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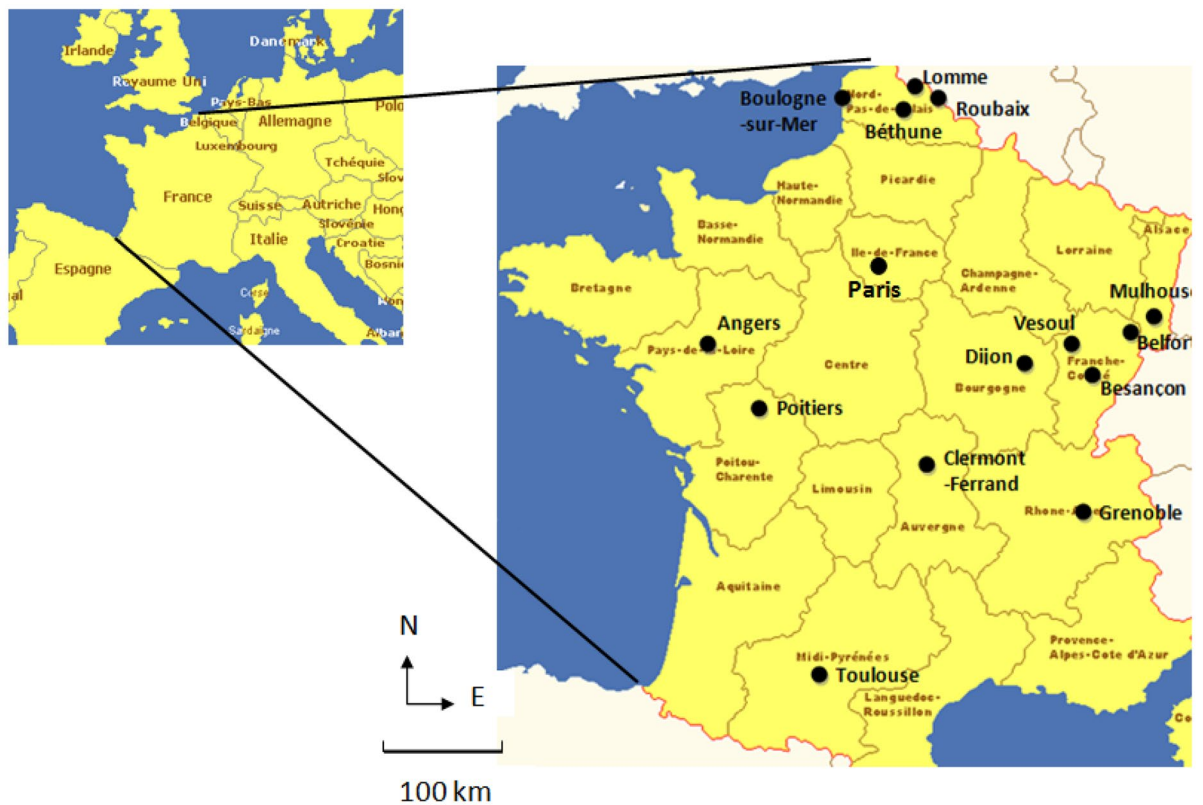
# Short term association between air pollution (PM<sub>10</sub>, NO<sub>2</sub> and O<sub>3</sub>) and secondary spontaneous pneumothorax

Tania Marx<sup>1,2,6</sup>✉, Nadine Bernard<sup>2,3,6</sup>, Anne-Laure Parmentier<sup>2,4,6</sup>, Marc Puyraveau<sup>2,4,6</sup>, Berenger Martin<sup>4</sup>, Madeleine Gantelet<sup>4,6</sup>, Jean-Baptiste Pretalli<sup>1</sup>, Jean-Charles Dalphin<sup>2,5,6</sup>, Frédéric Mauny<sup>2,4,6</sup> & Thibaut Desmettre<sup>1,2,6</sup>

Secondary spontaneous pneumothorax (SSP) occurs in the context of underlying pulmonary disease. Our objectives were to estimate the relationship between SSP and short term air pollution exposure with nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>) and particulate matter with a diameter ≤ 10 μm (PM<sub>10</sub>). Patients with SSP were included between June 1, 2009 and May 31, 2013, in 14 Emergency Departments in France. In this case–crossover design study, PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub> data were collected hourly from monitoring stations. Quantitative values, fast increase in air pollutant concentration, and air quality threshold exceedance were retained. These assessments were calculated for each of the 4 days prior to the event (Lag 1–Lag 4) for all case and control period, and for the entire exposure period. A total of 135 patients with SSP were included, with a mean age of 55.56 (SD 18.54) years. For short term exposure of PM<sub>10</sub>, NO<sub>2</sub> and O<sub>3</sub>, no differences were observed between case and control periods in terms of quantitative values of air pollutant exposure (P > 0.68), fast increase in concentration (P > 0.12) or air quality threshold exceedance (P > 0.68). An association between O<sub>3</sub> exposures cannot be ruled out, especially when considering the Lag 2 prior to the event and in warm seasons.

The link between air pollution and respiratory disease has been established, even if the role of each pollutant has not yet been clearly identified. Li et al.<sup>1</sup> demonstrated, with a case–crossover design, that air pollutants have a short term effect on a variety of acute respiratory diseases. Particulate matter with diameter ≤ 10 μm and ≤ 2.5 μm (PM<sub>10</sub> and PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>) and carbon monoxide (CO) had positive associations with outpatient visits for upper respiratory tract infection, acute bronchitis, community acquired pneumonia, acute exacerbation of bronchiectasis and acute exacerbation of chronic obstructive pulmonary disease (COPD). Two meta-analyses confirmed these results for COPD related emergency department visits, hospital admission and mortality<sup>2,3</sup>. Concerning ozone (O<sub>3</sub>), a positive association with outpatient visits for acute exacerbation of asthma and COPD was demonstrated<sup>4,5</sup>. For other respiratory diseases, such as pneumothorax, very few studies have documented the relationship with air pollution. Relationships were reported between the occurrence of primary spontaneous pneumothorax (PSP) and interactions with higher values of air pollutants and other meteorological parameters, such as atmospheric pressure, temperature and humidity<sup>6–9</sup>. Abul et al.<sup>10</sup> showed a link between an increase in O<sub>3</sub> and the occurrence of PSP. In a previous study, we demonstrated a lack of connection between PSP and NO<sub>2</sub> and PM<sub>10</sub> exposure, but could not rule out an association between O<sub>3</sub> exposure and PSP<sup>11</sup>. Secondary spontaneous pneumothorax (SSP) occurs in the context of underlying pulmonary disease.

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**Figure 1.** Geographical location of the 14 participating centers. Seven university teaching hospitals, namely Angers, Besançon, Clermont-Ferrand, Dijon, Grenoble, Poitiers and Toulouse; and seven general, non-academic hospitals, namely Belfort, Béthune, Boulogne sur Mer, Lomme, Roubaix, Mulhouse and Vesoul. Maximal distance between two hospitals: north–south 798 km; east–west 593 km (maps created with the software Microsoft Word 2013 15.0 and Paint 6.1 from Microsoft Windows 7 Professionnel <https://www.microsoft.com/fr>).

Among several recognized causes of SSP, the most common aetiology is COPD, which accounts for 70–80%<sup>12</sup>. Therefore, it is important to analyse a potential link between SSP and air pollution. The objectives of this study were: (1) to estimate the relationships between SSP and short term air pollution exposure with  $PM_{10}$ ,  $NO_2$  and  $O_3$ ; and (2) to investigate a time lag effect between exposure and the occurrence of SPP.

## Methods

The design of this study is a time-stratified case–crossover<sup>13</sup>. This design is used to study environmental conditions, particularly air pollution<sup>14–17</sup>. This study implicated Emergency Departments from 14 medium-sized cities distributed over all the territory of France (Fig. 1).

For each subject, a case period was compared to multiple other control periods dispersed over the month concerned by the occurrence of the event. The date of admission to the Emergency Department determined the date of occurrence of the SSP. Case period was defined as the period leading up to the date of admission, concerning the total time during which the subject was exposed to the risk of occurrence of SPP. A period of 4 days was retained, i.e., Lag 1–Lag 4, before the occurrence of the event. Control periods were defined as the same weekdays as the case period within the same month. The exposure period corresponded as all case and control periods for each subject.

**Study population.** All patients with pneumothorax aged over 18 years and who provided written informed consent from, the period of June 1, 2009, to May 31, 2013, were included. Patients with traumatic and PSP were excluded. Recurrent episodes, defined as a second episode of SSP during the period of inclusion, were excluded. Subjects living more than 30 km (19 miles) from an air pollutant monitoring station, or in a different study area were also excluded.

Data collected from the Emergency Department medical records were the following: age, sex, date of admission, home address, smoking status, and history of COPD, emphysema, pneumothorax and asthma. All research was performed in accordance with relevant regulations and informed consent was obtained from all the participants. The study was approved by the French National authority for the protection of privacy and personal data (CNIL) on December 23, 2014 under the number 913594.

**Environmental data.** Air pollution exposure was assessed using measurements provided by the French National AASQA Network, which is accredited by the French Ministry for the Environment and whose quality is guaranteed by ISO/TC146 standard for air quality. Measurements, data control and the maintenance of the instrumentation are standardized while respecting French and European standards. Hourly mean concentration of NO<sub>2</sub>, O<sub>3</sub> and PM<sub>10</sub> were collected from each monitoring station of the study area. The number of stations ranged between one to nine per area (mean 5.9). Each patient's home address was used to estimate the exposure to air pollutants for the case and control periods. The association between the patient's home address and the appropriate monitoring station was determined by the local AASQA team. To select the most representative station for measuring the exposure of each patient, different parameters were considered: the distance between the geolocated address and the station, the geomorphological situation and the proximity of significant sources of air pollution.

Three exposure assessments were selected. First, the maximum and mean absolute quantitative values of PM<sub>10</sub>, NO<sub>2</sub> and O<sub>3</sub> were determined. Second, the fast increase in air pollutant concentration was calculated, which was defined as a positive difference in concentration occurring in an interval of 3 h, noted as  $\Delta_{3h}$ . For each hour,  $\Delta_{3h}$  was calculated as the difference between the concentrations measured at hour h, minus the concentration measured at hour h-3. A fast increase was retained if a  $\Delta_{3h}$  exceeded: 20  $\mu\text{g}/\text{m}^3$  for PM<sub>10</sub>, or 40  $\mu\text{g}/\text{m}^3$  for NO<sub>2</sub> and O<sub>3</sub>. This threshold value was chosen as the third quartile of the observed distribution of the  $\Delta_{3h}$ .

Finally, the air quality threshold exceedance was defined by the European legislation on air quality<sup>18</sup>. The legal thresholds for each air pollutant were: PM<sub>10</sub> daily average = 50  $\mu\text{g}/\text{m}^3$ , NO<sub>2</sub> hourly average = 200  $\mu\text{g}/\text{m}^3$ , O<sub>3</sub> 8-h average = 120  $\mu\text{g}/\text{m}^3$ .

To highlight a lag effect, these assessments were calculated for each of the 4 days before the occurrence of SSP for all the case and control periods, and for the entire exposure period (Lag 1–Lag 4).

**Statistical analysis.** A conditional logistic regression was used to analyse the relationship between the exposure to air pollution for each case and control period. To control the false discovery rate with a high number of exposure indices, a correction for multiple testing was realized with Benjamini Yekutieli's adjustment, which is less conservative than a Bonferroni correction<sup>19–21</sup>. To verify that the effects of concentrations of pollutants were not modified by individual factors, sensitivity analyses were performed with age, sex, smoking status, history of pulmonary disease (COPD, emphysema, pneumothorax, and asthma) and centre. Complementary analyses were also performed with warm seasons (spring and summer) versus cool seasons (autumn and winter) to consider the variation of O<sub>3</sub> concentration with the amount of sunlight.

Statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA). A P value < 0.05 was considered statistically significant.

## Results

**Participants.** From June 1, 2009, to May 31, 2013, were admitted in the 14 Emergency department 1946 patients for pneumothorax. Among them, 358 patients presented a SSP. After excluding subjects living more than 30 km (19 miles) from an air pollutant monitoring station or with a recurrent episodes, 135 SSP were included (Fig. 2). The mean age of the population was 55.56 years (standard derivation 18.54 years). The male/female ratio was 4.4. Approximately 60% of the population presented with COPD or emphysema, and 39% declared a previous onset of pneumothorax. Current smokers accounted for 54%. Half of the SSPs were admitted in spring and summer seasons (Table 1).

**Air pollution exposure.** The pollutant exposures are presented according to the case and the control status in SI Table A (mean (SD), median, maximum, minimum and quartile) and SI Table B (correlation coefficients between the air pollutants).

The odds ratios associated with PM<sub>10</sub>, NO<sub>2</sub> and O<sub>3</sub> values of maximum and mean concentrations, for each Lag and the entire period exposure are presented in Table 2. The odds ratios associated with at least one fast increase ( $\Delta_{3h}$ ) are presented in Table 3. The odds ratios associated with at least one exceedance of air quality threshold are presented in Table 4.

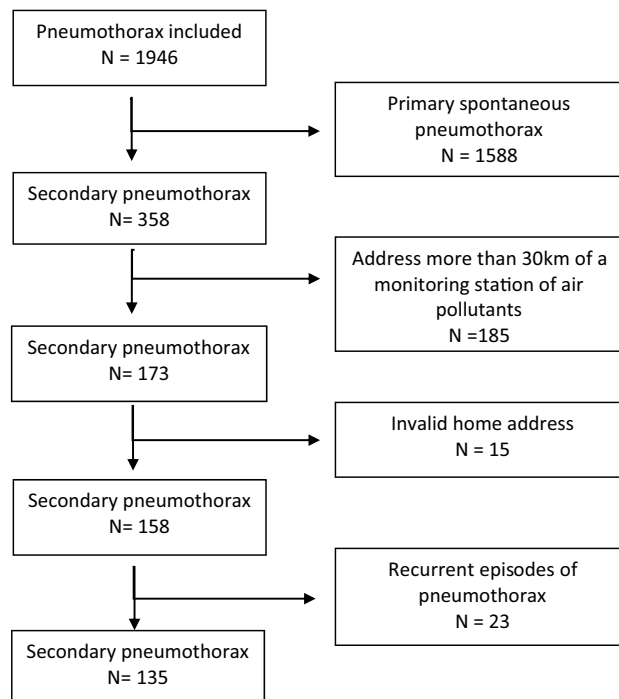
Concerning the PM<sub>10</sub> exposure assessment, the odds ratios associated with values of maximum and mean concentrations across Lag 1–Lag 4 ranged between 0.93 (0.77–1.13) and 0.99 (0.91–1.08) (Table 2). When considering each Lag, the odds ratios associated with PM<sub>10</sub> values of at least one fast increase ( $\Delta_{3h}$ ) ranged between 0.52 (0.27–1.00) and 1.02 (0.56–1.85) (Table 3); the odds ratios associated with at least one exceedance of air quality threshold ranged between 0.41 (0.11–1.49) and 1.00 (0.35–2.88) (Table 4).

Concerning the NO<sub>2</sub> exposure assessment, the odds ratios associated with values of maximum and mean concentrations across Lag 1–Lag 4 ranged between 0.87 (0.70–1.09) and 0.99 (0.82–1.21) (Table 2). When considering each Lag, the odds ratios associated with NO<sub>2</sub> values of at least one fast increase ( $\Delta_{3h}$ ) ranged between 0.37 (0.18–0.77) and 1.24 (0.65–2.38) (Table 3). No exceedance of air quality threshold of NO<sub>2</sub> was observed.

Concerning the O<sub>3</sub> exposure assessment, the odds ratios associated with values of maximum and mean concentrations across Lag 1–Lag 4 ranged between 0.95 (0.84–1.07) and 1.02 (0.93–1.13) (Table 2). When considering each Lag, the odds ratios associated with O<sub>3</sub> values of at least one fast increase ( $\Delta_{3h}$ ) ranged between 1.03 (0.61–1.74) and 1.40 (0.84–2.32) (Table 3); the odds ratios associated with at least one exceedance of air quality threshold ranged between 0.91 (0.29–2.81) and 1.77 (0.63–4.95) (Table 4).

The complementary analyses O<sub>3</sub> values separately performed on warm and cold seasons are presented in SI Figure A and SI Table C.

No significant association between the occurrence of SSP and the air pollutant exposure assessment were observed. All P<sub>Corr</sub> values were superior to 0.12.



**Figure 2.** Flow chart.

| N = 135                           | Mean (SD) or N (%) |
|-----------------------------------|--------------------|
| Age (years)                       | 55.56 (18.54)      |
| <b>Sex</b>                        |                    |
| Male                              | 110 (81.48)        |
| Female                            | 25 (18.52)         |
| <b>History of COPD</b>            | 82 (60.74)         |
| <b>History of emphysema</b>       | 78 (57.78)         |
| <b>History of pneumothorax</b>    | 53 (39.26)         |
| <b>History of asthma</b>          | 8 (5.93)           |
| <b>Smoking status<sup>a</sup></b> |                    |
| Current                           | 73 (54.07)         |
| Never                             | 5 (3.70)           |
| Former                            | 34 (25.19)         |
| <b>Season</b>                     |                    |
| Spring                            | 40 (29.63)         |
| Summer                            | 29 (21.48)         |
| Autumn                            | 33 (24.44)         |
| Winter                            | 33 (24.44)         |

**Table 1.** Baseline characteristics of study population. *COPD* chronic obstructive pulmonary disease. <sup>a</sup>Missing values N = 23.

## Discussion

In this study, no significant association between the occurrence of SSP and short term exposure to PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub> were identified for quantitative absolute values, fast increase in air pollutants and peak of pollution. Nevertheless, a link between O<sub>3</sub> and the occurrence of the event cannot be ruled out.

Our study had some strengths. We were careful to avoid selection bias. During the study period, all patients with a diagnosis of pneumothorax [International Classification of Diseases (ICD) 10th revision code = J93] were retrospectively identified by medical informatics queries of the emergency unit databases in the participating centres. The diagnosis of SSP (ICD code J93.12) was checked by research assistants in the medical files of the Emergency Department's admissions database.

| Variables      | PM <sub>10</sub>    |          |                         | NO <sub>2</sub>     |         |                        | O <sub>3</sub>      |         |                        |
|----------------|---------------------|----------|-------------------------|---------------------|---------|------------------------|---------------------|---------|------------------------|
|                | OR (95% CI)*        | P value† | P <sub>cor</sub> value‡ | OR (95% CI)         | P value | P <sub>cor</sub> value | OR (95% CI)         | P value | P <sub>cor</sub> value |
| <b>Maximum</b> |                     |          |                         |                     |         |                        |                     |         |                        |
| Lag 1          | 0.94<br>(0.83–1.06) | 0.33     | 1.00                    | 0.95<br>(0.86–1.05) | 0.30    | 0.95                   | 0.99<br>(0.89–1.09) | 0.80    | 0.80                   |
| Lag 2          | 0.97<br>(0.86–1.08) | 0.54     | 1.00                    | 1.02<br>(0.92–1.14) | 0.65    | 0.95                   | 1.02<br>(0.93–1.13) | 0.67    | 0.72                   |
| Lag 3          | 0.99<br>(0.91–1.08) | 0.90     | 1.00                    | 1.04<br>(0.95–1.14) | 0.39    | 0.95                   | 1.08<br>(0.98–1.20) | 0.12    | 0.68                   |
| Lag 4          | 0.98<br>(0.87–1.09) | 0.66     | 1.00                    | 1.02<br>(0.93–1.13) | 0.66    | 0.95                   | 0.97<br>(0.88–1.08) | 0.60    | 0.72                   |
| Entire period‡ | 0.96<br>(0.88–1.05) | 0.37     | 1.00                    | 1.04<br>(0.94–1.14) | 0.50    | 0.95                   | 1.04<br>(0.92–1.16) | 0.55    | 0.72                   |
| <b>Mean</b>    |                     |          |                         |                     |         |                        |                     |         |                        |
| Lag 1          | 0.94<br>(0.78–1.15) | 0.56     | 1.00                    | 0.87<br>(0.70–1.09) | 0.24    | 0.95                   | 1.02<br>(0.90–1.15) | 0.79    | 0.79                   |
| Lag 2          | 0.97<br>(0.80–1.18) | 0.77     | 1.00                    | 1.02<br>(0.83–1.25) | 0.85    | 0.95                   | 0.99<br>(0.87–1.12) | 0.83    | 0.83                   |
| Lag 3          | 0.93<br>(0.77–1.13) | 0.46     | 1.00                    | 0.97<br>(0.79–1.18) | 0.72    | 0.95                   | 1.03<br>(0.91–1.16) | 0.67    | 0.72                   |
| Lag 4          | 0.97<br>(0.82–1.15) | 0.71     | 1.00                    | 0.99<br>(0.82–1.21) | 0.95    | 0.95                   | 0.95<br>(0.84–1.07) | 0.41    | 0.68                   |
| Entire period  | 0.91<br>(0.72–1.15) | 0.41     | 1.00                    | 0.95<br>(0.72–1.25) | 0.71    | 0.95                   | 0.99<br>(0.84–1.17) | 0.94    | 0.94                   |

**Table 2.** Association between the maximum and mean concentration pollutants over the entire exposure period, and the occurrence of secondary pneumothorax. The OR were computed for a 10 µg/m<sup>3</sup> increase. CI confidence interval. \*Confidence interval without correction for multiple comparison procedure. †For conditional logistic regression. ‡Corrected P value with Benjamini Yekutieli's method. ‡Entire exposure period = Lag 1 to date Lag 4.

| Variables   | OR (95% CI)*     | P value† | P <sub>cor</sub> value‡ |
|---|------------------|----------|-------------------------|
| <b>PM<sub>10</sub> (concentration of 20 µg/m<sup>3</sup>)</b> |                  |          |                         |
| Lag 1   | 1.02 (0.56–1.85) | 0.95     | 1.00                    |
| Lag 2   | 0.96 (0.53–1.73) | 0.88     | 1.00                    |
| Lag 3   | 0.52 (0.27–1.00) | 0.05     | 0.97                    |
| Lag 4   | 1.01 (0.53–1.91) | 0.97     | 1.00                    |
| Entire exposure period‡                                       | 0.84 (0.55–1.29) | 0.43     | 1.00                    |
| <b>NO<sub>2</sub> (concentration of 40 µg/m<sup>3</sup>)</b>  |                  |          |                         |
| Lag 1   | 0.37 (0.18–0.77) | 0.01     | 0.12                    |
| Lag 2   | 1.07 (0.57–1.99) | 0.83     | 0.95                    |
| Lag 3   | 1.22 (0.65–2.29) | 0.53     | 0.95                    |
| Lag 4   | 1.24 (0.65–2.38) | 0.52     | 0.95                    |
| Entire exposure period  | 0.97 (0.59–1.57) | 0.89     | 0.95                    |
| <b>O<sub>3</sub> (concentration of 40 µg/m<sup>3</sup>)</b>   |                  |          |                         |
| Lag 1   | 1.40 (0.84–2.32) | 0.20     | 0.68                    |
| Lag 2   | 1.41 (0.84–2.35) | 0.19     | 0.68                    |
| Lag 3   | 1.26 (0.76–2.10) | 0.37     | 0.68                    |
| Lag 4   | 1.03 (0.61–1.74) | 0.91     | 0.91                    |
| Entire exposure period  | 1.06 (0.69–1.62) | 0.79     | 0.79                    |

**Table 3.** Association between the exposure to at least one episode of fast increase in air pollutant concentration and the occurrence of secondary pneumothorax. CI confidence interval. \*Confidence interval without correction for multiple comparison procedure. †For conditional logistic regression. ‡Corrected P value with Benjamini Yekutieli's method. ‡Entire exposure period = Lag 1 to date Lag 4.

Concerning the air pollution exposure for each patient, a partnership was realized with the French National AASQA Network. The aim was to identify the appropriate monitoring station in relation to each patient's address. Considering the geomorphological situation and the sources of primary pollutant, allows us to determine the most reliable level of air pollutant exposure.

| Variables  | OR (95% CI)*     | P value† | P <sub>cor.</sub> value‡ |
|--|------------------|----------|--------------------------|
| <b>PM<sub>10</sub> (daily average 50 µg/m<sup>3</sup>)</b> |                  |          |                          |
| Lag 1  | 0.41 (0.11–1.49) | 0.17     | 1.00                     |
| Lag 2  | 0.54 (0.15–1.90) | 0.34     | 1.00                     |
| Lag 3  | 1.00 (0.35–2.88) | 1.00     | 1.00                     |
| Lag 4  | 0.96 (0.34–2.73) | 0.94     | 1.00                     |
| Entire exposure period‡                                    | 0.82 (0.38–1.78) | 0.62     | 1.00                     |
| <b>O<sub>3</sub> (8-h average 120 µg/m<sup>3</sup>)</b>    |                  |          |                          |
| Lag 1  | 1.69 (0.71–4.02) | 0.23     | 0.68                     |
| Lag 2  | 1.77 (0.63–4.95) | 0.28     | 0.68                     |
| Lag 3  | 1.72 (0.58–5.08) | 0.33     | 0.68                     |
| Lag 4  | 0.91 (0.29–2.81) | 0.87     | 0.87                     |
| Entire exposure period                                     | 1.36 (0.66–2.79) | 0.40     | 0.68                     |

**Table 4.** Association between exposure to at least one air quality threshold exceedance of pollution and the occurrence of secondary pneumothorax. *CI* confidence interval. \*Confidence interval without correction for multiple comparison procedure. †For conditional logistic regression. ‡Corrected *P* value with Benjamini Yekutieli's method. ‡Entire exposure period = Lag 1 to date Lag 4.

The time-stratified case–crossover design, which is an advanced matching technique, makes it possible to take into account the characteristics of individual patients. This design is recognized to consider temporal trends and to reduce differential errors due to the measure of exposure. This methodology is specifically adapted to the analysis of associations between rapid onset disease with a short induction period, and acute exposure<sup>14,22</sup>.

To the best of our knowledge, our study is the first in the literature to evaluate the link between SSP and air pollution. Patients with SSP have mainly underlying chronic lung diseases, such as COPD. In their study on the epidemiology of pneumothorax, Gupta et al.<sup>12</sup> demonstrated that COPD causes 70–80% of SSP cases. In our study, approximately 60% of patients with SSP presented an underlying COPD or an emphysema. A significant impact between acute exacerbation of COPD and air pollution was demonstrated<sup>1–3,5</sup>. Long-term exposure to air pollutants is significantly associated with increasing emphysema<sup>23,24</sup>. With these chronic inflammatory diseases, these population are most vulnerable and present a greater risk of pulmonary complications. A diffuse histopathological change in the lung parenchyma under the visceral pleural could lead to the occurrence of a pneumothorax. Diffuse increased porosity at the periphery of both lungs has been identified, which could be associated with localized rupture of a bleb, or a bulla<sup>25,26</sup>. Short-term O<sub>3</sub> exposure could induce airway hyperresponsiveness, increase oxidant stress and stimulate inflammatory responses in the respiratory system associated with a chronic inflammatory disease, which could lend credence to the hypothesis of a stronger link between SSP and air pollutants<sup>27</sup>.

Nevertheless, in our study, a link between O<sub>3</sub> exposure and SSP cannot be ruled out. In the literature, Park et al.<sup>7</sup> showed that increased concentrations of O<sub>3</sub> on two previous days before the occurrence of PSP are significantly associated. Huang et al.<sup>5</sup> demonstrated that the strongest association between O<sub>3</sub> exposure and COPD mortality was found in the moving average concentration from the day of the occurrence of COPD to Lag 2. Yang et al.<sup>28</sup> concluded at an association among respiratory mortality and increased average O<sub>3</sub> 2 days before the occurrence of the event. Although non significant, our study results associated with the fast increase of 40 µg/m<sup>3</sup> and the peak of 8-h average of 120 µg/m<sup>3</sup> are compatible with the occurrence of SSP and a fast increase O<sub>3</sub> concentration to Lag 2 prior to the event.

The concentrations of O<sub>3</sub> are generally higher in warm seasons than in cool seasons. In fact, the concentration and distribution of O<sub>3</sub> are linked with regard to the main determinants: emissions and sunlight. Primary pollutant emissions from urban traffic include nitrogen oxides, carbon monoxide, and volatile organic compound produce O<sub>3</sub> through photochemical transformations. A strong correlation between O<sub>3</sub> concentrations and temperature is established<sup>29</sup>; increasing temperature also increases the emission of volatile organic compound by processes such as evaporation<sup>30</sup>. Ozone concentration increases almost linearly with the ambient temperatures and with greater intensity of sunlight, which is why O<sub>3</sub> concentrations are higher in warm seasons and in urban areas<sup>29,31,32</sup>. In the literature, Abul et al.<sup>10</sup> showed an association between the occurrence of PSP and higher levels of O<sub>3</sub> in the spring. Gryparis et al.<sup>33</sup> evaluated the relationship between acute effects of O<sub>3</sub> and respiratory mortality in 23 European cities. O<sub>3</sub> concentrations are higher during the summer and are associated with an increase respiratory mortality during warmer seasons. Zanobetti et al. and Peng et al.<sup>34,35</sup> demonstrated the same results for American and Canadian cities. Although our study results are non significant, the ORs concerning the associations between maximum and mean O<sub>3</sub> concentrations and the occurrence of SSP are higher in warm seasons than in cool seasons for each Lag and for the entire period of exposure before the event. A link between short term O<sub>3</sub> exposure and these diseases cannot be ruled out in warm seasons.

In this regard, two points merit discussion, namely the seasonality and the associations of different meteorological factors.

In the literature, the occurrence of pneumothorax and respiratory disease seems to have a seasonal effect. However, the results are contradictory. In fact, Park et al. and Aissa et al.<sup>7,36</sup> demonstrated a greater occurrence of pneumothorax in warm versus cold seasons. Schieman et al. and Motono et al.<sup>37,38</sup> concluded that there was an

absence of a significant link between pneumothorax and seasonality. Concerning respiratory diseases, such as COPD, a relationship is established with a higher concentration of O<sub>3</sub> during the summer<sup>33–35</sup>. However, Chen et al., Yin et al. and Wong et al.<sup>39–41</sup> showed in East Asia and southern China that O<sub>3</sub>, despite a higher concentration in warm versus cool seasons, had stronger effects on respiratory mortality in cool seasons. The main explanation for this finding is the people's behavior in relation to the climate. American, Canadian and European cities are exposed to a continental climate with extremely cold winters and hot summers with a great range of temperatures. People also spend longer amounts of time outdoors during warm seasons than in cool seasons. They are exposed in warm seasons to higher outdoors O<sub>3</sub> pollution and pollen concentration, which can increase respiratory disease exacerbation<sup>33</sup>. Southeast Asia has a subtropical climate with mild winter and hot and damp summers. During cool seasons, people are more likely to go outdoors and are also more exposed to O<sub>3</sub>. During warm stay at home with the air conditioner and are also less exposed to O<sub>3</sub><sup>5,41</sup>. Therefore, the exposition of air pollutants depends on lifestyle and people's behavior. Climate, with the associations of different meteorological factors, is therefore an interesting parameter to evaluate the occurrence of pneumothorax.

Concerning the different meteorological factors, the associations of air pollutants and different parameters, such as atmospheric pressure, temperature and humidity, were not included in our study. In fact, Bertolaccini et al.<sup>8</sup> concluded that the occurrence of PSP was significantly triggered by higher daily mean NO<sub>2</sub>, lower daily mean O<sub>3</sub> and daily decrement of standard variation of temperature and wind speed. In the second study of Bertolaccini et al.<sup>9</sup>, PSP was significantly more likely to occur on warm windy days with high atmospheric pressure and high mean NO<sub>2</sub> concentrations. Park et al.<sup>7</sup> demonstrated that increased concentrations of air pollutants associated with an abrupt change in atmospheric pressure were significantly associated with an increased incidence rate of PSP. Temperature and wind speed might affect the transport of air pollutants and allergens, leading to bronchiolar spasm, mucous retention and coughing<sup>7,37</sup>. The association with different factors could have a synergistic effect, and a resulting impact on air pollution. All environmental factors should be taken into account to evaluate their relationship with pneumothorax.

## Conclusions

Our study failed to identify any significant relationship between SSP and short-term PM<sub>10</sub> and NO<sub>2</sub> exposure. A link with O<sub>3</sub> exposures cannot be ruled out, especially when considering 2 days prior to the event and in warm seasons. Therefore, a potentiating effect of different meteorological factors remains to be demonstrated.

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## Author contributions

Study conception and design: N.B., A.L.P., M.G., J.C.D., F.M., T.D. Acquisition, analysis and interpretation of data: T.M., N.B., A.L.P., B.M., J.B.P., F.M., T.D. Statistical analysis: T.M., M.P., F.M. All the authors participated in drafting of the manuscript, approved the version to be published, and agree to be held accountable for all aspects of the work.

## Competing interests

The authors declare no competing interests.

## Additional information

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