

Short-Term Exposure to Air Pollutants and Acute Cardio-Cerebrovascular Events in Lombardy Region: A Case-Time Series Study (2016-2023)

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INTRODUCTION

Air pollution is a leading environmental risk factor for morbidity and mortality worldwide, with fine particulate matter ($PM_{2.5}$) among the most harmful pollutants for cardio-cerebrovascular health. The World Health Organization (WHO) estimates that air pollution contributes to millions of premature deaths annually, largely through cardiovascular diseases.

While Europe generally maintains lower average air pollution levels than other global regions, a substantial proportion of its population remains exposed to concentrations exceeding WHO guidelines. This pattern is evident in the Lombardy region due to Po Valley meteorology and intense anthropogenic emissions.

A large body of evidence has shown that short-term exposure $PM_{2.5}$ is associated with an increased risk of acute cardio-cerebrovascular events in the days following exposure. Proposed mechanisms include systemic inflammation, oxidative stress, endothelial dysfunction, autonomic imbalance, and pro-thrombotic pathways, which may trigger acute cardio-cerebrovascular events in susceptible individuals. However, traditional epidemiological designs have limited ability to capture exposure-lag-response dynamics, which require more flexible approaches.

OBJECTIVES

To evaluate the association between short-term exposure $PM_{2.5}$ and the risk of incident acute cardio-cerebrovascular events among residents of Lombardy.

METHODS

This population-based study used administrative health-care databases from Lombardy (~10 million inhabitants) and included residents aged ≥ 45 years with a first acute hospitalization for cardio-cerebrovascular event during 2016–2023. Incident cases were identified using a 5-year washout period.

Short-term effects were assessed using a case-time series design combined with Distributed Lag Non-linear Models to characterize exposure-lag-response associations. A lag window of 5 days was considered in the main analysis, with sensitivity analyses at 3 or 7 days.

Single- and multi-pollutant models were implemented to estimate the independent effect of $PM_{2.5}$, adjusting for NO_2 and O_3 . Effect estimates were expressed per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Models were adjusted for day of the week and meteorological variables (mean temperature,

relative humidity, wind speed) using natural splines, plus a binary indicator for rainfall.

RESULTS

During the study period, a total of 403,266 incident acute cardio-cerebrovascular events were recorded within a regional source population of approximately 5 million residents aged ≥ 45 years. In the main analysis, $[(PM)]_{2.5}$ was significantly associated with an increased risk of acute cardio-cerebrovascular events.

In the single-pollutant model, a $10 \mu\text{g}/\text{m}^3$ increase in $[(PM)]_{2.5}$ was associated with a 3.2% increase in risk (95% CI: 2.0–4.4%). The lag structure showed a peak effect at lag 0 (1.7%; 95% CI: 0.8–2.7%), declining to baseline by lag 3.

In multi-pollutant models, adjustment for O_3 slightly strengthened the association (4.0%; 95% CI: 2.8–5.2%), whereas adjustment for $[(NO)]_2$ attenuated the effect (1.9%; 95% CI: 0.8–3.1%), likely due to correlation between pollutants sharing emission sources. All results were stable across lag windows.

CONCLUSIONS

Short-term exposure to $[(PM)]_{2.5}$ was associated with an increased risk of acute cardio-cerebrovascular events, with effects concentrated mainly in the first days after exposure. These findings reinforce the evidence that air pollution acts as a trigger of cardio-cerebrovascular hospitalizations and highlight the need for effective strategies to reduce population exposure to fine particulate matter.