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# Lifetime exposure to particulate air pollutants is negatively associated with lung function in non-asthmatic children<sup>☆</sup>

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## ABSTRACT

**Background:** Pulmonary function is known to be affected by acute and subacute exposure to ambient air pollution. However, the impacts of lifetime exposure to air pollution on the pulmonary function of children have been inconsistent. The present study investigated the impact of lifetime residential exposure to intermediate levels of air pollution on the pulmonary function of schoolchildren.

**Methods:** In 2011, a survey of children aged 6–15 years was conducted in 44 schools in Taiwan. Atopic history, residential history, and environmental factors were recorded. Spirograms were obtained from a random sample of children without asthma. A total of 535 girls and 481 boys without a history of asthma were enrolled. Lifetime residential exposure to air pollutants, including particulate matter with an aerodynamic diameter less than 10  $\mu\text{m}$  (PM<sub>10</sub>), ozone (O<sub>3</sub>), sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>), and carbon monoxide (CO), was estimated using the kriging method, based on monitored data from the Taiwan Environmental Protection Administration. Multiple linear regression was used to analyze the association between lifetime air pollution exposure and pulmonary function, after adjustment for potential confounders and recent exposure.

**Results:** After adjustment for 7-day average air pollutant levels, a 10  $\mu\text{g}/\text{m}^3$  increase in PM<sub>10</sub> was related to reductions in the forced expiratory volume in 1 s (–2.00%; 95% confidence interval [CI] –3.09% to –0.90%), forced vital capacity (–1.86%; CI: –2.96% to –0.75%), and maximal midexpiratory flow (–2.28%; CI: –4.04% to –0.51%). These associations were independent of the other pollutants.

**Conclusion:** Lifetime exposure to 25–85  $\mu\text{g}/\text{m}^3$  of PM<sub>10</sub> has negative impacts on the pulmonary function of children.

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## 1. Introduction

Among the health effects of air pollution on humans, impaired pulmonary function has been a major source of concern because it is a predictor of mortality (Schunemann et al., 2000; Sin et al., 2005). Studies have observed an association between acute (within 2 weeks) (Health effects of outdoor air pollution, 1996; Chang et al., 2012; Chen et al., 1999; Rice et al., 2013; Int Panis et al., 2017), subacute (between acute and chronic) (Chen et al.,

2015), and chronic (3 months or longer) exposure to various air pollutants and pulmonary function (Hwang et al., 2015; Rojas-Martinez et al., 2007), including nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>), and particulate matter (PM).

The proliferation of alveolar cells and expansion of lung volume begin at birth and continue until adulthood (Kajekar, 2007). During this time, the respiratory bronchioles and alveolar ducts gradually mature and are therefore highly susceptible (Kajekar, 2007; Dietert et al., 2000). Respiratory cells are more susceptible to toxicants in early life than in adulthood (Pinkerton and Joad, 2000). In addition, children spend more time in outdoor activities than do adults. During these activities, children have higher frequencies of ventilation and respiration. Thus, they may be exposed to higher levels of air pollution than adults under the same circumstances.

Although early life is considered a susceptible period for the

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### Abbreviations

PM	particulate matter
PM <sub>10</sub>	particulate matter with an aerodynamic diameter less than 10 μm
NO <sub>2</sub>	nitrogen dioxide
O <sub>3</sub>	ozone
SO <sub>2</sub>	sulfur dioxide
CO	carbon monoxide
EPA	Taiwan Environmental Protection Administration
FEV <sub>1</sub>	forced expiratory volume in 1 s
FVC	forced vital capacity
MMEF	maximal-mid expiratory flow

adverse impacts of air pollutants, only a few studies have investigated the impacts of lifetime exposure to ambient air pollution on the pulmonary function of children and outcomes have been inconsistent (Oftedal et al., 2008; Schultz et al., 2012; Gehring et al., 2013). A study conducted in Sweden demonstrated that exposure to particulate matter with an aerodynamic diameter less than 10 μm (PM<sub>10</sub>) in the first year of life, but not in later life, is related to impaired forced expiratory volume in 1 s (FEV<sub>1</sub>) (Schultz et al., 2012). A study conducted in Norway revealed adverse impacts of early and lifetime exposure to PM<sub>10</sub> and NO<sub>2</sub> on peak expiratory flow (PEF) (Oftedal et al., 2008). However, the European Study of Cohorts for Air Pollution Effects (ESCAPE) in 4 countries reported contrasting results that decreases in pulmonary function parameters were associated with PM<sub>10</sub> and NO<sub>2</sub> levels at the current address, but not at the birth address (Gehring et al., 2013). The GINIplus and LISAPlus studies conducted in Germany did not observe the associations between long-term air pollution and pulmonary function variables (Fuertes et al., 2015).

The aforementioned studies have been conducted in countries with relatively low air pollution (e.g., mean PM<sub>10</sub> concentration: less than 30 μg/m (Health effects of outdoor air pollution, 1996)). However, many countries have higher levels of PM<sub>10</sub> and other pollutants. According to WHO (Organization WH, 2016), the mean PM<sub>10</sub> level worldwide is 71 μg/m<sup>3</sup>, and nearly 90% of the population is exposed to PM levels higher than that reported by the WHO air quality guidelines (annual mean values: 20 and 10 μg/m (Health effects of outdoor air pollution, 1996) for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively). Therefore, determining the impacts of both intermediate (25–85 μg/m<sup>3</sup>) and low levels of PM<sub>10</sub> is crucial. However, the information of the health effects under intermediate levels of pollution is lacking.

The present study investigated whether the pulmonary function of schoolchildren is impaired by lifetime exposure to intermediate levels of air pollution.

## 2. Methods

### 2.1. Design and study population

Fig. S1 shows the study design algorithm. The participants in this nationwide, cross-sectional, school-based survey were recruited between April and May 2011. (Chen et al., 2015) The children were selected from 22 junior high schools and 22 elementary schools within a 1-km radius of the Taiwan Environmental Protection Administration (EPA) monitoring station in each county. In elementary schools, participants were selected from one class in each grade, whereas in junior high schools, they were

selected from 3 classes in the first and second grades.

To determine the histories of the participants, 7154 copies of the modified Chinese version of the International Study of Asthma and Allergies in Childhood questionnaires were dispatched to their parents between April and May 2011. The questionnaire covered each participant's respiratory health, allergic conditions, demographic characteristics, and environmental exposures. Questions related to atopic conditions were identical to those used in 1995–1996 (Guo et al., 1999) and 2001 (Lee et al., 2007). Participants were excluded from the study if they reported a history of physician-diagnosed asthma or wheezing attacks.

Their residential history, starting from birth, was obtained from the questionnaire, and every move to a new township was recorded. If the participants moved to a new township in a specific year, they were considered to have lived in the new township throughout that year. Participants who moved twice in a year were deemed to have lived in each place for half a year. In addition, participants were excluded if they had ever resided abroad, if their residential history was incomplete, or if their current residence was not in the same county or immediate neighboring counties of the school they attended.

From the 44 schools participating in the study, 6346 questionnaires were retrieved (response rate: 88.7%). Among the participants who completed the questionnaire, 954 (15.0%) and 742 (11.7%) reported a history of wheezing attacks and physician-diagnosed asthma, respectively, whereas 1156 (18.2%) reported either condition. A total of 5190 (81.8%) participants reported no history of asthma or wheezing; among them, 1564 were randomly sampled. Among the remaining participants without asthma, 6 were randomly selected from each class. After the exclusion of participants with missing addresses, history of living abroad, or respiratory symptoms consistent with flu, 1070 were recruited for pulmonary function measurement. A total of 1016 children (95%; 535 girls and 481 boys) satisfactorily completed the pulmonary function study (Fig. 1).

#### 2.1.1. Lung function measurement

Three trained personnel used identical devices to conduct the pulmonary function measurements (Chest-graph HI-101; CHEST MI, Tokyo, Japan). The test was performed according to the guidelines of the American Thoracic Society and European Respiratory Society (Miller et al., 2005). To complete the test, each participant performed at least 3 acceptable maneuvers, defined as an extrapolation volume of <5% of forced vital capacity (FVC) or 150 mL, a smooth flow–volume curve without artifacts, and satisfactory exhalation with a forced expiratory duration of >6 s (>3 s for children younger than 10 years) or with a plateau of >1 s in the volume–time curve. The participants attempted a maximum of 8 blows in a session (Chen et al., 2015). Among the acceptable maneuvers, the highest value for each parameter was used in the following analysis. The recorded parameters included the FVC, FEV<sub>1</sub>, maximal midexpiratory flow (MMEF), and FEV<sub>1</sub>:FVC ratio.

#### 2.1.2. Air pollutant exposure assessment

In this study, PM<sub>10</sub>, O<sub>3</sub>, sulfur dioxide (SO<sub>2</sub>) NO<sub>2</sub>, and carbon monoxide (CO) were analyzed. Data on the pollutants were obtained from the EPA monitoring stations (from 69 stations in 1996 to 73 stations in 2010). Fig. 2 shows the location of these monitoring stations.

The air pollutant concentrations were measured and recorded every hour, and the annual averages were considered in the analysis. An effective annual average is calculated in cases of more than 250 effective days or 6000 effective hours annually. An effective day is defined as more than 16 effective hours daily; an effective hour is defined as more than 45 min sampled in 1 h (Environmental

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