國立臺灣大學公共衛生學院環境與職業健康科學研究所

碩士論文

Institute of Environmental and Occupational Health Sciences

College of Public Health

National Taiwan University

Master Thesis

2001 年、2011 年和 2016 年臺灣中學生氣喘、過敏性鼻炎和異位性皮膚炎盛行率趨勢

Trends of the prevalence of asthma, allergic rhinitis, dermatitis among middle school students in 2001, 2011 and 2016 in Taiwan

陳樂樂

Lele Chen

指導老師：郭育良教授

Adviser: Yue-Liang Guo, MD., MPH., PH.D

中華民國 113 年 1 月

January 2024

doi:10.6342/NTU202400166

中文摘要

背景：氣喘是最常見的過敏性疾病，特別是在兒童中。在過去的 20 年裡，氣喘在一些國家的發病率有所下降，而在另一些國家則有所增加。過敏性鼻炎（AR）影響了世界上 10%到 40%的人口，臺灣亦有類似的罹患情形。異位性皮膚炎（AD）是一種孩童常見的發炎性皮膚病。它也會在家庭和社會中產生一定的經濟負擔。在 21 世紀的亞洲，醫生診斷的 AD 的 1 年罹患率為 0.96%至 22.6%的兒童。臺灣亦有類似的罹患情形。

研究目的：本研究旨在通過過去 20 年對全臺灣中學生的一系列橫斷面研究，觀察氣喘、過敏性鼻炎和異位性皮膚炎的流行趨勢並探討相關之因子。

研究方法：本研究使用中文版的兒童哮喘和過敏症國際研究（ISAAC）問卷，在 2001 年、2011 年和 2016 年對全臺灣 12-15 歲的中學生進行了全國性的橫斷面研究。我們選擇問卷調查前 7 年的空氣污染物資料與氣候因子資料，這些資料來自於學校方圓 5 公裡內環境保護署（Environmental Protection Agency, EPA）的監測站。我們將醫生診斷的氣喘、過敏性鼻炎、異位性皮膚炎作為結果，將環境因素作為因變數，廣義估計方程（Generalized Estimating Equation, GEE）控制協同變量，並進行統計分析。在得出結果後，將三年的結果用 meta-analysis 進行整合。

研究結果：對過敏性疾病來說，2001-2016 年臺湾的氣喘症呈上升趨勢，2011 年後有所下降。過敏性鼻炎患者近期有所增加，異位性皮膚炎则没有什麼區別。同時，空氣污染物如 SO_2、NO、CO、PM10 和 PM2.5 在過去 20 年中呈現出先增後減的總體趨勢，而 O_3 一直在減少。在過去 20 年中，年平均環境溫度上升了將近 1℃。進一步 meta-analysis 研究發现，每增 0.1 ppm 的 CO 與每增 1 度環境溫

doi:10.6342/NTU202400166

度對孩童氣喘症盛行率的 OR 分別為 1.04（95% CI：1.02-1.06）、0.90（95% CI：0.83-0.98）；每增 0.1 ppm 的 CO、每增 1 ppb 的 NO、每增 1 ppb 的 NO2 對孩童過敏性鼻炎盛行率的 OR 分別為 1.02（95% CI：1.01-1.03）、1.004（95% CI：1.002-1.005）、1.011（95% CI：1.006-1.016）。這些空氣污染物與氣候因子對孩童異位性皮膚炎的盛行率則無統計上的顯著影響。

研究結論：結合三次的研究調查後，孩童氣喘症與過敏性鼻炎盛行率與交通源的空氣污染有相關。孩童的氣喘盛行率會受到溫度的影響。異位性皮膚炎則與空氣污染物或氣候因子無顯著相關。

中文关键词：氣喘，過敏性鼻炎，異位性皮膚炎，空气污染物，氣候因子，中學生

doi:10.6342/NTU202400166

Abstract

BACKGROUND: Asthma is the most prevalent allergic disease, particularly among children of school age. In some countries, asthma has decreased over the past two decades, while it has increased in others. Allergic rhinitis (AR) affects between 10 and 40 percent of the world's population. The prevalence of AR is comparable. Atopic dermatitis (AD) is a prevalent inflammatory skin condition in childhood, causing significant financial burden on health expenditure and society. In Asia in the 21st century, the 1-year prevalence of AD diagnosed by a physician ranged from 0.96 to 22.6% in children. In Taiwan, the prevalence of AD was similar.

STUDY AIMS: The purpose of this study was to observe the prevalence and determine the associated effects of asthma, allergic rhinitis, and atopic dermatitis through a series of cross-sectional studies of secondary school students throughout Taiwan over the past 20 years.

METHODS: This study used the Chinese version of the International Study of Asthma and Allergies in Children (ISAAC) questionnaire to conduct a cross-sectional study of secondary school pupils in Taiwan in 2001, 2011, and 2016. We gathered air pollutant and climate factor data from Environmental Protection Agency (EPA) monitoring stations within a 5-kilometer radius of the school for the seven years preceding the survey. We used asthma, allergic rhinitis, and atopic dermatitis diagnosed by a physician as outcomes, environmental factors as dependent variables, and generalized estimating equations (GEE) to control for co-variates and statistical analyses. After obtaining the findings, the three-year results were combined using meta-analysis.

RESULTS: Regarding allergic diseases, Taiwan's asthma trend increased from 2001 to 2016 before declining after 2011. Patients with allergic rhinitis have increased recently, while those with atopic dermatitis have shown little change. During the same period, air pollutants such as SO_2, NO, CO, PM10, and PM2.5 increased and decreased over the past 20 years, while O_3 decreased. Over the past two decades, the annual average ambient temperature has increased by approximately 1°C.

doi:10.6342/NTU202400166

Meta-analysis of the three cross-sectional studies showed that for life-time prevalence of asthma, the ORs of per 0.1 ppm increment of CO and 1 degree of ambient temperature were 1.04 (95% CI: 1.02-1.06) and 0.90 (95% CI: 0.83-0.98), respectively. For AR, the ORs of per 0.1 ppm increment of CO, per 1 ppb increment of NO, and per 1 ppb increment of NO2 were 1.02 (95% CI: 1.01–1.03), 1.004 (95% CI: 1.002-1.005), and 1.011 (95% CI: 1.006–1.005), respectively. AD was not associated with air pollutants and climate factors.

CONCLUSIONS: From the three cross-sectional studies, ttraffic-related air pollutants were related to the occurrence of asthma and allergic rhinitis in children, but not atopic dermatitis.

Key words: Asthma, Allergic rhinitis, Atopic dermatitis, air pollutant, climate change, middle school student

doi:10.6342/NTU202400166

目　錄

doi:10.6342/NTU202400166

圖 目 錄

doi:10.6342/NTU202400166

表目錄

doi:10.6342/NTU202400166

Chapter 1. Introduction

1.1 Allergic diseases

Allergy is an inappropriate immune response to an innocuous antigen that requires initial sensitization with a specific antigen. Subsequent exposure to the same antigen can result in pathological reactions mediated by immunoglobulin E (IgE), mast cells, and basophils (Aldakheel, 2021). There are three primary categories of anaphylactic conditions:

1.1.1 Asthma

Asthma is a chronic inflammatory disorder characterized by the immune cells, mast cells, eosinophils, neutrophils, T-lymphocytes, macrophages, and epithelial cells in susceptible individuals. Lymphocytes, macrophages, and epithelial cells all contribute to inflammation. Typically, these inflammations result in persistent wheezing and breathing difficulty. In the United States, asthma occurs most frequently in children, with an all-age group prevalence of 7.9%. Compared to adults aged 18 years or older, the prevalence of asthma in children is higher than in adults (Stern et al., 2020). In 2019, the all-age-group prevalence of asthma in Taiwan was 3.1%, and the prevalence among those 20 years of age and older was 0.22%. Risk factors for pediatric asthma include genetic factors, gastrointestinal and respiratory microbiomes, air pollution, exposure to tobacco smoke, etc(Stern et al., 2020).

1.1.2 Allergic rhinitis

Allergic rhinitis (AR) is a chronic inflammatory disease caused by the reaction of immunoglobulin E (IgE) in the patient's nasopharynx to a non-toxic environmental protein. Typical symptoms include nasal congestion, sneezing, and irritation. Some patients may also exhibit symptoms of combined eye syndrome. The prevalence of allergic rhinitis ranges from 10% to 40% in the United States and other developed nations (Schuler Iv & Montejo, 2019). 24.6% of adolescents in Taiwan were diagnosed with allergic rhinitis by a physician (Liao et al., 2005). The majority of

doi:10.6342/NTU202400166

patients show symptoms of AR before the age of 20 (Schuler Iv & Montejo, 2019). Environmental exposure (pollen exposure, etc.), climatic factors (variations in temperature, customs, etc.), and lifestyle factors (use of antibiotics, consumption of processed foods, etc.) are risk factors for allergic rhinitis (Zhang et al., 2021).

1.1.3 Atopic dermatitis

Atopic dermatitis (AD) is a chronic inflammatory, pruritic skin condition characterized by recurring flare-ups. The pathophysiology of AD is multifaceted, with genetic, immunological, and environmental variables all playing a role in skin barrier disruption and immune system dysregulation. Pruritus, itching, cutaneous erythema, edema, crusting, and mossiness are frequent clinical signs. It is frequently related to high IgE levels in the blood. Atopic dermatitis affects children more commonly than adults. Approximately 60% of patients have an attack within the first year of life, and 90% have an attack by age five (Eichenfield et al., 2014).

Asthma, allergic rhinitis, and allergic dermatitis are often associated. 38% of patients with AR have asthma, and 78% of those with asthma also have AR. Moreover, these three allergic diseases frequently burden individuals, families, and society. Asthma can result in significant resource consumption and increased emergency room visits (Loftus & Wise, 2015). The academic performance of adolescents with allergic rhinitis may be affected by symptoms such as fatigue, attention deficits, and learning and memory deficits (Schuler Iv & Montejo, 2019). Itching is a significant financial burden for patients with allergic dermatitis. The disease burden is even greater in adolescents with asthma, allergic rhinitis, and allergic dermatitis (Eichenfield et al., 2014).

1.2 Air pollutant

1.2.1 Carbon monoxide (CO)

Carbon monoxide (CO) is an odourless, colourless, and poisonous gas. The main sources of carbon monoxide (CO) in outdoor air are automobile and vehicle exhaust emissions and emissions from other fossil-fueled machinery. High levels of CO

doi:10.6342/NTU202400166

indoors can result in vertigo, confusion, unconsciousness, and even mortality. Outdoors, CO may be linked to lung cancer, angina pectoris, and other conditions(U. S. EPA, 2023a).

1.2.2 Nitrogen monoxide (NO), nitrogen dioxide (NO_2), and ozone (O_3)

NO and NO_2 are: Nitric oxide is colorless and is oxidized to nitrogen dioxide in the atmosphere. The gas nitrogen dioxide has an odor and is intensely acidic and corrosive. NO and NO_2 are primarily produced indoors by domestic appliances such as gas burners. NO_2 may have adverse health effects. Increased NO_2 air concentrations can cause injury to the human respiratory system and increase susceptibility to respiratory infections and asthma. Long-term exposure to excessive NO_2 concentrations can result in chronic respiratory disease. In addition, NO_2 impairs the ability to detect aromas by affecting the senses(Q. EPA, 2023).

Ozone is present in the upper atmosphere and at the surface of the Earth. Ozone has both positive and negative consequences on humans. Stratospheric ozone is naturally present in the upper atmosphere, where it forms a protective layer against the sun's ultraviolet radiation. Due to its effects on both humans and the environment, ground-level ozone is a detrimental air pollutant, and it is a primary component of photochemical smog. This study concentrates on ozone at the ground level. It is one of the causes of wheezing and shortness of breath that 4 O_3 causes airway muscles to contract, confining air in the alveoli. When O_3 concentrations exceed natural levels, they can negatively impact the cardiovascular system and cause or aggravate respiratory conditions.

oxides of nitrogen (NO_x) and ozone (O_3): Ground-level ozone is produced when oxides of nitrogen (NO_x) and volatile organic compounds (VOC) react chemically in the presence of sunlight(U. S. EPA, 2023b).

1.2.3 Particles: particulate matter with a diameter of 2.5 mm (PM2.5) and particulate matter with a diameter of 10 mm (PM10)

PM2.5 refers to airborne particulates with a diameter less than 2.5 micrometers.

doi:10.6342/NTU202400166

Combustion processes such as automobile engines, industrial furnaces, solid fuel burners, and fires are the main sources of these particles(Q. G. EPA, 2023). Due to its small particle size, PM2.5 can enter the gas exchange zone of the lungs and enter the circulatory system through the respiratory barrier, spreading throughout the body and causing adverse health effects such as airway damage, cardiovascular damage, inducing or worsening diabetes, causing birth weight loss and premature birth, and inflammation(Feng et al., 2016).

PM10: PM10 is defined as particulate matter in the air that is less than 10 microns in diameter. These particles are produced by combustion and non-combustion processes(Q. G. EPA, 2023). Its association with increased frequency of asthma is associated with reduced lung function in children and allergic rhinitis(Li et al., 2022; Weinmayr et al., 2010).

1.2.4 Climate factors

Ambient temperature: It mainly refers to the temperature in the ambient air. A decrease or increase in ambient temperature may have health effects, such as causing cardiovascular disease, asthma in children, etc(Hyrkas et al., 2014; Khraishah et al., 2022).

Relative humidity: Cold and dry weather can increase the prevalence and risk of atopic dermatitis attacks(Engebretsen et al., 2016).

1.3 The relationship between air pollutants, climate factors and allergic diseases

1.3.1 Air pollutant

1.3.1.1 Epidemiology

Multiple epidemiological studies have demonstrated a link between chronic exposure to high levels of outdoor air pollution and the incidence of allergic diseases. The exposure of school-aged children to PM and NO_x, according to a European birth cohort study, is associated with diminished respiratory function (Annesi-Maesano, 2015). Air pollution is a significant factor in the development of juvenile asthma, with effects that vary by population, region, and living environment (Paciencia et al., 2022).

doi:10.6342/NTU202400166

In a meta-analysis of allergic rhinitis, PM10, $PM_{2.5}$, NO_2, SO_2, and O_3 were positively associated with the prevalence of allergic rhinitis (Li et al., 2022). Another study demonstrated a positive correlation between allergic rhinitis and urban children. PM10, $PM_{2.5}$, NO_2, SO_2, and O_3 were found to have a positive correlation with the prevalence of allergic rhinitis (Maio et al., 2016). The prevalence of allergic rhinitis was found to be higher in urban than in suburban youth, according to a different study (Lee et al., 2008). In a cross-sectional study conducted in Taiwan, exposure to CO and NO_x was associated with the prevalence of eczema in both boys and girls (Gowers et al., 2012).

1.3.1.2 Mechanism of the role of air pollutants on allergic diseases

Lung cells are susceptible to air pollution, which induces inflammatory responses, stimulates oxidative stress, causes cytotoxicity, and modifies cell death and cell cycle (D'Amato et al., 2015). The UK Committee on the Medical Effects of Air Pollutants has identified four mechanisms through which air pollution contributes to the development and exacerbation of asthma: oxidative stress and injury, airway remodeling, inflammatory pathways, and immune responses, and enhanced respiratory sensitization to aeroallergens (Gowers et al., 2012). High air pollution concentrations may have direct stimulatory and inflammatory effects on airway neuroreceptors and epithelial cells. Certain pollutants, such as ozone and nitrogen dioxide in PM2.5, may affect asthma development. five may induce airway inflammation and promote oxidative stress, worsening asthma symptoms; ozone and nitrogen dioxide may cause airway hyperreactivity (Guarnieri & Balmes, 2014). Activation of aromatic receptor pathways, promotion of oxidative stress, disruption of the skin barrier, and initiation of proinflammatory responses are all linked to the development of atopic dermatitis (Lee et al., 2008).

1.3.2 Climate change

Climate change is closely linked to air pollution. The combustion of fossil fuels generates significant quantities of greenhouse gases such as carbon dioxide and

doi:10.6342/NTU202400166

methane. Excess greenhouse gases absorb an excessive amount of heat from the atmosphere, leading to global warming. Global warming accelerates plant growth and may alter the geographic location of plant growth, resulting in higher pollen levels in the air (Eguiluz-Gracia et al., 2020).

1.3.3 Current control strategies

The replacement of fossil fuels with renewable energy sources, the development of sustainable modes of transport (e.g., public transport, cycling, walking, etc.), government subsidies to encourage the use of electric vehicles, and the need for cities to have green spaces with a diversity of non-allergenic species 9 are all crucial to achieving the Sustainable Development Goals (Eguiluz-Gracia et al., 2020).

Study Aim:

Find the trends in asthma, allergic rhinitis, and atopic dermatitis associated with air pollution and climate change through serial cross-section questionnaire surveys in 1995, 2001, 2011, and 2016. And figure out what caused the trend.

doi:10.6342/NTU202400166

Chapter 2 Methods

2.1 Study Questionnaire

To conduct nationwide surveys from February to June 2001, from April to June 2011, and from April 2016 to July 2017, we used a modified and verified Chinese version of the ISAAC questionnaire. Students were required to bring home a standard ISAAC-C questionnaire for their parents to complete (Lee, Shaw, et al., 2003).

2.2 Study population

The response rate was 89% overall. 2001 and 2011 replicated the surveys from 1995–1996. Students from 22 elementary schools and 22 middle schools within a 1-km radius of an Environmental Protection Agency (EPA) air monitoring station in each county and city in Taiwan were selected for a stratified sample of children by grade level (one class for elementary school grades 1 through 6 and three classes for middle school grades 7 and 8). In 2011, 88.7% of the 7,154 sampled schoolchildren responded to the questionnaire, which 6,346 students completed. The study program was repeated between April 2016 and July 2017, and 20 elementary schools and 21 secondary schools participated in the 2016–2017 survey because schools in certain counties and municipalities did not participate. Each school received a grade-level stratified sample (five classes in grades 1-6 in elementary schools and nine in grades 7-8 in secondary schools). Out of a sample of 13,424 students, 11,585 schoolchildren completed the questionnaire (86.3% response rate) (Chen et al., 2019a, 2019b; Lee et al., 2007; Lee et al., 2005; Lee, Shaw, et al., 2003).

This study, we combined data from 2001, 2011, and 2016–2017 surveys, and students from secondary schools aged 12 to 15 were selected for further analysis. After removing the missing variables, a total of 7,296 secondary school students were included in 2001, 2,082 in 2011, and 4,022 in 2016.

2.3 Health outcome

The questionnaire collected data on the child's respiratory health history. If the

doi:10.6342/NTU202400166

parent answered "yes" to the question "Has a physician has ever diagnosed this child as having asthma?" then the child was defined as physician-diagnosed asthma; if the parent answered "yes" to the question "Has this child ever been diagnosed by a physician as having allergic rhinitis?" then the child was defined as physician-diagnosed allergic rhinitis. If "yes," then the child is defined as having been diagnosed by a physician as having allergic rhinitis, as reported by the parent; if the parent answered "yes" to the query "Has this child ever been diagnosed by a physician as having atopic dermatitis? ", then the child is defined as physician-diagnosed atopic dermatitis.

2.4 Exposure assessment

At the main island monitoring stations in Taiwan, the EPA has conducted comprehensive monitoring of sulfur dioxide (SO_2), nitrogen oxides (NO_x), ozone (O_3), carbon monoxide (CO), and particulate matter with an aerodynamic diameter of 10 m (PM10) since 1994. The concentration of each pollutant was measured continuously and reported every hour. For CO, this was done with non-dispersive infrared absorption, for NOx, with chemiluminescence, for O_3, with UV absorption, for SO_2, and with a beta-meter for PM10. Since 2005, the EPA's Aerodynamic Diameter 2.5 m ($PM_{2.5}$) monitoring instrument has provided hourly updates (Chen et al., 2019a, 2019b; Lee et al., 2007; Lee et al., 2005; Lee, Shaw, et al., 2003).

In this study, we selected the seven years of average air pollution information before the year when we took the questionnaire survey (2001 survey: 1994 1995, 1996, 1997, 1998, 1999, 2000; 2011 survey: 2004, 2005, 2006, 2007, 2008, 2009, 2010; 2016 survey: 2009, 2010, 2011, 2012, 2013, 2014, 2015）

2.5 Co-variates

We reviewed the English-language literature on the etiology of pediatric asthma, allergic rhinitis, and atopic dermatitis to identify individual risk factors such as genetics and the environment.

doi:10.6342/NTU202400166

Due to the few variables in the 1995–1996 survey questionnaire, we chose Co-variables: the child's sex, parental education level, and whether the child had ever been physician-diagnosed with atopic dermatitis. In 2001, 2011, and 2016–2017 surveys, we selected indoor environmental factors, such as cockroaches, visible mold on the walls, and water damage at home. The outdoor environmental factors included ambient temperature, CO, NO, O_3, PM10, SO_2, and NO_2; individual-related variables included the child's sex and parental education level; and genetic susceptibility factors included parental allergic disease history.

2.6 Data analysis

We combined data from 1995–1996, 2001, 2011, and 2016–2017 and eliminated invalid responses (missing data, invalid data, answers containing unknowns, etc.).

We employed the Fisher, ANOVA, K-W, and Chi-square tests for descriptive statistical analysis. Using the GEE (generalized estimating equations), univariate and multivariate analyses are conducted on three levels: air monitoring stations, institutions, and individuals. In the univariate analysis, the independent variables are the ambient temperature, CO, NO, O_3, PM10, SO_2, and NO_2. The dependent variables are physician-diagnosed asthma, allergic rhinitis, and atopic dermatitis. Add individual and environmental factors to the multivariate analysis if the Spearman correlation between air pollutants or climate factors is less than 0.70 or higher than -0.7. After analyzing the relationship between allergic diseases and air pollutants/climate factors, the adjusted ORs were pooled using meta-analysis to obtain the final OR.

doi:10.6342/NTU202400166

Chapter 3 Results

3.1 Characteristics of subject

Table 1 summarizes the demographic characteristics of the study population. Data were collected in 2001, 2011, and 2016, with sample sizes of 7,296, 2,082, and 4,022, respectively.

Approximately 45% of the population were males, while around 55% were females. In the survey conducted in 2001, the majority of the respondents were concentrated in the age range of 14-15 years old, accounting for approximately 72% of the total population. Additionally, only three individuals were 12 years old. In the 2011 survey, the age group with the fewest participants was 15 years old, representing 0.2% of the total population that year. The most prevalent age group was 13 years old, comprising approximately 52.6% of the total number of respondents. In the 2016 survey, the majority of the participants were concentrated in the 13-14 age range, with 38% of the total population being 13 years old and 40% being 14 years old.

Furthermore, it can be observed that the educational attainment of parents has increased. In the survey conducted in 2001, the percentage of parents with at least 9 years of education was only 23%. However, in the surveys conducted in 2011 and 2016, this percentage significantly rose to 90% and 92%, respectively.

Regarding maternal smoking behavior during pregnancy, the number of individuals who smoked during pregnancy remained relatively low, with a consistent proportion of around 2% in all three years surveyed, showing little variation.

As for the household indoor environment, there has been an increase in the proportion of households with water stains persisting for more than one day or visible mold on more than one wall surface, as observed in the surveys conducted over these three years. The percentage of surveyed students living in households with water stains lasting for more than one day increased from 3% in 2001 to 5% in 2016. Similarly, the proportion of students living in households with visible mold on more than one wall surface increased from 7% in 2001 to 12% in 2016. In the surveys conducted in 2001 and 2016, the proportion of households where at least two

doi:10.6342/NTU202400166

cockroaches were found was 35% and 36%, respectively, showing little difference. In the 2011 survey, a smaller percentage of students reported finding at least two cockroaches in their homes, approximately 25%.

In terms of parental allergic disease history, among the surveyed students, the percentage of fathers with a history of allergic rhinitis is 2-3% higher than that of mothers. The proportion of parents with a history of asthma and atopic dermatitis is similar. In the three research surveys, there is little difference in the allergic disease history of parents between 2011 and 2016, but there is an increase compared to 2001. The percentage of parents with a history of asthma increased from 1% in 2001 to 2% in the later years. The percentage of parents with a history of atopic dermatitis increased from 1.5-2% in 2001 to 4-5% in the later years.

Regarding the lifetime prevalence of allergic diseases, as shown in Table 1 and Figure 1, there has been an increase in physician-diagnosed allergic rhinitis and physician-diagnosed atopic dermatitis over the three years of the surveys. The prevalence of physician-diagnosed allergic rhinitis increased from 23% in 2001 to 33% in 2016. Similarly, the prevalence of physician-diagnosed atopic dermatitis increased from 3.5% in 2001 to 12.5%.

In addition, the prevalence of physician-diagnosed asthma experienced an initial increase and then a decrease. It rose from 6% in 2001 to 18% in 2011 and then decreased to 9% in 2016.

3.2 Distribution of air pollutants

Table 2 and Figure 2 illustrate the decreasing trends in the annual average values of CO, NO, NO_2, and SO_2 between 1994 and 2015. For CO, the annual average value decreased from 0.96 ppm in 1994 to 0.44 ppm in 2015. Regarding NO, the annual average value decreased from 15.86 ppb in 1994 to 4.8 ppb in 2015. Similarly, the annual average value of NO_2 decreased from 23.93 ppb in 1994 to 14.21 ppb in 2015. For SO_2, the annual average value decreased from 10.14 ppb in 1994 to 3.19 ppb in 2015.

doi:10.6342/NTU202400166

Table 2 and Figure 3 demonstrate a decreasing trend in the concentration of PM10 and PM2.5 in the atmosphere. The concentration of PM10 decreased from 70.78 $\mu m/m^3$ in 2001 to 47.62 $\mu m/m^3$. Similarly, the concentration of PM2.5 decreased from 36.03 $\mu m/m^3$ in 2005 to 21.80 $\mu m/m^3$ in 2015.

Table 2 and Figure 4 indicate an increase in the annual average concentration of O_3 over the past 20 years. The concentration of O_3 rose from 21.27 ppb in 2001 to 29.51 ppb in 2015.

Table 2 and Figure 5 demonstrate an increase in the annual average environmental temperature and relative humidity over the past 20 years. The annual average environmental temperature rose from 23.41°C in 2001 to 24.21°C in 2015, indicating an increase of approximately 1°C from 2001 to 2015. On the other hand, the relative humidity increased from 72.87% in 2004 to 75.32% over the same period.

3.3. Correlation between air pollutants and climate factors

Table 3-1 illustrates the correlation coefficients calculated by Spearman correlation analysis between air pollutants and climate factors in the 2001 survey, for which air pollution and climate data were selected between 1994 and 2000. The correlation coefficients of CO and NO were 0.71; the correlation coefficients of NO and NO_2 were 0.71; and the correlation coefficients of NO and O_3 were - 0.76.

Table 3-2 illustrates the correlation coefficients calculated by Spearman correlation analysis between air pollutants and climate factors in the 2011 survey, for which air pollution and climate data were selected between 2004 and 2010. The correlation coefficients of CO and NO were 0.77; the correlation coefficients of NO and NO_2 were 0.84; the correlation coefficients of CO and NO_2 were 0.87; and the correlation coefficients of PM2.5 and PM10 were 0.90.

Table 3-3 illustrates the correlation coefficients calculated by Spearman correlation analysis between air pollutants and climate factors in the 2016 survey, for which air pollution and climate data were selected between 2009 and 2015. The correlation coefficients of CO and NO were 0.74; the correlation coefficients of NO and NO_2 were 0.83; the correlation coefficients of CO and NO_2 were 0.92; The

doi:10.6342/NTU202400166

correlation coefficients of $PM_{2.5}$ and PM10 were 0.79; and the correlation coefficients of SO_2 and NO_2 were 0.74.

In summary, almost all air pollutant concentrations except O_3 showed a decreasing trend after 1994. O_3 showed an increased trend between 1994 and 2015. Climate factors such as ambient temperature and related humidity have increased in the last two decades. NO, and NO_2 show a positive correlation with CO; NO_2 shows a positive correlation with NO; and $PM_{2.5}$ shows a positive correlation with PM10 in these three surveys. In the 2001 survey, O_3 showed a negative correlation with NO. In the 2016 survey, NO_2 showed a positive correlation with SO_2.

3.4 Risk of allergic disease

3.4.1 Risk of asthma

Table 4-1 shows the relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed asthma in a single-pollutant model. In the survey conducted in 2001, there was a statistically significant relationship between the prevalence of asthma and the impact of CO and NO, indicating that they were risk factors for asthma prevalence. The point estimate for CO was 1.10, with a 95% confidence interval (CI) of 1.06 to 1.15. The point estimate for NO was 1.06, with a 95% CI of 1.03 to 1.09. In the survey conducted in 2016-2017, ambient temperature, CO, O_3, PM10, and $PM_{2.5}$ showed a statistically significant relationship with the prevalence of asthma. CO was identified as a risk factor for asthma prevalence, with a point estimate of 1.03 and a 95% CI of 1.01 to 1.06. Ambient temperature was found to be a protective factor for asthma prevalence, with a point estimate of 0.82 and a 95% CI of 0.68 to 0.97. O_3, PM10, and $PM_{2.5}$ exhibited a negative effect in this analysis.

After meta-analysis, the ORs of CO divided by ten times ppm and ambient temperature for the prevalence of asthma in children were 1.04 (95% CI: 1.02-1.06) and 0.90 (95% CI: 0.83-0.98), respectively.

3.4.2 Risk of allergic rhinitis

doi:10.6342/NTU202400166

Table 4-2 shows relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed allergic rhinitis in single-pollutant model. In the survey conducted in 2001, there was a statistically significant relationship between ambient temperature and the prevalence of allergic rhinitis. Ambient temperature had a positive effect on the prevalence of allergic rhinitis, with a point estimate of 1.06 and a 95% confidence interval (CI) of 1.03 to 1.09. In the survey conducted in 2011, ambient temperature showed a negative effect on the prevalence of allergic rhinitis, with a point estimate of 0.85 and a 95% CI of 0.77 to 0.93. In the survey conducted in 2016-2017, CO, SO_2, and NO_2 showed a statistically significant relationship with the prevalence of allergic rhinitis, and they were identified as risk factors for allergic rhinitis prevalence. The point estimate for CO was 1.02, with a 95% CI of 1.01 to 1.03. The point estimate for SO_2 was 1.09, with a 95% CI of 1.03 to 1.16. The point estimate for NO_2 was 1.04, with a 95% CI of 1.02 to 1.05.

After meta-analysis, the ORs of CO, which were divided by ten times ppm, NO/ppb, and NO_2/ppb for the prevalence of allergic rhinitis in children, were 1.02 (95% CI: 1.01–1.03), 1.004 (95% CI: 1.002-1.005), and 1.011 (95% CI: 1.006–1.005), respectively.

3.4.3 Risk of atopic dermatitis

Table 4-3 shows relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed atopic dermatitis in single-pollutant model. In the survey conducted in 2011, CO, NO, and NO_2 showed a statistically significant relationship with the prevalence of atopic dermatitis, and they were identified as risk factors for atopic dermatitis prevalence. The point estimate for CO was 1.12, with a 95% confidence interval (CI) of 1.05 to 1.19. The point estimate for NO was 1.05, with a 95% CI of 1.02 to 1.08. The point estimate for NO_2 was 1.18, with a 95% CI of 1.07 to 1.30.

After meta-analysis, we did not observe statistically significant effects of these air pollutants and climate factors on the prevalence of atopic dermatitis in children.

doi:10.6342/NTU202400166

Chapter 4 Discussion

4.1 Risk potential to lifetime prevalence of Asthma

4.1.1 Major finding

The prevalence of physician-diagnosed asthma showed an increase first and then a decrease after 2011.

We estimated the relationship between CO, NO, and asthma in the 2001 survey and discovered a 1.10-fold increase in the odds of asthma; for NO, every 1 ppb increase increased the odds of ever having a doctor's diagnosis of asthma among 12- to 15-year-old secondary school students by 1.06 times. And then, we evaluated the association between CO, O_3, $PM_{2.5}$, PM10, ambient temperature, and asthma in the 2016 survey and discovered substantial differences. In terms of CO, the odds of ever having it were 1.03 times higher for every 1 ppm increase in CO than the odds of ever being diagnosed with asthma by a physician. O_3, $PM_{2.5}$, and PM10, on the other hand, had a detrimental effect on the prevalence of asthma in children.

In meta-analysis, the ORs of CO divided by ten times ppm shows a risk factor for asthma prevalence and ambient temperature shows a protective factor for it.

4.1.2 Consistency with previous studies

In Taiwan, the prevalence of asthma in children aged 5 – 14 years declined significantly between 1994 and 2011; in Japan, it declined significantly after 1990 and began to rise in 2009; in mainland China, it was lower than in other countries at the beginning and began to rise rapidly around 2014, surpassing Japan in 2017, and then declining. Wei-Yu Chen et al. reported in Taiwan that the prevalence of physician-diagnosed asthma decreased after 2011, which is consistent with our findings (Chen et al., 2021). A 2016 Korean study found that all-age asthma-diagnosed cases declined from 2009 to 2014, with younger children under 10 diagnosed more often than older (Kim et al., 2016).

In a 2003 paper, the OR of CO on the prevalence of asthma in children was 1.37

doi:10.6342/NTU202400166

(95% CI: 1.14–1.65) (Lee, Lin, et al., 2003). According to Yuewei Liu et al., the OR of NO_2 on patient death due to asthma was 1.11 (95% CI: 1.01-1.22) (Liu et al., 2019). Chan Lu reported a prevalence of NO2 in asthmatic children of 1.17 (95% CI: 1.06-1.28) in 2022. Chan Lu et al. found that asthma prevalence in children increased with ambient temperature and decreased with it. However, rising and lowering temperature had different impacts (Lu et al., 2022).

In meta-analysis, the ORs of CO, which were divided by ten times ppm, NO/ppb, and NO_2/ppb shows risk factors for the prevalence of allergic rhinitis in children. However because of the heterogeneity in ambient temperature ORs, ambient temperature shows no significant effect on the prevalence of allergic rhinitis.

4.1.3 Potential explanations

In the case of high temperatures, reducing the temperature may be a protective factor for the occurrence of asthma in children. Higher temperatures may increase the prevalence of asthma in children by directly impacting the child's respiratory system or by influencing the mother's condition during pregnancy (Lu et al., 2022).

O_3 and NO are risk factors for childhood asthma prevalence. These traffic-related air pollutants (TRAP) can induce airway oxidative stress, which can lead to airway oxidative damage (Guarnieri & Balmes, 2014)

As shown in tables 3-1 and 3-3, the Spearman correlation coefficient of O_3 and NO in surveys conducted in 2001 and 2016 is close to -0.70, indicating a strong negative correlation. This may explain the negative effect of O_3 on asthma prevalence in children..

PM10 and PM2.5: Because the air measuring stations in eastern Taiwan (Hualien, Yilan, Taitung) have fewer air measuring stations but cover a greater area, the schools and measuring stations in eastern Taiwan were later deleted to avoid this effect. The statistical significance of the negative effect of PM10 on lifetime asthma vanished after excluding schools and stations in eastern Taiwan in the survey 2001, although its point estimate remained negative; in the survey 2016, the negative effect of PM10 and

doi:10.6342/NTU202400166

PM2.5 on lifetime asthma vanished. The statistical significance remained. We believe this is related to the faster decline in PM10 and PM2.5 concentrations in the atmosphere: the annual mean PM concentration decreased by 11 from 1994 to 2000; from 2009 to 2015, the annual mean PM10 temperature reduced by 8 and the annual mean PM2.5 concentration decreased by 11. Although the PM10 concentration in the survey 2016 did not decline as quickly as it did in the survey 2001, it did fall within the Taiwan EPA's recommended range (annual average yearly mean concentration of 50 $\mu g/m^3$).

4.2 Risk potential to lifetime prevalence of allergic rhinitis

4.2.1 Major finding

The prevalence of allergic rhinitis showed an increase between 2001 and 2016.

In 2001, we found a substantial association between ambient temperature and allergic rhinitis. For every degree Celsius increase in ambient temperature, the prevalence of allergic rhinitis among 12- to 15-year-old secondary school pupils increased 1.06 times. However, the Ambient temperature was the opposite in the 2011 survey. Secondary school children aged 12-15 had 0.85 times less allergic rhinitis per degree Celsius of ambient temperature. CO, SO_2, and NO_2 showed significantly affected allergic rhinitis prevalence in 2016. Among them, for every 1 ppm increase in CO, the prevalence of allergic rhinitis among schoolchildren ever diagnosed by a doctor increased by 1.02 times; for every 1 ppb increase in SO_2, it increased by 1.09 times; and for every 1 ppb increase in NO_2, it increased by 1.04 times. O_3 had a negative effect.

4.2.2 Consistency with previous studies

In Korea, which is close to Taiwan, the prevalence of allergic rhinitis increased in all age groups from 2009 to 2014, especially in children younger than 10 years old (Kim et al., 2016).

A 2021 meta-analysis found that for every 10 $\mu g/m^3$ NO2 rise, the prevalence of allergic rhinitis in the all-age population was 1.13 (95% CI: 1.07-1.20); for every 10

doi:10.6342/NTU202400166

μg/m^3 SO2 increased, it was 1.13 (95%: 1.04-1.22) (Li et al., 2022). The OR for the effect of CO on allergic rhinitis in children in Taiwan was reported to be 1.01 (1.04-1.11) for the period 2004-2013 (Hsieh et al., 2020).

4.2.3 Potential explanations

CO, SO_2, and NO_2 increase allergic rhinitis risk. Air pollutants may cause AR by mediating the response to nasal allergens, damaging the nasal mucosa, inducing nasal airway inflammation, and overproducing IgE antibodies that sensitize the airways to allergens (Chen et al., 2016). Air pollution may promote inflammation, oxidative stress, and immunosuppression, although the exact cause is unknown (Shankar & Mehendale, 2014). Meanwhile, higher SO_2, NO_2, and PM10 levels enhanced AR risk in the warm season compared to the cold season (Bousquet et al., 2008).

Cold temperature worsens asthma and AR (Hyrkas et al., 2014). In our 2001 survey, the average lowest temperature was 10.34°C in 1994-2000 and 8°C in 1999. The 2001 survey found a statistically significant association between ambient temperature and child AR prevalence. The chilly climate may be for a reason. The average highest temperature in the survey year of 2011 was 31°C and the lowest temperature was 11°C. We suspect various causes: 1) Taiwan's latitude leans toward the middle and low latitudes, which are more adapted to high temperatures; 2) it may be related to schoolchildren's personal activities, such as school vacations and air conditioning at home during hot summer holidays.

Since the concentration of air pollutants is gradually decreasing, basically down to within the annual average concentration range specified by the Taiwan EPA, while the prevalence of allergic rhinitis is increasing, we believe that other factors, such as urbanization, green space influence, pollen allergy, etc., also affect it.

As shown in tables 3-1 and 3-3, in surveys conducted in 2001 and 2016, the spearman correlation between O_3 and NO coefficient is close to -0.70, indicating a strong negative correlation. This may explain the negative effect of O_3 on the prevalence of allergic rhinitis in children.

doi:10.6342/NTU202400166

4.3 Risk potential to lifetime prevalence of atopic dermatitis

4.3.1 Major finding

The prevalence of physician diagnosis Atopic dermatitis showed an increasing trend from 2001 to 2016.

In our 2011 survey of 12-15-year-old middle school kids with physician-diagnosed atopic dermatitis, CO, NO, and NO_2 were substantially linked with prevalence. For each 1 ppm increase in CO, the prevalence of atopic dermatitis in schoolchildren increased by 1.12 times; for each 1 ppb increase in NO, it increased by 1.05 times; and for each 1 ppb increase in NO_2, it increased by 1.05 times. Atopic dermatitis in schoolchildren increased 1.14 times for each 1 ppb increase in NO_2;

The meta-analysis did not observe the statistically significant effects of these air pollutants and climate factors on the prevalence of atopic dermatitis in children. A possible explanation is that the incidence or prevalence of atopic dermatitis is extremely low across the entire dataset. Moreover, a cross-sectional analysis of these three years reveals a significant difference in the proportion or number of AD cases. This would lead to potential errors in the results due to an imbalance in the weight distribution of the three-year OR pooling in the meta-analysis.

4.3.2 Consistency with previous studies

Atopic dermatitis in children aged 5 – 12 years in Taiwan had a gentle upward trend from 2000–2010, a downward trend from 2010–2015, and then a slow rise. The lowest prevalence of atopic dermatitis in children was in mainland China, which remained steady from 1990 to 2015 and increased from 2017 to 2018, while Korean children remained stable.

In 2022, a literature from mainland China revealed that in Chongqing, children were 5.5 times (95% CI: 4.3 - 6.7) more likely to visit the hospital for AD for every 10 g/m3 NO_2 increase; 11 times (95% CI: 7.5-14.7) more likely to visit the hospital for AD for every 10 g/m^3 SO_2 increase; and 10.1 times (95% CI: 2.7-18.2) more likely to visit the hospital for every 11 mg/m^3 . The study also discovered that SO_2, PM10,

doi:10.6342/NTU202400166

and NO_2 had a greater impact during the colder months, and that children aged 0 to 3 years were more sensitive to air pollutants in AD (Luo et al., 2022).

4.3.3 Possible mechanism

Air pollution's effect on AD in children may be influenced by oxidative stress damage to the skin barrier, increased water loss, physicochemical damage, and effects on the skin microbiota. Furthermore, oxidative stress causes immunological dysregulation, which leads to increased sensitivity to allergens. Because of the many confounding factors in the current study, such as climate, synergistic effects of mixed pollutants, and the diversity of the study population, there are differences in the relationship between AD and air pollution between different years of investigation, so inconsistent effects may occur.

4.4 Strength

This study has several advantages. First, we use the study's nationwide scope to ensure that the study population is representative of the overall population (Chen et al., 2019b). Second, while our data comes from the station EPA, we apply GEE to overcome the problem of repeated measurements and determine each student's exposure to air pollutants and climate conditions at three levels: stations-school-sstudents. Third, compared to earlier studies, we gathered information from three questionnaire studies, 2001, 2011, and 2016. We pooled it to determine the association between allergy illnesses, air pollutants, and climate factors during the last ten years. Fourth, because there is no information on the onset of allergic diseases, we used air pollutant and climate data for the seven years preceding the study investigation, including the age at which children with asthma, allergic rhinitis, and atopic dermatitis were most commonly diagnosed, which is consistent with the causal relationship of exposure first and disease second.

4.5 Limitation

1. We do not know how much time people spend indoors or outside, which may

doi:10.6342/NTU202400166

affect air pollution exposure estimate.

2. Family migration may be a limitation in our study because we do not have this data. However, in 2009–2019, the migration rate of Taiwanese residents by county and city ranged from 82.22‰ to 70.06‰, according to the Ministry of the Interior (內政部統計處, 2020). We assume that the impact will not be substantial if Taiwan's migration rate is comparable to that of child families. Errors will occur if there is a mass migration of child families to the selected institutions.

doi:10.6342/NTU202400166

Chapter 5 Conclusion and Recommendation

Conclusion

Between 1994 and 2015, CO, NO, NO_2, SO_2, PM10, and PM2.5 levels drastically dropped. The prevalence of the three allergy disorders varied during the previous three survey years. Between 2001 and 2016, the prevalence of Lifetime physician-diagnosed asthma increased, then decreased; the prevalence of Lifetime physician-diagnosed allergic rhinitis increased and had the highest prevalence; and the prevalence of Lifetime physician-diagnosed atopic rhinitis was the highest. The prevalence of physician-diagnosed atopic dermatitis increased gradually.

The decrease rate in air pollutant concentrations may be related to a decrease in the prevalence of physician-diagnosed asthma over a lifetime. At low doses, lifetime physician-diagnosed allergic rhinitis and lifetime physician-diagnosed atopic dermatitis are not highly related to reducing air pollution concentrations. In terms of climatic conditions, the prevalence of asthma and allergic rhinitis was affected by ambient temperature.

Recommendation

We employed the longitude strategy in this work to review previous allergy illnesses. However, further research is needed to determine how specific temperatures and humidity affect asthma and allergic rhinitis in children.

doi:10.6342/NTU202400166

References

Aldakheel, F. M. (2021). Allergic Diseases: A Comprehensive Review on Risk Factors, Immunological Mechanisms, Link with COVID-19, Potential Treatments, and Role of Allergen Bioinformatics. *Int J Environ Res Public Health*, *18*(22). https://doi.org/10.3390/ijerph182212105

Annesi-Maesano, I. (2015). It is not time to lower the guard! *Eur Respir J*, *45*(3), 589-591. https://doi.org/10.1183/09031936.00008415

Bousquet, J., Khaltaev, N., Cruz, A. A., Denburg, J., Fokkens, W. J., Togias, A., Zuberbier, T., Baena-Cagnani, C. E., Canonica, G. W., van Weel, C., Agache, I., Ait-Khaled, N., Bachert, C., Blaiss, M. S., Bonini, S., Boulet, L. P., Bousquet, P. J., Camargos, P., Carlsen, K. H., Chen, Y., Custovic, A., Dahl, R., Demoly, P., Douagui, H., Durham, S. R., van Wijk, R. G., Kalayci, O., Kaliner, M. A., Kim, Y. Y., Kowalski, M. L., Kuna, P., Le, L. T., Lemiere, C., Li, J., Lockey, R. F., Mavale-Manuel, S., Meltzer, E. O., Mohammad, Y., Mullol, J., Naclerio, R., O'Hehir, R. E., Ohta, K., Ouedraogo, S., Palkonen, S., Papadopoulos, N., Passalacqua, G., Pawankar, R., Popov, T. A., Rabe, K. F., Rosado-Pinto, J., Scadding, G. K., Simons, F. E., Toskala, E., Valovirta, E., van Cauwenberge, P., Wang, D. Y., Wickman, M., Yawn, B. P., Yorgancioglu, A., Yusuf, O. M., Zar, H., Annesi-Maesano, I., Bateman, E. D., Ben Kheder, A., Boakye, D. A., Bouchard, J., Burney, P., Busse, W. W., Chan-Yeung, M., Chavannes, N. H., Chuchalin, A., Dolen, W. K., Emuzyte, R., Grouse, L., Humbert, M., Jackson, C., Johnston, S. L., Keith, P. K., Kemp, J. P., Klossek, J. M., Larenas-Linnemann, D., Lipworth, B., Malo, J. L., Marshall, G. D., Naspitz, C., Nekam, K., Niggemann, B., Nizankowska-Mogilnicka, E., Okamoto, Y., Orru, M. P., Potter, P., Price, D., Stoloff, S. W., Vandenplas, O., Viegi, G., Williams, D., World Health, O., Galen, & AllerGen. (2008). Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*, *63 Suppl 86*, 8-160. https://doi.org/10.1111/j.1398-9995.2007.01620.x

Chen, B. Y., Chen, C. H., Chuang, Y. C., Wu, Y. H., Pan, S. C., & Guo, Y. L. (2019a). Changes in the relationship between ambient fine particle concentrations and childhood lung function over 5 years. *Environ Res*, *179*(Pt B), 108809. https://doi.org/10.1016/j.envres.2019.108809

Chen, B. Y., Chen, C. H., Chuang, Y. C., Wu, Y. H., Pan, S. C., & Guo, Y. L. (2019b). Changes in the relationship between childhood asthma and ambient air pollution in Taiwan: Results from a nationwide survey repeated 5 years apart. *Pediatr Allergy Immunol*, *30*(2), 188-194. https://doi.org/10.1111/pai.12999

Chen, C. C., Chiu, H. F., & Yang, C. Y. (2016). Air pollution exposure and daily clinical visits for allergic rhinitis in a subtropical city: Taipei, Taiwan. *J Toxicol Environ Health A*, *79*(12), 494-501. https://doi.org/10.1080/15287394.2016.1182002

Chen, W. Y., Lin, C. W., Lee, J., Chen, P. S., Tsai, H. J., & Wang, J. Y. (2021). Decreasing ten-year (2008-2018) trends of the prevalence of childhood asthma and air pollution in Southern Taiwan. *World Allergy Organ J*, *14*(5), 100538. https://doi.org/10.1016/j.waojou.2021.100538

D'Amato, G., Holgate, S. T., Pawankar, R., Ledford, D. K., Cecchi, L., Al-Ahmad, M., Al-Enezi, F., Al-Muhsen, S., Ansotegui, I., Baena-Cagnani, C. E., Baker, D. J., Bayram, H., Bergmann, K. C., Boulet, L. P., Buters, J. T., D'Amato, M., Dorsano, S., Douwes, J., Finlay, S. E., Garrasi, D., Gomez, M., Haahtela, T., Halwani, R., Hassani, Y., Mahboub, B., Marks, G., Michelozzi, P., Montagni, M., Nunes, C., Oh, J. J., Popov, T. A., Portnoy, J., Ridolo, E., Rosario, N., Rottem, M., Sanchez-Borges, M., Sibanda, E., Sienra-Monge, J. J., Vitale, C., & Annesi-Maesano, I. (2015).

doi:10.6342/NTU202400166

Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ J*, *8*(1), 25. https://doi.org/10.1186/s40413-015-0073-0

Eguiluz-Gracia, I., Mathioudakis, A. G., Bartel, S., Vijverberg, S. J. H., Fuertes, E., Comberiati, P., Cai, Y. S., Tomazic, P. V., Diamant, Z., Vestbo, J., Galan, C., & Hoffmann, B. (2020). The need for clean air: The way air pollution and climate change affect allergic rhinitis and asthma. *Allergy*, *75*(9), 2170-2184. https://doi.org/10.1111/all.14177

Eichenfield, L. F., Tom, W. L., Chamlin, S. L., Feldman, S. R., Hanifin, J. M., Simpson, E. L., Berger, T. G., Bergman, J. N., Cohen, D. E., Cooper, K. D., Cordoro, K. M., Davis, D. M., Krol, A., Margolis, D. J., Paller, A. S., Schwarzenberger, K., Silverman, R. A., Williams, H. C., Elmets, C. A., Block, J., Harrod, C. G., Smith Begolka, W., & Sidbury, R. (2014). Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*, *70*(2), 338-351. https://doi.org/10.1016/j.jaad.2013.10.010

Engebretsen, K. A., Johansen, J. D., Kezic, S., Linneberg, A., & Thyssen, J. P. (2016). The effect of environmental humidity and temperature on skin barrier function and dermatitis. *J Eur Acad Dermatol Venereol*, *30*(2), 223-249. https://doi.org/10.1111/jdv.13301

EPA, Q. (2023). *Nitrogen oxides*. Retrieved 7/7 from https://www.qld.gov.au/environment/management/monitoring/air/air-pollution/pollutants/nitrogen-oxides#:~:text=The%20term%20nitrogen%20oxides%20(NOx,atmosphere%20to%20form%20nitrogen%20dioxide.

EPA, Q. G. (2023). *Particles*. Retrieved 7/7 from https://www.qld.gov.au/environment/management/monitoring/air/air-pollution/pollutants/particles

EPA, U. S. (2023a). *Basic Information about Carbon Monoxide (CO) Outdoor Air Pollution*. Retrieved 7/7 from https://www.epa.gov/co-pollution/basic-information-about-carbon-monoxide-co-outdoor-air-pollution

EPA, U. S. (2023b). *Ground-level Ozone Basics*. Retrieved 7/7 from https://www.epa.gov/ground-level-ozone-pollution/ground-level-ozone-basics#wwh

Feng, S., Gao, D., Liao, F., Zhou, F., & Wang, X. (2016). The health effects of ambient PM2.5 and potential mechanisms. *Ecotoxicol Environ Saf*, *128*, 67-74. https://doi.org/10.1016/j.ecoenv.2016.01.030

Gowers, A. M., Cullinan, P., Ayres, J. G., Anderson, H. R., Strachan, D. P., Holgate, S. T., Mills, I. C., & Maynard, R. L. (2012). Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; a review. *Respirology*, *17*(6), 887-898. https://doi.org/10.1111/j.1440-1843.2012.02195.x

Guarnieri, M., & Balmes, J. R. (2014). Outdoor air pollution and asthma. *Lancet*, *383*(9928), 1581-1592. https://doi.org/10.1016/S0140-6736(14)60617-6

Hsieh, S.-P., Hsieh, C.-J., Tseng, C.-C., & Yiin, L.-M. (2020). Allergic Rhinitis: Association with Air Pollution and Weather Changes, and Comparison with That of Allergic Conjunctivitis in Taiwan. *Atmosphere*, *11*(11). https://doi.org/10.3390/atmos11111152

Hyrkas, H., Jaakkola, M. S., Ikaheimo, T. M., Hugg, T. T., & Jaakkola, J. J. (2014). Asthma and allergic rhinitis increase respiratory symptoms in cold weather among young adults. *Respir Med*, *108*(1), 63-70. https://doi.org/10.1016/j.rmed.2013.10.019

doi:10.6342/NTU202400166

Khraishah, H., Alahmad, B., Ostergard, R. L., Jr., AlAshqar, A., Albaghdadi, M., Vellanki, N., Chowdhury, M. M., Al-Kindi, S. G., Zanobetti, A., Gasparrini, A., & Rajagopalan, S. (2022). Climate change and cardiovascular disease: implications for global health. *Nat Rev Cardiol*, *19*(12), 798-812. https://doi.org/10.1038/s41569-022-00720-x

Kim, B. K., Kim, J. Y., Kang, M. K., Yang, M. S., Park, H. W., Min, K. U., Cho, S. H., & Kang, H. R. (2016). Allergies are still on the rise? A 6-year nationwide population-based study in Korea. *Allergol Int*, *65*(2), 186-191. https://doi.org/10.1016/j.alit.2015.11.002

Lee, Y. L., Hwang, B. F., Lin, Y. C., Guo, Y. L., & Taiwan Childhood Allergy Survey, G. (2007). Time trend of asthma prevalence among school children in Taiwan. [corrected]. *Pediatr Allergy Immunol*, *18*(3), 188-195. https://doi.org/10.1111/j.1399-3038.2006.00504.x

Lee, Y. L., Lin, Y. C., Hsiue, T. R., Hwang, B. F., & Guo, Y. L. (2003). Indoor and outdoor environmental exposures, parental atopy, and physician-diagnosed asthma in Taiwanese schoolchildren. *Pediatrics*, *112*(5), e389. https://doi.org/10.1542/peds.112.5.e389

Lee, Y. L., Lin, Y. C., Hwang, B. F., & Guo, Y. L. (2005). Changing prevalence of asthma in Taiwanese adolescents: two surveys 6 years apart. *Pediatr Allergy Immunol*, *16*(2), 157-164. https://doi.org/10.1111/j.1399-3038.2005.00211.x

Lee, Y. L., Shaw, C. K., Su, H. J., Lai, J. S., Ko, Y. C., Huang, S. L., Sung, F. C., & Guo, Y. L. (2003). Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. *Eur Respir J*, *21*(6), 964-970. https://doi.org/10.1183/09031936.03.00094602

Lee, Y. L., Su, H. J., Sheu, H. M., Yu, H. S., & Guo, Y. L. (2008). Traffic-related air pollution, climate, and prevalence of eczema in Taiwanese school children. *J Invest Dermatol*, *128*(10), 2412-2420. https://doi.org/10.1038/jid.2008.110

Li, S., Wu, W., Wang, G., Zhang, X., Guo, Q., Wang, B., Cao, S., Yan, M., Pan, X., Xue, T., Gong, J., & Duan, X. (2022). Association between exposure to air pollution and risk of allergic rhinitis: A systematic review and meta-analysis. *Environ Res*, *205*, 112472. https://doi.org/10.1016/j.envres.2021.112472

Liao, M. F., Huang, J. L., Chiang, L. C., Wang, F. Y., & Chen, C. Y. (2005). Prevalence of asthma, rhinitis, and eczema from ISAAC survey of schoolchildren in Central Taiwan. *J Asthma*, *42*(10), 833-837. https://doi.org/10.1080/02770900500369892

Liu, Y., Pan, J., Zhang, H., Shi, C., Li, G., Peng, Z., Ma, J., Zhou, Y., & Zhang, L. (2019). Short-Term Exposure to Ambient Air Pollution and Asthma Mortality. *Am J Respir Crit Care Med*, *200*(1), 24-32. https://doi.org/10.1164/rccm.201810-1823OC

Loftus, P. A., & Wise, S. K. (2015). Epidemiology and economic burden of asthma. *Int Forum Allergy Rhinol*, *5 Suppl 1*, S7-10. https://doi.org/10.1002/alr.21547

Lu, C., Zhang, Y., Li, B., Zhao, Z., Huang, C., Zhang, X., Qian, H., Wang, J., Liu, W., Sun, Y., Norback, D., & Deng, Q. (2022). Interaction effect of prenatal and postnatal exposure to ambient air pollution and temperature on childhood asthma. *Environ Int*, *167*, 107456. https://doi.org/10.1016/j.envint.2022.107456

Luo, P., Wang, D., Luo, J., Li, S., Li, M. M., Chen, H., Duan, Y., Fan, J., Cheng, Z., Zhao, M. M., Liu, X., Wang, H., Luo, X. Y., & Zhou, L. (2022). Relationship between air pollution and childhood atopic dermatitis in Chongqing, China: A time-series analysis. *Front Public Health*, *10*, 990464. https://doi.org/10.3389/fpubh.2022.990464

Maio, S., Baldacci, S., Carrozzi, L., Pistelli, F., Angino, A., Simoni, M., Sarno, G., Cerrai, S., Martini, F., Fresta, M., Silvi, P., Di Pede, F., Guerriero, M., & Viegi, G. (2016). Respiratory

doi:10.6342/NTU202400166

symptoms/diseases prevalence is still increasing: a 25-yr population study. *Respir Med*, *110*, 58-65. https://doi.org/10.1016/j.rmed.2015.11.006

Paciencia, I., Cavaleiro Rufo, J., & Moreira, A. (2022). Environmental inequality: Air pollution and asthma in children. *Pediatr Allergy Immunol*, *33*(6). https://doi.org/10.1111/pai.13818

Schuler Iv, C. F., & Montejo, J. M. (2019). Allergic Rhinitis in Children and Adolescents. *Pediatr Clin North Am*, *66*(5), 981-993. https://doi.org/10.1016/j.pcl.2019.06.004

Shankar, K., & Mehendale, H. M. (2014). Oxidative Stress. In *Encyclopedia of Toxicology* (pp. 735-737). https://doi.org/10.1016/b978-0-12-386454-3.00345-6

Stern, J., Pier, J., & Litonjua, A. A. (2020). Asthma epidemiology and risk factors. *Semin Immunopathol*, *42*(1), 5-15. https://doi.org/10.1007/s00281-020-00785-1

Weinmayr, G., Romeo, E., De Sario, M., Weiland, S. K., & Forastiere, F. (2010). Short-term effects of PM10 and NO2 on respiratory health among children with asthma or asthma-like symptoms: a systematic review and meta-analysis. *Environ Health Perspect*, *118*(4), 449-457. https://doi.org/10.1289/ehp.0900844

Zhang, Y., Lan, F., & Zhang, L. (2021). Advances and highlights in allergic rhinitis. *Allergy*, *76*(11), 3383-3389. https://doi.org/10.1111/all.15044

內政部統計處. (2020). *內政統計通報*.

doi:10.6342/NTU202400166

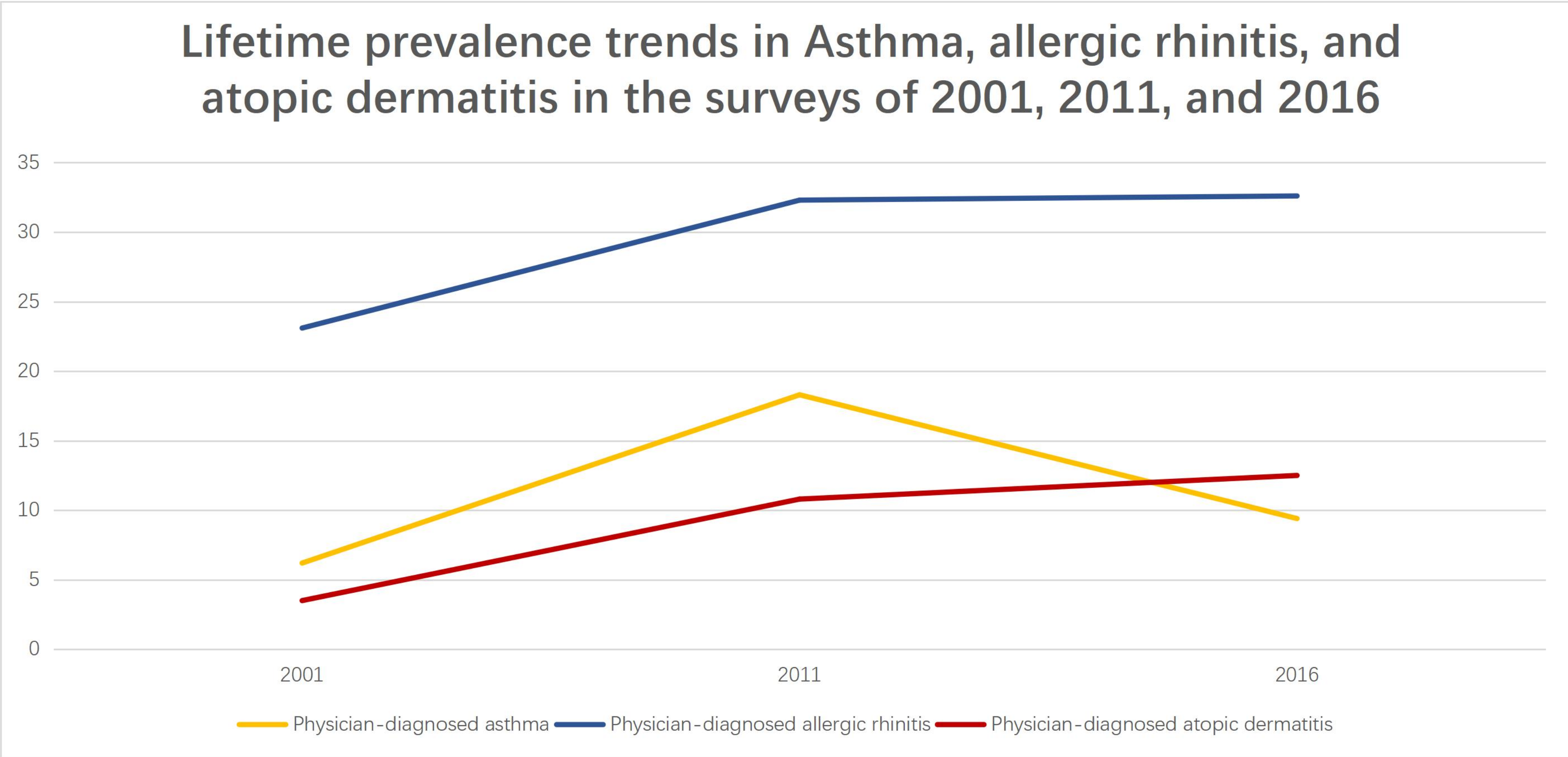

Figure 1 The trends of allergic diseases in Taiwan during the year 2001, 2011 and 2016

doi:10.6342/NTU202400166

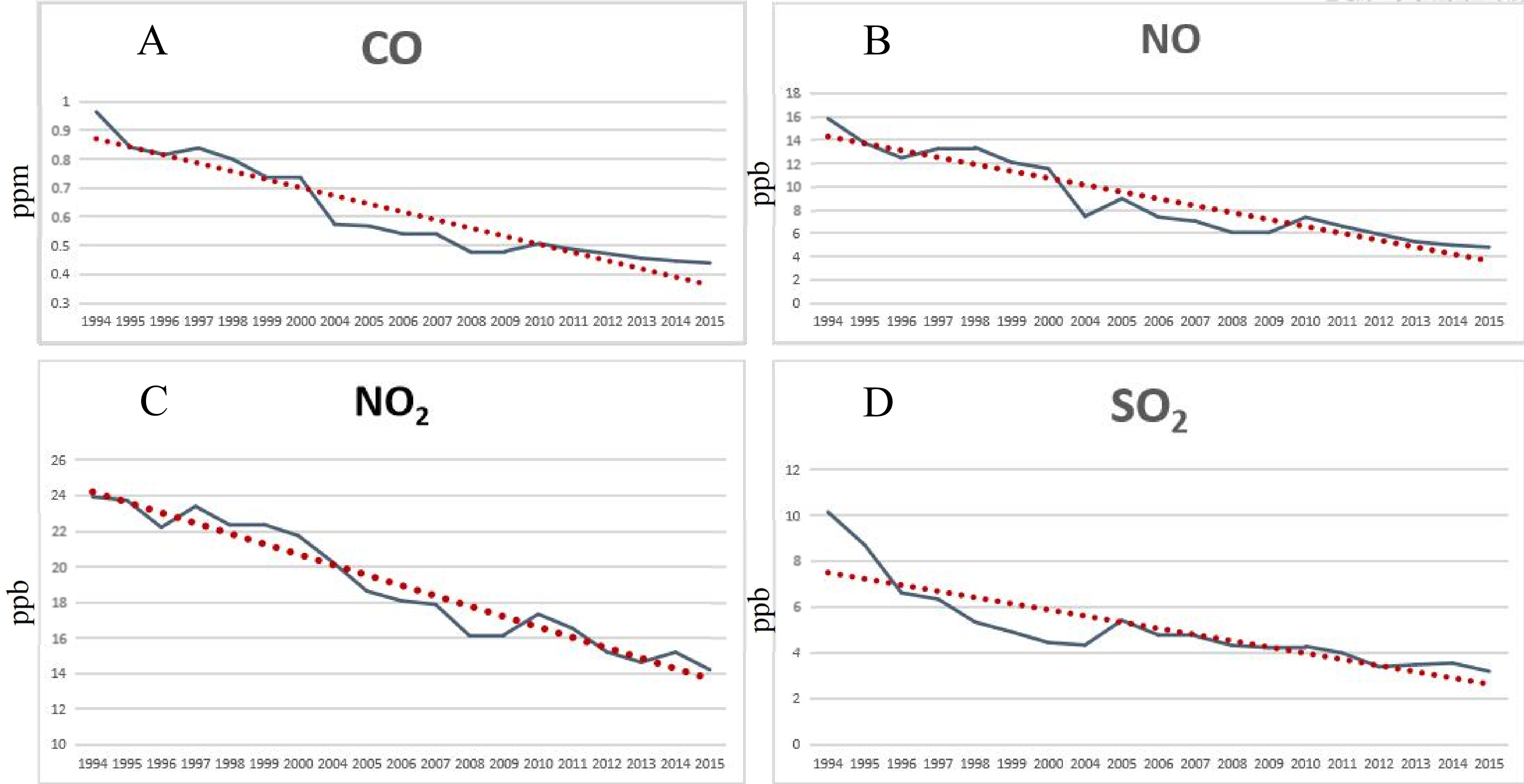

Figure 2 The trends of (A)CO, (B)NO, (C)NO_2 and (D)SO_2 in Taiwan during the year 1994 to 2015

doi:10.6342/NTU202400166

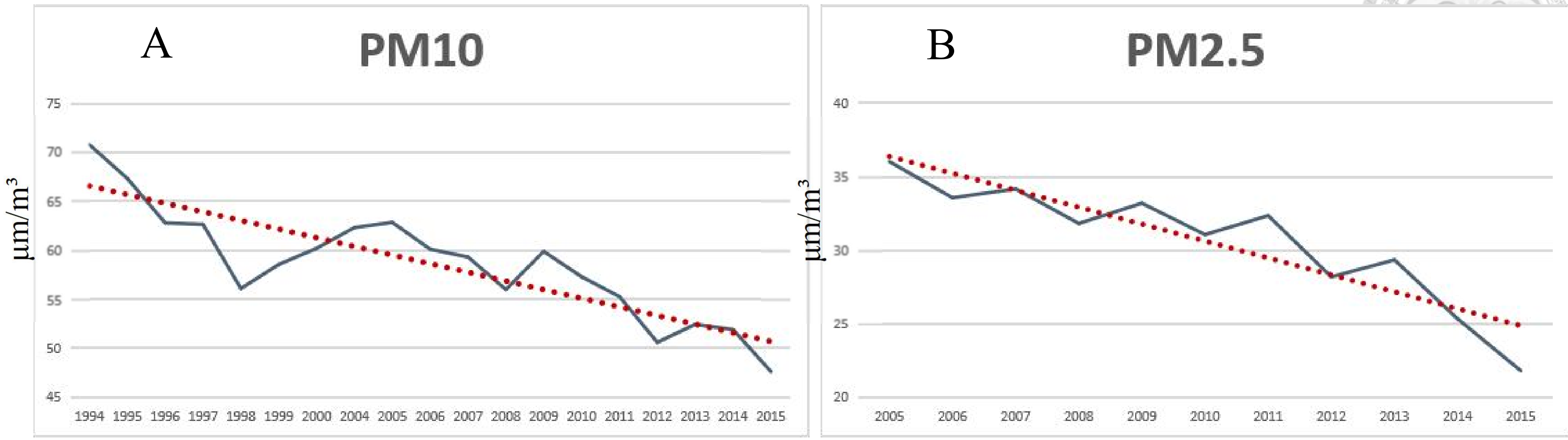

Figure 3 The trends of (A)PM10 and (B)PM2.5 in Taiwan during the year 1994 to 2015

doi:10.6342/NTU202400166

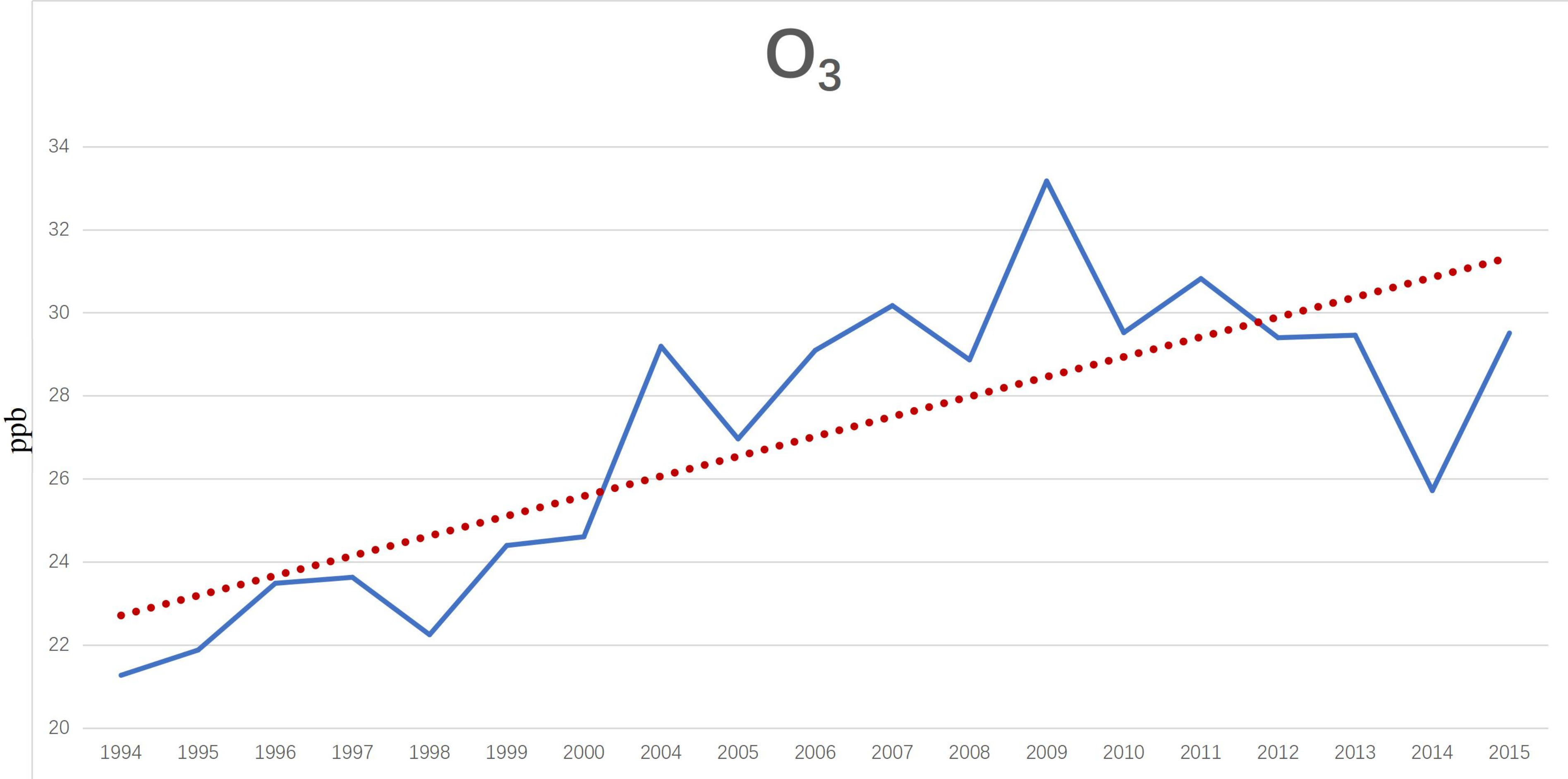

Figure 4 The trends of O_3 in Taiwan during the year 1994 to 2015

doi:10.6342/NTU202400166

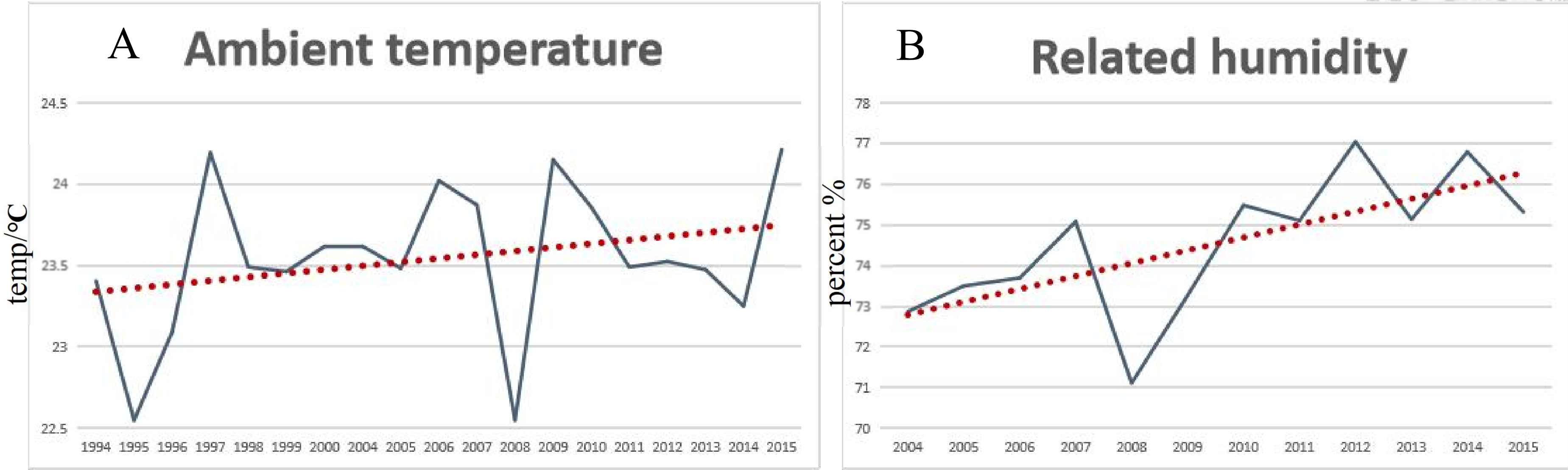

Figure 5 The trends of (A)ambient temperature and (B)related humidity in Taiwan during the year 1994 to 2015

doi:10.6342/NTU202400166

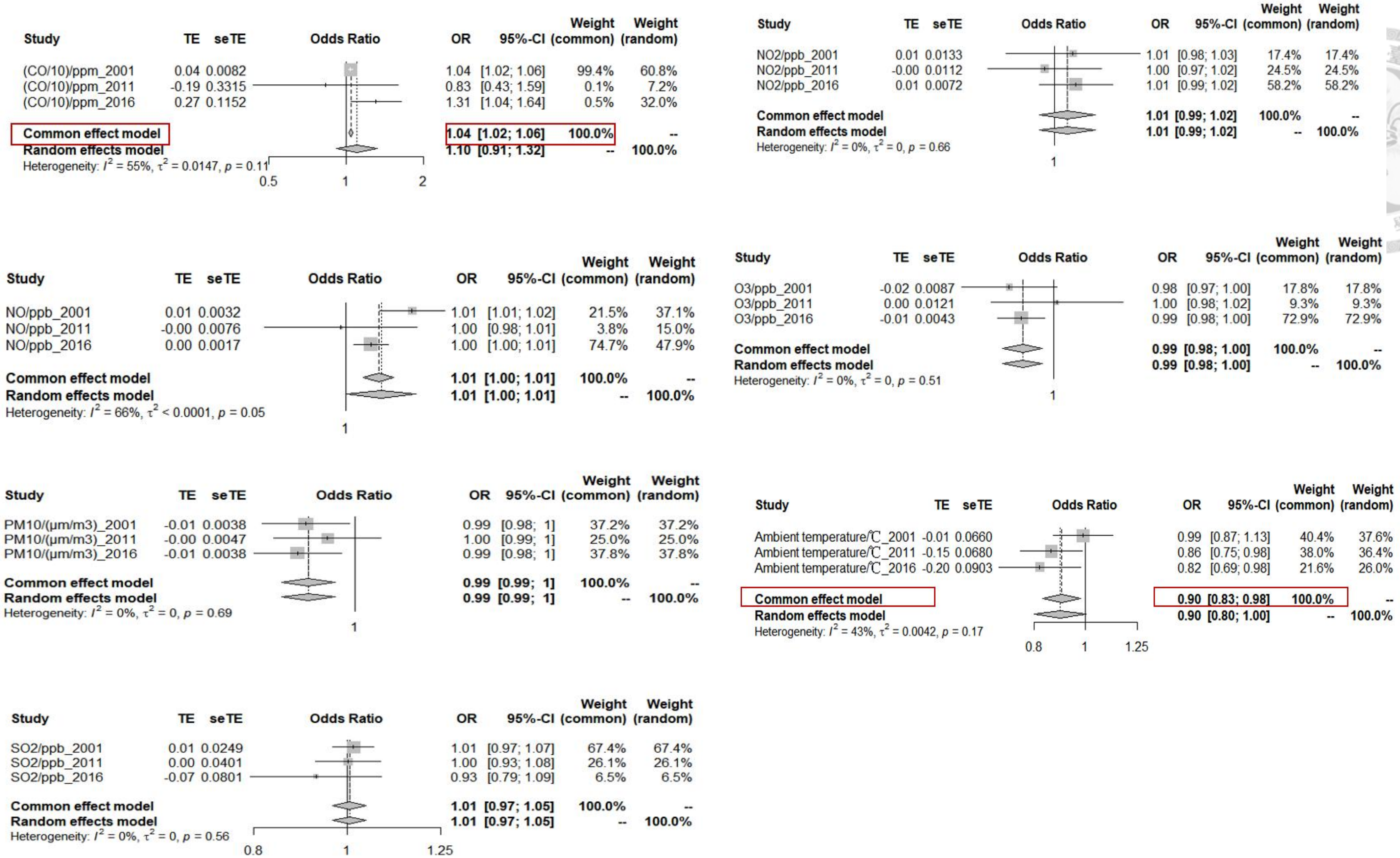

Figure 6 Meta-analysis for the odds ratio of asthma and air pollutant/climate factor in 2001, 2011, and 2016

doi:10.6342/NTU202400166

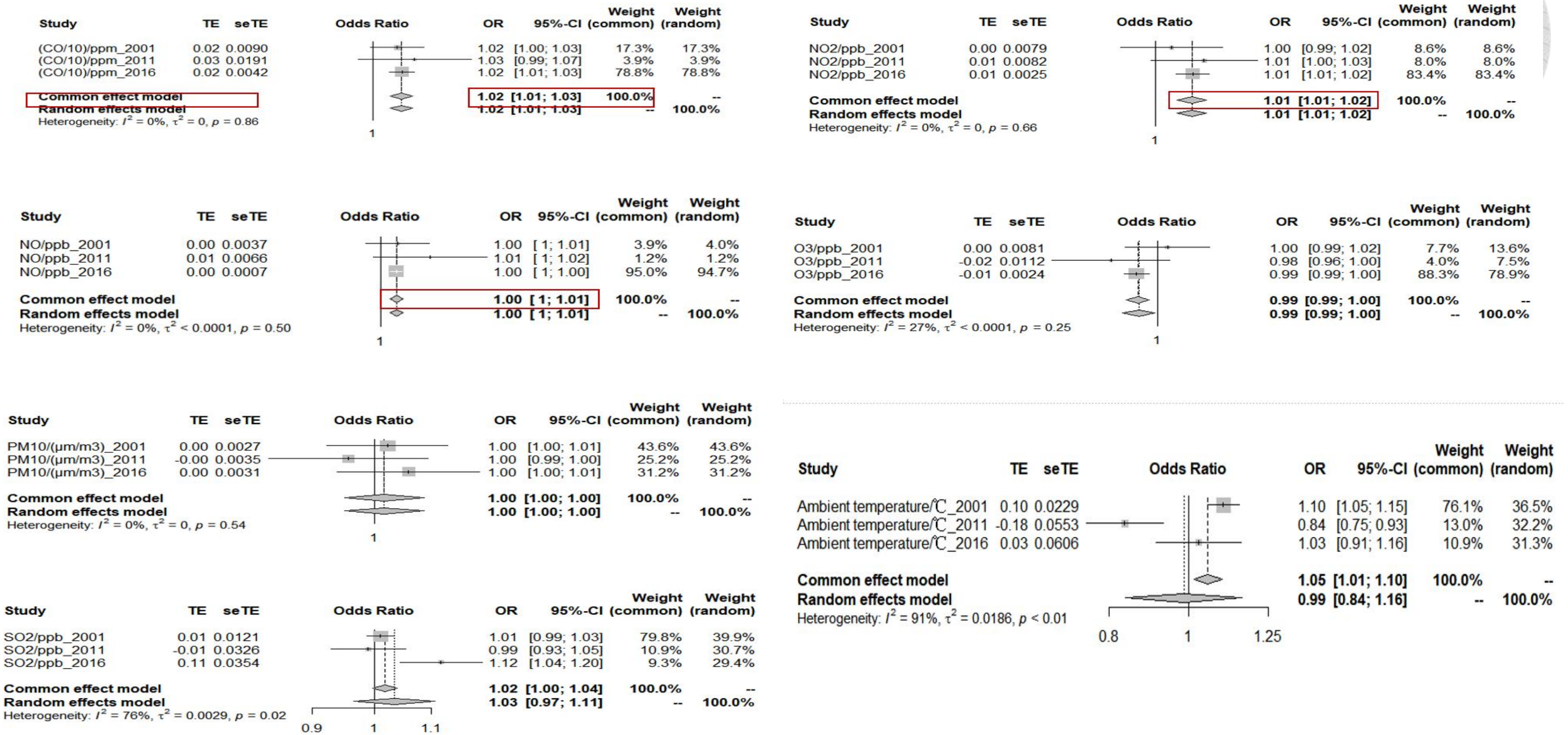

Figure 7 Meta-analysis for the odds ratio of allergic rhinitis and air pollutant/climate factor in 2001, 2011, and 2016

doi:10.6342/NTU202400166

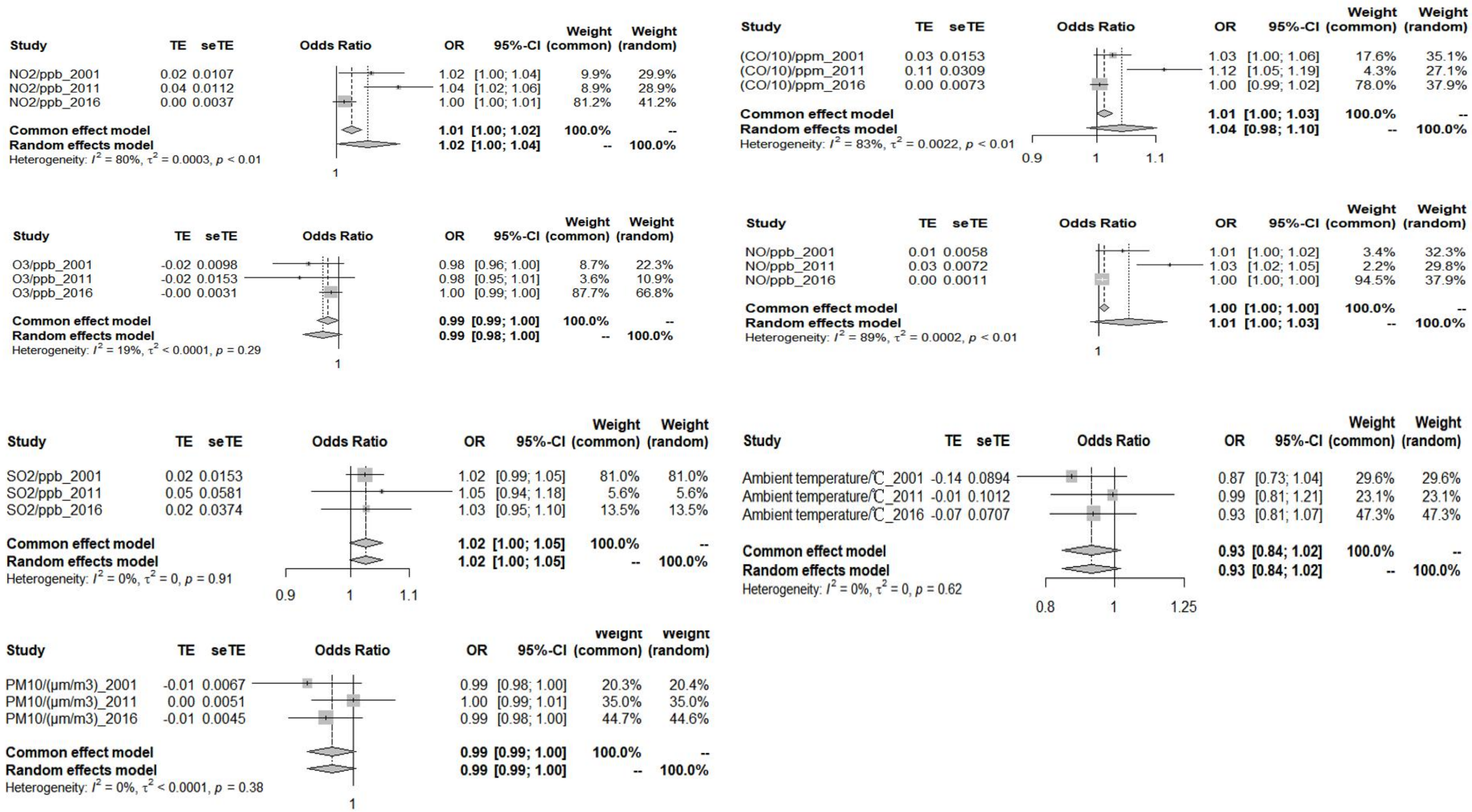

Figure 8 Meta-analysis for the odds ratio of atopic dermatitis and air pollutant/climate factor in 2001, 2011, and 2016

doi:10.6342/NTU202400166

Table 1. Characteristics of subjects

Variables	2001 (n = 7,296)	2011 (n = 2,082)	2016 (n = 4,022)	p
sex, n (%)				< 0.001
boy	3530 (48.4)	917 (44)	1743 (43.3)	
girl	3766 (51.6)	1165 (56)	2279 (56.7)	
age, n (%)				< 0.001
12	3 (0)	607 (29.2)	402 (10)	
13	1951 (26.7)	1096 (52.6)	1532 (38.1)	
14	2738 (37.5)	375 (18)	1603 (39.9)	
15	2604 (35.7)	4 (0.2)	485 (12.1)	
Parental education ≧ 9 y, n (%)	1654 (22.7)	1882 (90.4)	3714 (92.3)	< 0.001
Maternal smoking, n (%)	150 (2.1)	48 (2.3)	92 (2.3)	0.641
Household indoor environment				
Cockroaches seen ≧ 2 times/mo, n (%)	2552 (35)	528 (25.4)	1464 (36.4)	< 0.001
Water damage >1 d/y, n (%)	233 (3.2)	94 (4.5)	192 (4.8)	< 0.001

doi:10.6342/NTU202400166

Table 1 (Cont.)

Wall with visible mold ≧ 1 wall, n (%)	515 (7.1)	171 (8.2)	486 (12.1)	< 0.001
Parental allergic disease history				
Father asthma, n (%)	95 (1.3)	50 (2.4)	80 (2)	< 0.001
Father allergic rhinitis, n (%)	852 (11.7)	418 (20.1)	774 (19.2)	< 0.001
Father atopic dermatitis, n (%)	140 (1.9)	91 (4.4)	196 (4.9)	< 0.001
Mather asthma, n (%)	100 (1.4)	57 (2.7)	115 (2.9)	< 0.001
Mather allergic rhinitis, n (%)	668 (9.2)	385 (18.5)	666 (16.6)	< 0.001
Mather atopic dermatitis, n (%)	101 (1.4)	100 (4.8)	195 (4.8)	< 0.001
Physician-diagnosed allergic disease				
Physician-diagnosed asthma, n (%)	453 (6.2)	380 (18.3)	379 (9.4)	< 0.001
Physician-diagnosed allergic rhinitis, n (%)	1687 (23.1)	672 (32.3)	1311 (32.6)	< 0.001
Physician-diagnosed atopic dermatitis, n (%)	256 (3.5)	224 (10.8)	502 (12.5)	< 0.001

Analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina) and R version 4.1.3 software

doi:10.6342/NTU202400166

Table 2 Annual average of air pollutants/ climate factors from 1994-2015 (except the 2001-2003)

	1994	1995	1996	1997	1998	1999	2000	2004	2005
CO/ppm	0.96	0.84	0.82	0.84	0.80	0.74	0.73	0.57	0.57
NO/ppb	15.86	13.74	12.48	13.26	13.37	12.09	11.55	7.45	8.98
NO2/ppb	23.93	23.74	22.22	23.40	22.36	22.38	21.75	20.27	18.63
SO2/ppb	10.14	8.71	6.61	6.34	5.35	4.91	4.45	4.34	5.42
PM10/(μm/m³)	70.78	67.33	62.80	62.65	56.10	58.55	60.21	62.32	62.85
PM2.5/(μm/m³)	-	-	-	-	-	-	-	-	36.03
O3/ppb	21.27	21.88	23.48	23.63	22.24	24.39	24.60	29.19	26.96
Related humidity	-	-	-	-	-	-	-	72.87	73.50
Ambient temperature/℃	23.41	22.55	23.09	24.19	23.49	23.46	23.62	23.62	23.48

doi:10.6342/NTU202400166

Table 2 (Cont.)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
CO/ppm	0.54	0.54	0.48	0.48	0.51	0.49	0.47	0.46	0.45	0.44
NO/ppb	7.38	7.03	6.06	6.05	7.37	6.60	5.92	5.26	4.97	4.80
NO2/ppb	18.09	17.89	16.12	16.18	17.34	16.54	15.21	14.63	15.20	14.21
SO2/ppb	4.78	4.74	4.32	4.23	4.28	4.00	3.39	3.48	3.55	3.19
PM10/(μm/m³)	60.11	59.31	56.00	59.89	57.30	55.28	50.61	52.44	51.91	47.62
PM2.5/(μm/m³)	33.57	34.18	31.82	33.20	31.06	32.36	28.19	29.35	25.34	21.80
O3/ppb	29.09	30.17	28.86	33.17	29.52	30.82	29.40	29.46	25.71	29.51
Related humidity	73.69	75.08	71.12	73.26	75.48	75.10	77.04	75.13	76.79	75.32
Ambient temperature/°C	24.02	23.87	22.55	24.15	23.86	23.49	23.52	23.47	23.25	24.21

doi:10.6342/NTU202400166

Table 3-1 Correlation between Air pollutants and climate factors (2001 survey: 1994-2000)

	Ambient temperature	CO	NO	O3	PM10	SO2	NO2
Ambient temperature	1						
CO	0.26	1					
NO	-0.09	0.71	1				
O3	0.37	-0.42	-0.76	1			
PM10	0.55	0.35	0.09	0.29	1		
SO2	0.29	0.52	0.43	-0.13	0.51	1	
NO2	0.13	0.90	0.71	-0.37	0.49	0.65	1

doi:10.6342/NTU202400166

Table 3-2 Correlation between Air pollutants and climate factors (2011 survey: 2004-2010)

	Ambient temperature	CO	NO	O3	PM10	PM2.5	Humidity	SO2	NO2
Ambient temperature	1								
CO	0.06	1							
NO	-0.32	0.77	1						
O3	0.46	-0.36	0.63	1					
PM10	0.38	0.10	-0.15	0.53	1				
PM2.5	0.46	0.31	0.01	0.48	0.90	1			
Humidity	-0.28	-0.45	-0.30	-0.06	-0.34	-0.63	1		
SO2	0.11	0.51	0.40	0.14	0.53	0.59	-0.42	1	
NO2	-0.13	0.87	0.84	-0.35	0.19	0.38	-0.56	0.62	1

doi:10.6342/NTU202400166

Table 3-3 Correlation between Air pollutants and climate factors (2016 survey: 2009-2015)

	Ambient temperature	CO	NO	O3	PM10	PM2.5	Humidity	SO2	NO2
Ambient temperature	1								
CO	0.02	1							
NO	-0.35	0.74	1						
O3	0.47	-0.43	-0.69	1					
PM10	0.56	0.11	-0.06	0.46	1				
PM2.5	0.63	0.14	-0.03	0.51	0.79	1			
Humidity	-0.33	-0.63	-0.42	0.13	-0.20	-0.40	1		
SO2	0.22	0.69	0.52	0.06	0.55	0.56	-0.49	1	
NO2	-0.14	0.92	0.83	-0.38	0.46	0.20	-0.62	0.74	1

doi:10.6342/NTU202400166

Table 4-1 Relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed asthma, single-pollutant model

	Effect on the prevalence of asthma		
	2001 survey	2011 survey	2016-2017 survey
	ORa (95% CI)	ORa (95% CI)	OR (95% CI)
Ambient temperature	0.99 (0.91, 1.07)	0.93 (0.83, 1.05)	0.82 (0.68, 0.97)
Related humidity		0.91 (0.80, 1.04)	1.03 (0.89, 1.19)
CO	1.10 (1.06, 1.15)	0.98 (0.91, 1.05)	1.03 (1.01, 1.06)
NO	1.06 (1.03, 1.09)	0.99 (0.97, 1.02)	1.00 (1.00, 1.01)
O3	0.95 (0.90, 1.00)	1.00 (0.89, 1.13)	0.93 (0.89, 0.98)
PM2.5		0.93 (0.79, 1.10)	0.83 (0.77, 0.90)
PM10	0.84 (0.72, 0.98)	0.88 (0.69, 1.13)	0.84 (0.75, 0.96)
SO2	1.02 (0.94, 1.10)	1.00 (0.92, 1.08)	0.94 (0.82, 1.06)
NO2	1.05 (0.87, 1.25)	0.98 (0.89, 1.08)	1.02 (0.97, 1.08)

a The OR was calculated per interquartile range (IQR) increase in air pollutants. Models were adjusted for sex, parental education, household water damage, household mouldy walls, household cockroaches, and the history of a father or mother with asthma, allergic rhinitis, or atopic dermatitis.

The values of PM2.5 used in the 2011 survey were selected from 2005-2010

doi:10.6342/NTU202400166

Table 4-2 Relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed allergic rhinitis, single-pollutant model

	Effect on the prevalence of allergic rhinitis		
	2001 survey	2011 survey	2016-2017 survey
	ORa (95% CI)	ORa (95% CI)	ORa (95% CI)
Ambient temperature	1.06 (1.03, 1.09)	0.85 (0.77, 0.93)	1.03 (0.88, 1.21)
Related humidity		0.97 (0.85, 1.12)	0.92 (0.84, 1.01)
CO	1.04 (0.99, 1.09)	1.02 (0.98, 1.07)	1.02 (1.01, 1.03)
NO	1.01 (0.98, 1.05)	1.02 (0.99, 1.04)	1.00 (1.00, 1.01)
O3	1.01 (0.96, 1.06)	0.91 (0.82, 1.01)	0.95 (0.93, 0.98)
PM2.5		0.97 (0.84, 1.12)	1.07 (1.00, 1.14)
PM10	1.02 (0.91, 1.13)	0.93 (0.78, 1.12)	1.05 (0.94, 1.16)
SO2	1.01 (0.97, 1.05)	0.98 (0.92, 1.05)	1.09 (1.03, 1.16)
NO2	1.03 (0.92, 1.15)	1.06 (0.99, 1.14)	1.04 (1.02, 1.05)

a The OR was calculated per interquartile range (IQR) increase in air pollutants. Models were adjusted for sex, parental education, household water damage, household mouldy walls, household cockroaches, and the history of a father or mother with asthma, allergic rhinitis, or atopic dermatitis.

The values of PM2.5 used in the 2011 survey were selected from 2005-2010

doi:10.6342/NTU202400166

Table 4-3 Relationship between exposure to air pollutants in the 7 years before the survey and physician-diagnosed atopic dermatitis, single-pollutant model

	Effect on the prevalence of atopic dermatitis		
	2001 survey	2011 survey	2016-2017 survey
	ORa (95% CI)	ORa (95% CI)	ORa (95% CI)
Ambient temperature	0.91 (0.82, 1.02)	0.99 (0.83, 1.18)	0.91 (0.75, 1.09)
Related humidity		0.86 (0.67, 1.11)	1.04 (0.89, 1.21)
CO	1.07 (0.98, 1.15)	1.12 (1.05, 1.19)	1.00 (0.98, 1.02)
NO	1.04 (0.99, 1.10)	1.05 (1.02, 1.08)	1.00 (0.99, 1.00)
O3	0.95 (0.89, 1.00)	0.90 (0.78, 1.04)	0.97 (0.94, 1.01)
PM2.5		1.08 (0.86, 1.37)	0.93 (0.84, 1.04)
PM10	0.79 (0.60, 1.04)	1.00 (0.76, 1.30)	0.89 (0.77, 1.03)
SO2	1.03 (0.98, 1.08)	1.05 (0.93, 1.19)	1.02 (0.96, 1.08)
NO2	1.16 (1.00, 1.34)	1.18 (1.07, 1.30)	1.01 (0.99, 1.04)

a The OR was calculated per interquartile range (IQR) increase in air pollutants. Models were adjusted for sex, parental education, household water damage, household mouldy walls, household cockroaches, and the history of a father or mother with asthma, allergic rhinitis, or atopic dermatitis.

The values of PM2.5 used in the 2011 survey were selected from 2005-2010

doi:10.6342/NTU202400166