air pollution can serve as a trigger for ACS. We believe that in individuals without such comorbidity burden, a longer duration of exposure may be needed for the occurrence of ACS. Additionally, air pollution is also associated with an increased risk of atrial fibrillation,<sup>S15</sup> which, in turn, may contribute to an elevated risk of ACS through thromboembolic mechanisms or decreased oxygen supply with hypoperfusion during arrhythmia episodes.

### Vulnerable subgroups

In the present study, a higher risk of MI occurrence was observed in women as compared to men, with noticeable differences in relation to whether hospitalization was caused by STEMI or NSTEMI, and the influence of specific air pollutants. For STEMI, statistically significant increases in risk among women were noted in both short-term and mid-term exposures to PM<sub>2.5</sub> and BaP. In the case of NSTEMI, the risk was significantly increased by mid-term exposure to PM<sub>2.5</sub>. For other air

pollutants, no significant differences between men and women were observed.

Several potential explanations for this phenomenon have been proposed, including women being more susceptible to oxidative stress than men,<sup>18</sup> as well as differences in breathing patterns between women and men, leading to the deposition of a greater number of particles in the respiratory pathways of women.<sup>19</sup> The differences between men and women may also be influenced by the way time is spent and traditional roles assigned, for example, women still tend to be more involved in household chores, childcare, or cooking,<sup>20</sup> which may be associated with a greater cumulative effect on both indoor and outdoor air pollution. Additionally, there is a difference in exposure to air pollution associated with socio-economic status,<sup>21</sup> and inequalities still persist to the disadvantage of women.

The findings of prior studies on this matter have been inconclusive. For example, Nuvolone et al.<sup>S16</sup> found that women were recognized as a group more susceptible to the adverse effects of short-term air

	Air pollutant	GDP < 2Q			GDP ≥ 2Q			Ratio		
		RR	95% CI	P-value	RR	95% CI	P-value	RRR	95% CI	P-value
NSTEMI	SO <sub>2</sub>	1.002	0.999–1.004	0.21	1.000	0.998–1.003	0.7	1.001	0.998–1.005	0.49
	PM <sub>2.5</sub>	1.022	1.011–1.034	<0.001	1.013	1.003–1.023	0.01	1.009	0.994–1.025	0.24
	BaP	1.020	1.011–1.029	<0.001	1.006	1–1.011	0.051	1.014	1.004–1.025	0.008
	NO <sub>2</sub>	1.003	0.986–1.021	0.70	1.013	0.999–1.026	0.06	0.991	0.969–1.013	0.41
STEMI	SO <sub>2</sub>	1.008	1.005–1.011	<0.001	1.007	1.005–1.01	<0.001	1.001	0.997–1.004	0.75
	PM <sub>2.5</sub>	1.051	1.038–1.065	<0.001	1.051	1.04–1.061	<0.001	1.000	0.984–1.017	0.97
	BaP	1.012	1.001–1.023	0.03	1.004	0.998–1.009	0.21	1.008	0.996–1.021	0.19
	NO <sub>2</sub>	1.016	0.997–1.037	0.10	1.019	1.005–1.034	0.007	0.997	0.973–1.021	0.81

BaP, Benzo(a)pyrene; CI, Confidence Interval; GDP, Gross domestic product per capita; NO<sub>2</sub>, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; PM<sub>2.5</sub>, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Ratio; SO<sub>2</sub>, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction; RRR, Ratio of Relative Risk; SO<sub>2</sub>, Sulphur Dioxide.

**Table 2: Impact of increased air pollution concentrations on the risk of hospitalization due to myocardial infraction in areas with different gross domestic product.**

No. admissions above threshold	Threshold	AC (N)	95% CI AC (N)	AF (%)	95% CI AF (%)
NSTEMI					
49,612	Daily WHO norm	641	325–953	0.85	0.43–1.26
75,531	Yearly WHO norm	2033	1045–3099	2.69	1.38–3.98
76,542	Population attributable fraction	2693	1387–3977	3.52	1.81–5.2
STEMI					
41,244	Daily WHO norm	1159	1349–1831	3.9	3.3–4.4
62,384	Yearly WHO norm	5634	4566–6150	8.6	7.3–9.9
63,154	Population attributable fraction	7029	5997–8042	11.1	9.5–12.7

AC, attributable cases; AF, attributable fraction; CI, confidence interval; NSTEMI, Non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; WHO, World Health Organization.

**Table 3: Estimated number of avoided disease cases of hospital admissions associated with the reduction of PM<sub>2.5</sub> air pollution levels.**

pollution exposure without assessing STEMI and NSTEMI cases separately. In contrast, one study identified men as a more vulnerable group,<sup>S17</sup> with only STEMI cases being included.

We observed age strata differences, with mid and short-term exposures in relation to NSTEMI or STEMI. In the case of mid and short-term exposure to PM<sub>2.5</sub>, a statistically significant increase in the risk of hospitalization due to NSTEMI was observed among younger individuals compared to older ones. Next significant difference was observed in the case of short and mid-term NO<sub>2</sub> exposure and NSTEMI prevalence, which was also higher in the younger group. For STEMI, a statistically significant increase in the risk was noted among individuals who had reached the age of 65 compared to younger ones. This effect was noted in the case of both short- and mid-term exposure to PM<sub>2.5</sub> as well as short-term exposure to SO<sub>2</sub>. There were no statistically significant differences between older and younger individuals in the case of other air pollutants. We believe that a potential explanation for this phenomenon may be the fact that, initially, in the population of older individuals, atherosclerotic lesions in coronary arteries are more advanced and the age itself is also well-known STEMI risk factor. Consequently, the rupture of an atherosclerotic plaque leads to artery occlusion and the occurrence of STEMI.

Nevertheless, prior studies reported heterogeneous results. For example, Collart et al. found that young individuals are similarly sensitive to air pollution, but the negative effect in the form of both, STEMI and NSTEMI,<sup>22</sup> is more delayed. On the other hand, exposure to smog and the occurrence of MI was greater in older individuals, as stated by Li et al.<sup>23</sup> In the case-crossover study by Argacha et al.,<sup>24</sup> including over 11,000 STEMI patients, older individuals were more susceptible to the detrimental effects of PM<sub>2.5</sub>, while younger patients were more vulnerable to the harmful impact of NO<sub>2</sub> exposure. On the other hand, Zhou et al. found that the relationship between air pollution and CVD hospitalization was strongest for young people,<sup>25</sup>

perhaps related to more time spent outdoors by younger individuals. Indeed, increased exposure time to air pollution may lead to the occurrence of arrhythmias<sup>26</sup> and the presence of other CVD, thereby increasing the number of hospitalizations in this age group. The results of previous studies underscore the need for further investigations to elucidate the differential harmful impact of individual air pollutants in various age groups.

**Socioeconomic factors**

Another important information emerging from this study is the difference in the impact of air pollution between rural and urban areas. The risk of STEMI in the case of the influence of each analysed air pollutant, except for NO<sub>2</sub>, was higher in rural areas. People living in rural areas spend more time outdoors, which is possibly contributing to greater exposure to harmful effects of air pollution,<sup>27</sup> while the suboptimal heating choices in rural area residences, which involve also the emission of air pollutants other than those included in this study, may be related to the observed differences. Moreover, access to healthcare in rural areas is more difficult compared to residents of urban areas. According to 2020 data from the Central Statistical Office, a resident of the countryside had an average of 2.8 medical consultations, while a city dweller had an average of 10.6.<sup>28</sup> This perhaps contributes to the poorer health of the population living in rural areas and may be a reason for a stronger trigger effect of air pollution in these areas. Finally, air pollution related with agriculture practices, such as tillage, animal production and application of fertilizers to land, may be related with increased concentrations and temporal fluctuations of PM and atmospheric ammonia. Some reports suggest that long-term exposure to PM<sub>2.5</sub> from ammonium bisulphate and ammonium nitrate may be especially related with the development of CAD and MI incidence.<sup>S18,S19</sup>

Demonstrating how harmful exposure to polluted air is, even in rural, greenery-rich terrains, including the Podlaskie Voivodeship referred to as the “Green Lungs

of Poland” constitutes another novel aspect of this study. The results of the current study, along with our previous research<sup>7</sup> unequivocally demonstrate that even in such areas, air pollution plays an important role in adversely affecting human health.

Another important aspect of our research concerns the context of income inequalities. In this study, individuals living in regions with lower income had a higher risk of NSTEMI in the case of BaP exposure; however, no other significant impact of income inequalities was found. As demonstrated by Coughlin et al.,<sup>S20</sup> lower socioeconomic status is associated with a higher risk of MI. We believe that our observation could be one potential explanation for this phenomenon, but further studies are needed to confirm this.

In summary, this work, similar to our previous studies,<sup>2,3,7,S6</sup> highlights the significance of air pollution as a crucial factor for public health. It underscores the necessity for ongoing efforts for more precise monitoring of air quality, even in areas commonly perceived as free from air pollution.

### The pathways to reducing air pollution concentrations

The air quality standards were published by the WHO in 2021,<sup>S21</sup> noteworthy for significantly lower thresholds compared to the document released in 2005. The WHO recommends implementing a series of actions, including the use of renewable energy sources, changes in household heating methods, improving energy efficiency in planned buildings, adopting low-emission transportation, and introducing solutions contributing to waste reduction. However, the changes implemented so far are insufficient, and as this study clearly shows, there is no such thing as a safe level of air pollution. Indeed, an energy transition towards renewable energy sources, changes in household heating methods, and other emission reduction-focused actions, such as “Zero pollution action plan” by the European Union,<sup>S22</sup> along with efforts aimed at equalizing socioeconomic status should contribute to reducing the number of CVD in the future.

### Clinical implications and further directions

The current study underlines cohorts particularly vulnerable to specific air pollutants and emphasizes the need for implementing more individualized preventive strategies to mitigate the harmful effects. Apart from demographic data, socioeconomic characteristics of the inhabited region also influence susceptibility to air pollution. Thus, future actions could include the incorporation of environmental and residential factors in cardiovascular risk scales used for primary prevention. Concurrently, an increase in public awareness through health professionals and media will focus on clusters of people commonly perceived as not being at high

cardiovascular risk, such as young individuals and women, which may lead to systemic changes and subsequent decrease in the burden of ACS. Patients with a history of cardiovascular events should demonstrate even greater caution regarding the detrimental effects of air pollution, as part of their secondary prevention strategies. Raising awareness about the need for monitoring air quality before outdoor activities remains one of the simple, cost-effective, and feasible solutions, yet is underutilized, especially in rural areas—often falsely perceived as emission-free zones. High-quality scientific evidence, such as presented in the current study is essential to contribute to guideline modifications that form the basis of every day practice, incorporating individual strategies to mitigate the impact of specific air pollutants in particular groups.

### Strengths and limitations

This study has several limitations. First, indoor air pollution were not considered, although current evidence suggests that the issue of household air pollution, primarily caused by smoke from poorly ventilated cookstoves, mainly affects developing countries with relatively smaller in high-income regions.<sup>29</sup> However, the impact of passive and active air pollution infiltration from outdoor sources such as car traffic, indoor smoking, and cleaning activities—the main sources of indoor pollution in high-income countries, is not yet well investigated.<sup>S23</sup> Another limitation is the lack of consideration of other environmental risk factors such as light pollution or noise, whose impact on cardiovascular risk, often overlapping with that of air pollution, is being increasingly explored.<sup>S24,S25</sup> The combined effect of both air pollution and transportation noise may increase the risk of major adverse cardiac events including cardiovascular death, unstable angina, MI, cerebrovascular accidents, heart failure and coronary or peripheral artery revascularisations.<sup>S24</sup>

This study also did not account for the movement of individuals between communes, but as mentioned earlier, the unique GEM-AQ model was used in order to reduce this potential bias. In Poland, internal migrations at the communes level, according to data from the Central Statistical Office, does not exceed 5% on an annual basis.<sup>30</sup> Lastly, our study did not assess the relationship between air pollution exposure and mortality during the course of ACS, given the lack of data on deaths that would have occurred before hospital admission which would impact the quality of the obtained results. On the other hand, no data on out of hospital cardiac arrest due to MI might have caused potential underestimation of the influence of air pollution on MI incidence. However, the large population of this study was already sufficient to capture the temporal trends, lag patterns and draw important conclusions from subgroup analyses.

Several strengths are also worth noting in our study. First, the 10-year analysis covered 80,000,000 person-years across more than 700 communes, constituting a vast study population.

The unique approach of this study based on analysing such a large amount of data at the level of individual patients allows us to generalize the obtained results and has adequate statistical power for drawing clinically important conclusions. Additionally, the analysis was conducted with consideration for demographic and socioeconomic factors. Second, the GEM-AQ model was used, providing high spatiotemporal resolution data that facilitated precise statistical analysis. Third, we evaluate of not only short-term but also mid-term exposure effects to air pollution. Indeed, as mentioned earlier, we show there is no such thing as a 'safe' level of air pollution.

### Conclusions

There are significant disparities in the influence of air pollution depending on the demographic and socioeconomic factors. Air pollution exposure is associated with the threat of a higher risk of NSTEMI and STEMI, especially in younger people, women, residents of rural areas, and those with lower income.

### Contributors

Conceptualization, funding acquisition, methodology, project administration, were performed by Ł.K. Investigation, validation and visualization were performed by Ł.K. and E.J.D. Data curation and formal analysis were performed by Ł.K., M.Ś., E.J.D. All authors contributed to the original draft, review and editing. Ł.K., P.K., S.D., G.Y.H.L. supervised the project.

Ł.K. and E.J.D. directly accessed and verified the underlying data reported in the manuscript.

All authors had full access to all the data in the study, read and approved the final manuscript.

### Data sharing statement

Data used for all analyses and analytic code whenever applicable are available from the corresponding author upon reasonable request.

### Editor note

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### Declaration of interests

GYHL: Consultant and speaker for BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, Anthos. No fees are received personally. He is a National Institute for Health and Care Research (NIHR) Senior Investigator and co-PI of the AFFIRMO project on multimorbidity in AF (grant agreement No 899871), TARGET project on digital twins for personalised management of atrial fibrillation and stroke (grant agreement No 101136244) and ARISTOTELES project on artificial intelligence for management of chronic long term conditions (grant agreement No 101080189), which are all funded by the EU's Horizon Europe Research & Innovation programme. Other authors declare no conflicts of interest.

### Acknowledgements

The study was financed from the funds of the National Science Center granted under the contract number UMO-2021/41/B/NZ7/03716 and Medical University of Bialystok contract numbers: UMB-B.SUB.23.509,

UMB- B.SUB.23.290, UMB- B.SUB.23.102. Study sponsors had no influence on any stages of the study course.

The study was registered at [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT05198492) (NCT05198492).

### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanepe.2024.100910>.

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