



Increased incidence of allergic rhinitis, bronchitis and asthma, in children living near a petrochemical complex with SO₂ pollution



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ABSTRACT

This study aims to investigate incidence of allergic rhinitis, bronchitis and asthma, in children living near a petrochemical complex with SO₂ pollution obtained by air monitoring stations. A total of 587 children aged 11 to 14 were recruited and classified into high and low exposure groups based on a radius of 10 km from the complex. To study the influence of health on children since the operation of complex in 1999 and observe the difference of these diseases' short-term and long-term impact, we obtained the incidence rates of allergic rhinitis (ICD-9: 477), bronchitis (490–491) and asthma (493) from the Taiwan Health Insurance Database for three periods: 1999–2002, 1999–2006, and 1999–2010. Since 2001, the mean and 99th percentile of SO₂ concentrations in the high exposure area have been significantly higher than those in low exposure area. There were significant differences between the high and low exposure groups in the percentage of smoking, alcohol consumption, passive smoking exposure and incense burning habits. The incidence rates of three intervals were 26.9%, 35.7%, 41.7%; 8.3%, 8.8%, 10.2%; 18.5%, 25.0%, 26.9% for allergic rhinitis, bronchitis and asthma in high exposure group. Significant differences were found between groups for allergic rhinitis in all periods, bronchitis in the first two periods, and asthma in the first period using Student's *t*-test. After we adjusted age, gender, group, living near roads, incense burning and passive smoking exposure, the hazard ratios between exposure groups were 3.05, 2.74, and 1.93 for allergic rhinitis with significant difference in three periods, and 2.53, 1.92 and 1.72 for bronchitis with significant difference in first period and 1.60, 1.28 and 1.29 for asthma with significant difference in first period by Cox regression. The higher incidence of allergic rhinitis was related to boys and living near roads and the higher incidence of asthma was also related to younger children, boys, and passive smoking exposure.

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1. Introduction

Previous studies on pediatric respiratory diseases and exposure to sulfur dioxide (SO₂) from petrochemical complexes have been inconclusive. Some of the studies have reported positive associations between SO₂ exposure due to petrochemical complexes and respiratory diseases. For example, a case-crossover study showed that elevated SO₂ exposure from refinery factories was associated with an increased number of asthma episodes (Smargiassi et al., 2009). Other cross-sectional studies have indicated that children living near a petrochemical site have a higher prevalence of respiratory hospitalizations and symptoms such as nocturnal cough (Rovira et al., 2014). A significantly higher prevalence of acute irritative symptoms, including eye and throat irritation and nausea, has also been reported in children living near petrochemical factories in Taiwan (Yang et al., 1997). However, other

studies have shown no or a moderate association between petrochemical exposures and respiratory diseases. A cross-sectional study showed only moderately lower lung function and no excess of lifetime asthma and wheezing symptoms in children who lived near refinery factories (Rusconi et al., 2011). Furthermore, case-crossover studies have indicated an only moderately increased risk of emergency department visits and hospitalization due to respiratory diseases from SO₂ exposure and no association between SO₂ concentrations and emergency department visits (Lee et al., 2006; Lin et al., 2005). Another cross-sectional study in Taiwan similarly did not find a significantly higher prevalence rate of sinusitis, wheezing, asthma, allergic rhinitis, bronchitis, or pneumonia in children living near petrochemically polluted areas (Chen et al., 1998).

These inconsistent results may be due to several factors. For one, the studies conducted to date have predominantly used different questionnaires to compare respiratory diseases, such as International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires and the American Thoracic Society questionnaire (Rovira et al., 2014; Rusconi et al., 2011; Chen et al., 1998; Yang et al., 1998); the different questionnaires may have caused the difference in results. Additionally, several studies have used yearly or weekly averages to indicate daily SO₂

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exposure. However, this approach may neglect the influence of short-term exposures (Rovira et al., 2014; Yang et al., 1998; Rusconi et al., 2011). Moreover, the studies mentioned above primarily used a case-crossover or cross-sectional design to investigate the prevalence rate within a short period of time, i.e., <5 years (Deger et al., 2012; Rovira et al., 2014; Rusconi et al., 2011; Smargiassi et al., 2009); these study designs make it difficult to precisely infer the effects of changes in age and length of exposure.

The No. 6 Naphtha Cracking Complex in Yunlin County covers an area of 2603 ha and includes >64 factories, including harbors, oil refineries, coal-fired power plants, boilers, co-generation plants, naphtha cracking plants, and petrochemical processing plants (Formosa Petrochemical Corporation, Internet, 2015). The complex began its operations in 1999 and became the largest source of industrial emissions in Yunlin County. Our previous studies have shown that people living near this complex experienced higher levels of urinary vanadium (V), arsenic (As), and urinary 1-hydroxypyrene (1-ohp) (Yuan et al., 2015a, 2015b), and the residents of this county showed a smaller increase in life expectancy over time than the change in life expectancy in another less-industrialized county. The average difference in life expectancy between these counties ranged from 0.89 to 1.62 years at different intervals after the complex began its operations (Chen et al., 2014). However, the impact on the health of the children who live near this complex is still under debate. The establishment and operation of the No. 6 Naphtha Cracking Complex in a previously unindustrialized area of central Taiwan provided a rare opportunity to investigate the respiratory diseases in children that were related to petrochemical pollution from a historical perspective. By comparing the health indicators of children's diseases, we can better estimate the associations between petrochemical exposure and pediatric respiratory diseases over several years after the start of the complex's operations. In addition, the availability of hourly SO₂ concentrations in the study area allowed us to reveal acute exposure effects that were shorter than a day, a metric that was not reported in the studies mentioned above. A study that we previously conducted analyzed the concentrations of SO₂ observed in the Taishi air monitoring station in Yunlin County to present the complex's effects on exposure and found that there were elevated levels of SO₂ from 1995 to 2010. However, these results have not been correlated with health data and no comparisons with other air monitoring stations have been made (Shie et al., 2013a).

Accordingly, our study aims to investigate the relationship between exposure to SO₂ and the incidence of respiratory diseases including allergic rhinitis, bronchitis and asthma in children living near a petrochemical complex using SO₂ exposure data from air quality monitoring stations and data on individual demographics, health, and environmental characteristics generated from a questionnaire and a health insurance database.

2. Material and methods

2.1. Study area, period and subjects

Our study area included nine townships with similar socioeconomic factors that were located between 0 and 30 km away from the No. 6 Naphtha Cracking Complex. The Taishi, Mailiao and Dongshih townships were within a 10 km radius of the complex and were thus classified as high exposure (HE) areas. The Erlun, Lunbei, Huwei, Baojzhong, Sihhu, and Yuanchang townships were farther than 10 km away from the complex and were thus classified as low exposure (LE) areas, as shown in Fig. 1.

This study covered a time period from 1999 to 2010. To observe the incidence rates of diseases based on different lengths of exposure, we divided the overall time frame (1999 to 2010) into three periods including four (1999–2002), eight (1999–2006), and 12 years (1999–2010) after the beginning of the complex's operations. Our study subjects, who were aged between 11 and 14 years old and have lived >5 years

at the same addresses, were directly recruited from the junior high schools in each of the 9 townships near the petrochemical complex in Yunlin County from 2009 to 2011. After excluding children who did not have an available identity card number and complete information, our final study population consisted of 587 children. There were 216 (37%) children in the HE areas and 379 (63%) in the LE areas. Fig. 1 shows the locations of the study subjects in the HE and LE areas.

2.2. Health data

Taiwan Health Insurance database, which was managed by the Ministry of Health and Welfare, Taiwan, includes database of outpatient visits, hospital administration, and medication. According to the 2015–2016 National health insurance annual report, the coverage of insured population is about 99.6% of total population in Taiwan. We chose outpatient data to calculate the incidence rate of the diseases of interest among the study subjects. These outpatient data included the date, location, and main causes [International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM)]. The observed disease in our study were allergic rhinitis (ICD-9-CM: 477) (Hankin et al., 2010; Hwang et al., 2010; Sazonov Kocevar et al., 2005), bronchitis (ICD-9-CM: 490–491) (Choi et al., 2004; Hsu et al., 2014; Sin et al., 2002) and asthma (ICD-9-CM: 493) (Cree et al., 2006; Sin and Tu, 2001). Children who had a code of interest more than three times in each study period were defined as the cases. For this study, the cases that were present in 1998 were excluded to retain only new cases.

During the recruitment period from 2009 to 2011, we collected demographic characteristics, including age, gender, smoking, alcohol consumption, living near roads, passive smoking exposure, and indoor environmental factors such as incense burning, mosquito incense burning, and use of carpets, dehumidifiers, gas cookers, and gas tea kits. Among these variables, "Passive smoking" was defined as passive smoking exposure at home. "Living near roads" was defined by reaching main road in 3 min on foot.

2.3. Exposure assessment and SO₂ air monitoring

Our study focused on SO₂ as an indicator of exposure from petrochemical factories. We used monitoring data of hourly SO₂ concentrations that were measured at Taishi, which is located 8.1 km south of the complex, and Lunbei, which is located 16.2 km east and south of the complex. These two air quality monitoring stations (Taishi and Lunbei) are parts of the Taiwan Environmental Protection Administration (TEPA) and represent the air pollution in the HE and LE areas, respectively (Fig. 1). To investigate the differences before and after the complex's operations, we collected SO₂ concentrations from 1995, which was four years before its operation, to 2010. The temperature, relative humidity, wind direction, wind speed, and rainfall at the two stations were also measured hourly. The SO₂ analyzer was based on an optical spectroscopy method (Ecotech model 9850; Ecotech Inc., Australia). A complete quality assurance protocol was regularly maintained by TEPA to ensure the accuracy and reliability of the data. In addition, our indicators of the exposure from the complex were adherent with standards used by the United States Environmental Protection Agency (USEPA), including the number of hourly SO₂ concentrations above 75 ppb and the three-year average of the 99th percentile of SO₂ concentrations.

2.4. Statistical analyses

We defined the location of the No. 6 Naphtha Cracking Complex's main petrochemical factory and the locations of the study subjects using Google Earth 6.1 and Quantum Geographic information system 1.74. The data analysis began with comparisons of the differences of continuous variables in the HE and LE groups using Student's *t*-test. Chi-square tests were used to compare the differences in categorical

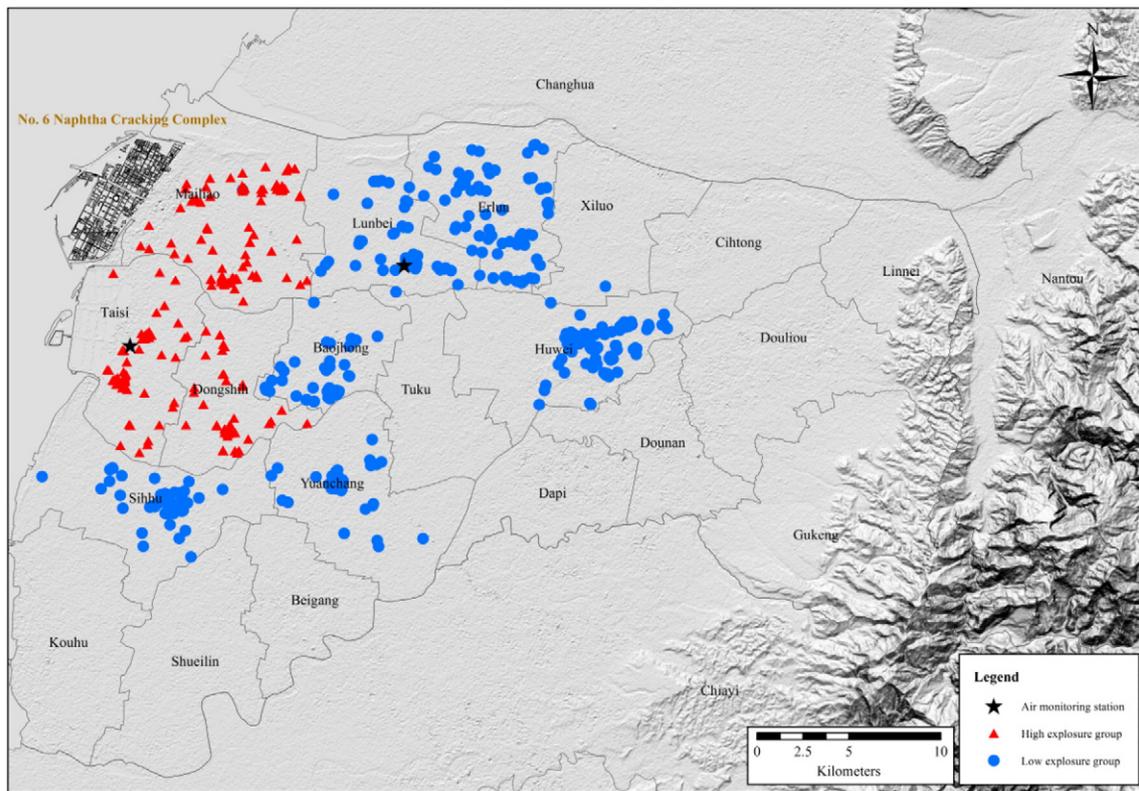


Fig. 1. The locations of the study subjects and the air quality monitoring stations near the No. 6 Naphtha Cracking Complex in Yunlin County, Taiwan.

variables and incidence rates of diseases. Time-to-event probability functions were calculated by the Kaplan–Meier method for the incidence of allergic rhinitis, bronchitis and asthma, from 1999 to 2010, and a log-rank test was used to test the difference between functions of these three diseases of HE and LE groups. Cox proportional hazards regression model was applied to assess the associations between demographic, environmental factors and the incidence rates of allergic rhinitis, bronchitis and asthma, we excluded variables with no significant difference between HE and LE groups but forced variables of age, gender and living near roads, an important traffic pollution factor, in the Cox

model. An alpha level of 0.05 with a two-tailed distribution determined statistical significance. All analyses were performed using SAS software (Version 9.3; SAS Institute).

3. Results

A summary of the annual data on the hourly SO₂ concentrations in the HE and LE areas between 1995 and 2010 is presented in Table 1. The averages of the annual SO₂ concentration in the HE area were all lower than those in the LE area from 1995 to 2000. Starting in 2001,

Table 1
SO₂ concentrations in high exposure (HE) and low exposure (LE) areas from 1995 to 2010.

	High exposure (HE) area			Low exposure (LE) area		
	Annual average ^a	No. of SO ₂ measurements >75 ppb ^c	Three-year annual average 99th percentile ^b	Annual average	No. of SO ₂ measurements >75 ppb ^c	Three-year annual average 99th percentile ^b
1995	3.72	0	–	6.23	2	–
1996	3.26	0	–	4.47	3	–
1997	3.56	0	54.8	5.08	2	67.6
1998	3.24	0	52.5	4.34	1	67.7
1999	2.60	0	48.4	3.31	0	63.1
2000	2.31	0	39.2	2.34	0	45.9
2001	3.23	6	49.6	2.55	0	31.6
2002	3.19	10	67.6	2.20	0	20.9
2003	3.49	13	85.8	2.02	0	22.6
2004	3.46	15	94.8	2.66	0	25.4
2005	5.17	61	131.8	3.46	2	32.0
2006	4.06	10	137.3	3.78	0	29.3
2007	4.48	4	126.6	3.54	0	24.1
2008	5.05	23	107.2	3.62	0	19.4
2009	4.36	11	101.3	3.44	0	19.0
2010	3.89	1	101.8	3.25	0	17.6

Abbreviations: SO₂, sulfur dioxide.

Unit: ppb.

^a The annual 99th percentile (fourth highest daily maximum hourly value) of hourly maximum concentrations.

^b The three-year average of the annual 99th percentile of hourly maximum concentrations.

^c The USEPA's latest standard (75 ppb) is based on the three-year average of the 99th percentile concentration of the hourly maximum concentrations.

Table 2
Demographic and environmental characteristics of the HE and LE groups from 2009 to 2011.

	All (N = 587)	HE group (N = 216)	LE group (N = 371)	p ^a
Distance from complex (km)	15.72 (6.70)	9.03 (3.51)	19.56 (4.81)	<0.0001
Age at recruitment (years)	13.65 (0.69)	13.59 (0.69)	13.68 (0.70)	0.1356
Gender (male)	313 (53%)	126 (58%)	187 (50%)	0.0633
Smoking	16 (3%)	10 (5%)	6 (2%)	0.0280
Alcohol consumption	11 (2%)	8 (4%)	3 (1%)	0.0125
Passive smoking exposure	49 (8%)	27 (13%)	22 (6%)	0.0050
Living near roads	303 (52%)	119 (56%)	184 (50%)	0.1708
Indoor environmental factors				
Incense burning	207 (35%)	86 (40%)	121 (33%)	0.0485
Mosquito repellent burning	227 (40%)	90 (42%)	137 (38%)	0.5285
Carpet use	71 (12%)	25 (12%)	46 (12%)	0.7803
Dehumidifier use	114 (20%)	42 (20%)	72 (20%)	0.9733
Gas cooker use	556 (95%)	210 (98%)	346 (94%)	0.1588
Gas tea kit use	163 (28%)	58 (27%)	105 (28%)	0.7052
Indoor dampness ^b	29 (6%)	12 (7%)	17 (5%)	0.5600

Abbreviations: km, kilometer; HE, high exposure; LE, low exposure.

The values shown are mean (SD) or N (%). The number of subjects with missing data was very low.

^a Student's *t*-tests were used to compare continuous data, and chi-square tests were used to compare categorical data. Fisher's exact test was used when 20% cell frequency < 5.

^b Defined as experiencing dampness every day.

the average annual SO₂ concentrations began to increase and reached their highest concentration of 5.17 ppb in 2005, whereas in the LE areas, the concentrations remained between 2.02 and 3.78 ppb from 2001 to 2010. Using the new SO₂ standards from the USEPA, the three-year annual average of the 99th percentile of SO₂ concentrations in the HE and LE areas did not reach 75 ppb before 2003. In 2002, this value was 67.6 ppb in the HE areas, whereas it was 20.9 ppb in the LE areas. However, after 2003, the three-year annual average of the 99th percentile of SO₂ concentrations began to increase in HE areas with a concentration above 75 ppb in each year, whereas the concentrations gradually decreased in LE areas. The three-year average of the 99th percentile of SO₂ concentrations reached 137.3 ppb and 32.0 ppb in the HE and LE areas respectively between 2003 and 2006. From 1999 to 2002, the HE areas had a total of 16 h above 75 ppb and the LE areas had zero. Yet from 2003 to 2010, there were 138 h with hourly SO₂ concentrations above 75 ppb each year in the HE areas and only two hours meeting that criteria in LE areas.

Table 3
Incidence of allergic rhinitis, bronchitis and asthma in children living in high exposure (HE) and low exposure (LE) areas since the start of the No. 6 Naphtha Cracking Complex's operations in 1999.

	HE area			LE area			p
	N	Age at the end of period	Incidence	N	Age at the end of period	Incidence	
Allergic rhinitis							
1999–2002	216	6.59 (0.69)	26.9%	371	6.68 (0.70)	9.4%	<0.0001
1999–2006		10.59 (0.69)	35.7%		10.68 (0.70)	14.6%	<0.0001
1999–2010		13.59 (0.69)	41.7%		13.68 (0.70)	24.3%	0.0276
Bronchitis							
1999–2002	216	6.59 (0.69)	8.3%	371	6.68 (0.70)	3.5%	0.0116
1999–2006		10.59 (0.69)	8.8%		10.68 (0.70)	4.6%	0.0402
1999–2010		13.59 (0.69)	10.2%		13.68 (0.70)	5.9%	0.0590
Asthma							
1999–2002	216	6.59 (0.69)	18.5%	371	6.68 (0.70)	11.0%	0.0114
1999–2006		10.59 (0.69)	25.0%		10.68 (0.70)	18.9%	0.0792
1999–2010		13.59 (0.69)	26.9%		13.68 (0.70)	20.2%	0.0640

Abbreviations: HE, high exposure; LE, low exposure; data was presented by % or mean (SD).

Chi-square tests were used to compare the incidence between the high and low exposure groups.

Allergic rhinitis was defined by ICD-9 code: 477. Bronchitis was defined by ICD-9 codes: 490–491. Asthma was defined by ICD-9 code: 493.

Table 2 shows the demographic and environmental characteristics of the 587 study subjects. The average distance from the complex of the HE group was 9.03 ± 3.51 km, whereas the average distance of the LE group was 19.56 ± 4.81 km. During the 2009 to 2011 recruitment period, the HE and LE groups were 13.59 ± 0.69 years old and 13.68 ± 0.70 years old, respectively. The proportion of boys were 58% and 50% in the HE and LE groups, respectively. A significant difference was found regarding the prevalence of smoking, alcohol consumption, passive smoking exposure, and incense burning between the two groups. It should be noted that the number of children with smoking and alcohol consumption habit was very small in either one of the two groups.

The incidence rates of allergic rhinitis, bronchitis and asthma, during the different study periods are shown in Table 3. The incidence rates of allergic rhinitis in the HE group (26.9%, 35.7%, and 41.7%) were significantly higher than those in the LE group (9.4%, 14.6%, and 24.3%) in the four, eight and 12 years after the start of the complex. The incidence of bronchitis in the HE group (8.3% and 8.8%) were significantly higher than that in the LE group (3.5% and 4.6%) four and eight years after the start of the complex, but there was no difference between the two groups when extending the study period to 12 years. The incidence rate of asthma in the HE group (18.5%) was significantly higher than that in the LE group (11.0%) in the first four years after the complex began its operations. In the 8 and 12 years after the start of the complex, the higher incidence of asthma in the HE group but did not reach statistical significance. Extending the study period to eight and 12 years after the start of the complex, only moderately significant differences were found in the incidence of asthma between the two groups.

The time-to-event probability functions of allergic rhinitis, bronchitis and asthma, in the 12 years after the operation of the complex were shown in Fig. 2. Children in the HE group showed lower non-event probabilities of allergic rhinitis, bronchitis and asthma, than those in LE group. The difference in the incidence of allergic rhinitis between the two groups emerged after 18 months and the maximum difference was at 40 months lasting stable significant difference with the non-event probabilities were 67% in the HE group and 89% in the LE group (p < 0.0001). The curves for bronchitis were driven apart obviously after 18 months and showed steadily slight difference (p = 0.0547). The curves for asthma were separated clearly after 12 months, and the maximum difference appeared at 40 months and lasted stable borderline significant difference for two groups (p = 0.0485).

Table 4 illustrates the hazard ratios of the incidences of allergic rhinitis, bronchitis and asthma, during the different study periods after adjusting for group, age, gender, living near roads, incense burning and passive smoking exposure by Cox proportional hazard regression. Smoking and alcohol consumption were not included in our final

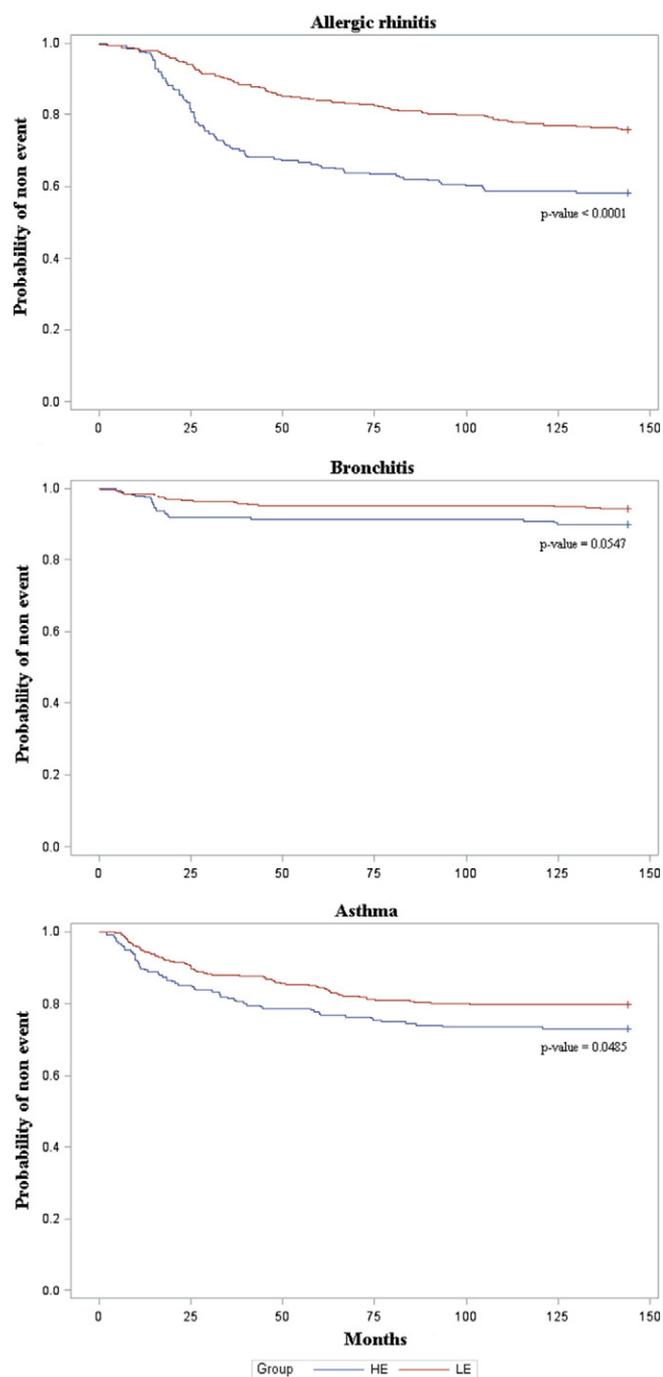


Fig. 2. Probabilities of non-event for the incidences of allergic rhinitis, bronchitis and asthma in the 12 years after the start of the complex.

models because they became divergent in our models, possibly due to fewer cases in our study subjects. Through Cox regression, we found that the incidence rates of allergic rhinitis in the HE group were 3.05 [95% Confidence Interval (CI): 1.98, 4.68], 2.74 (95% CI: 1.91, 3.93), and 1.93 (95% CI: 1.43, 2.61) times higher than that in the LE group in the four, eight, and 12 years after the start of the complex's operations, respectively, which was a significant finding. Boys and children living near roads had a higher risk of allergic rhinitis in our models. In the four, eight, and 12 years after the complex's operations began, the incidence rates of bronchitis in the HE group were 2.53 (95% CI: 1.22, 5.24), 1.92 (95% CI: 0.99, 3.75), and 1.72 (95% CI: 0.94, 3.14) times higher than those in the LE group, which was also a significant difference in first period. No other factors in our models significantly influenced the

incidence rate of bronchitis. The incidence rates of asthma in the HE group were 1.60 (95% CI: 1.03, 2.48), 1.28 (95% CI: 0.89, 1.83), and 1.29 (95% CI: 0.91, 1.83) times higher than those in the LE group in the four, eight, and twelve years after the complex's operations began, respectively, which had significant difference only in the first four years. In our models, we also found that younger children, boys, and children passively exposed to smoking had a significantly higher risk of developing asthma.

4. Discussion

This is the first study using three-year annual averages of the 99th percentile of hourly SO_2 concentrations to report that the higher incidence rates of allergic rhinitis, bronchitis and asthma in children living near a petrochemical complex were associated with SO_2 exposure from the complex.

Our findings confirmed the association between SO_2 exposure from petrochemical complexes and acute respiratory effects, which is consistent with several previous studies (Smargiassi et al., 2009; Schwartz et al., 1994). It should be noted that the association we found between SO_2 exposure and the incidence of respiratory diseases occurred as early as <2 years and lasted for 8 to 12 years. Our findings thus showed that the acute respiratory effects experienced continued to affect nearby children and developed into long-term effects. Previous studies that used yearly and weekly averages of SO_2 exposure also found an association between relatively long-term SO_2 exposure and the prolonging of respiratory diseases (Rusconi et al., 2011; Rovira et al., 2014).

The finding that children living near the complex had higher incidence rates of allergic and respiratory diseases was also consistent with previous cross-sectional and case-crossover studies on the prevalence rates of allergic rhinitis (Chen et al., 1998; Yang et al., 1998), bronchitis near petrochemical complexes (Chen et al., 1998; Yang et al., 1997) and asthma (Chen et al., 1998; Rovira et al., 2014; Yang et al., 1997; Yang et al., 1998).

The Taishi Township used to be a comparison site for the Linyuan petrochemical factory, which was one of the largest petrochemical factories in southern Taiwan in 1994 before the No. 6 Naphtha Cracking Complex was constructed. In our previous studies on the Linyuan factory (Linyuan Industrial Park Service Center, Internet, 2015) (Chen et al., 1998; Yang et al., 1998), we reported that children living near the Taishi air monitoring station had a lower one-year prevalence rate of asthma (1.6%) and bronchitis (16.0%) than children living near the Linyuan petrochemical factories, who had a prevalence rate from 1994 to 1995 of 4.0% for asthma and 16.4% for bronchitis (Chen et al., 1998; Yang et al., 1998). Moreover, a historical comparison found that the three-year annual average of the 99th percentile of hourly SO_2 concentrations in 1995 was 46.3 ppb in the Taishi air monitoring station and 170.1 ppb in the Linyuan air monitoring station. However, these values reversed to 101.8 ppb in the Taishi station and 59.6 ppb in the Linyuan station in 2010 (see Supplemental Material, Table S1). Thus in the past 15 years, the high SO_2 exposures and prevalence of allergic and respiratory diseases that the children living near the Linyuan petrochemical factories experienced seemed to occur again in the children living near the No. 6 Naphtha Cracking Complex, despite the factories being located in two different areas of Taiwan.

Air pollution from petrochemical complexes is more complicated and diverse than the SO_2 pollution alone. Previous studies showed a distance-to-source pattern of existed for resident's exposures to metals (Yuan et al., 2013; Yuan et al., 2015a), Polycyclic Aromatic Hydrocarbon (PAH) (Yuan et al., 2015b), and Volatile Organic Compound (VOC) (Shie and Chan, 2013b) near the No. 6 Naphtha Cracking Complex area. Significantly higher concentrations of V in the air and urinary V, Mn, As and Sr were reported for inhabitants living in the HE area than those living farther away from the petrochemical complex (Yuan et al., 2013; Yuan et al., 2015a). A clear relationship between ambient PAHs concentrations and urinary 1-ohp, a PAH metabolite, of residents in areas near

the petrochemical complex was established in a previous study (Yuan et al., 2015b). A significantly high vinyl chloride monomer (VCM) level, a specific pollutant emitted from plastic factories, was measured in the HE area during the downwind period after an industrial fire occurred at the petrochemical complex (Shie and Chan, 2013b). It is possible that more air pollutants than SO₂ alone may be associated with the increased incidence of the diseases among the children we observed in the study.

The associations we found between demographic and environmental factors and the incidence of asthma and allergic rhinitis were consistent with previous studies. Older children had a lower risk of developing asthma than young children (Hwang et al., 2010; Nirel et al., 2015). In addition, boys had a higher incidence rate of allergic rhinitis and asthma than girls in our study, which had similar children male predominance as other studies (Pausjensen and Cockcroft, 2003). They believed that the result was because of airway hyper-responsiveness which commonly was evaluated by challenge of methacholine or histamine (Peat et al., 1992). Besides, there are also study explaining higher rate of asthma for children male by intrinsic state of their airways, and some possible diagnostic biases favoring males which needs more studies to clarify (Pausjensen and Cockcroft, 2003; Habbick et al., 1999).

Individuals who were passively exposed to smoking (Fernández-Plata et al., 2016) which is an important risk factor in previous studies had higher incidence rates of asthma and allergic rhinitis because smoke does harm to the mucosa and worsen clinical pathology as many studies (Higgins and Reh, 2012; Jaakkola et al., 2001). Living near roads was reported to increase study subject's exposure levels of traffic-related pollutants, such as carbon monoxide (CO), nitrogen dioxide (NO₂), and particle matter with size <10 μm (PM₁₀), and can possibly affect children's airway and cause damages (Johannessen et al., 2013; Lee et al., 2003; Weiland et al., 1994). Our findings should not be confounded by traffic air pollution as air monitoring data in the study area showed that ambient concentrations of CO, NO₂, and PM₁₀ were actually lower in the HE areas than those in the LE areas (see Supplemental Material, Table S2).

Our study has several limitations to be noted. First, misclassification of individual study subject's air pollution exposure may occur as area-wide statistics were used to represent individual levels of exposure. Although misclassification is a common problem in epidemiological studies, it would not have changed the results of the present study because of the multiple-years analysis design and the non-directional data emphasizing the difference between the two groups (Nirel et al., 2015; Wichmann et al., 2009). Second, our study used the levels of SO₂ in the air quality monitoring stations instead of individual exposure data, which might be more representative. Additional studies that obtain

more accurate individualized data should be conducted to clarify the association between exact SO₂ exposure and respiratory diseases in children. Other studies using modeled SO₂ exposure data, such as the AERmic model (AREMOD), to simulate individual exposure data which might be one solution (Deger et al., 2012). Third, we did not obtain the health data of the children from birth to investigate the complete incidence rates of these diseases; however, we missed only a few cases that occurred on average under 2 years old, which would not significantly alter the present findings of our study. Fourth, we cannot totally exclude the influence of smoking and alcohol consumption as significant risk factor of these diseases among our study subjects as reported in previous studies (Hedman et al., 2011; Thakur et al., 2009) because the small number of children with these two factors prevented us from reaching reliable risk estimates of either one of these factors in this study. Lastly, we still cannot fully account for the contribution of social economic status to the difference in incidence of diseases as family income data were not available for direct comparisons between two study areas. We also didn't get clear social economics status for these two groups.

5. Conclusions

Regardless of these limitations, our study concluded that children living in the vicinity of a petrochemical complex were exposed to significantly higher levels of SO₂ and had significantly higher incidences of allergic rhinitis in the 12 years after the petrochemical complex began operating. A significantly higher incidence of bronchitis and asthma were also found in the high exposure group in the first four years after the complex's operations began. Thus, stricter guidelines should be set, particularly for susceptible groups, such as children, elders, and people with previous respiratory diseases. Further studies should be conducted to better understand the relationships between exposures from the petrochemical industry and the incidence of allergic and respiratory diseases.

Competing financial interests

The authors declare they have no actual or potential competing financial interests.

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Table 4

The hazard ratios of children's allergic rhinitis, bronchitis and asthma over three periods since the start of the operations of the No. 6 Naphtha Cracking Complex in 1999.

	Age at the end of the period	Group	Age	Gender	Living near roads	Incense burning	Passive smoking exposure
Allergic rhinitis							
1999–2002	6.65 ± 0.69	3.05 [¥] (1.98–4.68)	1.01 (0.83–1.24)	2.03 [¥] (1.29–3.19)	0.97 (0.65–1.47)	0.88 (0.57–1.36)	1.26 (0.66–2.42)
1999–2006	10.65 ± 0.69	2.74 [¥] (1.91–3.93)	1.03 (0.87–1.22)	1.99 [¥] (1.36–2.91)	1.11 (0.79–1.58)	0.88 (0.61–1.27)	1.30 (0.75–2.25)
1999–2010	13.65 ± 0.69	1.93 [¥] (1.43–2.61)	0.98 (0.85–1.12)	1.85 [¥] (1.35–2.54)	1.38 [¥] (1.02–1.87)	0.89 (0.65–1.22)	1.25 (0.76–2.07)
Bronchitis							
1999–2002	6.65 ± 0.69	2.53 [¥] (1.22–5.24)	0.89 (0.63–1.25)	1.07 (0.52–2.19)	0.63 (0.31–1.29)	0.55 (0.25–1.25)	2.14 (0.76–6.05)
1999–2006	10.65 ± 0.69	1.92 [¥] (0.99–3.75)	0.81 (0.59–1.12)	0.99 (0.51–1.92)	0.88 (0.46–1.70)	0.79 (0.39–1.59)	2.47 [¥] (0.95–6.41)
1999–2010	13.65 ± 0.69	1.72 [¥] (0.94–3.14)	0.84 (0.63–1.12)	1.07 (0.59–1.96)	0.97 (0.54–1.76)	0.93 (0.50–1.73)	1.89 (0.75–4.75)
Asthma							
1999–2002	6.65 ± 0.69	1.60 [¥] (1.03–2.48)	0.83 [♣] (0.67–1.03)	1.99 [¥] (1.24–3.19)	1.22 (0.78–1.90)	1.16 (0.74–1.82)	1.88 [♣] (0.96–3.70)
1999–2006	10.65 ± 0.69	1.28 (0.89–1.83)	0.79 [¥] (0.67–0.94)	2.32 [¥] (1.57–3.42)	1.26 (0.88–1.81)	1.02 (0.71–1.48)	1.84 [¥] (1.04–3.26)
1999–2010	13.65 ± 0.69	1.29 (0.91–1.83)	0.80 [¥] (0.68–0.94)	2.30 [¥] (1.58–3.34)	1.23 (0.87–1.73)	1.01 (0.71–1.45)	1.70 [♣] (0.96–3.00)

Data are presented as the HR ratio (95% CI). The reference groups are as follows: area-low exposure area; gender-girl; living near roads-no; incense burning-none; passive smoking exposure-none.

Allergic rhinitis was defined by ICD-9 code: 477. Bronchitis was defined by ICD-9 codes: 490–491. Asthma was defined by ICD-9 code: 493.

[¥] p-Value < 0.05.

[♣] p-Value < 0.1.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.envint.2016.08.009>.

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