

## Impact of Short-Term Exposure to Below Recommended PM<sub>10</sub> Pollution Levels on Asthma Exacerbations

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Air pollution significantly affects health, causing up to 7 million premature deaths annually and generating an even larger number of hospitalizations and days of sick leave [1]. The negative impact of pollutants on human health is well known. Several epidemiological studies have reported positive associations between exposure to particulate matter (PM) and morbidity and mortality associated with obstructive pulmonary diseases, including asthma [2-3]. Although there is well-documented evidence that short-term exposures to PM<sub>10</sub>, ozone, and NO<sub>2</sub> contribute to asthma exacerbations [4], no threshold for PM<sub>10</sub> concentrations has been established below the maximum recommended by World Health Organization (WHO) [5]. This study aims to analyze whether levels and duration of exposure to PM<sub>10</sub> can have an impact on asthmatic patients who visit the emergency department (ED) with an asthma exacerbation.

We conducted a retrospective, observational cohort-study using data collected at the ED of Hospital Universitario La Paz, Madrid, Spain from January 1 to December 31, 2014. The hospital is a tertiary referral center serving a population of 500 000 in northern Madrid. The search procedure, enrolment, and data collection have been addressed elsewhere [6]. The study population comprised 831 patients aged >14 years, who attended the ED with an asthma exacerbation. For each event, data were collected on 84 variables—considering patient characteristics in terms of epidemiology and comorbid conditions—according to the consensus criteria of the 2009 Spanish guideline on asthma management (GEMA 2009) [7]. The study was approved by the local ethics committee, and permission was obtained for the use of confidential data.

Hourly PM<sub>10</sub> concentrations collected from 3 different stations (Cuatro Caminos, Paseo de la Castellana, and Plaza de Castilla) in the hospital catchment area were retrieved from the institutional database of Madrid City Council between December 28, 2013 and December 31, 2014 [8]. Hourly PM<sub>10</sub>

data were measured using a heated tapered element oscillating microbalance. Average hourly concentrations were calculated using the hourly concentration of the referred measurement stations. We limited data to PM<sub>10</sub> concentrations of between 10 µg/m<sup>3</sup> and 40 µg/m<sup>3</sup> and exposure times from 4 hours to 16 hours, in 2-hour intervals, with a 2-day lag to each individual ED visit. A total of 11 025 models were examined to validate the procedure, considering different PM<sub>10</sub> levels and duration of exposure for each patient. Significance was set at 95%. The parameters of the models were evaluated using both maximum likelihood estimators and a bootstrap approach (50 replications); both models yielded the same results (Supplementary Figure 2).

The association between PM<sub>10</sub> levels, exposure times, and asthma episodes was studied using a logistic regression model for binary outcomes and both continuous and binary independent variables. The independent variables were age, sex, and a binary variable that explains the level of exposure to PM<sub>10</sub> pollutants for a 2-day lag prior to the ED visit. The initial data processing to build the model was performed using MATLAB-R2020, while the models were developed using STATA-V24. The outcome of the analysis was the probability of an exacerbation in asthmatic patients who visited the ED.

According to the model results (Figure), if there is a PM<sub>10</sub> concentration of 22 µg/m<sup>3</sup> for a 10-hour period the day prior to the ED visit and a PM<sub>10</sub> level of between 14 µg/m<sup>3</sup> and 30 µg/m<sup>3</sup> for a 10-hour period 2 days prior to the visit (see blue line), there is a moderate probability of an asthma exacerbation (0.18-0.26, *P*<.05). When the PM<sub>10</sub> concentration and exposure time are increased (38 µg/m<sup>3</sup> for 16 hours the day prior to the ED visit and a PM<sub>10</sub> level between 26 µg/m<sup>3</sup> and 30 µg/m<sup>3</sup> for 16 hours 2 days prior to the ED visit), the probability of an asthma exacerbation rises to 48%.

In the real world, dynamic changes in air pollutants and meteorological factors coexist [9]. Age, temperature, allergen concentrations, and various pollutants play a role in increasing or decreasing the risk of an asthma exacerbation [10], although it remains unclear how PM<sub>10</sub> affects this risk. A recent meta-analysis concluded that an increase of 10 µg/m<sup>3</sup> in acute PM<sub>10</sub> exposure was associated with a change of -0.19 L/min

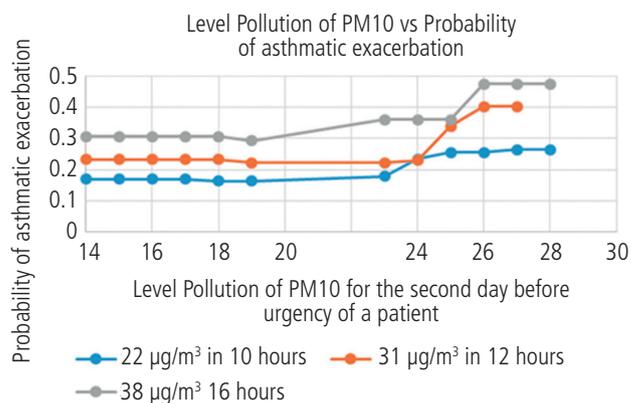


Figure. Probability of an asthma exacerbation in asthma patients with a confirmed diagnosis who visited the emergency department, considering different exposure times and PM<sub>10</sub> levels. PM indicates particulate matter.

(95%CI, -0.30 to -0.09) in peak expiratory flow, particularly among nonsmoking asthmatics [11]. We cannot provide lung function data, because these were not recorded on the clinical charts, although, overall, we recorded a positive association between PM<sub>10</sub> and visits to the ED owing to asthma exacerbations. Previous studies consistently conclude that increasing concentrations of PM<sub>10</sub> were associated with more frequent asthma attacks. Similarly, a 10- $\mu\text{g}/\text{m}^3$  increase in PM<sub>10</sub> concentration was strongly associated with a higher risk of respiratory outpatient visits, with the highest effect noted on lag day 2 [12]. Unfortunately, as our study is retrospective, it was difficult to obtain the precise probability of experiencing an asthma exacerbation, because it is unknown whether an individual patient has been exposed or not. Moreover, we were unable to explore the associations between daily variations in meteorological factors that could influence our results [13,10]. However, the major strength of our study is that the model analyzed the impact of PM<sub>10</sub> on each patient with an exacerbation by comparing individual characteristics and different levels of PM<sub>10</sub> concentration and times of exposure.

We identified the maximum risk for PM<sub>10</sub> levels to be above 38  $\mu\text{g}/\text{m}^3$  with an exposure time >16 hours, which is consistent with previous reports [14-15]. However, this study confirms the hypothesis that exposure to PM<sub>10</sub> at levels below those established by the WHO could also be dangerous for health and increase the probability of visiting the ED with an asthma exacerbation.

In summary, although high levels and longer times of exposure to PM<sub>10</sub> are clearly associated with worsening of asthma, exposure to PM<sub>10</sub> at even lower concentrations than previously recommended could also increase the risk of exacerbations. Further evidence from well-designed studies is required to definitively establish a safe threshold for this pollutant in asthmatic patients.

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#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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