Short-term Effects of Air Pollution and Temperature on Daily Morbidity in Chiang Mai, Thailand

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Abstract

Air pollution is associated with mortality and morbidity worldwide. Hot and cold temperature is also related to increased deaths and possibly hospital visits and admissions in many settings. Climate change is anticipated to pose increasing risks of deaths and illnesses associated with air pollution and temperature variations, particularly in developing world. To date, research studies about health effects of air pollution and temperature have been conducted in developed countries with cool climate more than in developing countries with subtropical or tropical climate. Furthermore, studies to identify susceptible populations are still limited. This study aims to investigate heath effects of air pollution and temperature and to identify people who are more susceptible to air pollution and temperature in a developing, tropical country, Thailand.

A regression analysis of retrospective time series data was employed to assess the short-term effects of air pollution and temperature on daily out-patient visits and hospital admissions in Chiang Mai, Thailand, from October 2002 to September 2006. Generalised negative binomial regression was used to model the relationships between the exposure and health outcomes, controlling for seasonal patterns and other possible potential confounders. Lag effects up to 4 days for air pollution, and up to 13 days for temperature were considered. Effect modification by age, sex, occupation, season, and previous out-patient visits before admissions were also examined.

There were positive, but not significant, effects of air pollution for some pollutants (particularly for SO_2), with notably larger effect sizes compared to previous studies in Western countries. There was evidence of hot temperature effects (though wide confidence intervals), with an increase in diabetic visits of 26.3% (95% CI, 7.1% to 49.0%), and in circulatory visits of 19.2% (95% CI, 7.0% to 32.8%) for each 1°C increase in temperature above 29°C. There was a rise of both the visits (3.7% increase, 95% CI, 1.5% to 5.9%) and admissions (5.8% increase, 95% CI, 2.3% to 9.3%) due to intestinal infectious disease for each 1°C increase across the whole temperature range. Despite no statistically significant differences between subgroups, air pollution effects were stronger in the elderly, females

and manual workers, whereas temperature effects were stronger in the elderly, male and unemployed people.

This study suggests that while there was little evidence of air pollution effects, there was significant evidence of high temperature effects on daily morbidity in Chiang Mai. The elderly seemed to be more vulnerable to the daily changes of both air pollution and temperature.

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Abbreviations and Acronyms

AIC: Akaike Information Criterion

APHEA: Air Pollution and Health: a European Approach

CHF: Congestive heart failure

COPD: Chronic Obstructive Pulmonary Disease

CVD: Cardiovascular disease

df: Degree(s) of freedom

HEI: Health Effects Institute

HN: Hospital number

ID: Identification number

IHD: Ischemic heart disease

NCS: Natural cubic spline

NAAQS: National Ambient Air Quality Standard

NMMAPS: National Mortality, Morbidity and Air pollution Studies

PACF: Partial autocorrelation function

PAPA: Public Health and Air Pollution in Asia

PCD: Pollution Control Department

SD Standard deviation

WHO: The World Health Organization

TSP: Total suspended particles

PM: Particulate matter

PM_{10}: The particulate matter less than 10 μm in aerodynamic diameter

$PM_{2.5}$: The particulate matter less than 2.5 μm in aerodynamic diameter

T: Temperature

RH: Relative humidity

CO: Carbon monoxide

NO_2: Nitrogen dioxides

SO_2: Sulphur dioxide

O_3: Ozone

μg: Micrograms

$\mu g/m^3$: Micrograms per cubic meter

ppb: Parts per billion

ppm:	Parts per million
mm/h:	Millimetre per hour
sqm:	Square metres
sq km:	Square kilometres
°C:	Degree Celsius
95% CI:	95% Confidence Interval

Chapter 1: Introduction

1.1. Background

1.1.1 Air pollution, temperature, and health

A large body of epidemiological evidence has suggested that exposure to air pollution, even at moderate concentrations, is associated with increased morbidity and mortality in many cities worldwide [1-5]. Numerous observational studies about temperature effects have also shown increased morbidity and mortality in relation to temperature changes [6-13]. However, health effects of air pollution and temperature are not equally spread [14, 15]. Children, the elderly, and people with pre-existing illnesses, such as heart and lung diseases, are more vulnerable to air pollution exposure than general population [16-21]. An increase in daily deaths and hospitalizations due to temperature exposure is also pronounced among older people [22-25]. It has been found that the risk of hospital admissions and premature deaths related to either air pollution or temperature are more likely to be enhanced by individual health conditions, such as respiratory diseases, cardiovascular diseases, and diabetes [26-38]. To date, studies to indentify the characteristics of those vulnerable to the effects of air pollution and temperature are still limited and need further investigations in order to gain a better understanding of their special susceptibility characteristics, which are crucial for developing targeted public health interventions.

It is important to note that most research studies about air pollution and temperature effects have been carried out in developed countries and in cool, temperate regions. The likely adverse health effects in developing countries with subtropical or tropical climates may however be different from those settings. The characteristics determining the vulnerability of a population may also be different. This could include several factors, such as genetic factors, lifestyles, health behaviours, socioeconomic status (SES), and environments. Therefore, assessment of regional specific vulnerabilities to temperature and air pollution variations is very important.

Chiang Mai is the second biggest city in Thailand, a tropical country in Southeast Asia. Chiang Mai is a growing city with an increasing population, intensifying traffic density,

and an increased consumption of natural resources to serve the growing economic development and urbanization. Since few investigations have been undertaken in low-income settings, the investigations of adverse health effects associated with current levels of air pollution and temperature in Chiang Mai, as well as identifications of its vulnerable population are needed for determining, developing and implementing appropriate public health mitigation measures and interventions.

1.1.2 Chiang Mai profile

Geographical location

Chiang Mai is located about 750 kilometres north of Bangkok, the capital city of Thailand, with 16 north of latitude, 99 east of longitude, and with 1,027 feet above sea levels [39]. The northern part of Chiang Mai connects to Myanmar, while other parts connect to other provinces of Thailand.

Weather

The weather in Chiang Mai is moderate throughout the year, with the average temperature of 25.4 °C (min = 20.1 °C and max = 31.8 °C), relative humidity of 72%, and annual rainfall of 1,000-1,200 mm [39]. There are three seasons in Chiang Mai: cool season (November-February), warm season (March-May), and rainy season (June-October).

Population

The total area of Chiang Mai is 20,107.057 sq km, with a total population of about 1.6 million (about 80/sq km, information obtained in 2006). Among all districts of Chiang Mai, Maung district is the most crowded, with the population density of about 1,947.2/sq km (total area = 152.4 sq km and total population = 296,753 people, December 2005) [39].

Approximately 80% of the total area is mountainous. The mountains in Chiang Mai are more than 500 feet above sea levels and are located in the northern and western parts of the province. Most of this area consists of forests and rivers, and is unsuitable for agriculture. Thus, there are significant numbers of Chiang Mai population living on the highland, which account for 19.5% of the total, including hill tribes (14.3%), minority ethnic groups such as Chinese and Mianmese minority (2.2%), and local Thais (3.0%).

Agricultural activities are the most common occupation in Chiang Mai. Approximately 60% of working people in Chiang Mai work in the agricultural sectors, followed by 13.6% in industry, 10.2% in business and trading. Regarding industrial activities, there is no major industry that may cause a substantial air pollution problem in the city. However, there are total of 2,192 various small factories in the province. The three most prevalent industries include agricultural factories (43.8%), 207 transportation factories (9.4%), and 200 food factories (9.1%).

Chiang Mai pollution and health

Air pollution in Chiang Mai has been of great concern in recent years due to its rapid economic growth, development and urbanization to serve an increasing population and also an influx of international tourists. Levels of air pollutants, especially PM_{10}, have occasionally exceeded the National Ambient Air Quality Standard levels [40, 41]. In addition to the already polluted air from the vehicle exhausts during traffic jams, burning of fallen leaves and agricultural residues in adjacent areas and open burning for cooking (such as food street vendors) have caused polluted air in a wider area [42]. Moreover, Chiang Mai is located in a valley surrounded by mountains and also influenced by the low pressure weather from China, which make it difficult for air pollutants to disperse [42].

In 1994, the statistics also showed the high number of about 500,000 hospitalized patients suffering from respiratory diseases [43]. In 1995, the prevalence of allergic diseases and asthma among children in Chiang Mai was observed, with 8.8% of total Chiang Mai children reported to suffer from asthmatic problems [44]. Furthermore, the annual health report has indicated that respiratory disease is the first leading cause of out-patient visits among the general population in Chiang Mai [39]. However, there is a lack of investigations as whether these respiratory health problems are influenced by the current levels of air pollution and/or temperature in the city.

1.1.3 Global climate change and public health risks

It is estimated that global climate change may pose increasing health risks and regional vulnerability associated with air pollution and temperature variations in the future [45, 46]. Climate change may influence weather, distribution of airborne allergens, anthropogenic emissions of pollution, and dispersion and concentrations of air pollutants, which may all in

turn lead to fluctuations of either temperature or air pollution [46]. Temperature and air pollution variations may directly affect people's health by increasing deaths and illnesses due to inability to adapt and tolerate to the changes [47]. Hence, greater attention should be paid to determining specific vulnerabilities in low-income countries because these settings are more likely to be highly affected by the climate variability due to less capacity to assess vulnerabilities and to develop and implement cost-effective mitigation and adaptation strategies [48].

1.1.4 Summary

Levels of air pollution and temperature can vary from country to country, corresponding with variation in geographical locations, climatic conditions, and human activities. Health effects of air pollution and temperature found in different regions can also vary. To date, most studies that illustrate the vulnerability to air pollution and temperature are conducted in developed regions like America and Europe with cooler temperate climates more than in developing regions with subtropical or tropical climates. Among those studies, either air pollution or temperature studies, more consistent findings have been found for mortality than those for morbidity. In this context, the investigation of the effects of air pollution and temperature on morbidity and the identification of susceptible populations in a tropical climate and less developed country is warranted.

1.2 Research topic

Short-term effects of air pollution and temperature on daily morbidity in Chiang Mai, Thailand

1.3 Research questions

1. How do daily changes in air pollution and temperature affect daily out-patient visits and hospital admissions in a tropical climate country, such as Thailand?
2. Do people with many counts of out-patient visits have a greater risk of hospital admissions associated with air pollution and temperature exposure?
3. What factors modify a person's risk of getting illness associated with air pollution and temperature exposure?

1.4 Hypotheses

1. Daily increase in air pollution levels increases daily out-patient visits and hospital admissions.
2. Daily increases in either heat or cold temperatures can affect daily out-patient visits and hospital admissions.
3. People with many counts of previous out-patient visits are at increased risk of a hospital admission associated with air pollution and temperature exposure.
4. The effects of air pollution and temperature on daily out-patient visits and hospital admissions may be modified by factors, such as age, sex, occupation, and season.

1.5 Aim and objectives

The aim of the study was to describe and quantify the short-term effects of air pollution and temperature on the health of people in Chiang Mai, Thailand and to identify people who were more susceptible to air pollution and temperature.

The specific objectives of the study were:

1. To assess the association between air pollution (SO_2, NO_2, CO, O_3, PM_{10}, and $PM_{2.5}$) and daily out-patient visits and hospital admissions, and the association between temperature and out-patient visits and hospital admissions.
2. To quantify the effects of air pollution and temperature on daily counts of out-patient visits and hospital admissions, with all causes of the visits and admissions and with specific disease groups, including respiratory, circulatory, diabetic, and intestinal infectious diseases, in the selected health centres and hospitals in Chiang Mai.
3. To determine whether people who had many counts of out-patient visits at the selected health centres and hospitals were at increased risk of a hospital admission for all causes, and for specific disease groups, including respiratory, circulatory, diabetic, and intestinal infectious diseases.
4. To determine whether factors, such as age, sex, occupation, and season had modified the effects of air pollution and temperature on daily out-patient visits and hospital admissions in the selected health centres and hospitals in Chiang Mai.

1.6 Conceptual framework

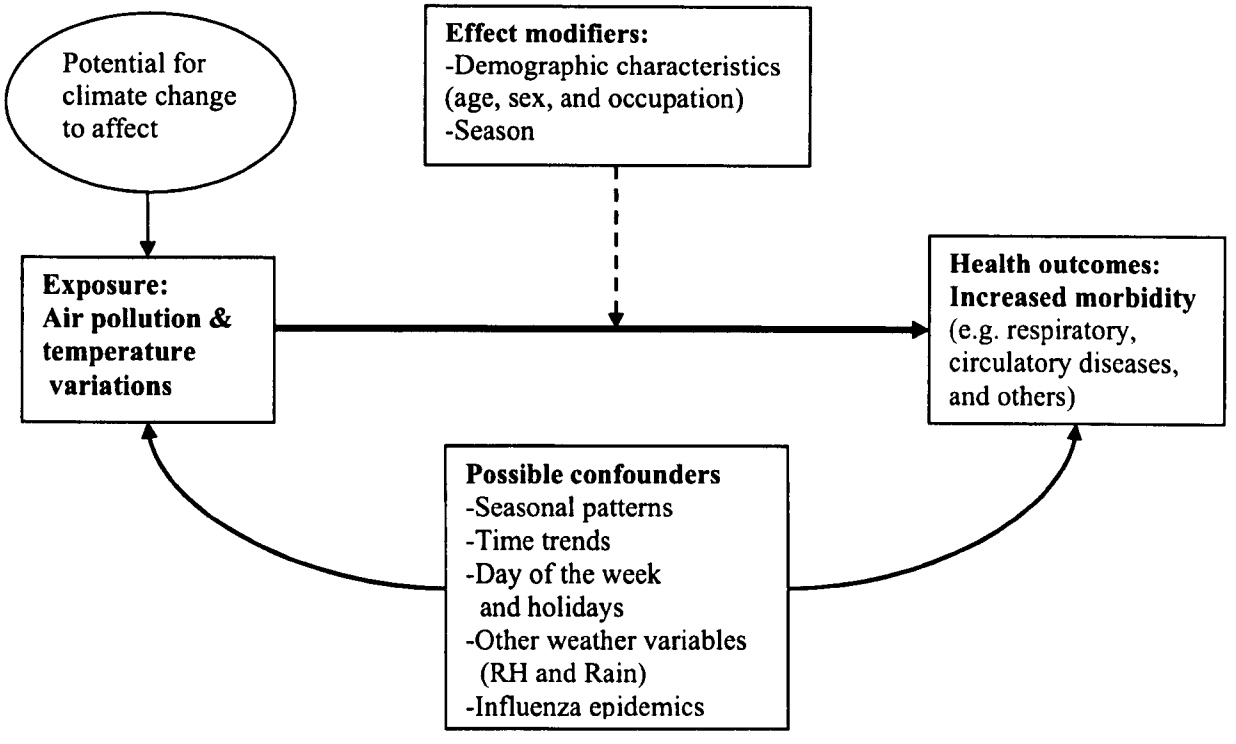


Figure 1. 1 Conceptual framework in assessing morbidity in relation to air pollution and temperature exposure.

1.7 Significance of the study

It was expected that the findings of the study would raise awareness of the general population, government, and private sectors regarding the effects of current levels of air pollution and temperature on the health of people in Chiang Mai, Thailand. This may lead to implications for public health to implement appropriate mitigation measures to reduce air pollution in the city and to prevent adverse health effects, especially among the vulnerable population. Since there was an establishment of a linkage between the history of hospital admissions and subsequent deaths, but not between daily counts of out-patient visits and subsequent hospital admissions, the study was unique due to identifying the susceptible population by linking the frequency of out-patient visits with subsequent hospital admissions. This study could increase understanding of the susceptibility to air pollution and temperature in less developed countries with tropical climates, could add more epidemiological evidence of time series studies in Asia, and could also be a sound basis for further research conducted within this area.

1.8 Structure of the thesis

In addition to this introduction chapter, there are 8 remaining chapters as follows:

Chapter 2 reviews previous literatures on air pollution and temperature effects on health, mainly focusing on time series studies.

Chapter 3 outlines the methods of developing the models to be used for quantifying the short-term effects of air pollution and temperature.

Chapter 4 discusses the characteristics and quality of the health data, and air pollution and meteorological data used in the study.

Chapter 5 presents the descriptive analysis results of the data used in this study, both exposure and health outcomes data.

Chapter 6, 7, and 8 describes the regression analysis results from the three series: out-patient visits series, hospital admissions series, and linkage series (linkage between out-patient visits and hospital admissions). The results of sensitivity analyses of each series are also presented.

Chapter 9 provides the discussion about the main findings of the study with respect to previous literatures as well as specific issues of concern, such as analytical issues, multiple testing, harvesting, and confounding. The strengths and limitations of the study are discussed. The conclusion of the key findings, implications for public health in regard to the short-term effects of air pollution and temperature, and recommendations for future research are also included.

Chapter 2: Literature review

This chapter presents a review of literature regarding health effects of air pollution and temperature. Due to a huge number of research studies on air pollution and health, this document is mainly focused on time series studies of air pollution in different countries, particularly in Asia. However, some relevant case-crossover studies of either air pollution or temperature, which have been shown to give similar results to time series studies, are also included. The specific health conditions and other related factors that are more likely to enhance the susceptibility to air pollution and temperature are described.

2.1 Air pollution and Health

2.1.1 Time series studies of air pollution and health

Time series regression is a method used for evaluating short-term effects of time-varying exposures [49]. A time series study generally aims to understand how explanatory variables influence health outcomes over time, and usually employs regression analysis for the investigation [50]. The time series method has been widely used to detect the short-term effects of air pollution on daily mortality and morbidity in many cities worldwide. The key advantage of the time series method is that the study population serves as its own control, and this, therefore, eliminates the influence of other underlying risk factors (such as smoking) that may vary among subjects, but do not vary from day to day [49]. However, there are some limitations of using this method, including the likelihood of measurement error due to using single or central monitoring sites to represent exposure for large mobile population, and the need for sophisticated statistical methods to adequately control for possible potential confounders such as long-term time trends, seasonal patterns, weather variables, and unusual events (e.g. influenza epidemics) [51]. Moreover, the time series method does not provide the information about long-term exposure to air pollution. Despite the limitations, time series studies have increased understanding about the influence of daily changes in ambient air pollution on health in various aspects, such as an increased daily mortality, exacerbation of asthma, and increased hospital visits and admissions [52]. Epidemiological evidence showing the effects of air pollution on daily mortality and morbidity are presented in this section. The morbidity effects are specific to out-patient visits and hospital admissions only.

2.1.2 Criteria air pollutants

A brief description of five criteria air pollutants, which are commonly used for time series studies, is provided here in order to give general information about the unique characteristics of each pollutant. The five criteria air pollutants include sulphur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3), and particulate matter (PM).

Sulphur dioxide (SO_2)

SO_2 is an irritant gas, mainly released into the atmosphere through industrial combustion of coal and oil. In a humid environment, SO_2 can be oxidized to sulphuric acid, and partially neutralised sulphate salts [53]. Thus, humidity and photochemical processes can accelerate the formation of acid aerosols in the atmosphere. Health effects of exposure to SO_2 may range from mild effects, such as irritation of the eyes, nose, and throat, to severe effects, such as bronchial spasm and deaths due to respiratory insufficiency and concomitant effects on the central nervous system [54].

Nitrogen dioxide (NO_2)

NO_2 is a secondary air pollutant, formed by the reactions of oxides of nitrogen and atmospheric oxidants such as O_3 in the presence of sunlight [53]. Oxides of nitrogen are generally emitted to the atmosphere by the combustion of fossil fuels from stationary sources, such as heating and power generation, and motor vehicles [54]. Exposure to NO_2 has been shown to increase airway reactivity to stimuli such as inhaled allergens, and enhance bacterial infection and colonization by reducing the ciliary beat frequency of bronchial epithelial cells [55]. The health effects of NO_2 exposure may range from cough and haemoptysis to lung oedema [54].

Carbon monoxide (CO)

CO is generated by the incomplete combustion of fossil fuels. Ambient concentrations of CO are highly related to traffic congestion, domestic combustion devices (such as heating and cooking), and smoking [54]. The effects of CO on health are due to the binding of CO to haemoglobin, which produces carboxyhaemoglobin, resulting in a reduction of haemoglobin capacity to transport or release oxygen [53]. Thus, when exposed to CO,

human body organ is likely to become hypoxia, leading to fainting, increased respiratory and pulse rate, intermittent convulsions, coma, and death [54].

Ozone (O_3)

O_3 is a photo-oxidant, formed by a complex series of reactions of nitrogen oxides and hydrocarbons in the presence of sunlight in the troposphere [56]. O_3 is a highly reactive pollutant. Therefore, exposure to O_3 may lead to inflammation of the nasal mucosa and of bronchoalveolar lining, leading to an increase in airway hyper reactivity and a decrease in lung function [53].

Particulate Matter (PM)

Particulate matter is a complex mixture of solid particles and liquid droplet suspended in the air. It can originate either from natural sources, such as windblown dust, bushfires, volcanoes, and the oceans, or from anthropogenic activities, such as industrial processes, motor vehicle exhaust, domestic fuel burning, and industrial and domestic incineration [57]. Mechanical processes, including grinding, breaking, or dust resuspension generate coarse particles (larger than 2.5μm in aerodynamic diameter), whereas combustion processes generally create fine particles (those smaller than 2.5μm in aerodynamic diameter, $PM_{2.5}$) [58]. Thus, particles suspended in the air comprise a variety of sizes and mass composition. They may consist of various substances, including inorganic and organic carbon (such as polycyclic aromatic hydrocarbon), fine soil dust, acidic nitrates and sulphates, heavy metals (such as lead), asbestos, and other fibres [53]. PM_{10} refers to particulate matter less than 10μm in aerodynamic diameter, sometimes called thoracic particles, while $PM_{2.5}$ or fine particles can be called respirable particles [51]. The small particles are of great concern because they can deposit in the deeper parts of the respiratory system and cause various adverse health effects.

It is noteworthy that there are several substances mixtures in the air. Generally, most air pollutants are highly correlated, which make it difficult for air pollution studies to separate the effects of one pollutant from one another pollutant [59]. Thus, the issue of collinearity is one common problem in epidemiological studies of air pollution [60].

2.1.3 Air pollution effects on mortality

Exposure to air pollution, even at moderate levels, is associated with increased mortality in many cities [51, 61]. Although the expression of the risk of dying due to air pollution exposure can vary from study to study, time series studies conducted in different locations have shown consistent findings of the association between air pollution and mortality.

For example, the APHEA (Air pollution and Health: a European approach) studies undertaken in 29 European cities indicated that each $10\mu g/m^3$ increase in PM_{10} concentrations was associated with an increase in all cause mortality of 0.6% (95% CI, 0.4, 0.8) [62]. Similarly, the National Mortality, Morbidity and Air pollution Studies (NMMAPS) conducted in the 20 largest metropolitan areas in the USA suggested that each $10\mu g/m^3$ increase in PM_{10} concentrations was associated with an increase in all cause mortality of 0.5% (95% CI, 0.1,0.9) [63]. All cause mortality in London (1992-1994) was also found to be associated with various pollutants (NO_2, SO_2, PM_{10}, CO, and black smoke), but the strongest association was found between PM_{10} and respiratory mortality (4.0% increase in deaths of all ages for a 10th-90^{th} percentile increment) [64].

Air pollution is associated with not only an increase in all-cause mortality, but also an increase in respiratory and cardiovascular mortality, particularly in the elderly [65-72]. Moreover, it has been speculated that the risk of dying in relation to air pollution is more likely to occur in general population, not only persons who are very ill or are about to die [73, 74].

2.1.4 Air Pollution effects on morbidity

Daily out-patient visits to different care settings and hospital admissions have been used as health outcomes to evaluate short-term effects of air pollution on morbidity. Similar to mortality, a daily change in air pollutant levels are related to increased daily hospital visits and admissions. The changes in air pollution have been found associated with all causes of the visits and admissions, and with several health conditions, including respiratory illnesses (such as upper respiratory infections (URI), lower respiratory infections (LRI), chronic obstructive pulmonary disease (COPD) and asthma), and cardiovascular diseases [5, 16, 23, 75-82]. The risk of the visits and admissions appears to be pronounced in children and the

elderly [5, 23, 75, 80, 81, 83]. The study results of some previous time series studies on morbidity effects of air pollution reviewed for this document can be seen in **Appendix 2A**. Similar to mortality studies, literature showed the increased risk of illnesses could occur among general population, not just only those who are very ill and would enter the hospital within a few days or weeks, anyway [73].

2.1.5 Time series studies of air pollution in Asia

In Asia, the pattern of mortality and morbidity in low-income countries is currently in a transition, that is, life expectancy in those countries is increasing and health risk factors tend to be related to lifestyles, urbanization, and environmental deterioration. Generally, the diffuse, small-scale burning (such as burning garbage and biomass) is the main contribution to air pollution in many Asian countries. It has been found that total suspended particle (TSP) is the major outdoor air pollutant, followed by PM_{10}, SO_2, and NO_2, respectively [84]. Like other regions, time series studies in Asian regions have also demonstrated an association between ambient air pollution and increased risks of deaths and illnesses.

According to the Public Health and Air Pollution in Asia (PAPA) project of the Health Effect Institute (HEI), a meta-analysis of 28 time series studies (of the total 45 studies) in Asia showed that all criteria pollutants were associated with daily mortality and morbidity, but the estimated risks varied, depending on study areas and their selected study pollutants (see table in **Appendix 2B**) [84]. Levels of SO_2, TSP, and PM_{10} were highly related with mortality and morbidity in this region. The health effects of O_3 and NO_2 were found in some areas in Hong Kong and Korea [33, 38, 85-92], while the health effects of CO were found predominantly in industrial areas in Korea [93]. The more recent publications of the PAPA project and of other Asian studies (Shanghai and Bangkok) also confirmed the adverse effects of PM_{10}, O_3, SO_2, and NO_2 on both mortality and morbidity in this region [94-96].

Most literature has indicated that current levels of pollutants, even at levels well below recommended standards (WHO or national standards), are significantly associated with increased mortality and morbidity [4, 75, 97, 98]. In addition, the most vulnerable groups appear to be children, the elderly ($\geq$ 65year), and people with pre-existing diseases, such as cardiovascular diseases (congestive heart failure, ischemic heart disease, and stroke), chronic obstructive pulmonary disease (COPD), and asthma [87, 88, 91, 93, 97, 99-102]. There is

only one study mentioning sex, indicating that risk of stroke mortality associated with particulate pollution is higher in the elderly female population [89].

In summary, air pollution is associated with an increase in daily deaths and illnesses all around the world. Children, the elderly, and people with pre-existing health problems are particularly vulnerable compared to general population. Among all five criteria pollutants (SO_2, NO_2, CO, O_3, and PM_{10}), which are commonly used for time series studies of air pollution, particulate matter (PM) has demonstrated more consistent adverse health effects than other pollutants [77, 94, 103-116].

2.2 Temperature and Health

There is a growing concern over temperature effects on health. Exposure to extreme hot and cold weather can affect people's health directly, such as hyperthermia or heat stress as a result of exposure to very hot temperatures and hypothermia and ischemic stroke due to exposure to very cold temperatures, leading to a rise in deaths and hospitalizations [8, 117-120]. Besides direct effects from extreme weather events, a bigger burden from indirect effects of exposure to small changes of temperature over time has been shown. The increasing heat and cold temperatures have been found to be associated with increased risks of deaths and illnesses (e.g. due to CVDs and respiratory diseases) in many places [8-10, 118, 121].

2.2.1 Temperature effects on mortality

An attempt to detect mortality risks associated with variations of heat and cold temperature has been done in many countries. It has been suggested that comfort temperatures (temperatures that people are able to adapt or live with) could vary across different geographical locations [122]. For example, the comfort temperatures in Valencia, Spain, were about 15°C in colder months and 24°C in hotter months [123]. Thus, an increase in heat (from 24°C) during hot periods and a decrease in temperatures (from 15°C) during cold periods could result in a rise of mortality in the city [123]. In a subtropical country, Taiwan, the comfort temperature ranged from 26°C to 29°C, and therefore, the mortality from coronary heart disease was detectable when temperature dropped below this range [124].

As a consequence of consistent observations that an increase in either hot or cold temperature can result in increased mortality, the relationship between temperature and

mortality can be visualised as a U-, V-, or J-shaped relationship [6, 13, 122, 125, 126]. In addition, due to increasing evidence of high temperature effects on deaths in many settings, it has been pointed out that heat-related mortality can be a major public health problem, not only in cool climate regions but also in temperate and warm climate regions [12].

Several studies have suggested that the risk of dying due to temperature effects is more likely to be higher in the elderly [8, 25, 123, 126, 127]. Furthermore, respiratory and cardiovascular diseases have constituted the major causes of deaths associated with temperature changes [6, 8, 123]. With respect to sex difference, some studies illustrated that females had a higher risk of dying associated with temperature changes [128-130], while some studies found that males were prone to die from heat-related deaths [131, 132]. However, a recent review of mortality effects of high temperature suggested a higher risk among females [127].

Literature has also suggested that there might be interactions between air pollutants and temperature on mortality effects of high temperature. However, to date, this issue remains unclear as some studies found a significant confounding or effect modification by air pollutants (particularly by O_3 and PM_{10}) on the association between temperature and mortality, whereas some studies did not [127].

2.2.2 Temperature effects on morbidity

By comparison to mortality, there are fewer research studies on the association between temperature and morbidity. Moreover, the risk of illnesses or hospitalizations in relation to temperature changes derived from morbidity studies appears to be less consistent compared to that obtained from mortality studies.

Hot temperature

Increased morbidity can be found following exposure to extremely hot temperatures. For example, a study in Australia suggested that the majority of hospital presentations during a ten day heat wave were older people (60 years or over), those who lived in institutional care or live alone, and those with pre-existing health problems such as cognitive impairment, alcoholism and diabetes [118]. Excess hospital admissions during a 1995 heat wave in Chicago were found to be mainly due to the direct effects of high temperatures, such as

dehydration, heat exhaustion, and heat stroke, and mostly in person aged 65 or older [119]. The admissions significantly increased in patients with underlying health conditions, including cardiovascular disease, diabetes, renal disease, and nervous system disorders [119]. An observational study during a 2003 heat wave in France also demonstrated that infected critically ill patients were more likely to suffer from hyperthermia than non-infected critically ill patients [133].

In addition to extreme temperature, a small increase in temperature may affect daily morbidity. For example, a study in London demonstrated that a 10.5% increase in hospital admissions due to respiratory disease among the elderly (over 75 years) was associated with each 1°C increase in daily mean temperature above 23°C [10].

Hot temperature has also been found to be associated with hospital admissions for heart diseases. A study in 12 US cities illustrated that an association between hot temperature and hospital admissions for heart diseases [121]. This was corresponding to a study in Denver, Colorado, which found the link between high temperature and an increase in hospital admissions for myocardial infarction and congestive heart failure [24]. Another study in New York City also suggested an increase in hospitalizations in association with high temperatures, ranged from 28.9°C - 29.4°C [134]. While a study in the US demonstrated the relationship between high temperature and heart disease admissions, studies in London, Madrid, California, and 12 European cities did not find the relationships between them [10, 135-137]. The lower effects of high temperature on hospital admissions than on mortality in those places suggest that many people may die before receiving medical treatment or admission to hospital [136].

Cold temperature

Daily variations of low temperature can also increase the risk of getting illness. For example, the excess winter morbidity among older people living in cold homes (those with insufficient energy to keep warm) in London was observed [138]. Another study in London found that a 10.5% (95% CI 7.6, 13.4) rise in all respiratory GP consultations among people age 65 or over was associated with each 1°C decrease in mean temperature below 5°C [23].

A study in Athens also showed that, with each 1°C decrease in mean temperature (linear), there was a 5% increase in hospital admissions due to acute coronary diseases, which was stronger in females and the elderly [139]. A study in Chicago illustrated the magnitude of CO effects on hospital admissions for congestive heart failure (CHF) increased with decreasing temperature, suggesting that the CO effects was temperature dependent [31]. The relative risks of hospital admissions for CHF associated with the 75th percentile of exposure to CO were 1.02 (95% CI 0.95, 1.10) for high temperature range, 1.09 (95% CI 1.04, 1.14) for medium temperature range, and 1.15 (95% CI 1.09, 1.12) for low temperature range.

In brief, small changes of temperature can induce morbidity, not only extreme temperatures. The elderly and ill people are particularly vulnerable to temperature effects in comparison to others. In addition, the manifestation of adverse health effects may be due to the interactions between temperature and air pollutants, not temperature alone.

2.2.3 Health effects of temperature in Asia

Few investigations of association between temperature and health have been made in Asia. Nevertheless, evidence shows that temperature changes may also affect mortality and morbidity in Asia, but the magnitude of the risk may differ from that in other regions in accordance with variability of climates and population characteristics.

Mortality studies

In China, Kan et al reported that the lowest mortality risk occurred at a temperature of 26.7°C (optimum value) in Shanghai [140]. It was found that the total mortality increased by 0.73% for each 1°C increase in temperature above this optimum value, but decreased by 1.21% for each 1°C increase in temperature below this value.

In Taiwan, Pan et al found that the temperature range for the minimum mortality risks due to coronary artery disease (26-29°C) and cerebral infarction (27-29°C) was higher than that observed in colder climate countries [124]. Each 1°C decrease in temperature from 27-29°C was associated with a 3% increase in the risk of cerebral infarction in the elderly.

The increased cardiovascular mortality, such as heart disease and ischemic stroke, were also found in Israel [141], Japan [142], and Korea [143]. The increased deaths appeared to be higher in winter and highly associated with cold temperature.

Morbidity studies

In Japan, Ye et al indicated that daily maximum temperatures were associated with hospital emergency transport for pneumonia, but not for other diseases [144]. They also found that increased daily maximum temperatures were associated with decreased hospital emergency transport for hypertension.

In Taiwan, an increase in acute coronary syndrome of about 30-40% was observed when the average daily temperature was below 26.2 °C [145].

2.3 Susceptible populations

Individual susceptibility is one important factor affecting relationships between air pollution and health and between temperature and health. Each individual has different ways and different degrees in responding to environmental exposure. Therefore, individual susceptibility can vary greatly among a population, which can be influenced by individual variability and diversity, such as levels, dose, and duration of exposure, physiology, biological mechanisms, and behaviour [15]. Furthermore, the increased susceptibility is likely to be enhanced by frail health status. An establishment of a link between history of hospitalizations and mortality has suggested that a risk of dying associated with air pollution and temperature is higher among persons who were hospitalized before deaths with chronic health conditions, such as congestive heart failure, myocardial infarction, and diabetes [14, 27, 28]. However, there is a lack of identifying characteristics of frail populations by linking the history of out-patient visits with subsequent hospital admissions to see whether the risk of admissions associated with the exposure is modified by history of previous visits before the admissions.

2.3.1 Health conditions and enhancement of vulnerability

Pre-existing health problems, including respiratory disease, circulatory disease, diabetes, and intestinal infectious disease, are more likely to increase the risks of deaths and hospitalizations in association with air pollution and temperature.

Respiratory disease

Air pollution effects are more likely to manifest in persons with respiratory disease such as asthma and chronic obstructive pulmonary diseases (COPD). Experimental human studies showed that exposure to ozone (O_3) could limit ability of people with COPD to perform deep inspiration through reflex mechanisms, resulting in a significant decrease in vital capacity of the lung [146]. The significant effects (both single and combined) of exposure to relatively low concentrations of air pollution have been shown in asthmatic patients, including the reduction of force expiratory volume (FEV) after exposure to O_3, the enhancement of airway reactivity to allergen and airway inflammation when exposed to NO_2, and the increase in bronchoconstriction due to SO_2 exposure [146]. The pulmonary infections may occur due to the single and combined effects of O_3 and NO_2 on alveolar macrophage by reducing its ability to react against infectious agents [147]. Air pollution may increase the vulnerability of lung defence mechanisms by causing the changes of immunological response such as suppressing and increasing antibody production of immune system [148].

The vulnerability to temperature appears to increase in persons with COPD. This may be because these people usually have cardiovascular problems, and therefore, their blood components are particularly vulnerable to temperature changes [14]. Respiratory infections during cold weather in persons with COPD can occur easily because their lungs are typically colonized by bacteria [149]. Furthermore, an increase in red cell counts, platelet, blood viscosity, and bronchospasm can also be enhanced by cold weather [150].

Circulatory disease

It has been suggested that acute episodes of cardiovascular diseases (such as myocardial infarction and cardiac arrhythmia) are probably due to the impairments of lung functions, inflammation of alveolar, increased coagulability of the blood, alterations of the nervous system control of the heart, and decrease of heart rate variability following the exposure to air pollutants [151-153]. In addition, persons with myocardial damage or cardiac disease are more likely to develop congestive heart failure (CHF) due to an enhancement of acute pulmonary diseases, such as bronchitis and pneumonia, after exposure to air pollution [154].

In order to adapt to hot temperature, cardiac output in human bodies is generally increasing to increase blood circulation [121]. This process can be limited by dehydration, which reduces blood volume in the body. Increased cholesterol and blood viscosity has also been found on exposure to high temperatures [155]. Thus, people with impairment of cardiac functions are probably less able to adapt to increasing temperature compared to healthy persons, resulting in increased deaths and hospitalizations during heat waves. Furthermore, some medications used in chronic disease of the heart and lungs may interfere with heat loss mechanisms and reduce adaptive responses during hot temperature [25, 117]. In addition, people with pre-existing hypertension or hypercholesterolemia are more likely to develop ischemic stroke on exposure to cold temperature [143]. Cold temperature may facilitate the development of ischemic heart disease by causing hemoconcentration, which can lead to thrombosis [156]. Moreover, angina pectoris and myocardial infarction can be facilitated by physical activity during cold weather [121].

Diabetes

Recent studies suggested that people with diabetes were at greater risk of death and illness associated with air pollution [28, 29, 32, 157]. For example, a study in Brazil showed that an increase in cardiovascular emergency room visits in association with SO_2 levels was higher in diabetic patients than non-diabetic patients [157]. It has been pointed out that the increased risk among diabetic patients appears to be related to cardiovascular risk factors associated with PM pollution, including increased plasma fibrinogen levels and other makers of systemic inflammation, increased C reactive protein levels, and reduced heart rate variability [28, 29]. In addition, exposure to particles was also found to be associated with impairment in vascular reactivity and endothelial function in diabetes, which was also related to cardiac functions [32]. An increased risk of deaths on hot days among people with diabetes was found to be higher than other people [14, 158]. This may be because of the interaction between increased demands on the circulatory system under extreme thermal stress and impairment of endothelial function and autonomic control in people with diabetes.

Intestinal infectious disease

There is evidence suggesting that climate variability may lead to an increase in frequency and severity of some particular infectious diseases, such as intestinal infectious diseases. For example, an increase in hot temperature may not only increase the frequency of occurrences of infectious diarrhoea, but may also increase the severity of the illness. Since exposure to hot temperature can cause dehydration through heat loss mechanisms [117], the body of persons with infectious diarrhoea may not be able to balance fluid intakes and outputs easily during high temperatures. This could result in an increased severity of their dehydration and electrolyte imbalance. In addition, an increase in temperature may promote the growth of bacteria and transmission of intestinal infectious diseases, such as bacteria enteric infections, diarrhoeal diseases, and food poisoning, leading to a rise of numbers of visits or admissions to hospitals [159-162]. For instance, the number of food poisoning cases in European countries was found to increase in association with a 1°C increase in average temperature above indentified threshold value [160]. The hospital visits and admissions for diarrhoea in children also increased by 8.0% and 5.6% per 1°C increase in mean temperature over lag 0-4 weeks, in Peru and Bangladesh, respectively [159, 162].

Other diseases relating to air pollution and temperature exposure

Apart from the diseases mentioned above, there are some other diseases that may also be related to air pollution and temperature exposure, such as cancer, suicide, and traffic accidents. Evidence has suggested that the incidence of cancer, such as lung cancer, is associated with outdoor air pollution emitted from industrial sources, power plants, and motor vehicles [163-165]. It has been speculated that carcinogenic effects of air pollution may be derived from an exposure to combustion emissions, including particles, semivolatile, and gaseous pollutants, which usually contain chemical compounds, such as polycyclic aromatic hydrocarbons (PAH) and nitrated PAH [166]. It has also been suggested that the particularly vulnerable people may not be only those with cardiorespiratory health problems, but also those with failing health causing difficulty in regulating their physiologic set points, such as cancer [Frank et al cited in 70]. For example, it was found that an increase in daily deaths from cancer of 3.9% (95% CI, 1.0 to 6.91) among people age 65 years or over in Quebec was associated with an increase in the changes of mean concentrations of O_3 of 21.3% $\mu g/m^3$ [70].

Accidental events, such as traffic accidents, have also been suggested to increase in association with increasing temperature. For example, during hot days in Tokyo, the occurrence of motor vehicle collisions was significantly associated with the high temperatures [167]. Similarly, road traffic accidents in Riyadh were also found to be related to the high temperatures in summer [168]. Hot temperature may lead to increased stress, decreased performance in intellectual tasks (which require physical efforts and motor skills), and increased heart rate that exacerbates existing pathological conditions of heart and lung diseases of drivers, resulting in road traffic accidents [168].

In addition, an increased risk of suicide in England and Wales was also found to be associated with hot weather [169]. For each 1°C increase in mean temperature, there was an increase in suicide and violent suicide by 3.8% and 5.0%, respectively [169]. The hot temperature may lead to excessive alcohol drinking, and aggressive and violent behaviour among individuals, which might result in an increase in suicidal acts.

2.3.2 Effect modifiers

Besides the pre-existing health problems, some characteristics of population such as age, sex and occupation may also increase vulnerability to air pollution and temperature.

Age

Numerous research studies have indicated that the elderly are particularly vulnerable to air pollution and temperature. This may be due to the deterioration of their physical bodies with increasing age. The functional impairment of important physical organs (such as heart, lungs, and kidneys) may make it difficult for the body of people in older age to adapt or recover after exposure to high concentrations of pollutants or temperature changes compared to the young. Research evidence has also suggested that older people may have a higher risk of suffering from air pollution effects due to a decline of antioxidant defences [170]. With regard to temperature effects, an experimental study demonstrated that older people (>60 years) were less able to maintain core temperature under a given cold temperature compared to younger people because of a reduction in thermal sensitivity of the skin (such as vasoconstrictive response to cold) and in subjective thermal perception during cooling [171]. In addition, the cognitive impairment and reduced mobility may limit

their abilities to perform behavioural defences or may delay their access to health care services after exposure [117, 118].

Sex

The role of sex in association between health and air pollution or between health and temperature are not consistent. Some studies showed an increased risk of the exposure in females [8, 18, 172, 173], while some studies showed a higher risk of exposure in males [24, 174]. Nevertheless, by comparison, it appears that females are more vulnerable than males as indicated by the majority of published literature [127]. First of all, the increased susceptibility may be related to differences in the growth and development of physical organs and the maturity of immune system. Due to smaller sizes of the lung and air way calibre, but higher levels of bronchial and airway reactivity, females are more likely to be vulnerable to air pollution than males [18]. A smaller proportion of the heart relative to body size (approximately two-thirds) as well as higher pulse rates in females in comparison to males may also increase their vulnerability to pollution and temperature [18].

It has also been postulated that fluctuations of hormones during menstrual, pregnancy, and menopause periods may be responsible for female susceptibility to air pollution (such as exacerbation of asthma) [18]. Finally, the differences in lifestyle and behaviour between females and males, in terms of domestic exposure, daily activities, and occupation may influence their susceptibility differently. This could result in different exposure hazards as well as different does, levels, and duration of exposure. It should be noted that much of the evidence indicating sex differences has been found in older populations [14, 28, 89, 129, 130, 172, 175, 176]. The differences may be attributed to confounding by age, as the increased vulnerability among elderly female populations may be due to age related declines in physiological functions.

Occupation

Occupation may also influence individual susceptibility to air pollution and temperature because people who work in different places may be exposed to air pollution and temperature differently. The mixtures and concentrations of air pollutants may vary from workplaces to workplaces. For example, a study in Thailand showed that there was a

decline in lung functions among traffic police who work at roadside in Bangkok, which was associated with higher levels of exposure to particles from motor vehicle exhausts [177]. Another study in Bangkok also demonstrated that street vendors, who sell clothes or foods, were highly exposed to genotoxic air pollutants such as particle-associated polycyclic aromatic hydrocarbons (PAHs) and benzene [178]. Similarly, workers will experience thermal stress (heat and cold stress) to different degrees in relation to different working environments. For example, people who worked outdoors during winter periods were found to suffer from cold stress, whereas people who worked in a glass factory experienced intensive heat exposure [179]. Therefore, occupation (or employment status) has also been used as a proxy of socioeconomic status (SES) in some studies for examining the interaction between SES and environmental exposure-related health outcomes [180-183].

Season

In general, levels of air pollution and temperature vary throughout the year, from season to season. This is due to the fact that several factors in the atmosphere, such as pressure, wind, and sunshine, can influence the emission, formation, and dispersion of pollutant mixtures in the air. The interactions between various mixtures of pollution components and meteorological variables may occur differently in different seasons, which could also influence exposure levels of individuals differently [184]. For example, ozone (O_3) is known to be a secondary pollutant, formed by a series of reactions between nitrogen oxides and hydrocarbons in the presence of sunlight [56]. Therefore, a higher level of ozone in summer would be expected, and people would then be more likely to be affected by O_3 in summer than in other seasons. Furthermore, it may be possible that patterns of outdoor activity of individuals may vary from season to season, resulting in differences in both duration of exposure and exposure levels [185]. For example, people tend to go out for outdoor activities summer or warm season, which may lead them to be more exposed to outdoor air pollution and hot temperature than other seasons. The use of air conditioning or opening windows for cooling may be more prevalent during hot period, while the use of heating or closing windows to keep warm may be more prevalent during cold period.

2.4 Lag effects of air pollution and temperature

In general, the effects of air pollution are acute, which usually occur at current day of exposure (lag 0) or at 3-5 days after exposure. For example, the effects of particulate air pollution on daily mortality in Seoul, Korea, were found to occur on the same day of exposure [186]. Another study in Atlanta, U.S.A., showed that the effects of particulate air pollution on respiratory visits in ambulatory care setting occurred at lag 3-5 days [76].

For temperature effects, it has been suggested that hot temperature effects are immediate, with occurrence at short lag (e.g. from lag 0 up to 5-7 days), while cold temperature effects are prolonged and may appear after lag 3 days to at least 2 weeks or 1-2 months [9, 125, 187-189]. For example, a study in the Netherlands found that the lag effects of hot temperature occurred at current day of exposure, whereas the lag effects of cold temperature occurred at lag 0-5 days [125]. Another study in Sofia and London demonstrated that there were short lag effects of hot temperature at around 3 days, while there were longer lag effects of cold temperature at 2 weeks [188].

Although evidence from previous studies has suggested short lag effects for air pollution and for hot temperature, and longer lag effects for cold temperature, it is important to note that the lag effects could vary depending on geographical locations and on characteristics of study populations. The geographical locations may influence intensity of air pollution and temperature, resulting in different exposure levels and duration. The population characteristics may also mean the variability in susceptibility to air pollution and temperature exposure, which could make the magnitude and lag structures of the effects vary from study to study. In addition, since there are several factors affecting hospital visits/ admissions (e.g. necessity to make appointments in advance, availability of transport, and availability of hospital beds), the morbidity outcomes may induce lag effect structures that differ from those observed in the mortality studies.

2.5 Conclusion

Research evidence has suggested an increase in daily mortality and morbidity is associated with daily changes of air pollution and temperature. The young, the elderly and persons with pre-existing health problems are particularly vulnerable. However, there are few

investigations in developing countries with tropical climates. Furthermore, more consistent findings of association between air pollution and health, and between temperature and health have been found for mortality than those for morbidity. With regard to future impacts of climate variability that are more likely to affect low-income settings than high-income settings, there is a need for more research studies in developing countries with different types of climate to assess regional specific vulnerabilities and to identify the populations susceptible to air pollution and temperature variations.

Chapter 3: Methods

The methods used for conducting this study are presented in this chapter. The study design and period, area of the study, and the study population are described. Sources of health data as well as air pollution and meteorological data are explained. The analytical methods employed for the study are also detailed.

3.1 Study design and period

This study was a regression analysis of retrospective time series data to assess the effects of air pollution and temperature on daily out-patient visits and hospital admissions among people in Chiang Mai province, Thailand, from October 2002 to September 2006.

3.2 Study area

This study was undertaken in Muang district of Chiang Mai, the inner area of the city. There were three main reasons to select Muang district for the study.

First of all, it is an urban area with growing infrastructure development, and higher population density and traffic congestion than other districts. Thus, it is more likely to be affected by air pollution and temperature changes. It has also been suggested that heat effects are usually higher in urban areas than rural areas ('urban heat island effect', which occurs due to abundance of heat-retaining surfaces, such as concrete and black asphalt) [47]. In addition, evidence has showed that respiratory illness has become an important health problem in Chiang Mai. For example, in 1994, health statistics showed that there was the high number of 500,000 hospitalized patients due to respiratory diseases [43]. In 1995, it was observed that 8.8% of the total children in Chiang Mai was suffering from asthmatic problems [44]. Moreover, the annual health report has also indicated that respiratory disease is the first leading cause of out-patient visits among the Chiang Mai population [39]. Therefore, it is interesting to know whether this health problem is exacerbated by short-term changes of air pollution and/or temperature in the city.

The second reason for undertaking the study in the Muang district was due to the feasibility in obtaining health data as well as air pollution and meteorological data at the same period

of time. The two air monitoring stations are located within the area of Muang district, which is among the few cities in Thailand that has more than one fixed air monitoring station. The use of two fixed sampling sites could help reduce bias in regard to misclassification of exposure that commonly occurs in epidemiological studies when using only one fixed sampling site to estimate exposure of large population [190]. Because one station is located in the inner city and another one is located in the outskirts (about 10 kilometres away), it was expected that the average exposure levels from the two stations located in different geographical locations would be the reasonable average exposure levels for the study population since personal exposure could not be known. The use of data from two stations could also help reduce a problem of missing data because when data from one station were missing, data from another station were used for calculating the replacements (detailed later in section 3.4.2).

The final reason of choosing Muang district for the study was to avoid the likely influences of differences between people living in urban area and people living in the highland (e.g. tribal people living in remote area on the mountains) on study results, in relation to socioeconomic status and lifestyle such as levels of education, nutritional status, and indoor cooking activities (which is common among tribal people in the highland).

3.3 Study population

Study population were all people who had visited and/or had been hospitalized at the selected health centres and hospitals in Muang district in Chiang Mai, from October 2002 to September 2006. During the study period, the district comprised a population of 296,753 people (December 2005), with 16% of 0-14 year, 73% of 15-59 year, and 11% of > 60 year) [39].

3.4 Data collection

3.4.1 Health data

Health outcome data of this study were daily morbidity data , which were the routine daily health records of two different data sets: out-patient visits (all ambulatory care settings, including primary care) and hospital admissions, of selected health centres and hospitals within Chiang Mai public health systems. The daily out-patient visit data were obtained

from the Chiang Mai Provincial Health Office, and the daily hospital admission data were obtained from the National Security Health Office. Therefore, only health centres and hospitals that provided a monthly report of daily out-patient visits for the provincial health office and of hospital admissions for the National Health Security Office were included in the study. These consisted of 10 sub-district health centres and 11 hospitals (6 private hospitals and 5 government hospitals). The time period of health data collection covered a four-year period from October 2002 to September 2006. However, over this study period, there were different numbers of health centres and hospitals contributing to the health data in each month. Health information on individual visits and admissions selected for the study comprised hospital number, date of visits, date of birth, age, sex, occupation (out-patient visits only), a unique individual identification number (ID), and diagnosis based on diagnostic codes of the International Classification of Disease, the 10th version (ICD-10) of the WHO [191].

3.4.2 Air pollution and meteorological data

Data on daily levels of selected criteria air pollutants, including SO_2, NO_2, CO, O_3, PM_{10}, and $PM_{2.5}$, were obtained from the two air monitoring stations: Chiang Mai City Hall station (35T) and Yuparaj College station (36T), in Muang district, Chiang Mai. The Yuparaj College station (36T) is located in the Muang district central, and is a roadside station. The Chiang Mai City Hall station (35T) is located about 10 kilometres away from the central district, which is an urban area station (description of the two types of air monitoring station is presented in chapter 4, section 4.3.1). The two stations are operated by the Pollution Control Department (PCD), Bangkok, which is the centre for controlling the real-time air monitoring stations all around the country.

The real-time monitoring equipments can provide readings of air pollutant levels at any time interval such as at every 30 minute or at every one hour, depending on settings. The PCD is responsible for calculating the daily mean levels of the pollutants and provides this information to the public via the PCD's website. Daily mean levels of all pollutants (only $PM_{2.5}$ data are not shown via the website) are calculated from 10am to 9am of a day. The data presented on the website are the daily mean of a pollutant measured every one hour, the first reading begins at 10am (starting the measurement from 9am) every day and ends at 9am on the following day, which is the day of reporting. The data of most pollutants were

the report of a one-hour average for 24 hours, with exceptions for CO (8-hr average) and PM_{10} (24-hr average). Daily mean levels of temperature, relative humidity, and rainfall were also obtained from these two stations during the same period.

In this study, the meteorological data from the district central station were used for the analysis because levels of meteorological variables were not greatly different between the two stations, and also the data from the district central station had less missing values compared to the outskirt station.

For air pollution, levels of air pollutants from these two air monitoring stations were calculated as representative of the city's mean daily levels for the analysis. If there was a missing value of one station, the mean daily value from another station on the same day was used to estimate the missing value on that particular day. By adopting the APHEA (Air Pollution and Health: a European Approach) protocol, the mean value from the remaining station was multiplied by a factor equal to a ratio of the three-month mean for the missing station over the corresponding mean from this remaining station on that day [192]. If there were missing values from both stations on the same day, the mean values of both stations on the previous day and the day after were used for the estimation by adopting the same approach. However, if there was a gap (e.g. 2 days upward) of missing data from the two stations at the same period of time, the estimation could not be made and, therefore, those particular days with missing data were left as they were.

3.5 Analytical methods

The purpose of time series analysis was to explore whether there was a short-term association between exposure and outcome. Regression analyses of daily counts of the visits and admissions were employed. In general, for count data, a Poisson distribution is assumed and a Poisson regression model, allowing for overdispersion, is commonly used for time series studies [193]. However, when the overdispersed Poisson (OP) regression model is not sufficient to accommodate the high overdispersion of the data, negative binomial (NB) distribution can be assumed and NB regression can be applied for the analysis [105, 194] Since the health data in this study were heavily overdispersed, the NB were used for the analysis.

For the NB model, the probability distribution is given by the expression:

$$\Pr(Y = y \mid x) = \frac{\Gamma(y + a^{-1})}{y!\Gamma(a^{-1})}\left(\frac{a\mu(x)}{1 + a\mu(x)}\right)^{y} \times \left(\frac{1}{1 + a\mu(x)}\right)a^{-1}, y = 0,1,K,$$

Where x is the vector of explanatory variables and a is the dispersion parameter, which represents the degree of extra-Poisson variation. When overdispersion is not present, $a = 0$ and the NB will be equal to a Poisson distribution. The variance of the NB model is: $\text{var}(Y|x) = \phi[\mu(x) + a\mu(x)^2]$. The model holds negative binomial distribution when $\phi = 1$ and the model is overdispersed when $\phi > 1$ or underdispersed when $\phi < 1$ [194].

Generalized linear models(GLMs) were applied for the modelling [195]. The NB model is in the following form:

$$Log[E(Y)] = \beta_0 + \beta_1 X_1 + ... + \beta_p X_p$$

Where $E(Y)$ is the expected daily counts of out-patient visits or hospital admissions, $X_1 \ldots X_p$ are explanatory variable (predictors) of Y, and $\beta_1 \ldots \beta_p$ are the regression coefficients for the predictors.

3.5.1 Adjustment for potential confounders

Seasonality

In general, there is a systemic variation in air pollution, weather, and health outcomes over time. The seasonal patterns of each variable may induce correlations among them, even though they may not be causal relation. The changes in out-patient visits and hospital admissions over time may not be due to the changes in levels of air pollution and temperature. The changes of the visits and admissions may be due to the changes of something else such as the changes of hospital systems or people's lifestyles in relation to season change.

With respect to the problem of having different numbers of hospitals contributing to the health data in each month, when building the models, a monthly indicator representing

months of the visits/ admissions over the study period from 1 to 48 (4-year data) was used for seasonal control.

Long-term trends

In this study, long-terms trends can be defined as long-term changes in the mean daily hospital visits and admissions (outcomes) over a certain period of time. It is also possible that there are long-term trends of air pollution and temperature (exposure) over a certain period of time. The long-term changes of exposure and of outcomes over a certain period of time may make it look like they have had a causal relationship even though they do not. Thus, long-term trends must be addressed in time series studies.

To account for long-term trends, the smooth function of time was used to capture long-terms trends in the data. The splines created by 'frencurv' command were used in this study. The 'frencurv' is an extension of b-splines, which generates a set of reference splines to be used in the design matrix of a regression model, with the property that the parameters fitted will be values of the spline at a list of reference points. The core model was developed with the starting of using one degree of freedom (df) for the smooth of time at the first place.

Day of week

Day of week can affect daily hospital visits and admissions. There are usually higher counts of visits and admissions on Monday than any other weekdays, while there are usually less counts of visits and admissions on the weekend [193]. To account for day of week effects, day of week indicator was incorporated in the models.

Holidays

Similar to day of week, holidays may also have effects on hospital visits and admissions. Besides including indicator variables of public holidays during the study period into the models, indicator variables of the two long-holiday periods in Thailand: international new year period (30 Dec-2 Jan) and Thai new year period (13-16 Apr), were also included into the models. This was because the plots of residuals showed relatively high positive and negative residuals during these two periods. In general, daily hospital visits and admissions,

particularly due to accidents (e.g. car accidents or head injuries because of drinking and driving, and high traffic congestion) are usually high during these periods. Thus, the increased visits/ admissions during these periods may confound the relationships between air pollution and the visits/ admissions, and between temperature and the visits/ admissions.

Influenza or respiratory epidemics

There is no information on influenza or respiratory epidemics in Thailand. It has been suggested that this variable may confound the findings in time-series study because they may co-vary with the environmental exposures or may be more prevalent during cold weather period [196]. Therefore, the period comprising daily counts of the visits/ admissions due to respiratory diseases above the 99th centile of the total respiratory visits/ admissions was used as an indicator for influenza or respiratory epidemics in this study.

Meteorological variables

Three meteorological variables: temperature, relative humidity, and rain, were included in the models by using natural cubic splines (3df over the range of the values of these three variables). When air pollution was the exposure of interest, temperature was considered as a potential confounder to be controlled for, whereas, when temperature was the exposure of interest, air pollution was controlled for. When either air pollution or temperature was the exposure of interest, humidity and rain were also incorporated into the model as possible potential confounders. Functional forms of meteorological, specific to temperature, in terms of smoothing and linear (or threshold models), are described below.

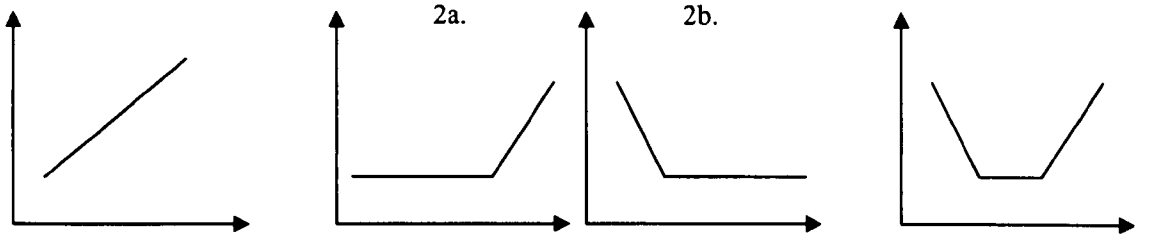
Smoothing

Graphical assessment was used for visualising general relationships between temperature and the visits/ admissions, by using natural cubic splines (NCSs) to identify the general relationships between them. The NCSs were used to avoid too much flexibility at the edges as these splines would become straight at the edges if there were not too many values of the temperature. The NCSs fit cubic polynomials to temperature-the visits/ admissions relationships in each interval. The polynomials of each interval are joined smoothly by knots, the boundaries of the intervals. Therefore, the number of knots determines the degree

of smoothing of the data. In this study, two knots (3df) were chosen for allow for flexibility of the relationships between the exposure and the outcomes.

Linear or threshold models

It was expected that the general relationships between temperature and the visits/ admissions would be shown in three-possible figures below [197]:



(1) Linear (2) Threshold models (3) Double threshold models

Figure 3. 1 Conceptual models of temperature-hospital visits/ admissions.

Simple linear models were considered when a log-linear association through the whole range of temperature as shown in **Figure 3.1-1**. For simplicity, a threshold temperature used for quantifying temperature effects in the present study was chosen visually (integer value only) from the plots of their general relationships. A likelihood ratio test between the model fitted with linear terms of temperature and the model fitted with non-linear terms of temperature was also performed to ascertain the non-linearity of the relationships. If the temperature threshold was not apparent from a graphical assessment and the test showed that there was no evidence of non-linearity, a linear term of temperature was used for quantifying temperature effects.

When a plot of the smoothed relationships between temperature and the visits/ admissions was shown as **Figure 3.1-2**, a threshold model was assumed, which could be two possible directions. **Figure 3.1-2a** shows a log-linear increase in the risk of the visit/admissions above the temperature threshold and no increase (or decrease) in the risk of the visit/admissions below the temperature threshold. **Figure 3.1-2b** illustrates a log-linear increase in the risk of the visit/admissions below the temperature threshold and no increase (or decrease) in the risk of the visit/admissions above the temperature threshold.

If a smoothed plot of the relationships suggested U or V shape as shown in **Figure 3.1-3**, the double thresholds model was assumed. There would be two temperature thresholds: low and high temperature thresholds for quantifying temperature effects. This meant that there was a log-linear increase in the risk of the visits and admissions below a 'low temperature' threshold, and above a 'high temperature' threshold.

3.5.2 Lag structure (delayed effects)

The effects of air pollution and temperature may be immediate and/or may occur several days after exposure (delayed effects occurring with some lags). This can be called a distributed lag structure, which means that air pollution or temperature could affect morbidity on many days. Thus, the effects of air pollution or temperature on morbidity (at any day) would be the sum of the effects on those days. However, the magnitude of the effects of today's air pollution (or temperature) and of yesterday's air pollution (or temperature) could be different.

In the present study, distributed lag models were employed to investigate the effects of air pollution and temperature on daily hospital visits and admissions. The overall effects of a unit increase in air pollution (or in temperature) on a single day are its impact on that day plus its impact on subsequent days. For air pollution, lag effects at 0-1 day and at 0-4 days were chosen for the analysis because of two reasons: first, literature reviews suggested that air pollution effects were more likely to be immediate or relatively short-term [3, 125, 192, 198, 199], and second, to make the study results comparable to the PAPA protocol (**Appendix 3A**). For temperature, lag effects at 0-1 day (short lag) and 0-13 days (long lag) were selected for the analysis since previous literature suggested that heat effects were acute (about 0-1 day after exposure), while cold effects were more delayed up to 2 weeks or even a month [10, 121]. In addition, the plots of constrained lags of temperature effects on the health outcomes in the study illustrated that the effects were less likely to increase after 13 days.

3.5.3 Effect modification

Because different groups of people may be exposed to different levels of air pollution and temperature, and some people may be more vulnerable than others, identification of the vulnerable population in different disease groups was made. Daily counts of the visits/

admissions were divided into six main groups, including all-cause visits/ admissions, respiratory diseases (J00-J99), circulatory diseases (I00-I99), diabetes (E10-E14), intestinal infectious diseases (A00-A99), and 'other' visits/ admissions (the rest of the counts). The primary diagnosis based on the International Classification of Disease, 10th version (ICD-10) of the WHO was used for this purpose. Then, the effects of air pollution and temperature in different disease groups were assessed in separate series.

There were three effect modifiers: age, sex, and occupation, considered in this study. The data was divided into three age groups, including 0-14 years (children), 15-64 years (adult), and ≥65 years (the elderly). The data was also stratified by sex (male and female). In addition, there were three occupational groups for the analysis, including unemployed and economically inactive people, non-manual workers, and manual workers (details of occupational grouping can be seen in **Appendix 3C**). All occupational groups were restricted for working age (15-64 year) only, excluding children and the elderly. To investigate the possible modifications, the series were developed separately for each group and then the test for interaction was undertaken to see whether there was evidence of effect modification by each subgroup. In addition, the effect modification by season (winter, summer, and rainy seasons) was also examined. The analysis for each season was done separately. The test for interaction between seasons was also done.

3.5.4 Autocorrelation

Daily counts of hospital visits and admissions are likely to be correlated and are not independent. That is, today's visits or admissions are likely to be correlated with yesterday's visits and admissions. To account for autocorrelations in the models, the partial autocorrelation function (PACF) was plotted to visualise the serial correlation of the time series at lag 1 day, 2 days...etc, with the value of each lag corrected for the previous lags. In general, the autocorrelation in time series is usually removed after adequate adjustment for seasonality and other potential confounding factors. However, the remaining autocorrelations can be adjusted for by including autoregressive terms at any order that shows strong autocorrelations into the models.

In this study, the PACF plots of the out-patient visits series showed that there were apparently strong positive autocorrelations at lag 1 day and every seven lag days (1, 7, 14,

21, and 28 lags), even though and indicator of day of the week was already included in the models, which suggested the remaining of day of the week effects in the models. Therefore, autoregressive terms at order 1, 7, 14, 21, and 28 were created and incorporated into the models.

3.5.5 Overdispersion

As previously mentioned, overdispersion is the phenomenon that the variance of the residual distribution is greater than the mean of the distribution of the visits/ admissions, which may be due to several reasons (e.g. the influence of some unmeasured factors on the heath outcome variables). If the overdispersion is not addressed, it can lead to the underestimation of coefficient standard errors. Thus, after applying overdispersed Poisson (OP) or negative binomial (NB) models, a presence of remaining overdispersion was checked by looking at the model overdispersion parameters (ϕ), which was expected to be close to 1.

3.5.6 Diagnostic plots

Time series plots

The health outcome data were plotted against time to help identify cyclical or other seasonal patterns that needed to be addressed in the analysis [200]. The time plots were also useful for checking if there were any unusual events that could have occurred. After regressing a potential confounder, plots of the predicted values over time were also undertaken to see whether the fitted model provide an adequate description of the data in relation to the specific confounder.

Residual plots

Plots of residuals (residual = observation - fitted value) versus time were used to examine whether the patterns seen in the original data series had been effectively removed. When a smooth curve was also fitted in the model, the residual plots could help identify if long wavelength patterns remained in the data. If the seasonal patterns appeared in both the original data series and in the residual plots, this would have suggested an insufficient fitting in the model. In contrast, if the patterns presented in the residual plots, but did not show in the original data series, this would have suggested overfitting in the model [201].

Partial autocorrelation function (PACF)

As described earlier, the PACF plots were employed to check whether there were any remaining serial autocorrelation in the series. To account for the autocorrelations, autoregressive terms at order that showed relatively strong positive autocorrelations were included in the models. The autoregressive terms were created by extracting the residuals at any significant order (strong positive autocorrelations) and then lagging them for the number of days seen from PACF plots (at lag 1, 7, 14, 21, and 28 days for out-patient series, and at lag 1 day for hospital admission series). The PACF plots were checked each time when including a new variable into the model, and were checked again after including all variables into the models.

3.5.7 Model building process

After data cleaning and corrections, Pearson pairwise correlations were applied to examine the correlations among air pollutants and meteorological variables. The model building process began with plotting count numbers of the visits and admissions against time in order to see the general patterns of the outcomes over time. Then, the baseline or 'core' model was developed by inclusions of the terms of potential confounders into the model. Plots of residuals and of predicted values over time were used at each time adding variables to the core model to check the adequacy of the modelling.

When seasonality, long-term trends, meteorological variables, and pollution (when temperature was the main exposure) were adequately adjusted for, PACF of residuals were explored to assess the presence of any remaining autocorrelation of the data. If autocorrelation was present, autoregressive terms at significant order were established and added into the model. The contribution of the air pollution variables and of the temperature variable to the prediction of daily morbidity (out-patient visits and hospital admissions) was examined after an establishment of the core model was completed. The effects of air pollution and temperature were estimated by including variables of air pollutants and temperature into the core model. Regression coefficients and 95% confidence intervals for each exposure of interest on different health outcomes were then obtained. The relative risk (RR) for one degree Celsius increase (°C) in temperature, and for a 10-unit increase in air pollution levels for all pollutants (except CO, one-unit increase) were used for presenting the results.

The RR was determined by the natural exponential of the regression coefficients from the models as follows:

Temperature: RR = exp(regression coefficients)
Air pollution: RR = exp(regression coefficients × 10)

Where exp is the natural exponential.

For air pollution, in the first instance, the risk estimates of each pollutant were analysed separately to determine the effects of a single pollutant. Based on the results of a single pollutant model, two-pollutant models were also developed by inclusion of two pollutants (those that mostly provided positive effects on the health outcomes) into the models. Since pollutants in the air are highly correlated, to determine the effects of multi-pollutants may not be very useful. The inclusions of three or more pollutants in the same model may make it difficult for interpretations. Thus, only single pollutant and two-pollutant models were developed in the present study.

All statistical procedures were undertaken using the STATA statistical software for professional, the 10th version.

3.5.8 Linkage between hospital admission data and out-patient visit data

Linking the two data sets

To examine whether people who have many out-patient visits (OPD visits) are more susceptible to a subsequent hospital admission in association with air pollution and temperature exposure, a new data set was established by linking hospital admission data with out-patient visit data. This linkage data was then used for investigating whether there was an effect modification of air pollution and temperature by the history of out-patient visits prior to the hospital admissions.

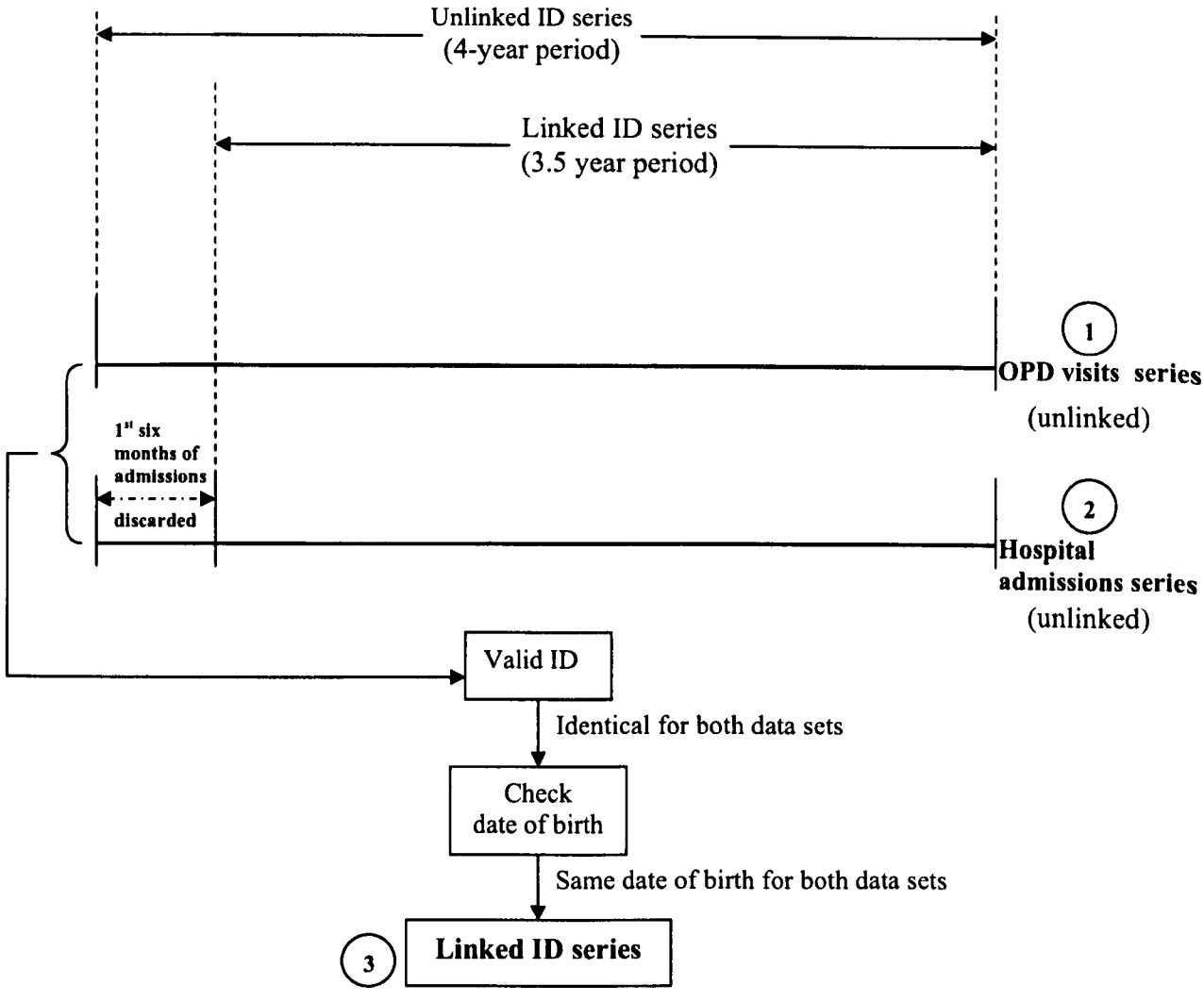
First of all, individual daily records in the hospital admission data were linked to all of their records in the out-patient visit data by using individual identification (ID) numbers. That is, the ID number of a hospitalized patient in the hospital admission data was matched with the ID number of an out-patient visit in the out-patient visit data. The ID number is chosen for

linking the two data sets because all Thai people have their own unique 13-digit ID numbers. If the ID number of a hospitalized patient and of an out-patient visit was identical, a patient's date of birth was then used to recheck for validation to ensure that the records in the two data sets belonged to the same person.

Then, the numbers of out-patient visits prior to admission were counted. Only the visits that occurred within the 6-month period prior to the admission were included in the count. A 6-month period of OPD visits prior to the hospital admission was chosen under because it was believed that using a shorter period, there might be too few counts of out-patient visits for each individual and the visits might be highly correlated or they might be due to the same exposure. On the other hand, using a longer period, the out-patient visits might be due to other reasons, not due to the short-term effects of the exposure. The sensitivity test was also carried out to investigate the impact of different time periods chosen for obtaining the linkage data.

With this process, data from the first 6 months (October 2002 to March 2003) of the hospital admission data could not be used for linking and therefore, were discarded. Thus, in this study, there were three main time series: two unlinked ID series (out-patient visits and hospital admissions series described previously), and one linked ID series (presented in section) as illustrated in the following figure.

Figure 3. 2 Process for data analysis in this study.



Inclusion and exclusion criteria of hospital admission cases in the linkage data

1. Hospital admissions that had only one out-patient visit occurring on the same date of their admission were kept as a baseline group of the admissions with no history of the visits prior to their admissions.

As mentioned earlier, since Thai patients need to visit the out-patient department (OPD) for preliminary investigations before admissions, there is a record of an out-patient visit on the same date as a hospital admission for each patient. Thus, in the linkage data, the out-patient visit recorded on the same date of the admission was not counted as a history of the visit

prior to that admission. But this admission was still retained for the analysis as a baseline group of hospital admissions with 'no history' of previous visits.

2. Only hospital admissions of a patient where ID numbers were matched with the ID numbers in the out-patient visit data were kept.

It is important to note that not all hospital admissions could be linked with the out-patient visits, which might be due to the general problem of missing data or errors in inputting individual information (e.g. the 13-digit ID number). Thus, it was decided to include only matched ID, hospital admission cases in the linkage data by assuming that all matched ID cases had their actual numbers of previous visits in the out-patient data set.

However, due to the problem of missing data or errors in routine health records, it could not be certain that these hospitalized people truly had only one out-patient visit recorded on the same date of their admissions (i.e. these patients in the 'no visit' group for the linkage series) or they actually had several visits, but their out-patient visit records were just missing or errors. To address this problem, another data set that included all unmatched hospital admission cases was created for sensitivity tests by assuming that those unmatched cases also had 'one out-patient visit' only (results presented in chapter 8, section 8.3.2, p. 196).

3. Only hospital admissions where the dates of birth were the same in both OPD visit data set and hospital admission data set were kept.

Because one hospital admission could be matched with several out-patient visits prior to that admission, date of birth was also used to double check that a hospital admission was the same person shown in the out-patient data set. If the ID number of both data sets was matched, and all dates of birth in both data sets were also the same, all records of this person were kept in the linkage data for further analysis. However, if some of their dates of birth were not the same, all records of that patient were excluded from the linkage data because it could not be known for sure which date of birth (the one in the OPD data set or the one in the hospital admission data set) was the correct one for this person.

4. Only the first admission of each person was kept, if his/her re-admission was due to the same diagnosis within 6-month period.

If a patient had more than one hospital admission with the same diagnosis within the 6-month period, only his/her first admission was included in the linked ID series because hospital admissions occurring within 6 months might be due to the same condition. But, if the same person had been re-admitted within the 6-month period due to different diagnoses, those re-admissions were still kept for the linked ID series.

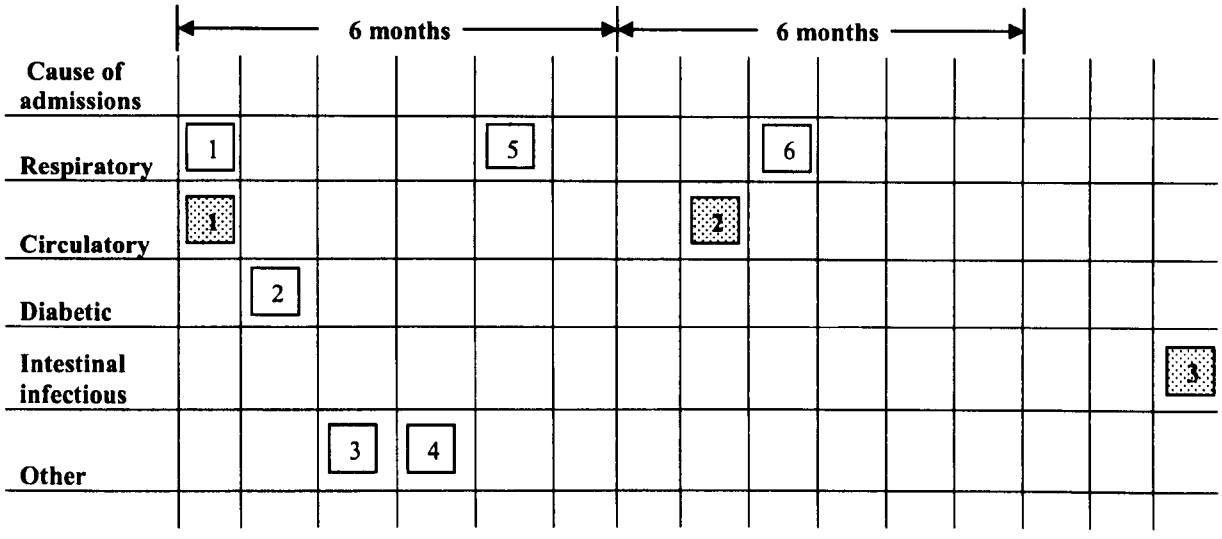
5. Hospital admissions greater than 6 months apart were considered as a new episode.

If the same patients had hospital admissions greater than 6 months apart, all of his/her admissions (even though the same diagnoses) were included in the series.

Please note that a 6-month period was used in two different situations. First, it was used to obtain the linkage data or as a certain time period for counting the numbers of previous visits before admissions of a patient. Second, it was used for including or excluding the daily counts of hospital admissions of each individual in the linkage data with regard to the diagnoses of the hospital admissions.

In order to make it clearer about the use of individual hospital admission records for the linkage series, an example of daily records of a patient presented in the linkage data is given below.

Figure 3. 3 Example of a patient in the linkage data by causes of his/her admissions.



Note: 1. Linkage data was a subset of hospital admissions data – the hospital admissions with no history or with at least one visit or more prior to their admissions.

2. Each admission generally had its own number of previous visits before the admission (not shown). But there might be an overlap of the previous visits for each admission e.g. the same visit could be counted for 1st admission and also for the 2nd admission.

Patient number 1: ☐

- Patient number 1 is an example of a patient, who had 6 hospital admissions in the linkage data. The number in each block represents a sequel of his admissions from the 1st to the 6th admissions.
- Since the first admission and re-admissions with different diagnoses within a 6-month period were kept, the 1st, 2nd, and 3rd admissions of this person were kept in the linkage data, but the 4th and the 5th were excluded. However, the 6th admission was retained as the first new episode of respiratory admissions for this person because the interval between the 1st and the 6th admissions was greater than 6 months.

Patient number 2: ▒

- Patient number 2 is an example of a patient, who had 3 hospital admissions in the linkage data. Each admission of this patient was greater than 6 months apart. Therefore, all of his admissions were included in the series, even though the 1st and 2nd admissions were due to the same diagnosis.

In summary, the linkage data was the hospital admissions, which could be linked with out-patient visits by using ID numbers. The data comprised two main groups:

1. Hospital admissions with no history of out-patient visits within a 6-month period prior to their admissions.
2. Hospital admissions with one or more out-patient visits within a 6-month period prior to their admissions.

After data cleaning and corrections, the linkage data was collapsed into a time series format and a regression model of this linked ID series was developed.

Analytical methods of the linkage ID series

The analytical methods applied for the linkage ID series were generally the same as those used for out-patient visits and hospital admissions series. However, the aim of the linkage series was to explore whether there was a modification of air pollution effects, and of temperature effects by the history of previous out-patient visits, which might have an impact on subsequent hospital admissions of each individual.

To investigate whether the patterns of air pollution and temperature effects would have changed in relation to the frequency of the out-patient visits prior to the hospital admissions, the numbers of previous visits before admissions were counted and divided into 4 groups: 0 visit (no history), 1 visit, 2-5 visits, and >5 visits. The grouping was done for analysis purposes to have reasonable numbers for each visit-category group.

Then, the effects of air pollution and temperature on each health outcome were examined for all visit-category groups. In order to see whether there were any patterns of air pollution and temperature effects across these 4 groups, the estimated effects (RRs and confidence intervals) of air pollution and temperature for each group were plotted.

In addition, tests for trends of air pollution and temperature effects across the 4 groups were also done. The distribution of the count numbers of previous visits before admissions in each group was explored. The median of the count numbers of the visits was used as a weight score for testing for the trends of air pollution and temperature effects across the

visit-category groups: 0 for '0 visit' group , 1 for '1 visit' group, 3 for '2-5 visits' group, and 8 for '>5 visits' group.

Variables and related factors in the analysis of the study are detailed below.

Outcome variables:

Health outcomes of interest are based on diagnostic codes in accordance with the International Classification of Disease, 10th version (ICD-10). The six main groups of health outcomes include:

- All causes of visits/ admissions
- Respiratory diseases (J00-J99)
- Circulatory diseases (I00-I99)
- Diabetes (E10-E14)
- Intestinal infectious diseases (A00-A99)
- Other visits/ admissions (the rest of daily counts in the data, apart from above disease groups)

Explanatory variables:

1. Air pollutants: SO_2, NO_2, CO, O_3, PM_{10}, and $PM_{2.5}$
2. Temperature

Possible confounding factors:

- Time trends
- Seasonal patterns
- Other weather variables: relative humidity and rainfall
- Day of weeks and holidays
- Influenza epidemics

Possible modifiers

- Age groups (0-14, 15-64, 65+)
- sex (male /female)

- Occupation (unemployed & economically inactive people, non-manual workers, manual workers)
- Season (winter, summer, rainy)
- Previous history of out-patient visits (0, 1, 2-5, >5)

3.6 Sensitivity analyses

The section described two main sensitivity analyses when building the core model for the study, which were done for the first series (out-patient visits series) only. Other sensitivity tests specific to the hospital admissions and the linkage series were explained in their result chapters. With regard to model building, the main issues of concern were: model distributional assumption and model seasonality.

3.6.1 Model distributional assumption

Conventionally, time series studies of air pollution and temperature effects usually employ Poisson regression, allowing for overdispersion. This is due to the assumption that count data mostly follow Poisson distribution [195]. Failure to allow for overdispersion can lead to underestimation of the variance of the coefficients and exaggerated significant levels. In the present study, however, due to heavily extra variation of the data, negative binomial regression was then chosen for analyses instead. In order to see how much impacts on the coefficient estimates in regard to using different types of regression analysis, comparison of the estimates obtained by using negative binomial regression and those obtained by using Poisson regression was made.

Modelling air pollution

For both negative binomial regression (NB) and overdispersed Poisson (OP), the models were the following form:

$\log[E(Y)] = \alpha$ + i.dow + i.movisit (1-48) + holidays + time splines (sdate) + splines of unusual peak visits (sodd) + interny + thainy + influ + autoregressive terms (1, 7, 14 21, 28) + temperature splines + humidity splines + rain splines + a pollutant (lag 0-1 day or lag 0-4 days).

Where i.dow = indicator variables of day of the week,

i.movisit	=	indicator variables of month of the visits (1-48),
holidays	=	indicator variable of public holidays,
sdate	=	time variables using splines of date (frencurvnk, 1df/year),
sodd	=	splines of a three-month unusual peak visits from April 2005 to June 2005 (frencurvnk, 1df/year),
interny	=	indicator variable of international new year period (30 Dec-2 Jan),
thainy	=	indicator variable of Thai new year period (13-16 Apr),
influ	=	indicator variable of possible influenza epidemic using the period that respiratory visits were above 99th percentile.

In addition, the autoregressive terms at order 1, 7, 14, 21 and 28, were incorporated to account for the remaining autocorrelations. The natural cubic splines (3df) of temperature, humidity, rain were also included into the model. To determine air pollution effects, pollutant variables at average lag 0-1 day or lag 0-4 days were added into the model.

The probability function of a Poisson model is:

$$\Pr(Y = y) = \frac{e^{-\mu}\mu^{y}}{y!}; y = 0,1,2,K,$$

Where μ is the mean and the degree of dispersion can be estimated by the overdispersion parameter:

$$\phi = \sum \frac{(y_i - \mu_i)_2}{\mu_i} \; / \; (n - p),$$

Where μ is the mean, n is the number of observations, and p is the number of parameter in the model. When ϕ = 1, the assumptions of the Poisson have been met – variance is equal to the mean. The model is overdispersed when ϕ > 1. Thus, the variance of the OP model is var(Y) = $\phi\mu$.

Modelling temperature

The regression analysis form used to model temperature was based on the same structure as that used for modelling air pollution. The only difference is that temperature variables from lag 0 to 13 were incorporated into the model, instead of air pollutant variables.

3.6.2 Model seasonality

Adequacy of controlling for seasonal and long-term trends in time series studies is of great concern. The inclusion of a smooth function of time, such as natural splines and penalized splines, in regression model is commonly used to adjust for seasonality and long-term trends. However, degrees of smoothing or numbers of degree of freedom (df) used for splines of time may influence estimates of exposure effects in time series analysis. Oversmoothing in the series may lead to confounding bias, whereas undersmoothing in the series may result in attenuation of a true effect [202]. Since there are no absolute degrees of smoothing, evaluating various numbers of df used in time series studies to ensure adequacy of adjustment for seasonality has been recommended [203]. In the present study, time splines used for modelling referred to the b-splines of date and the 1 df per year was chosen for developing the core model at the beginning for both air pollution and temperature models. To assess the sensitivity of the results in regard to the degrees of smoothing, varying degrees of freedom of the b-splines of date from 1 df to 10 df per year was examined. Then, the number of df of time was adjusted as suggested by the sensitivity test results. According to the sensitivity test results, in this study, 1df was used for modelling air pollution, while 6 df was used for modelling temperature.

Chapter 4: Data Quality

This chapter describes characteristics of health, air pollution, and meteorological data in Thailand. It begins with broad description of Thai health care systems, followed by specific characteristics of health data used in this study, both out-patient visits and hospital admissions. Information about air pollution and meteorological data is also included.

4.1 Thai Health care system

This section describes the general characteristics of Thai health care system in relation to the two main data sets (out-patient visits and hospital admissions) used for the study. The out-patient data were routine daily health records obtained from the Chiang Mai provincial health office, while the hospital admission data were the hospital claim data obtained from the National Health Security Office. Information about the health care system and the health data are detailed as follows.

4.1.1 Health and welfare of Thai population

According to the 2003 Health and Welfare Survey (HWS), approximately 95% (60.7 million) of the total Thai population were covered by different health insurance schemes, including the universal coverage (UC) scheme (74.7%), the social security scheme (SSS) – for private employees and temporary public employees (9.6%) – , the civil servants medical benefit scheme (CSMBS) – for civil servants, public employee, and their dependants (9%) – , and private insurance (1.7%) [204]. Therefore, only 5% (3.2 million) of the total population were still uninsured (e.g. they need to pay for health care services themselves at the point of delivery).

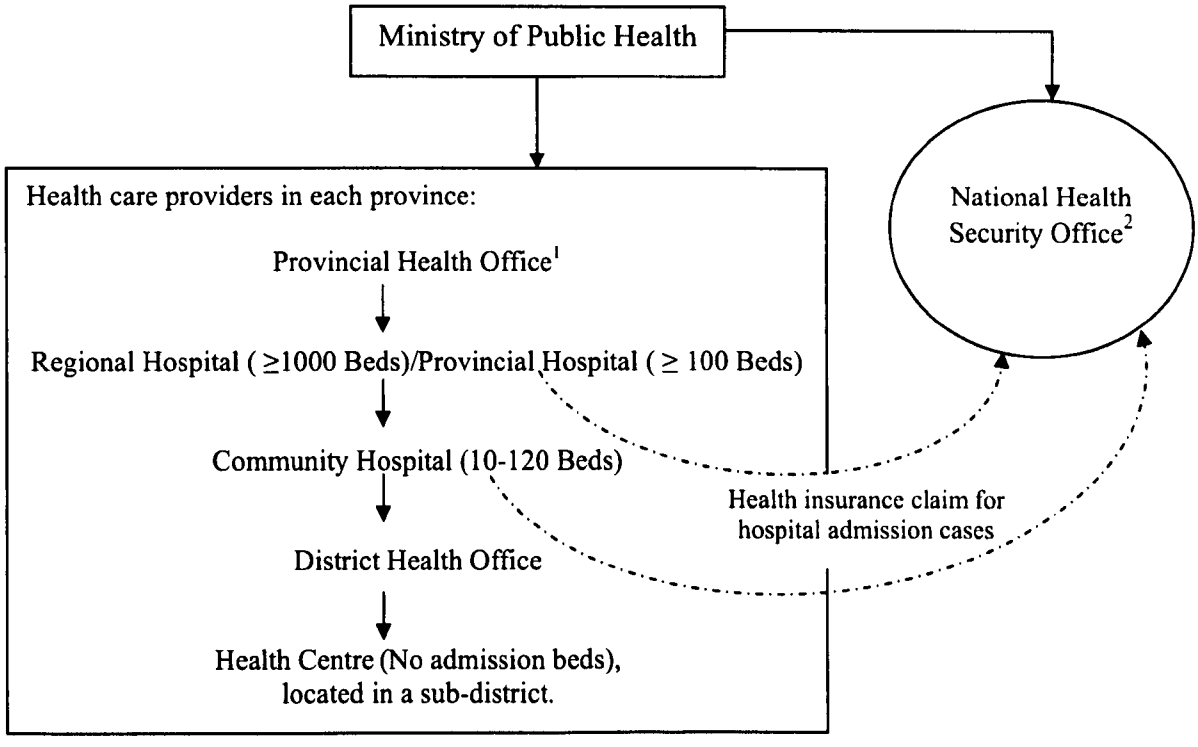
When Thai people are ill, they generally visit their assigned health centres and hospitals under their own health insurance schemes, which are usually located near their homes. After providing health care services for patients, health centres and hospitals will claim the cost of the services from the main offices of the health insurance schemes. To receive health care services, an individual health care card needs to be presented. If people forget their cards, they still receive health services from those health centres and hospitals as necessary. They will be given some period of times (e.g. 3-7 days) for presenting their

documents. However, an inability to provide the documents by the due date means they have to pay for their health care services by themselves.

For out-patient services, health care providers generally receive the subsidy for their services from their provincial health offices as an annual budget based on their public health activities (e.g. primary health care services, health promotion activities). In other words, a provincial health office is responsible for distributing the annual budget received from the Ministry of Public Health to all government health care providers in a province. Thus, a primary health care provider usually sends daily out-patient records to its provincial health office, which is a centre for keeping all public health information of a province. However, there is no financial incentive for health care providers specifically to reporting their out-patient records to the provincial health office.

For hospital admissions, in each month, hospitals will send the daily routine health records of hospital admissions, which include personal information (e.g. identification number, age, and sex), and details of medical treatments used during the admissions, to the National Health Security Office – a government health sector that is responsible for providing reimbursement for hospitals under health insurance schemes throughout the country – in order to get the reimbursement.

Figure 4. 1 Health care providers under control of the Ministry of Public Health in a province of Thailand.



[1]**Sources of OPD records, keeping health records from hospitals and health centres in a province.**
[2]**Source of hospital admission records, keeping hospital claim data of the country.**

Note: ⟶ = the direction of administration systems. The higher levels is generally bigger and has more authority than the lower one.
-·-·▶ = the route of reporting hospital admission data for reimbursement.

4.1.2 Health centre

In general, health centres in Thailand are located in every sub-district (known as 'Tam-bon' in Thailand) to provide primary health care services for people in the community. Each health care centre is assigned to be a main contractor for the population registration in the UC scheme for its community. Although health centres are entrusted with providing comprehensive care to their registered population, in practice, they also provide primary care services for all people (with every type of health insurance schemes, and without insurance) in the community. For Thai people who have a health centre as a main contractor (some people who live near hospitals will register with a primary care unit of their nearest hospitals instead), they have to visit their assigned health centres first when

they are ill. Direct access to hospital care is not permitted, except in the event of an accident or the need for emergency care. If local health centres cannot handle their own patients, such as patients with severe illness or injuries that exceed their capacity, they will transfer these patients to hospitals for more advanced care (secondary or tertiary care) as necessary. Hence, there is no bed occupancy in a health centre and its health records are normally called 'out-patient visits', which can be both elective and emergency situations.

4.1.3 Hospital

For each district in Thailand, there is at least one community hospital of the government to provide the ambulatory care and in-patient care for the population in the community. The number of hospital beds is an indicator of the size of a hospital, which can range from 10 to 120 beds. For the district located in the inner area of a province, usually named 'Muang district', it will have a big, provincial hospital (≥100 beds). If the city has a large population, such as Muang district in Chiang Mai, it can also have a big regional hospital (≥ 1000 beds) as well as several government hospitals (such as a military hospital, a medical school or university hospitals, and other specialized hospitals) and private hospitals with various sizes.

In terms of hospital care, hospitals in Thailand generally consist of two big departments: an out-patient department (OPD) and in-patient department (IPD or hospital admissions).

Out-patient Department (OPD)

Out-patient department (OPD) is responsible for ambulatory care (including primary care) in a hospital. Apart from health care centres, out-patient departments of hospitals in Thailand also have a primary care unit to serve as a main contractor for population registration in regard to the UC Scheme for its nearest community. Health services at the OPD consist of both scheduled and unscheduled visits to several health care units (e.g. Paediatric unit, Medicine unit, Surgical unit, and Gynaecological unit), and emergency visits to an emergency room (ER) of a hospital. Therefore, health records of out-patient department in Thailand are the records of all ambulatory care settings in a hospital, which comprise both elective and emergency visits. The process of health services at OPD in hospitals in Thailand can vary depending on the administration system of each hospital.

However, the overall process is very similar. Examples of health services at OPD and ER are shown in **Appendix 4A**.

In-patient Department (IPD) or Hospital admissions

The in-patient department (IPD) of a hospital provides in-patient care for hospital admission cases. When patients go to a hospital, all patients have to visit the OPD of a hospital first. If patients are considered to be severe illness cases and need admissions, they will be transferred from OPD to IPD for the admissions. Even if patients have appointments to admit at a hospital (such as for elective operations), they still have to visit the OPD and see OPD doctors for primary investigations before their admissions. Therefore, one patient generally has a record of an out-patient visit and a hospital admission on the same day in the routine health record data sets. This means that although out-patient visit data and hospital admission data in the present study were obtained from the different sources, it is possible that, on the same day, some individual records in the hospital admission data were also presented in the out-patient visit data (if there is no missing record of out-patient visit data, all hospital admission records should have at least one out-patient visit records on the same day of their admissions). Thus, for the linkage series, it was decided that an out-patient visit recorded on the same day of the hospital admission would not be counted as its history of the previous visit before admission on that day (see Chapter 3: Methods, section 3.5.8).

With regard to bed capacity, if hospital beds are fully occupied and there is an out-patient visit considered as a severe case and needed to be admitted, a hospital in Thailand always provides an additional bed (or extra bed) for his/her admission. For example, during an outbreak of diarrhoea or of dengue hemorrhagic fever or mass causalities (from accidents or disaster events), additional beds can be seen between the usual fixed beds in hospital wards or along the hallway of a hospital building when necessary. In some cases, if there is too much workload for a small hospital and there is a bigger hospital available in the city, patients from the smaller hospital may be transferred to the bigger hospital for admissions. Therefore, daily count numbers of hospital admissions in Thailand are unlikely to be artificially restricted by bed capacity.

4.2 Quality of health data

4.2.1 An overlap of health records between OPD visits and hospital admissions

As mentioned earlier, in general, every patient who has been admitted to a hospital in Thailand also has an OPD visit (for preliminary physical examination before admissions) on the same date of that admission. Thus, there is an overlap of health data used for the analysis in the present study. Because the OPD data comprised not only OPD visits, but also hospital admissions, it may be possible that the observed effects of air pollution and temperature from the OPD visits series may not truly represent the effects on daily OPD visits due to some possible contributions of hospital admission cases in the data.

Since the hospital admission data in this study were the hospital claim data, which were obtained from one institute (The National Health Security Office) only, even if we exclude OPD visit records that were the same cases of these hospital admissions, the OPD data set would still contain hospital admissions from other institutes (those that were not used for health insurance claims, which we were unable to know how many they were). Therefore, it was decided to use the whole original OPD data set, without any exclusion for this study.

4.2.2 Coding system of health records

Daily routine health records used in this study derived from some parts of the diagnosis related group (DRG) records of health centres and hospitals. DRG was established in the U.S.A. in 1983 because of the increasing cost of services. The Health Care Financing Administration (HCFA) had changed the methods of reimbursement of treating patients under the Medicare program for hospitals. Thailand began to use the DRG system for routine health records almost 10 years before it officially adopted this system for reimbursement of Thai health care cost in 1998 [205]. However, the reimbursement of hospital care services in Thailand have been applied for IPD (or hospital admissions) only and mainly for patients with health insurance schemes introduced by the Ministry of Public Health.

Like all provincial health offices in the country, the Chiang Mai provincial health office also employs the DRG system and requires their registered health centres and hospitals to report the daily health records of out-patient visits in each month to be used for providing

subsidy (not for health insurance claim, but for other budgetary needs for public health activities e.g. primary health care services and health promotion activities) for those health centres and hospitals. Thus, out-patient data in the present study were the daily routine health records (October 2002 to September 2006) obtained from health centres and hospitals registered with the Chiang Mai provincial health office only.

By comparison, health records of IPD (or hospital admissions) are more reliable than OPD visits in regard to accuracy of diagnoses, and completeness and accuracy of coding practices. This is because of two important reasons. First, DRG records of IPD are used for reimbursement of health insurance claims, while DRG records of OPD visits are requested by the government for co-operation in keeping health records (for statistical reports) for the country. Thus, there is financial incentive for hospitals to provide complete and accurate records of hospital admissions, whereas there is no financial incentive for a provision of OPD records. Hence, in this study, the missing data in some months of some hospitals were found in the out-patient visit data more than those found in the hospital admission data.

Second, on a daily basis, there are less numbers of hospital admissions compared to OPD visits. At OPD, medical doctors, nurses and other health care workers have to complete their jobs and health records within a day. Thus, decisions in diagnosis, records of health reports, and all medical investigations at OPD have to be made quickly and are likely to have mistakes. At IPD, on the other hand, health records of hospital admissions are discharge records. Thus, health care workers (such as doctors, nurses, or coders) at IPD can gradually fill in health reports while patients are staying in a hospital. They are generally able to spend more time thinking and writing discharge records, and more importantly doctors can also request for more medical investigations (e.g. laboratory and x-ray) to ensure their diagnoses. Therefore, IPD records are more likely to have fewer mistakes in comparison to OPD records.

4.2.3 Coding practices of health records

According to the survey about medical coding practices in Thailand [206], approximately 60% of the survey hospitals had certificated medical coders in coding practices, but 46.20% of the coders had to work in other jobs as well. Hospitals that did not have certificated medical coders, health personnel such as nurses, doctors, or public health practitioners

would be trained to take responsibility for coding instead. It was found that, 85% of coders had attended in a diagnosis/procedure coding training course. Approximately 44% of the coders had 1-3 year experiences in coding practices, whereas 13.66 % of them had < 1 year experiences. The most common method of coding was using only ICD books (53.90%), followed by using ICD books with computer-aided coding program (27.80%) and using only computer-aided program (18.31%).

The survey also revealed opinions of administrators and academic experts about reliability of health records in Thailand. It was found that 34.13% of administrators and academic experts in Thailand believed that ≥86% of health records were reliable, 33.15% of them thought that 76-85% of health records were reliable. Approximately 30% of the administrators and academic experts believed that the reliability of health records was 50-75%, whereas only 3.75% of them thought that the reliability of health records was less than 50%.

Regarding the error in coding, the survey found that there were several types of error in coding, such as wrong codes, incomplete/missing codes, and codes uncorrelated with age and sex of patients. The survey indicated that the error in coding practices in Thailand was due to three main causes: first, insufficiency of coders; second, lack of knowledge and experience and carefulness in rechecking codes; and third, lack of motivation in their work due to an inappropriate career ladder and a lack of supportive measures in professional knowledge and skill.

It is important to note that this survey was conducted in 322 hospitals in Thailand and it cannot be known whether hospitals in Chiang Mai province were included in the survey. Even so, the results have demonstrated the likely situation of diagnostic records as well as the procedure of coding practices in Thailand. During the data collection for this study, the officer of the biggest hospital in Chiang Mai, which had large number of missing diagnoses, also acknowledged that the main cause of missing code was due to insufficient coders of the hospital. This information is in agreement with the first leading cause of coding error of the above survey. In general, monthly reports of daily routine health records will be sent to the Chiang Mai provincial health office by the due date although there is

incomplete coding. In each month, the coders usually work with health records (input the ICD-10 diagnostic codes into the individual health records) and stop coding in order to hand in the reports to the provincial health office by the due date with non-specific to particular patients or diseases in the data set. Thus, if this practice would cause bias to the study results with respect to the missing information, it would be non-differential.

4.2.4 Factors affecting quality of health data

There are three main issues of concern regarding the quality of the health data: the distinction between elective and emergency cases, the representativeness of the Chiang Mai population, and the completeness of the data and the diagnostic accuracy.

Firstly, it is impossible to distinguish between elective and emergency cases for both out-patient visits and hospital admissions series in this study. In general, one would expect short-term effects of exposure to air pollution and temperature to only be associated with emergency visits or admissions [19, 78, 199, 207]. The use of combined data on elective and emergency patients will render the series more 'noisy' and therefore, make an assessment of air pollution and temperature effects more difficult. Since this situation could only serve to reduce the apparent effects, any association observed will not be invalidated.

Secondly, the out-patient visits and hospitalizations in the health centres and hospitals may not truly represent the entire residents of Muang district in Chiang Mai. This may be due to two reasons: health care seeking behaviours and population mobility. First, health care seeking behaviours among individuals in the city could vary greatly. For example, some inhabitants may choose alternative medicines, such as Thai traditional medicines (e.g. massage, herbs) or buying medicines from drug stores to treat themselves [204]. Some people may visit private clinics or other hospitals, which are not included in the study. Second, there is also the possibility of an influx of people from neighbouring areas into the study area, which may introduce bias into the study and cause some distortions of the study results. However, we would expect that most people in the northern region would share similar characteristics in terms of behavioural and cultural lifestyle. In addition, it is possible to assume that health care seeking behaviours or an influx of neighbouring population would have not changed enormously in terms of a day-to-day variation. The

proposed study is designed for assessing short-term effects only, which would reduce an influence of this situation on study results.

Thirdly, this study is based on routinely collected health data from several health centres and hospitals. Thus, the completeness of the data and the degree of diagnostic accuracy could vary greatly among those selected health centres and hospitals. However, it is possible to assume that the error in both diagnosis and data records would have acted randomly over time.

4.3 Quality of air pollution and meteorological data

4.3.1 Air monitoring station

Daily mean levels of air pollutants and meteorological variables for Chiang Mai province were obtained from the Pollution Control Department (PCD), Bangkok, Thailand. The PCD is the central air monitoring system for the whole country. By using the standard computer software called "AIRVIRO", the PCD can control air monitoring stations and obtain levels of air pollutants from those stations throughout the country via telephone systems. Thus, the PCD is able to monitor air pollution situations (real-time monitoring) and is able to forecast the air pollution situation in some particular areas of the country. The real-time monitoring equipments can provide readings of air pollutant levels at any time interval such as at every 30 minute or at every one hour, depending on the setting. Daily levels of pollutants are provided for the public via the PCD's website, presenting daily mean levels of pollutants measured every one hour ending at 9am on the day of reporting.

An air monitoring station in Thailand is a movable container with 3 metres wide, 4 metres long, and 2.4 metres high. It is usually located on a concrete base with an area of about 25 square metres (5 metres wide and 5 metre long). In general, there are two types of air monitoring stations: an urban area station – located approximately 50 metres or more from the nearest road, and a roadside station – located less than 10 metres from the nearest road. Thus, in general, levels of air pollution obtained from a roadside station should be higher than those obtained from an urban area station. The air data used for this study were the average from the only two stations in the city of Chiang Mai, one roadside station and one urban area station. The roadside station is located in the inner area of Muang district,

whereas the urban area station is located in the outskirts of the district (approximately 10 kilometres from each other). Using the data from the station in the city central might represent higher levels of exposure, while using data from the station in the outskirts might represent lower levels of exposure. Thus, by using the average levels of air pollution from both types of air monitoring stations within the same district, the air pollution data in this study would reasonably represent exposure levels of the study population (though not the same as personal exposure).

Figure 4. 2 The urban area air monitoring station in Chiang Mai.

Figure 4. 3 The roadside air monitoring station in Chiang Mai.

4.3.2 Factors affecting quality of air pollution and meteorological data

Completeness

Completeness of the air pollution and meteorological data is also important in assessing morbidity in relation to daily changes of air pollutant and temperature. Based on preliminary investigation of two-year data (October 2003- September 2005) obtained from the PCD, the daily missing values of air pollutants and meteorological factors (temperature, relative humidity, and rainfall) of the two air monitoring stations ranged from approximately 4% (rainfall) to 27% (CO) of the total. Summary of daily average levels of air pollution and meteorological factors from the preliminary findings can be seen in **Appendix 4B**. As mentioned previously in the method chapter (section 3.4.2), the missing data in one station were replaced by using the data from another station by adopting the Air Pollution and Health: a European Approach (APHEA) protocol.

Measurement error

To obtain levels of air pollutants and temperature from the fixed air monitoring stations is more likely to cause the so-called 'measurement error' in the study. Like many other time-series studies, the use of fixed point sampling may not represent true exposure of the large mobile population [190]. However, as mentioned earlier, instead of obtaining the exposure levels of air pollutants from only one station, the average exposure levels from the two air monitoring stations in two different geographical locations would be a better estimate of exposure levels for the study population since the individual exposure could not be known. For weather variables (temperature, humidity, and rain), it was decided to use the data from one station only because there were little differences in the levels of weather variables between the two stations. The levels of weather variables from the city station were used because there were less missing data than another station.

Summary of data quality for the present study

Health data:

- Hospital admission data in Thailand are generally more reliable than out-patient data due to the financial incentives of reimbursement from the government.
- Routine health records in Thailand have officially been using DRG coding system since 1998 (with 10 years of a trial period earlier). Although the problems of

missing and error in coding the data still remain, the reliability in coding practice should be acceptable. This is supported by the survey of medical coding practices in Thailand that approximately 70% of administrators and academic experts believed in its reliability being >76% or more. Furthermore, most coders have also been trained before practicing. In addition, missing and/or error in coding practices that would have caused bias in the study appeared to be non-differential.

- Any observed effects in the study would have been reduced by not only an overlap of health records between OPD visits and admissions, but also other factors, such as an inability to differentiate between elective and emergency cases, a mobile population, and an incompleteness of the data as well as inaccuracy of diagnosis.

Air pollution and meteorological data:

- Due to having two monitoring stations in the city, missing data of one station could be replaced by calculations using data from another station.
- Like other time series studies, measurement error due to using data from fixed sampling sites to represent an exposure of individuals from a large and mobile population was unavoidable.

Chapter 5: Descriptive results

5.1 Out-patient visits

Daily counts of out-patient (OPD) visits were obtained from the Chiang Mai provincial health office for a 4-year period from October 2002 to September 2006. After data cleaning and corrections, there were 1,398,369 visits recorded during this period. Of total daily visits, 0.6% (8,092 counts) had missing information on age, 0.8% (10,431 counts) had missing information on sex, and 18.6% (259,522 counts) had missing information on occupation. Thus, when the data were stratified by age, sex or occupation, these observations were excluded.

Figure 5.1 presents the total count of OPD visits on a monthly basis. Due to the fact that there were different numbers of hospitals and health centres contributing to total counts of OPD visits in each month, a steep increase or decrease of total counts of the visits had occurred in some particular months throughout the study period.

5.1.1 Characteristics of study population of out-patient visits

Following the ICD-10 coding system, the out-patient data were divided into six disease groups: respiratory disease (J00-J99), circulatory disease (I00-I99), diabetes (E10-E14), intestinal infectious disease (A00-A09), 'other' diseases (those not included in the four first categories), and all-cause visits. The distribution of the disease groups by three main characteristics (age, sex, and occupation) of the study population are presented in **Table 5.1**.

Three age groups were defined for children (0-14 years), adults (15-64 years), and the elderly (≥ 65 years). The majority of study population were adults (67.1%), followed by the elderly (19.3%) and children (13.1%). It was found that approximately 50-70% of all six disease groups were adults. However, children had higher OPD visits because of respiratory (40.2%) and intestinal infectious (42.2%) diseases, compared to other diseases. Among elderly people, the visits due to diabetes (31.2%) and circulatory diseases (37.4%) were higher than other diseases.

The daily visits among females were slightly higher than males in all disease groups. In total, the distribution is approximately 60% females and 40% for males. Regarding occupational groups, which were restricted among people at working ages (15-64 year) only, approximately 25% of the study population were unemployed and economically inactive people. This was followed by non-manual workers (21.6%) and manual workers (7.6%). The grouping was done according to the 3-digit occupation code (see **Appendix 3C**). Among these three groups, unemployed and economically inactive people had higher visits in diabetes (33.0%) and circulatory (26.5%) disease, while non-manual workers had higher visits in respiratory (24.3%), intestinal infectious (22.6%), and 'other' (30.2%) diseases. Compared to other occupations, manual workers held the lowest visits in all diseases, ranging from 3.4% (intestinal infectious disease) to 7.0% (circulatory disease).

When the data were broken down into specific disease groups, there were limited counts in some selected characteristics, which can be seen **Appendix 5A**. Besides all-cause visits, the analysis could be done for all stratified groups for respiratory and 'other' visits. For circulatory and diabetic visits, there were very small count numbers, preventing the analyses for children (0-14 years), whereas, for intestinal infectious visits, there were limited count numbers to analyze for the elderly (≥ 65 years) and manual workers.

5.1.2 Daily variation of the OPD visits

To visualize the daily variation of the OPD visits over a year, the mean daily count of all-cause visits and the proportion of each disease group compared to all-cause visits throughout a 4-year study period were plotted against day of the visits in one year (**Figure 5.2**). In general, approximately half of the total visits were the visits by 'other' diagnoses. There was also a seasonal pattern of the visits by 'other' diseases over a year. The visits by 'other' diagnoses increased during the middle of winter to early summer (Jan-Mar) and dropped after that. Then, the 'other' visits tended to increase during the changes of one season to another season, such as early on the rainy season (May) and later on the rainy season (Oct) up to early winter (Nov). Among the rest of the disease groups of interest, respiratory visits held the highest percentage of 12.6%, while intestinal infectious visits held the lowest percentage of 1.3%. The respiratory visits were found to be higher during winter time from January to February than other period of a year. There were also some

peaks of the visits due to respiratory and circulatory diseases in the middle of rainy season (August), and in early winter (Nov).

The daily mean count of each disease groups of OPD visits are illustrated in **Table 5.2**. As can be seen, the mean (SD) daily counts of OPD visits by all causes were 957 (680). Of which, regardless 'other' diagnoses, respiratory visits were the most common causes of the visits (mean=95.3, SD=53.4), followed by circulatory visits (mean=83.6, SD=61.1), diabetic visits (mean=30.8, SD=23.7) and intestinal infectious visits (mean=9.17, SD=5.53), respectively.

5.2 Hospital admissions

Daily counts of hospital admissions were obtained from the National Health Security Office at the same period of time, obtaining out-patient visits from October 2002 to September 2006. The hospital admission data were the health care insurance claim data. This data is used by involved hospitals in order to claim for budget that they had spent on admitted patients who had health care insurance registered with their hospitals. After data cleaning and corrections, there were 168,829 counts of the hospital admissions over the study period.

Monthly variation of total counts of hospital admissions over the 4-year study period is illustrated in **Figure 5.3**. The total counts of admissions were lowest during the beginning of the study period and began to rise at the beginning of year 2. There was a fluctuation of total counts in each month, ranging from about 3,000-4,000 from year 2 to year 4, with one dramatic drop in month 31 (about 2,500 counts) and one considerable peak in month 35 (about 5,000 counts).

5.2.1 Characteristics of study population of hospital admissions

Similar to out-patient visit data, the hospital admission data were categorised in six disease groups in accordance with the ICD-10 coding system. These included admissions due to respiratory disease (J00-J99), circulatory disease (I00-I99), diabetes (E10-E14), intestinal infectious disease (A00-A09), 'other' diseases (those not included in the four first categories), and all-cause admissions. The distribution of the disease groups in three main characteristics (age, sex, and occupation) of the study population are presented in **Table 5.3**.

Overall, the total admissions by all causes were highest in adult (15-64 year, 64.0%), followed by the elderly (≥ 65 years, 21.7%), and children (0-14 years, 14.0%), respectively. Adults also held the highest counts of admissions in all disease groups, which accounted for about 50-70%. By comparison, the admissions in the elderly due to circulatory, diabetic, respiratory diseases were higher than in children, whereas the admissions in children due to intestinal infectious diseases were higher than for the elderly.

Although males and females shared similar counts of hospital admissions (approximately half of the total), the numbers of female patients were slightly higher than those of male patients in all disease groups, except for respiratory admissions. The respiratory admissions in males (52.18%) were slightly higher than those in females (47.52%).

Taking into account their occupation, hospital admissions in unemployed and economically inactive people (5.5%-14.9%) were highest in all disease groups, followed by manual workers (4.2%-7.6%), and non-manual workers (0.5%-1.8%). However, there were large numbers of missing occupational codes in the data, which were more than 40% of the data. Thus, the analysis in different occupational groups for hospital admissions series was excluded.

The breakdown of the data into specific disease groups by sex and age can be seen in **Appendix 5B**. According to the count numbers, we could analyze the data for both sex and age for respiratory and other admissions only. For circulatory admissions, there were very limited count numbers to analyze for children (0-14 years), while for intestinal infectious admissions, there were limited count numbers preventing to analyze for all age groups. In addition, the analysis for both age and sex could not be done for diabetic admissions.

5.2.2 Daily variation of the hospital admissions

The plot of the mean daily counts of all-cause admissions over the 4-year study period, and the proportion of each disease groups compared to all-causes admissions against day of the admissions in one year is shown in **Figure 5.4**. Overall, the admissions due to other diagnoses held the highest percentage of about 80% of all-cause admissions. Regardless the admissions by 'other' diagnoses, circulatory admissions held the highest percentage (11.0%), followed by respiratory (7.9%), intestinal infectious (3.5%), and diabetic

admissions (0.8%), respectively. The respiratory and circulatory admissions were slightly higher in winter from late November to early January. There were no obvious seasonal patterns for the rest of the disease groups.

The distribution of daily hospital admissions by causes of the admissions in accordance with the ICD-10 coding systems are presented in **Table 5.4**. The mean (SD) hospital admissions by all causes were 103.9 (47.9). When looking at specific disease groups, the admissions by 'other' diagnoses held the highest daily counts of admissions (mean=80.4, SD=40.1), followed by circulatory (mean=11.1, SD=8.9), respiratory (mean=7.8, SD=4.3), intestinal infectious (mean=3.3, SD=2.5) admissions, respectively. The admissions due to diabetes had the lowest mean (SD) of admissions, which were only 0.8 (1.0).

5.3 Linkage data between hospital admissions and out-patient visits

As described previously in chapter 3 (methods), the linkage data between hospital admissions and out-patient visits was created by matching an identification number (ID) of a patient between the two data sets. Sixteen percents of total counts of hospital admissions (169,829 counts) were missing ID, while 16.1% of total counts of out-patient visits (1,398,369 counts) were missing ID. After matching the two data as well as cleaning and corrections, there were remaining 29,937 counts (17.6% of total hospital admissions) of the hospital admissions in the linkage data. The diagram of liking the two data sets can be seen in **Appendix 5C**.

Monthly variation of total counts of hospital admissions in the linkage data over the 4-year study period is shown in **Figure 5.5**. The monthly counts of this data began at month 7th of the study period, which were generally fluctuated (approximately ranged from 600 to 1000 counts). However, the counts of admissions started to drop below 600 counts from the month 41th, and dropped steadily to about 100 counts in the last month (48th). This may be due to the low number of counts of the OPD visits during this period (see **Figure 5.1**), resulting in low number of matched cases between OPD visits and hospital admissions for the linkage data. Since the number of the visits prior to the admissions is an important factor considered for the linkage series, the data from month 41th to 48th were excluded

from the analysis. Therefore, the linkage data used for the study were the data from month 7th to 40th (April 2003 to January 2006) only.

5.3.1 Characteristics of study population in the linkage data

After excluding data from month 41th to 48 (2095 observations), there were 29,937 counts remaining in the linkage data. Of total 29,937 counts, there were only 9.1% (2,733 counts) that had no history of the visits prior to their admissions (**Table 5.5**). The breakdown of people with history of the visits prior to their admissions was shown in **Table 5.6**. As can be seen, about half of the total (51.4%) were people with 2-5 visits prior the admissions, while about one in four of the total were people with 1 visit (26.0%) and people with more than 5 visits (22.5%) prior to their admissions.

Table 5.7 presents the proportion of disease groups of hospital admissions and out-patient visits prior to their admissions relative to number of the visits before admissions. Overall, approximately 30-40% of hospitalized people due to respiratory and circulatory diseases had the history of out-patient visits with the same diseases prior to their admissions. These people also had a history of visits due to 'other' diagnoses in about 20-30%, except only those hospitalized by circulatory disease with no visits (11.3%) and with ≤ 5 visits (16.3%) prior to their admissions. For people admitted by intestinal infectious disease, between 8-20% had a history of visits by the same diseases, and almost 20% had a history of visits by respiratory disease. People admitted by intestinal infectious disease and 'other' disease groups had similar history of previous visits due to 'other' diagnoses of about 40-50%. However, it should be noted that the diagnoses of previous visits in some people cannot be known due to the relatively high percentages of missing diagnoses of the out-patient visit data.

The distribution of the disease groups in the linkage data by three main characteristics (age, sex, and occupation) of the study population are illustrated in **Table 5.8**. Since the linkage data is actually one part of the hospital admissions data – hospitalized people with no visit and with at least one visit or more prior to their admissions –, the distribution of the disease groups in the linkage data was similar to the hospital admissions data. The majority of the patients were adults aged 15-64 years (68.6%), followed by the elderly aged ≥ 65 years (17.4%) and children aged 0-14 years (14.0%), respectively. The elderly had the higher

admissions due to diabetic (31.0%) and circulatory (27.5%) diseases, whereas children had the higher admissions due to intestinal infectious (40.2%) and respiratory (33.8%) diseases. The proportion of females was generally higher than males in all disease groups, except only respiratory admissions. In addition, there were large numbers of missing data on occupational group, which accounted for about 21%. Thus, the stratified analysis of the linkage data by occupation was excluded.

The data of specific disease groups stratified by the number of the visits prior to their admissions can be seen in **Appendix 5D**. When the data were divided into subgroups according to the number of out-patient visits prior to admissions, there were limited count numbers to analyze for most diseases (except only all-cause and 'other' diseases). When the data were broke down further by age and sex (not shown), there was also limited count numbers to analyze for age and sex in different disease groups relative to the history of the visits before admissions.

5.3.2 Daily variation of the hospital admissions in the linkage data

The plot of the mean daily counts of all-cause admissions over the study period, and of the proportion of each disease group compared to all-cause admissions against day in one year in the linkage data is presented in **Figure 5.6**. Similar to hospital admissions data, the admissions in the linkage data due to 'other' diagnoses held the highest percentage with approximately 80%. The percentage of circulatory and respiratory admissions was very similar, which accounted for about 9%, followed by intestinal infectious admissions (4%). The diabetic admissions had the lowest percentage of the admissions, which was about 1% only.

The distribution of daily hospital admissions in the linkage data by causes of admissions in accordance with the ICD-10 coding systems are presented in **Table 5.9**. The mean (SD) of all-cause admissions was 28.9 (14.4). While the admissions by other diagnoses had the highest daily mean of 22.9 (12.6), the diabetic admissions had the lowest daily mean of 0.2 (0.5). The daily mean of respiratory (mean = 2.1, SD = 1.6) and circulatory (mean = 2.6, SD = 2.1) admissions was relatively similar, and the daily mean of intestinal infectious was 0.9 (1.0) only.

5.4 Air pollution and meteorological data

5.4.1 Daily levels and seasonal variations of air pollutants in Chiang Mai

As mentioned previously in chapter 3 (methods), levels of air pollutants used for the analysis were the daily mean levels from the two air monitoring stations located in the Muang district, Chiang Mai province. Daily mean levels of air pollutants calculated from the two stations from October 2002 to September 2006 are presented in **Figure 5.7**.

As can be seen, PM_{10}, O_3, and NO_2 exhibited a strong seasonal variation, compared to other pollutants. According to Thailand's ambient air quality standards, there is a 24-hour average standard of 120μg/m^3 for PM_{10}. In **Figure 5.7-e**, the straight line represents the 24-hour average standard levels in Thailand. As shown in the figure, during the study period, daily mean levels of PM_{10} occasionally exceeded the recommended standards of 120μg/m^3.

In general, levels of PM_{10} were comparatively higher during the winter. In Thailand, however, the peak of PM_{10} levels was usually observed from the end of winter (February) to early summer (March) because of two main reasons. Firstly, the occurrence of forest fires is common during this period due to very dry conditions. Secondly, open burning of crop residues to prepare soil for new crops is an agricultural tradition of local people among three border countries (Thailand, Myanmar, and Lao), causing a rise of PM_{10} levels in the Northern Thailand during this period of every year.

The daily levels of ozone appeared to be higher during summer (March-May) in relation to the presence of higher sunlight in comparison to other periods in the same year. Daily levels of NO_2 are generally related to motor vehicle emissions. In this study area, the peak concentrations of NO_2 were observed during winter (Jan and Feb), which might be because of poor local dispersion conditions together with light winds during the colder period. The daily levels of NO_2 dropped during rainy season of a year. This may due in part to the wash out by rains. Overall, there is no obvious trend for air pollutants in Chiang Mai. However, as can be seen in **Figure 5.7-f**, daily levels of $PM_{2.5}$ tended to be increasing over time.

5.4.2 Daily levels and seasonal variations of meteorological variables

Figure 5.8 shows seasonal variations of daily mean levels of selected meteorological variables observed in Chiang Mai for a 4-year period from October 2002 to September 2006. The minimum daily levels of temperature were about 20°C in winter (November-February) and the maximum daily levels of temperature were just above 30°C in summer (March-May). Relative humidity in Chiang Mai was very high during rainy season (June-October), with the maximum levels of about 100%. The lower levels of relative humidity were usually found in winter and possibly in early summer, which were below 40%. The peak levels of rainfall were observed in rainy season, particularly during the end of July to early September, which reached the maximum levels of about 7 mm/hr. While there was no trend for daily mean levels of relative humidity and of rain, a slight increase in daily mean level of temperature in Chiang Mai over the 4- year period was observed.

5.4.3 Correlations among air pollutants and meteorological variables.

Correlations among daily mean levels of air pollutants and meteorological variables in Muang, Chiang Mai are presented in **Table 5.10**. Generally, there were low correlations among air pollutants, with only one exception – the correlation between $PM_{2.5}$ and NO_2. These two pollutants had a high correlation of about 0.81. There were also low correlations among the three meteorological variables. The daily mean levels of temperature were negatively correlated with humidity and rain, while the daily mean levels of relative humidity and rain were positively correlated with each other. In addition, there was a low, negative correlation between air pollutants and meteorological variables. The only one positive correlation was found between O_3 and temperature, but was also low ($r=0.24$). However, it is important to note that the correlations among air pollutants and meteorological variables may be different during different seasons.

Table 5. 1 Characteristics of study population of the out-patient visits data in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Respiratory (J00-J99)	Diabetic (E10-E14)	Circulatory (I00-I99)	Intestinal infectious (A00-A09)	Other	Missing	All-cause
Total count	139,256	45,040	122,177	13,396	617,184	461,316	1,398,369
Age (year)							
0-14	40.2%	1.0%	1.1%	42.2%	11.7%	10.2%	13.1%
15-64	49.1%	67.4%	61.2%	48.9%	67.9%	73.4%	67.1%
≥ 65	10.1%	31.2%	37.4%	8.3%	20.0%	15.5%	19.3%
Missing	0.6%	0.5%	0.3%	0.6%	0.4%	0.9%	0.6%
Sex							
Male	46.6%	41.0%	41.2%	46.4%	43.0%	40.9%	42.5%
Female	52.9%	58.8%	58.2%	53.1%	56.3%	58.2%	56.8%
Missing	0.5%	0.2%	0.6%	0.5%	0.7%	0.9%	0.8%
Occupation*							
Unemployed & economically inactive	19.0%	33.0%	26.5%	21.3%	27.1%	23.3%	25.2%
Non-manual	24.3%	27.5%	25.4%	22.6%	30.2%	7.6%	21.6%
Manual	3.8%	6.2%	7.0%	3.4%	6.8%	7.7%	6.8%
Missing	2.8%	1.2%	2.6%	2.3%	4.2%	35.7%	17.2%

*Excluding children (0-14) and the elderly (≥ 65).

Table 5. 2 Daily OPD visits by causes of the visits in accordance with ICD-10 coding systems in Muang, Chiang Mai, from October 2002 to September 2006.

Causes of visits	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Respiratory (J00-J99)	1461	95.3	53.4	3	30.2	53	87	131	166	318
Circulatory (I00-I99)	1461	83.6	61.1	0	9	22	85	122	163	323
Diabetic (E10-E14)	1461	30.8	23.7	0	2	9	30	44	59	162
Intestinal infectious (A00-A09)	1461	9.17	5.53	0	3	5	8	13	17	33
Other	1461	422	253	16	120	198	373	630	775.8	1163
All-cause	1461	957	680	28	210.2	363.5	912	1473	1749.6	3649

Table 5. 3 Characteristics of study population of hospital admissions data in Muang, Chiang Mai, from October 2003 to September 2006.

Group	Respiratory (J00-J99)	Diabetic (E10-E14)	Circulatory (I00-I99)	Intestinal infectious (A00-A09)	Other	Missing	All-cause
Total count	12,006	1,184	16,694	4,867	133,189	889	168,829
Age (year)							
0-14	23.9%	4.5%	2.3%	28.5%	14.1%	18.6%	14.0%
15-64	47.2%	58.3%	56.9%	60.1%	66.7%	52.9%	64.0%
≥ 65	28.7%	37.3%	40.7%	11.2%	19.0%	14.6%	21.7%
Missing	0.2%	0.0%	0.1%	0.2%	0.2%	13.9%	0.3%
Sex							
Male	52.2%	41.6%	48.8%	40.5%	46.8%	43.9%	47.2%
Female	47.5%	58.5%	50.9%	59.3%	52.8%	39.7%	52.4%
Missing	0.3%	0.0%	0.3%	0.3%	0.3%	16.4%	0.4%
Occupation*							
Unemployed & economically inactive	8.9%	12.8%	14.9%	5.5%	14.2%	9.6%	13.5%
Non-manual	1.8%	1.2%	0.5%	1.0%	1.0%	0.3%	1.0%
Manual	4.2%	7.4%	7.0%	4.6%	7.6%	3.7%	7.2%
Missing	32.7%	37.1%	34.8%	49.6%	44.4%	53.5%	42.6%

*Excluding children (0-14) and the elderly (≥ 65).

Table 5. 4 Daily hospital admissions by causes of the admissions in accordance with ICD-10 coding systems in Muang, Chiang Mai, from October 2003 to September 2006.

				Percentile						
Causes of admissions	**n (day)**	**Mean**	**SD**	**Min**	**10th**	**25th**	**50th**	**75th**	**90th**	**Max**
Respiratory (J00-J99)	1461	7.8	4.3	0.0	3.0	5.0	7.0	10.0	14.0	29.0
Circulatory (I00-I99)	1461	11.1	8.9	0.0	4.0	6.0	10.0	15.0	19.0	32.0
Diabetic (E10-E14)	1461	0.8	1.0	0.0	0.0	0.0	1.0	1.0	2.0	6.0
Intestinal infectious (A00-A09)	1461	3.3	2.5	0.0	1.0	1.0	3.0	5.0	7.0	13.0
Other	1461	80.4	40.1	13.0	32.0	45.0	75.0	115.0	137.0	203.0
All-cause	1461	103.9	47.9	18.0	45.2	63.0	96.0	146.0	172.0	233.0

Table 5. 5 Summary of the linkage data between out-patient visits and hospital admissions by history of the visits prior to the admissions from April 2003 to January 2006.

OPD visits within 6 months prior to admissions	Count of admissions
Total	29,937 (100.0%)
No visit	2,733 (9.1%)
1 visit or more	27,204 (90.9%)

Table 5. 6 The breakdown of people with history of out-patient visits prior to their admissions by number of the visits from April 2003 to January 2006.

History of the visits prior to the admissions	Count of admissions
Total	27,204 (100.0%)
1 visit	7,085 (26.0%)
2-5 visits	13,990 (51.4%)
>5 visits	6,129 (22.5%)

Table 5. 7 Proportion of disease groups of hospital admissions and disease groups of out-patient visits prior to their admissions from April 2003 to January 2006.

5.7a) People with one visit prior to the admissions

Disease groups of hospital admissions	Disease groups of out-patient visits prior to their admissions						
	Respiratory	Diabetic	Circulatory	Intestinal infectious	Other	Missing	All-cause
Respiratory (J00-J99)	117 (27.9%)	2 (0.5%)	19 (4.5%)	3 (0.7%)	96 (22.9%)	182 (43.4%)	419 (100.0%)
Diabetic (E10-E14)	1 (4.6%)	4 (18.2%)	3 (13.6%)	0 (0.0%)	2 (9.1%)	12 (54.6%)	22 (100.0%)
Circulatory (I00-I99)	12 (1.6%)	20 (2.7%)	285 (37.9%)	2 (0.3%)	85 (11.3%)	349 (46.4%)	753 (100.0%)
Intestinal infectious (A00-A09)	24 (17.1%)	0 (0.0%)	5 (3.6%)	17 (12.1%)	59 (42.1%)	35 (25.0%)	140 (100.0%)
Other	157 (2.7%)	31 (0.5%)	121 (2.1%)	24 (0.4%)	2,374 (41.4%)	3,029 (52.8%)	5,736 (100.0%)
Missing	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	13 (86.7%)	15 (100.0%)
All-cause	311 (4.4%)	58 (0.8%)	433 (6.1%)	46 (0.7%)	2,617 (36.9%)	3,620 (51.1%)	**7,085** (100.0%)

5.7b) People with 2-5 visits prior to the admissions

Disease groups of hospital admissions	Disease groups of out-patient visits prior to their admissions						
	Respiratory	Diabetic	Circulatory	Intestinal infectious	Other	Missing	All-cause
Respiratory (J00-J99)	355 (34.8%)	8 (0.8%)	40 (3.9%)	25 (2.5%)	277 (27.2%)	314 (30.8%)	1,019 (100.0%)
Diabetic (E10-E14)	1 (1.1%)	24 (26.4%)	4 (4.4%)	0 (0.0%)	28 (30.8%)	34 (37.4%)	91 (100.0%)
Circulatory (I00-I99)	35 (2.9%)	26 (2.1%)	371 (30.6%)	1 (0.1%)	198 (16.3%)	583 (48.0%)	1,214 (100.0%)
Intestinal infectious (A00-A09)	75 (17.5%)	2 (0.5%)	16 (3.7%)	93 (21.7%)	166 (38.7%)	77 (18.0%)	429 (100.0%)
Other	385 (3.4%)	88 (0.8%)	235 (2.1%)	64 (0.6%)	4,848 (43.3%)	5,586 (49.9%	11,206 (100.0%)
Missing	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.8%)	22 (71.0%)	31 (100.0%)
All-cause	852 (6.1%)	148 (1.1%)	666 (4.8%)	183 (1.3%)	5,525 (39.5%	6,616 (47.3%)	**13,990** (100.0%)

5.7c) People with > 5 visits prior to the admissions

Disease groups of hospital admissions	Disease groups of out-patient visits prior to their admissions						
	Respiratory	Diabetic	Circulatory	Intestinal infectious	Other	Missing	All-cause
Respiratory (J00-J99)	193 (34.6%)	9 (1.6%)	33 (5.9%)	10 (1.8%)	176 (31.5%)	137 (24.6%)	558 (100.0%)
Diabetic (E10-E14)	2 (2.0%)	39 (39.4%)	5 (5.1%)	0 (0.0%)	34 (34.3%)	19 (19.2%)	99 (100.0%)
Circulatory (I00-I99)	23 (5.1%)	23 (5.1%)	129 (28.4%)	2 (0.4%)	111 (24.5%)	166 (36.6%)	454 (100.0%)
Intestinal infectious (A00-A09)	36 (19.1%)	6 (3.2%)	15 (7.9%)	16 (8.5%)	89 (47.1%)	27 (14.3%)	189 (100.0%)
Other	170 (3.5%)	105 (2.2%)	193 (4.0%)	24 (0.5%)	2,284 (47.5%)	2,036 (42.3%)	4,812 (100.0%)
Missing	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	9 (52.9%)	7 (41.2%)	17 (100.0%)
All-cause	424 (6.9%)	182 (3.0%)	376 (6.1%)	52 (0.9%)	2,703 (44.1%)	2,392 (39.0%)	**6,129** (100.0%)

Table 5. 8 Characteristics of study population of the linkage data in Muang, Chiang Mai, from April 2003 to January 2006.

Group	Respiratory (J00-J99)	Diabetic (E10-E14)	Circulatory (I00-I99)	Intestinal infectious (A00-A09)	Other	Missing	All-cause
Total count	2,226	232	2,684	934	23,790	71	29,937
Age (year)							
0-14	33.8%	3.5%	2.5%	40.2%	12.5%	19.7%	14.0%
15-64	46.8%	65.5%	70.0%	49.0%	71.3%	62.0%	68.6%
≥ 65	19.4%	31.0%	27.5%	10.8%	16.2%	18.3%	17.4%
Missing	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Sex							
Male	53.3%	41.8%	47.1%	45.3%	44.2%	43.7%	45.1%
Female	46.6%	58.2%	52.9%	54.7%	55.8%	56.3%	54.9%
Missing	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Occupation*							
Unemployed & economically inactive	18.9%	29.3%	32.3%	11.8%	30.2%	26.8%	29.0%
Non-manual	2.4%	0.0%	0.6%	1.8%	1.0%	0.0%	1.1%
Manual	9.7%	13.4%	18.0%	12.2%	18.7%	12.7%	17.7%
Missing	15.9%	22.8%	19.1%	23.2%	21.5%	22.5%	20.9%

*Excluding children (0-14) and the elderly (≥ 65).

Table 5. 9 Daily hospital admissions of the linkage data by causes of the admissions in accordance with ICD-10 coding systems in Muang, Chiang Mai, from April 2003 to January 2006.

				Percentile						
Causes of admissions	n (day)	Mean	SD	Min	10th	25th	50th	75th	90th	Max
Respiratory (J00-J99)	1037	2.1	1.6	0	0	1	2	3	4	9
Circulatory (I00-I99)	1037	2.6	2.1	0	0	1	2	4	5	10
Diabetic (E10-E14)	1037	0.2	0.5	0	0	0	0	0	1	3
Intestinal infectious (A00-A09)	1037	0.9	1.0	0	0	0	1	1	2	6
Other	1037	22.9	12.6	1	7	11	23	33	39	60
All-cause	1037	28.9	14.4	2	10	15	30	40	47	70

Table 5. 10 Correlations among air pollutants and meteorological variables.

	SO_2	NO_2	CO	O_3	PM_{10}	$PM_{2.5}$	Temperature	Humidity	rain
SO_2	1								
NO_2	0.36	1							
CO	0.17	0.58	1.00						
O_3	0.19	0.51	0.34	1					
PM_{10}	0.36	0.81	0.60	0.63	1				
$PM_{2.5}$	-0.01	0.46	0.66	0.40	0.62	1			
Temperature	-0.05	-0.24	-0.22	0.24	-0.07	0.14	1		
Humidity	-0.18	-0.50	-0.46	-0.66	-0.53	-0.58	-0.22	1	
Rain	-0.08	-0.18	-0.14	-0.23	-0.22	-0.15	-0.05	0.28	1

Figure 5. 1 Monthly variation of total counts of OPD visits in the selected heath centres and hospitals Muang, Chiang Mai, from October 2002 to September 2006.

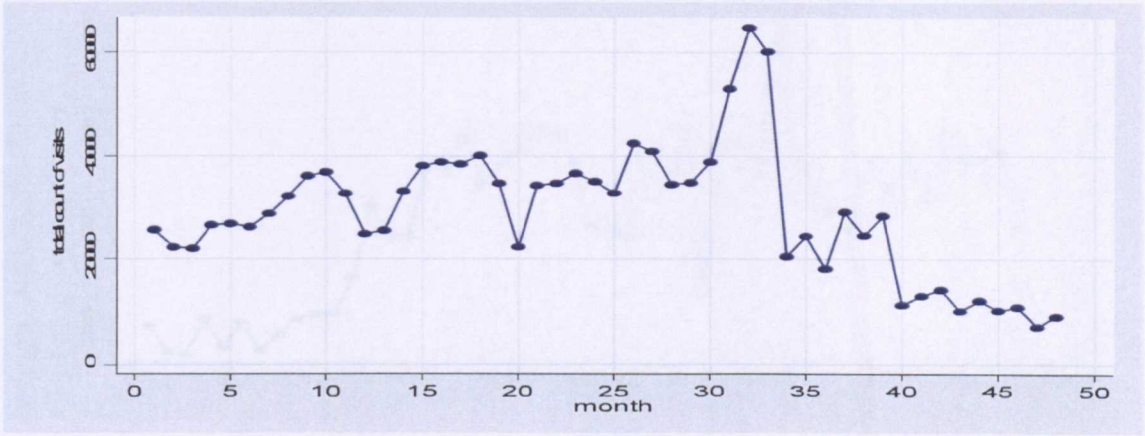
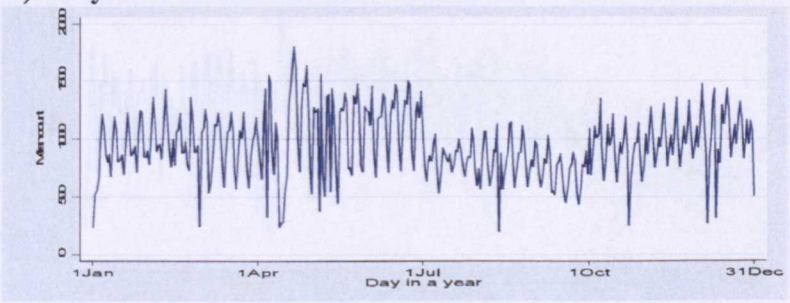


Figure 5. 2 Overview of a one-year variation of out-patient visits by causes of the visits over the study period.

5.2a) Daily mean count of all-cause visits



5.2b) Daily mean percentage of each disease group compared to all-cause visits.

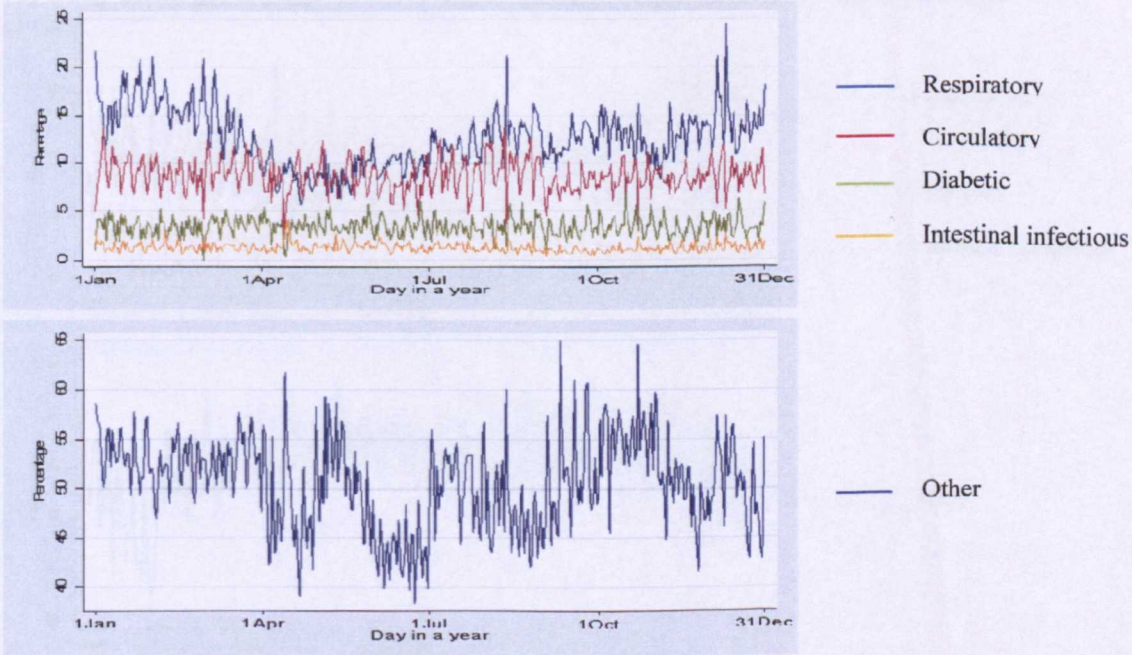


Figure 5. 3 Monthly variation of total counts of hospital admissions in the selected hospitals in Muang, Chiang Mai, from October 2002 to September 2006.

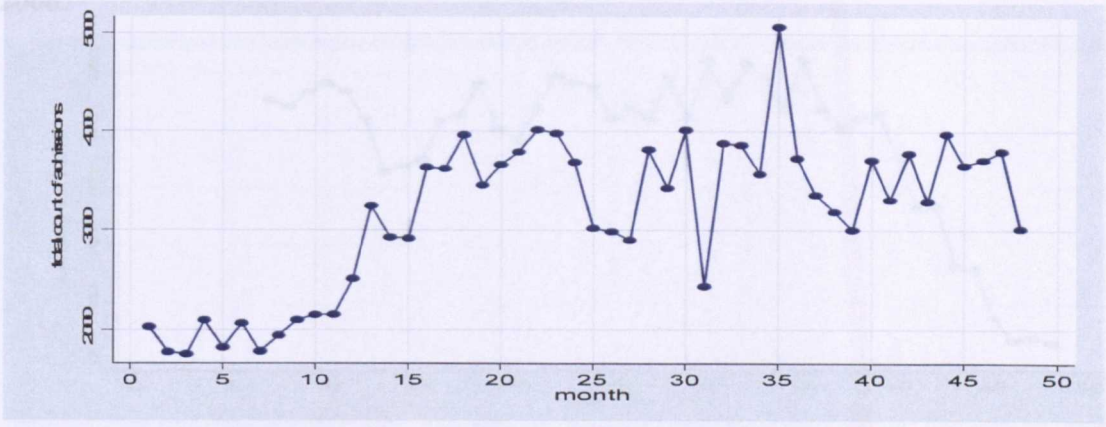
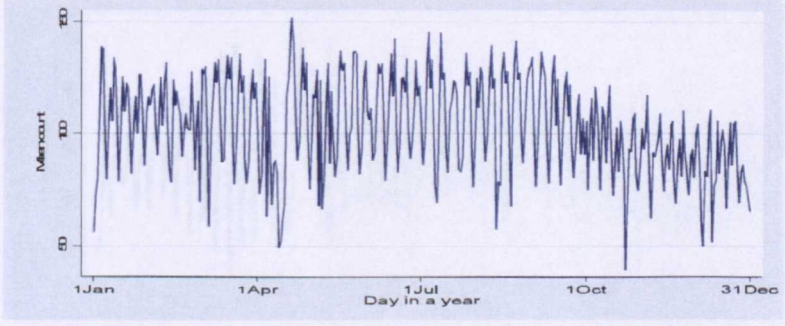
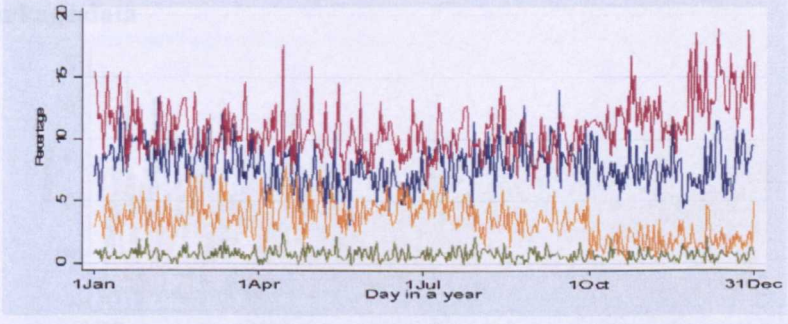


Figure 5. 4 Overview of a one-year variation of hospital admissions by causes of the admissions over the study period.

5.4a) Daily mean count of all-cause admissions



5.4b) Daily mean percentage of each disease group compared to all-cause admissions.



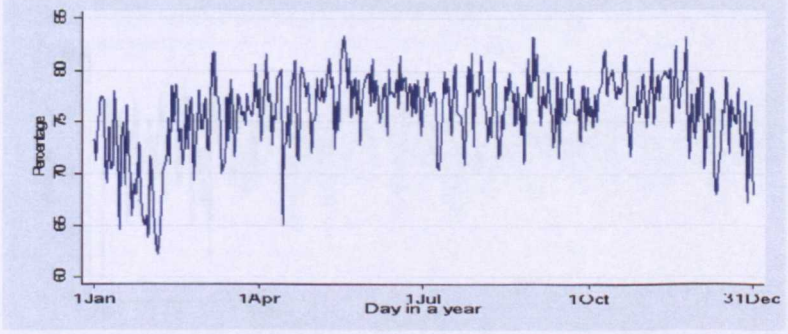


Figure 5. 5 Monthly variation of total counts of linkage data (between out-patient visits and hospital admissions) in Muang, Chiang Mai, from April 2003 to September 2006.

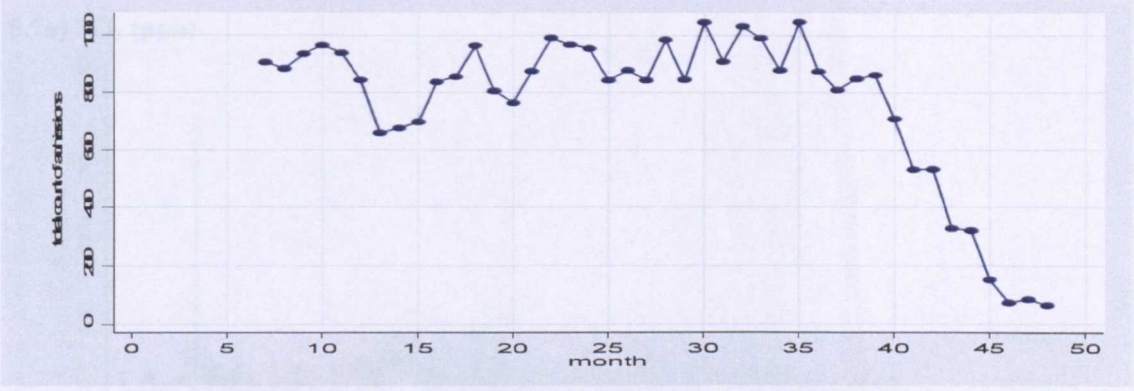
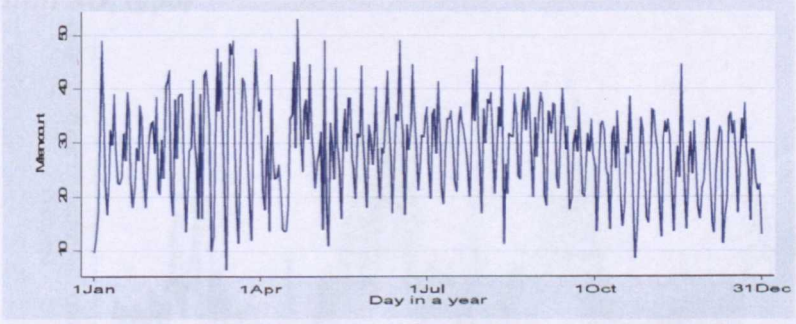


Figure 5. 6 Overview of a one-year variation of hospital admissions in the linkage data by causes of the admissions over the study period.

5.6a) Daily mean count of all-cause admissions in the linkage data



5.6b) Daily mean percentage of each disease group compared to all-cause admissions in the linkage data

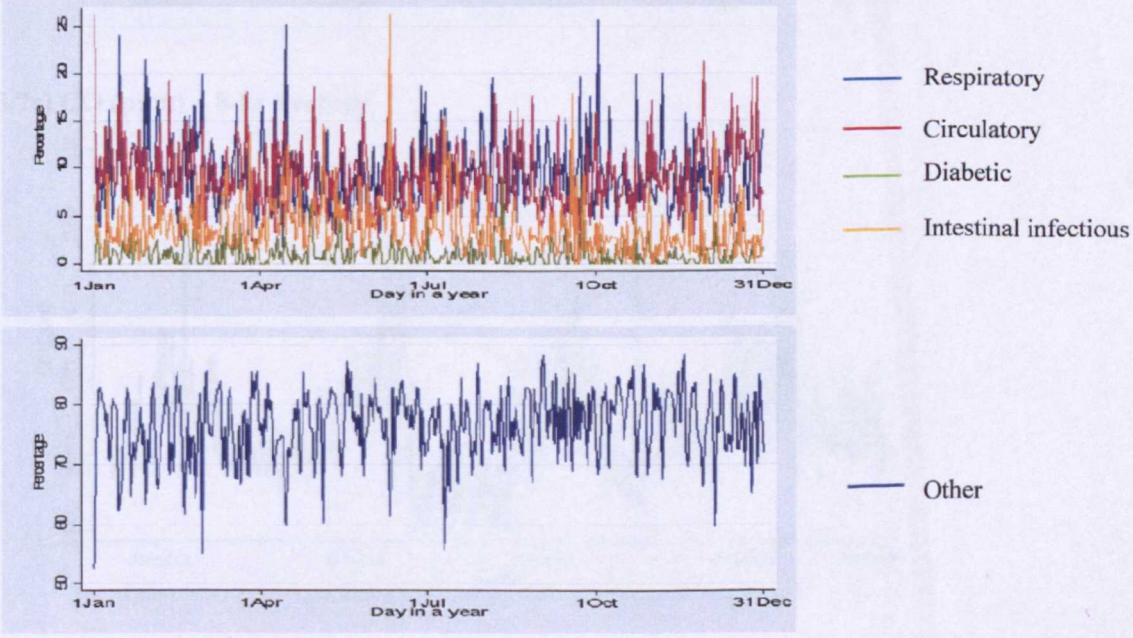
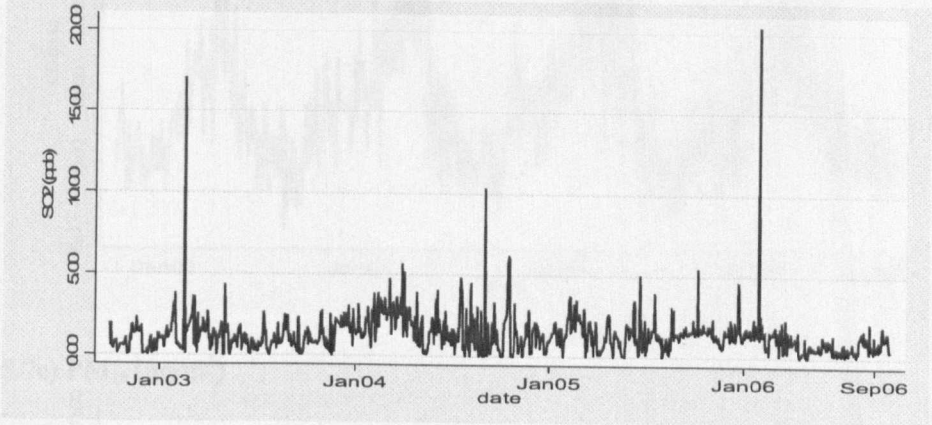


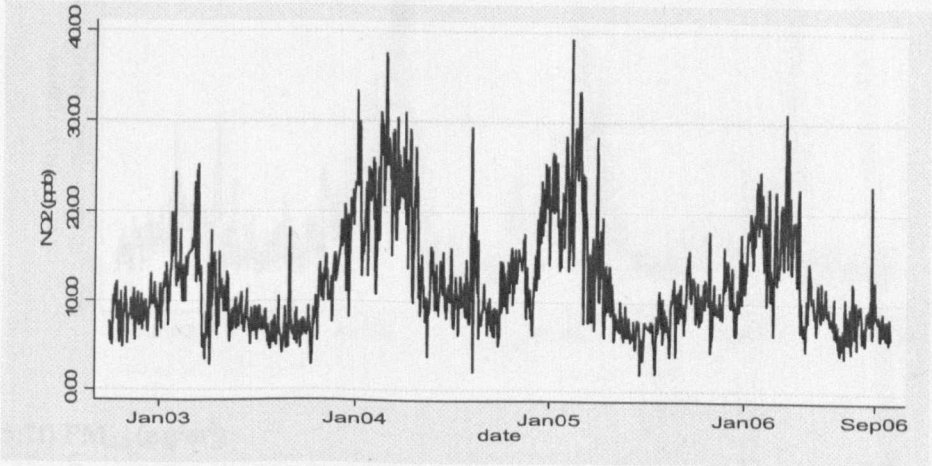
Figure 5. 7 Daily levels of air pollutants in Chiang Mai for 4-year period measured from October 2002 to September 2006.

Note: Daily mean levels of 1-hr average for all pollutants, except noted.

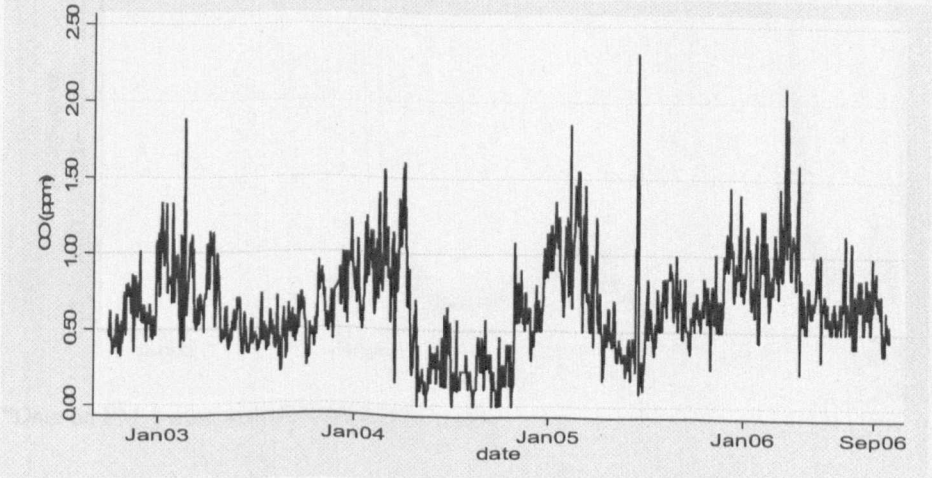
5.7a) SO_2 (ppb)



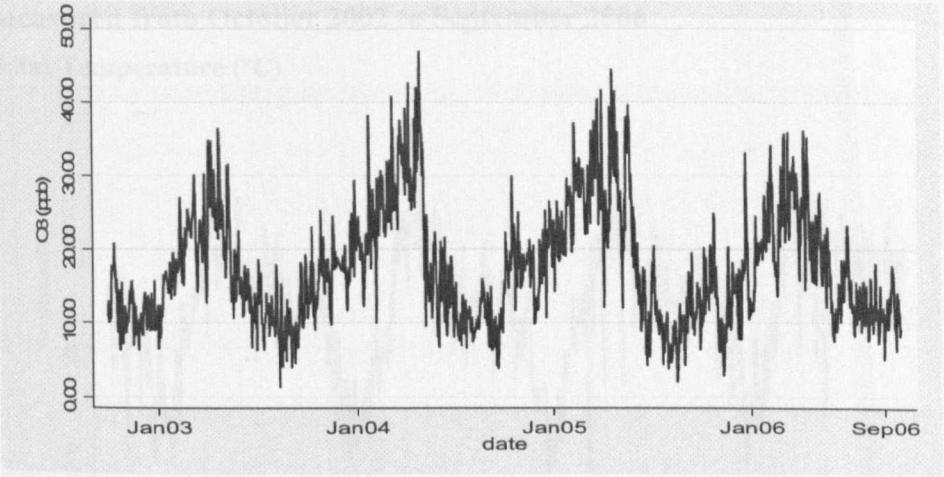
5.7b) NO_2 (ppb)



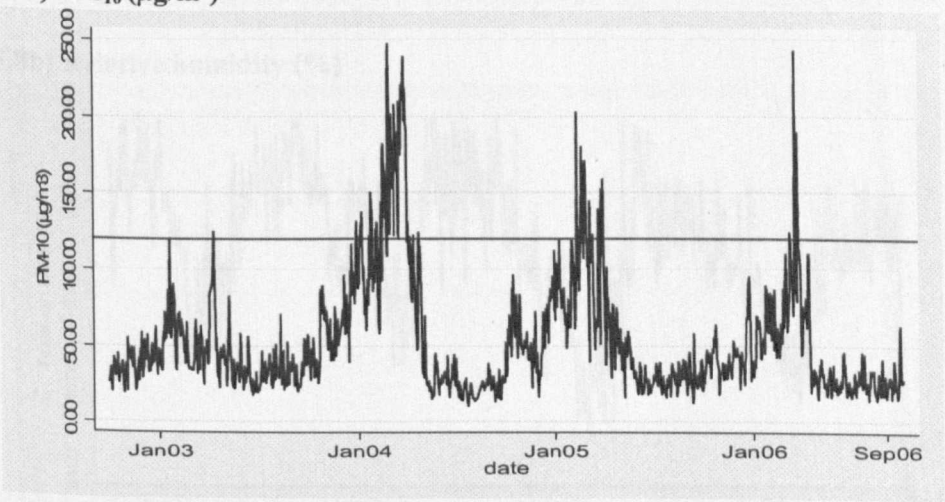
5.7c) CO (ppm) – 8-hr average



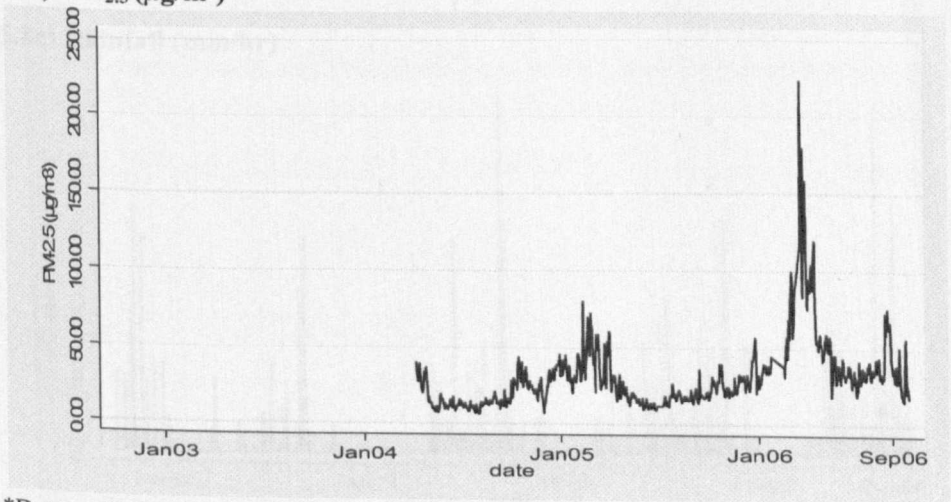
5.7d) O_3 (ppb)



5.7e) PM_{10} ($\mu g/m^3$)



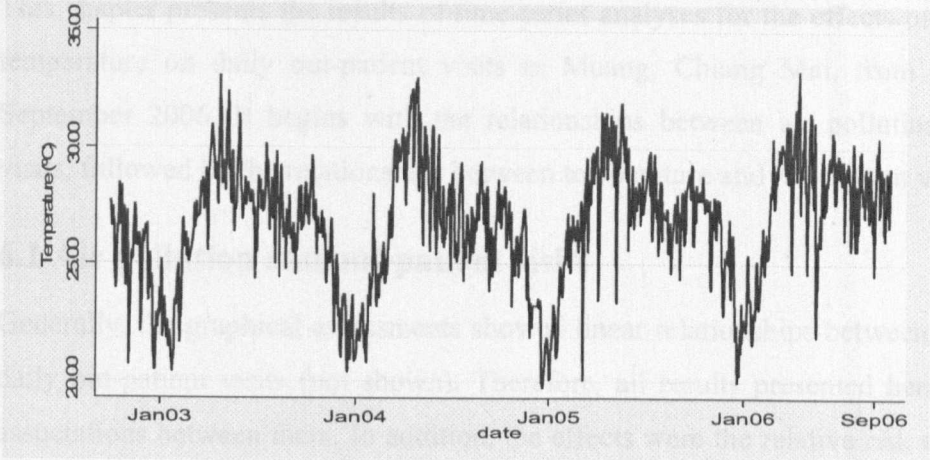
5.7f) $PM_{2.5}$ ($\mu g/m^3$)



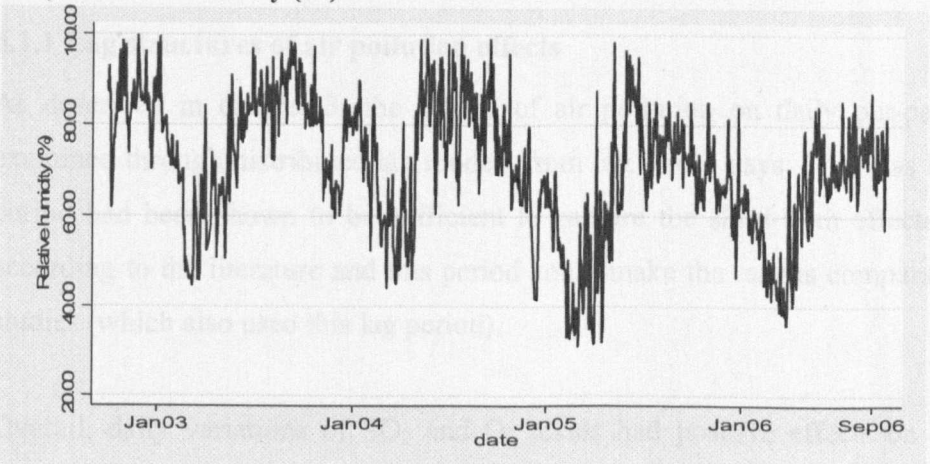
*Data on $PM_{2.5}$ were available from April 2004.

Figure 5. 8 Daily levels of meteorological variables in Chiang Mai for 4-year period measured from October 2002 to September 2006.

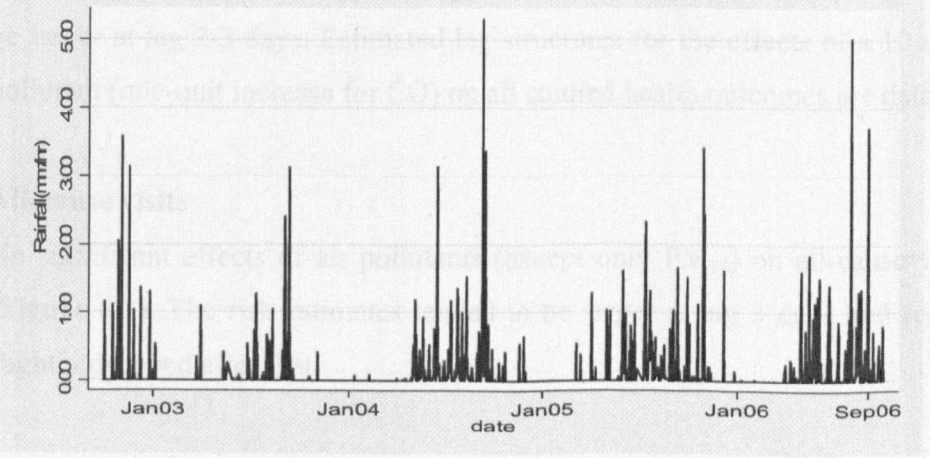
5.8a) Temperature (°C)



5.8b) Relative humidity (%)



5.8c) Rainfall (mm/hr)



Chapter 6 Regression results: Out-patient visits

This chapter presents the results of time-series analyses for the effects of air pollution and temperature on daily out-patient visits in Muang, Chiang Mai, from October 2002 to September 2006. It begins with the relationships between air pollution and out-patient visits, followed by the relationships between temperature and out-patient visits.

6.1 Air pollution and out-patient visits

Generally, the graphical assessments showed linear relationships between air pollution and daily out-patient visits (not shown). Therefore, all results presented here were the linear associations between them. In addition, the effects were the relative risk estimates of a 10-unit increase of a pollutant (one-unit increase for CO) on the daily out-patient visits.

6.1.1 Lag structures of air pollution effects

As described in chapter 3, the effects of air pollution on daily out-patient visits were examined through distributed lag models from lag 0 to 4 days. This was because this time period had been shown to be sufficient to capture the short-term effects of air pollution according to the literature and this period could make the results comparable to the PAPA studies (which also used this lag period).

Overall, daily variations of SO_2 and O_3 levels had positive effects on daily out-patient visits, but not statistically significant. The effects of other pollutants were generally negative, and also not statistically significant. The effects of most pollutants were found to be larger at lag 2-3 days. Estimated lag structures for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on all studied health outcomes are detailed below.

All-cause visits

No significant effects of air pollutants (except only PM_{10}) on all-cause visits were found (**Figure 6.1**). The risk estimates tended to be larger at lag 3 days and remained stable or slightly dropped after that.

Respiratory visits

Some small positive effects of SO_2 and O_3 were found, particularly at lag 2 days (**Figure 6.2**). NO_2, CO, and $PM_{2.5}$ effects were found to be larger at lag 3 days, while PM_{10} effects relatively fluctuated over 0-4 days. However, none of these effects were statistically significant.

Circulatory visits

The risks of circulatory visits were larger at lag 4 days in association with a 10-unit increase in SO_2, NO_2, PM_{10} and one-unit increase in CO (**Figure 6.3**). The risk of circulatory visits at lag 3 days was also found to be associated with a 10-unit increase in O_3 and $PM_{2.5}$.

Diabetic visits

The risk estimates of diabetic visits in association with a 10-unit increase in selected air pollutants were relatively small and close to 1, with little fluctuations over the 0-4 days period (**Figure 6.4**).

Intestinal infectious visits

Similar to diabetic visits, the estimated effects of each pollutant on intestinal infectious visits were relatively small and close to 1 (**Figure 6.5**). A small increase in positive effects of most pollutants was found at lag 2-3 days.

Other visits

Some positive effects on 'other' visits were found at lag 0 day for NO_2, O_3, and PM_{10}, and found at lag 2 and 3 days for CO and SO_2, respectively (**Figure 6.6**). However, the risk estimates were not statistically significant.

6.1.2 Air pollution effects on daily out-patient visits

In general, positive effects were predominantly found for SO_2, O_3, and NO_2, but did not reach the statistically significant at 5% level. The negative, but significant, effects were occasionally found for PM_{10} and $PM_{2.5}$. The estimated effects presented here are the sum of all lags (lag 0-1and lag 0-4 days) from single pollutant, distributed lag models, and are described separately for each selected health outcome.

All-cause visits

There were only two pollutants: SO_2 and O_3 that had positive effects on all-cause visits (**Table 6.1**), with 4.7% (95% CI, -0.91% to 20.5%) increase in all-cause visits per 10-unit increase in SO_2 (ppb) and 0.1% increase in all-cause visits per 10-unit increase in O_3 (ppb). This was found at lag 0-4 days, but not statistically significant. At the same lag, a negative effect with borderline significance was found for PM_{10} (RR = 0.988, 95% CI, 0.977 to 1.000, p-value = 0.053) and for $PM_{2.5}$ (RR=0.985, 95% CI, 0.970 to 1.001, p-value = 0.062).

Respiratory visits

Positive effects on respiratory visits were found for SO_2 and NO_2, while negative effects were found for other pollutants (**Table 6.2**). For instance, at lag 0-4 days, the respiratory visits increased by 4.4% (95% CI, -10.9% to 22.4%) per 10-unit increase in SO_2 (ppb), and by 1.0% (95%CI, -2.3% to 4.5%) per 10-unit increase in NO_2 (ppb). Negative, but significant, effects were found for O_3 at lag 0-1 day (RR = 0.969, 95% CI, 0.942 to 0.998, p-value = 0.036). The negative effects of $PM_{2.5}$ were also found to be significant, with the RR of 0.986 (95% CI, 0.973 to 1.000, p-value = 0.042) at lag 0-1 day, and of 0.976 (95% CI, 0.959 to 0.993, p-value = 0.006) at lag 0-4 days.

Circulatory visits

As can be seen in **Table 6.3**, SO_2 effects on circulatory visits were relatively large, although the effects were not statistically significant at the 5% level. It was found that circulatory visits increased by 11.2% (95% CI, -6.0% to 31.5%) and by 22.2% (95% CI, -2.8% to 53.6%) in association with a 10-unit increase in SO_2 (ppb) at lag 0-1 day and at lag 0-4 days, respectively. Circulatory visits also increased by 1.7 % (95% CI, -3.6% to 7.3%) in association with a 10-unit increase in O_3 (ppb) lat lag 0-4 days. The other pollutants provided negative association with circulatory visits, but none of the estimates was statistically significant (except only $PM_{2.5}$ at lag 0-1 day).

Diabetic visits

As shown in **Table 6.4**, the relatively large estimated effects on diabetic visits were found for SO_2, while smaller effects were found for NO_2 and CO. There was a rise in diabetic visits of 5.3% (95% CI, -19.2% to 37.2%) per 10-unit increase in SO_2 (ppb) at lag 0-1 day

and of 25.5% (95%CI, -12.1% to 79.2%) per 10-unit increase in SO_2 (ppb) at lag 0-4 days. The effects of other pollutants were found to be negative. However, all estimated effects of all pollutants on diabetic visits were non-significant.

Intestinal infectious visits

As can be seen in **Table 6.5**, none of the air pollutants provided positive effects on intestinal infectious visits in the present study. In addition, the effects of PM_{10} and $PM_{2.5}$ were found to be statistically significant at 5% level. For example, at lag 0-1 day, the relative risks were 0.987 (95% CI, 0.976 to 0.999, p-value = 0.033) for PM_{10}, and were 0.962 (95% CI, 0.932 to 0.993, p-value = 0.018) for $PM_{2.5}$.

Other visits

Some small positive effects on 'other' visits were found for SO_2 and O_3, but not statistically significant (**Table 6.6**). A 10-unit increase in SO_2 (ppb) at lag 0-4 days was associated with a 1.3% (95% CI, -12% to 16.6%) increase in 'other' visits, whereas a 10-unit increase in O_3 (ppb) at lag 0-4 days was associated with a 2.5% (95% CI, -0.7% to 5.8%) increase in 'other' visits. Negative effects were found for other pollutants and were found to be significant for CO (both lags) and $PM_{2.5}$ (lag 0-4 days). At lag 0-4 days, the relative risks were about 0.935 (95% CI, 0.877 to 0.997, p-value = 0.040) for CO, and were about 0.981 (95% CI, 0.965 to 0.997, p-value = 0.017).

6.1.3 Air pollution and effect modification

The estimated effects of air pollution on selected health outcomes when the out-patient visit data was stratified by age, sex, and occupation are presented in this section. To determine whether air pollution effects were modified by these subgroups, the test for heterogeneity between subgroups was carried out. Effects of season on association between air pollution and daily out-patient visits were also examined.

I. Effect modification by age

There was no evidence of effect modification by age on the association between air pollution and daily out-patient visits in the present study (**Figure 6.7**). Overall, the effects of air pollution were found to be stronger in the elderly in comparison to adults and

children. However, most effects were not significant, and there were no differences in the estimated effects between age groups.

II. Effect modification by sex

In general, air pollution effects did not vary by sex in this study (**Figure 6.8**). The estimated effects of most pollutants seemed to be negative and centred around one, except only SO_2 effects, but not significant. By comparison, the risks of all-cause, circulatory, diabetic, and 'other' visits were slightly higher in males than in females, whereas the risks of respiratory and intestinal infectious visits were higher in females than in males. However, there was no significant difference in the estimated effects between males and females.

III. Effect modification by occupation

Overall, there was little evidence of modification of air pollution effects by occupation in the present study (**Figure 6.9**). The effects of air pollution varied from pollutant to pollutant, and did not consistent across all disease groups. Larger, positive effects on the visits in different occupational groups were found for SO_2 than for other pollutants. Generally, the effects of most pollutants were relatively stronger manual workers for most diseases, except for circulatory visits, which the effects of all pollutants were higher in non-manual workers. However, most results from the test for heterogeneity between groups were not significant.

IV. Effect modification by season

As described earlier, there are three seasons in Chiang Mai, including winter (November-February), summer (March-May), and rainy (June-October) season. Thus, it was decided to examine whether air pollution effects on daily out-patient visits were modified by season. To investigate air pollution effects in different seasons, an indicator variable of season was incorporated into the models (1= winter, 2=summer, and 3=rainy). The risk estimates of daily out-patient visits per 10-unit increase of a pollutant (one-unit increase for CO) in different seasons are shown in **Figure 6.10**.

Overall, there was no evidence of effect modification by season on association between air pollution and out-patient visits, with only one exception – the association between air pollution and respiratory visits (p-value of the test for interaction < 0.05 for the effects of

all pollutants). By comparison, the effects of SO_2 were larger than those of other pollutants in all seasons, but the confidence intervals were relatively wide. The effects of SO_2 were higher in summer for all-cause and respiratory visits, but were higher in rainy season for circulatory and diabetic visits. The estimated effects of other pollutants seemed to centre around 1 in all seasons. In addition, although the risk estimates for O_3 effects were small, as one would expected, the O_3 effects were stronger in summer compared to other seasons.

6.1.4 Air pollution effects for two-pollutant models

There is a mix of air pollutants in the air. In general, individuals are not exposed to only one pollutant at a time. Since air pollutants are either positively or negatively correlated, with each other, to distinguish the most affecting pollutant is very difficult. Nevertheless, the two-pollutant models may help determine which pollutant is the better predictor of the health outcomes.

Based on positive effects of single pollutant model results, three pollutants, including SO_2, O_3, and NO_2, were selected for developing two-pollutant models as they provided more positive effects than other pollutants studied. The two-pollutant models used the same basic structure as the single-pollutant models, with the inclusion of linear terms of selected two pollutants at one time. The two-pollutant analyses focused on main health outcomes, including all-cause, respiratory, circulatory, diabetic, intestinal infectious and 'other' visits. In addition, the analyses were undertaken for all ages and for the elderly ($\geq$ 65 year) only because the positive associations in this study were mostly found in the elderly compared to other age groups.

The results of single pollutant models and two-pollutant models for the effects of a 10-unit increase in a pollutant at average lag 0-4 days on daily out-patient visits in all ages and in the elderly ($\geq$65 year) are presented in **Table 6.7**. As can be seen, when including SO_2 and O_3 into the models, the risk estimates of each pollutant were not different from those obtained from the single pollutant models. Similarly, when including O_3 and NO_2 into the same models, there was also no significant difference in the risk estimates of each pollutant in the models compared to the single pollutant models. When SO_2 and NO_2 were included in the models, only one considerable reduction of the effects of SO_2 on circulatory visits was observed. That was, the risk estimates of SO_2 decreased from 14.7% (95% CI, -7.8% to

42.8%) in single pollutant model to 3.4% (95% CI, -1.9% to 9.0%) in the two-pollutant model.

In brief, there were generally no significant changes of the risk estimates of each selected pollutants in the two-pollutant models when compared to those obtained from the single pollutant models.

6.2 Temperature and out-patient visits

6.2.1 General relationships between temperature and out-patient visits

General relationships between temperature and out-patient visits were investigated by plotting the counts of the visits against average temperature at lag 0-1 days (for short lag) and at lag 0-13 days (for long lag). Adjustments were made for humidity, rain, and the two selected pollutants: SO_2 and O_3. These two pollutants were selected with respect to the air pollution results as they predominantly provided positive effects on daily out-patient visits than other pollutants. In addition, O_3 is likely to be a confounder as its occurrence related to the presence of sunlight or warm climate. Since literature suggests that PM_{10} is more likely to confound the association between temperature and health outcomes [127], replacing SO_2 with PM_{10} in the models was also done, but there were little changes in the risk estimates (not shown). The plots of adjusted relationships between temperature and out-patient visits are shown in **Figure 6.11**.

All-cause visits

When adjusting for meteorological variables (humidity and rain) and air pollution (SO_2 and O_3), there was a linear increase in all-cause visits when temperature was above 29°C, but found for temperature at a long lag (0-13 days) only.

Respiratory visits

The plots of the relationship between temperature and respiratory visits showed a somewhat linear decrease of respiratory visits with increasing temperature, which was more apparent for the short lag (0-1 day) than that for the longer lag (0-13 day) period. The likelihood ratio test between the models with and without splines of temperature also showed that the

model without the splines of temperature fitted better than that with the splines of temperature, suggesting a linear association between them.

Circulatory visits

The plot of the relationship between temperature and circulatory visits showed that there was a linear increase in circulatory visits at temperature above 29°C, which was more apparent for temperature at a long lag (0-13 days) than for temperature at short lag (0-1day).

Diabetic visits

The plot of the relationship between temperature and diabetic visits showed a flat line of the estimated risks, which centred around 1 for temperature at a short lag (0-1 day). For temperature at a long lag (0-13 days), there was a linear increase in diabetic visits with temperature threshold of about 29°C.

Intestinal infectious visits

By comparison, the linear relationship between temperature and intestinal infectious visits was more visible for temperature at a short lag (0-1 day) than for temperature at longer lag (0-13 days). The plot of the relationship at short lag showed a linear increase in the visits with increasing temperature, although the visits declined slightly when temperature was above 29 °C.

Other visits

The plot of the relationship between 'other' visits and temperature illustrated that there was a linear increase in 'other' visits with increasing temperature for both shot lag (0-1 day) and long lag (0-13 days), but the slope of the relationship was steeper for longer lag.

To sum up, based on the graphical assessments, a linear association between out-patient visits and temperature with temperature threshold at about 29 °C was visible at longer lag (0-13 days) for all-cause, circulatory, and diabetic visits. Therefore, the quantification of hot temperature at above 29 °C was carried out for these three diseases. Since a linear association with no temperature threshold was obviously shown for respiratory, intestinal

infectious and 'other' visits, quantifying temperature effects by using linear terms of temperature was done for these diseases. However, the quantification of temperature effects at long lag (0-13 day) was undertaken for 'other' visits, whereas the quantification of the effects at a short lag (0-1 day) was done for respiratory and intestinal infectious visits.

6.2.2 Lag structure of temperature effects

The effects of temperature on daily out-patient visits for specified lag period are presented in **Figure 6.12**. Generally, there was no significant effect of temperature on out-patient visits over 0-13 day lag period. Larger, positive effects were mostly observed at lag 2, while larger, negative effects were shown at lag 1 for most diseases. The estimated effects remained stable from lag 3 to lag 13. There was also no increase or decrease in temperature effects beyond 13 days (not shown). Thus, the use of temperature at lag 0-13 days for further investigations of temperature effects in the present study should be sufficient.

6.2.3 Temperature effects on out-patient visits

As mentioned earlier, a temperature threshold of 29°C was used for quantifying temperature effects for all-cause, circulatory, and diabetic visits, while a linear term of temperature was used for respiratory, intestinal infectious, and 'other' visits. The quantification was examined through the distributed lag models of temperature for short lag (0-1 day) for respiratory and intestinal infectious visits, and longer lag (0-13 days) for the rest of the disease groups. The same core model used for determining air pollution effects was employed for the quantification, but using 6df of the spline for time and adjusting for two pollutants: SO_2 and O_3. Thus, the estimated effects were the sum of all lags from lag 0 to 1day and from lag 0 to 13 days. Generally, without stratification, the temperature effects on all people reached the statistically significant at 5% level for most health outcomes. The test for heterogeneity between each stratified group (age, sex, and occupation) was also investigated. The analysis results are detailed separately for each health outcomes as the followings.

All-cause visits

Overall, there were positive effects of hot temperature (above 29°C) on all-cause visits, but the effects were not statistically significant for all subgroups (**Table 6.8**). There was a 9.4% (95% CI, 2.8% to 16.5%) increase in all-cause visits in all people per 1°C increase in

temperature above 29°C. When the data were stratified by age, the risk estimates in adults (15-64 years) and the elderly (≥ 65 years) were found to be significant and broadly the same, while the smallest and non-significant estimates were found in children (0-14 years). For each 1°C increase in temperature above 29°C, the risk of all-cause visits in males (11.6% increase, 95% CI, 4.7% to 19.0%) was almost two-times higher than that in females (6.3% increase, 95% CI, -0.6% to 13.7%). For occupation, the estimate was significant and slightly higher in unemployed and economically inactive people (9.9% increase, 95% CI, 3.1% to 17.1%) than those in non-manual and manual workers, which were similar and not significant.

Respiratory visits

Generally, there was a reduction in respiratory visits with increasing temperature, but the reduction was not significant for all subgroups as shown in **Table 6.9**. For each 1°C increase in temperature (no threshold), there was a borderline significant reduction of respiratory visits in all people of about 0.9 % (95% CI, -1.9% to 0.0%). The decreased risks of the visits were found to be similar for all age groups, ranging from 0.2% to 1.0%. The risk of respiratory visits significantly decreased in females (-2.0%, 95% CI, -3.1% to -0.9%), but not in males (which was in opposite direction and not significant). A significant decline in the visits was also observed in unemployed and economically inactive people (-1.1%, 95% CI, -2.1% to 0.0%), whereas a decline in the visits and an increase in the visits were found for non-manual and manual workers, but none of them was significant.

Circulatory visits

There was an increase in circulatory visits by 19.2% (95% CI, 7.0% to 32.8%) per 1°C increase in temperature above 29°C in all people (**Table 6.10**). The increased risk of circulatory visits in adults (20.4%, 95%CI, 8.2% to 34.0%) was slightly higher than that in the elderly (17.5%, 95%CI, 3.2% to 33.9%). The increased risk found in males (22.7%, 95% CI, 9.8% to 37.1%) was higher compared to females (17.3%, 95% CI, 4.5% to 31.7%). When stratified by occupation, the risks were highest in unemployed & economically inactive people (23.2%, 95% CI, 8.9% to 39.3%), followed by manual workers (19.1%, 95% CI, -0.8% to 43.0%), and non-manual workers (10.9%, 95% CI, -2.3% to 25.8%), respectively.

Diabetic visits

There was an increase in diabetic visits by 26.3% (95% CI, 7.1% to 49.0%) per 1°C increase in temperature in all people when temperature >29°C (**Table 6.11**). The estimated risks of diabetic visits in adults (25.9%, 95% CI, 6.8% to 48.5%) were higher than those in the elderly (17.5%, 95% CI, -4.5% to 44.6%). The increased risks in males (28.6%, 95% CI, 7.7% to 53.6%) were slightly higher than females (23.3%, 95% CI, 3.0% to 47.7%). For occupation, the significant, positive effects of hot temperature were found in non-manual workers (32.5%, 95% CI, 8.7% to 61.6%) and in unemployed & economically inactive people (24.0%, 95% CI, 2.9% to 49.5%), whereas a non-significant, negative effect was found in manual workers (-2.2%, 95% CI, -22.9% to 34.4%).

Intestinal infectious visits

In general, for each 1°C increase in temperature (no threshold), there was an increase in intestinal infectious visits for all diseases, but the increased risks were not statistically significant at 5% level for all diseases (**Table 6.12**). There was a 2.6 % (95% CI, 0.4% to 4.8%) increase in the visits per 1°C increase in temperature in all people. The smallest, non-significant, increase of 0.2% (95% CI, -2.7% to 3.2%) was found in children, while the largest, significant increase of 7.7% (95% CI, 0.2% to 15.6%) was found in the elderly.

Other visits

Most estimated effects of temperature on 'other' visits were found to be statistically significant at 5% level, but the effects were relatively small in all people and all subgroups studied (**Table 6.13**). Overall, the risk estimates of 'other' visits of all groups of people were very similar, which ranged about 0.6% to 5.5% only. The lowest estimate, but not significant, was found in manual workers (0.6%, 95% CI, -3.4% to 4.8%), while the highest, significant estimate was found in children (5.5%, 95% CI, 1.2% to 10.1%).

Neoplasm visits

Neoplasms or cancers were not the main outcome of interest in this study at the first place. However, due to the significant effects of temperature on 'other' visits (and admissions), this raised a question about which particular sub-disease groups could be the contribution of the effects. In general, diagnoses in 'other' disease groups vary greatly and therefore

make it difficult to divide into subgroups. However, among several kinds of diseases in this category, it was found that the visits and admissions due to neoplasms (ICD-10: C00-D48) were relatively large count numbers compared to other diseases, which accounted for 6.1% for the visits and 28.4% for the admissions. Therefore, further investigations of both air pollution (results are shown later for hospital admissions only) and temperature effects on this group were undertaken.

There was a significant association between hot temperature and neoplasm visits in this study (though wide confidence intervals), as can be seen in **Table 6.14.** It was found that there was an increase in neoplasm visits by 28.3% (95% CI, 4.2% to 58.1%) among all people for each 1°C increase in temperature above 29°C. In addition, the positive, significant effect was shown in adults (29.8% increase, 95% CI, 4.1% to 61.9%), whereas the negative, but not significant effects was shown in the elderly (15.4% decrease, 95% CI, -37.4% to 14.4%).

6.2.3 Effect modification by age, sex, and occupation

According to the results shown in **Table 6.8-6.14**, there was generally no evidence of effect modification by subgroups (age, sex, and occupation) of people on the association between temperature and daily out-patient visits in this study. There were only some significant differences between subgroups obtained from the tests for heterogeneity.

6.2.4 Effect modification by season.

To investigate whether temperature effects on daily out-patient visits were modified by season, the general relationships between temperature and the visits in each season: winter (November-February), summer (March-May), and rainy (June-October) season, were plotted separately. The plots of the relationships between temperature and the visits in each season are shown in **Figure 6.13**. Overall, the somewhat linear relationships were seen in each season for most health outcomes. Thus, the quantification of temperature effects in different seasons was done by assuming that there was no temperature threshold. The risk estimates of temperature effects for each 1°C increase in temperature in each season are presented in **Table 6.15**.

As can be seen, there were positive effects of temperature in all seasons for most health outcomes, except only respiratory and circulatory visits. For each 1°C increase in temperature, there was an increase in respiratory visits in rainy season, but a decrease in winter and summer. For circulatory visits, the increase in the visits per 1°C increase in temperature was found in summer and rainy season, but not in winter. Overall, there were no significant differences between seasons, with only one exception, all-cause visits (p-value =0.019). It was found that the temperature effect on all-cause visits was much higher effects in summer (17.5% increase) than winter (2.1% increase) and rainy (3.0% increase) seasons.

6.3 Sensitivity analyses for out-patient visits series

To examine how using different approaches would have influenced the study results, two sensitivity tests were performed for out-patient visit series. Firstly, with regard to model distributional assumption, the effect estimates obtained by using negative binomial (NB) regression (used in this study) were compared with those obtained by using overdispersed Poisson (OP) regression (the conventional method commonly used in time series studies). Secondly, to assess the adequacy of seasonal control, the effect estimates from choosing different degrees of freedom for the splines of time in the models were explored. The sensitivity of the results was tested for all main health outcomes (all people only). For air pollution, the sensitivity of estimates was assessed for three pollutants: SO_2, O_3 and NO_2, since these pollutants mostly provided the notable associations with the health outcomes in this study.

6.3.1 Results of the sensitivity tests for model distribution assumption

Table 6.16 presents the risk estimates of the effects of the selected pollutants on daily out-patient visits obtained by using NB and OP models. Overall, the effects of air pollution estimated by both models are relatively similar with some occurrences of opposite directions of the estimates (one provided negative effects and another one provided positive effects).

Table 6.17 shows the risk estimates of out-patient visits in association with 1°C increase in temperature obtained by NB and OP models. As can be seen, the estimates derived from

both models are broadly similar in terms of the direction of the effects (positive or negative), with slightly higher estimates provided by NB model compared to OP model.

6.3.2 Results of the sensitivity tests for model seasonality

Varying degrees of freedom for time used for modelling was done to explore the impact of the changes on the estimated effects of air pollution and temperature.

Degree of freedom for time and air pollution effects

Sensitivity of the results on air pollution effects when using different degrees of freedom (df) were shown in **Figure 6.14 to 6.16**. As can be seen, there was no significant difference in the estimated effects of the selected air pollutants (SO_2, O_3, and NO_2) on daily out-patient visits when changing degrees of freedom of the time splines from 1df to 10 df per year.

Besides the estimated effects, model diagnostics was also examined in determining the impact of different degrees of freedom for the time splines on the study results. It was found that the more degrees of freedom, the more negative autocorrelations provided by the PACF plots, which can be seen in **Appendix 6A (Figure 6A-1 to 6A-3)**. When using 1 df/year for the splines of date, the negative autocorrelations in the PACF plots were the least compared to those when using higher degrees of freedom. In addition, the (1/df) deviance values obtained by using 1df were also lowest compared to those obtained by using higher degrees of freedom. However, the AIC values of the models with 1df were slightly higher than those with higher degrees of freedom.

Degree of freedom for time and temperature effects

The estimated risks of 1°C increase in temperature on daily out-patient visits with respect to different degrees of freedom of the time splines are illustrated in **Figure 6.17**. The estimated splines curves of the risks and their confidence intervals can be seen in **Appendix 6A (Figure 6A-4)**. It was found that there was an increase in temperature effects when using 5 df upward for most health outcomes. Although there was a slight increase with some fluctuations of the effects when using 5 df up, the overall effects were generally stable. This suggested that the model was found to be adequately controlled when using 5 df upward, whereas the model was uncontrolled when using 1-4 df of the spline for time.

Model diagnostics for temperature effects

The model diagnostics for temperature effects with regard to changing degrees of freedom were also examined (for all-cause visits only). This can be seen in **Appendix 6A (Figure 6A-5)**. Similar to the model diagnostics for air pollution effects, the PACF plots shows higher presence of negative autocorrelations when increasing degrees of freedom. The use of 1 df provided the least negative autocorrelations in comparison to the use of higher degrees of freedom. When looking at the (1/df) deviance values, the model with 1df also provided the lowest values compared to other models with higher degrees of freedom. However, the AIC values derived from the model with 1df were slightly higher than those derived from the models with higher degrees of freedom.

In brief, according to the above results, it was decided to continue using 1df for time for modelling air pollution effects since there were little changes of the estimated effects. However, when modelling temperature effects, because the model was stabilised when using 5 df up, the core model with the use of 6 df for time was chosen in the present study. At first, the use of 5df was used, but there were some problems with collenearity of variables when running the model with 5df for time in Stata (reported by Stata, and this made it unable to perform the estimations). Therefore, 6df was selected for the modelling temperature effects instead because it provided the lowest values of overdispersed parameters, which were very similar to using 5df (ϕ=1.12 for using 5df, and ϕ=1.13 for using 6df).

Estimation of fitted values over time with regard to the choice of seasonal adjustment

As described previously in the analytical method section in Chapter 3, dummy variables of month of the visits over the study period (i.movisit 1-48, 4-year data) were used to control for seasonality in this study with respect to different number of hospitals contributing to the data in each month. According to Schwartz et al 1996 [193], the use of dummy variables of the month of the study may cause an over specifying the model. Thus, in addition to examining the model diagnostics, scatter plots of the fitted values of all-cause visits over time (date) when modelling without adjusting for anything and with adjusting for only 'i.movisit' were also explored to see whether this dummy variables reasonably captured the changes of the outcome over the study period, which can be seen in **Appendix 6B (Figure**

6B-1 and 6B-2). As shown in the Figure, the use of month of the visits over the study period (1-48) was presented an adequate control for the changes of the health outcome over time.

Summary of out-patient visits series:

Air pollution effects

- There was little evidence of air pollution effects on daily out-patient visits in Chiang Mai in the present study. The effects were found to be larger for SO_2, followed by O_3, and NO_2 respectively, although imprecisely estimated.
- The use of lag 0-4 days for the investigation were sufficient to capture the short-term effects of air pollution since lag effects were predominantly found at lag 2-3 days.
- There was no evidence of effect modification of air pollution by age, sex, occupation, and season in the present study as there were generally no statistically significant differences between subgroups. However, the air pollution effects were seen to be stronger in the elderly and in manual workers for some pollutants for some diseases.
- By comparison, there was no significant difference in air pollution effects between those obtained by single pollutant models and those obtained by two-pollutant models.

Temperature effects

- There was some significant evidence of hot temperature effects on daily out-patient visits in the present study. The most significant effects of temperature were found for diabetic visits and circulatory visits (though wide confidence intervals). For each 1°C increase in temperature, there was an increase of 26.3% (95%CI, 7.1% to 49.0%) for diabetic visits and of 19.2% (95%CI, 7.0% to 32.8%) for circulatory visits.
- Because lag effects of temperature were mostly found at longer lag (0-13 days) and did not increase or decrease beyond lag 13 days, the use of temperature at a long lag (0-13 days) for the investigation was sufficient to capture temperature effects in this study.

- There was little consistent evidence of effect modification by age, sex, and occupation, although there were some noticeable differences between subgroups. For example, the effects of temperature on some disease groups, such as all-cause, circulatory, and diabetic visits, were found to be stronger in males than in females.
- The temperature effects were partly modified by season. Some differences in the magnitude and directions of the effects between seasons were shown, but most of them were not significant.

Sensitivity analyses

- There were no significant changes in the risk estimates of air pollution and temperature effects obtained by NB models in comparison to those obtained by OP models.
- There was no significant impact of changing degrees of freedom of the time splines on air pollution effects.
- When increasing degrees of freedom of the time splines for temperature models, the risk estimates increased considerably at 5df, but remained fairly stable after that.

Table 6. 1 Risk estimates for single pollutant, distributed lag models for the effects of a10-unit increase of a pollutant (one-unit increase for CO) on daily all-cause visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.931	0.841	1.029	0.162
	0-4 days	1.047	0.909	1.205	0.525
NO_2(ppb)	0-1 day	0.978	0.950	1.006	0.127
	0-4 days	0.988	0.953	1.024	0.512
CO-8hr(ppm)	0-1 day	0.956	0.912	1.002	0.060
	0-4 days	0.952	0.893	1.014	0.126
O_3(ppb)	0-1 day	1.004	0.980	1.030	0.733
	0-4 days	1.001	0.969	1.033	0.961
$PM_{10}(\mu g/m^3)$	0-1 day	0.997	0.990	1.003	0.296
	0-4 days	0.988	0.977	1.000	0.053
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.985	0.970	1.001	0.062
	0-4 days	0.985	0.970	1.001	0.062

*The estimates are the sum of all lags.

Table 6. 2 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily respiratory visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.982	0.874	1.104	0.763
	0-4 days	1.044	0.891	1.224	0.592
NO_2(ppb)	0-1 day	1.010	0.977	1.045	0.541
	0-4 days	1.007	0.966	1.049	0.749
CO-8hr(ppm)	0-1 day	0.994	0.941	1.051	0.835
	0-4 days	0.989	0.918	1.066	0.774
O_3(ppb)	0-1 day	0.969	0.942	0.998	0.036
	0-4 days	0.966	0.930	1.004	0.078
$PM_{10}(\mu g/m^3)$	0-1 day	0.998	0.992	1.004	0.457
	0-4 days	0.997	0.990	1.005	0.435
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.986	0.973	1.000	0.042
	0-4 days	0.976	0.959	0.993	0.006

*The estimates are the sum of all lags.

Table 6. 3 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily circulatory visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	1.112	0.940	1.315	0.216
	0-4 days	1.222	0.972	1.536	0.086
NO_2(ppb)	0-1 day	0.984	0.939	1.032	0.513
	0-4 days	0.995	0.938	1.055	0.868
CO-8hr(ppm)	0-1 day	0.949	0.878	1.026	0.189
	0-4 days	0.978	0.882	1.084	0.671
O_3(ppb)	0-1 day	0.981	0.941	1.022	0.364
	0-4 days	1.017	0.964	1.073	0.538
$PM_{10}(\mu g/m^3)$	0-1 day	0.994	0.986	1.003	0.178
	0-4 days	0.998	0.988	1.008	0.689
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.976	0.955	0.997	0.028
	0-4 days	0.980	0.953	1.006	0.134

*The estimates are the sum of all lags.

Table 6. 4 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily diabetic visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	1.053	0.808	1.372	0.702
	0-4 days	1.255	0.879	1.792	0.211
NO_2(ppb)	0-1 day	1.004	0.932	1.082	0.910
	0-4 days	0.990	0.903	1.086	0.832
CO-8hr(ppm)	0-1 day	1.003	0.888	1.133	0.960
	0-4 days	0.944	0.803	1.111	0.488
O_3(ppb)	0-1 day	0.980	0.919	1.047	0.554
	0-4 days	0.985	0.906	1.071	0.726
$PM_{10}(\mu g/m^3)$	0-1 day	0.996	0.983	1.009	0.530
	0-4 days	0.993	0.977	1.009	0.380
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.981	0.950	1.013	0.240
	0-4 days	0.968	0.930	1.008	0.111

*The estimates are the sum of all lags.

Table 6. 5 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily intestinal infectious visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.830	0.637	1.082	0.168
	0-4 days	0.876	0.616	1.247	0.462
NO_2(ppb)	0-1 day	0.975	0.910	1.044	0.469
	0-4 days	0.996	0.913	1.086	0.928
CO-8hr(ppm)	0-1 day	0.932	0.831	1.046	0.232
	0-4 days	0.876	0.751	1.023	0.094
O_3(ppb)	0-1 day	0.968	0.911	1.028	0.288
	0-4 days	0.963	0.891	1.041	0.342
$PM_{10}(\mu g/m^3)$	0-1 day	0.987	0.976	0.999	0.033
	0-4 days	0.985	0.970	1.000	0.047
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.962	0.932	0.993	0.018
	0-4 days	0.981	0.942	1.021	0.337

*The estimates are the sum of all lags.

Table 6. 6 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase in air pollutants (one-unit increase for CO) on daily other visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.917	0.828	1.016	0.098
	0-4 days	1.013	0.880	1.166	0.860
NO_2(ppb)	0-1 day	0.979	0.951	1.008	0.150
	0-4 days	0.978	0.943	1.014	0.226
CO-8hr(ppm)	0-1 day	0.951	0.907	0.996	0.034
	0-4 days	0.935	0.877	0.997	0.040
O_3(ppb)	0-1 day	1.011	0.986	1.036	0.392
	0-4 days	1.025	0.993	1.058	0.131
$PM_{10}(\mu g/m^3)$	0-1 day	0.998	0.994	1.003	0.547
	0-4 days	0.997	0.991	1.004	0.399
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.989	0.977	1.001	0.068
	0-4 days	0.981	0.965	0.997	0.017

*The estimates are the sum of all lags.

Table 6. 7 Risk estimates for single pollutant and two-pollutant models for a 10-unit increase of a pollutant (average lag 0-4 days) on daily out-patient visits in all ages and in the elderly (≥ 65 year) in Muang, Chiang Mai, from October 2002 to September 2006.

Outcome		Single pollutant RR (95%CI)	SO_2 & O_3 RR(95%CI)	SO_2 & NO_2 RR(95%CI)	O_3 & NO_2 RR(95%CI)
All-cause					
all ages	SO_2	1.053 (0.918-1.208)	1.050 (0.915-1.205)	1.070 (0.930-1.231)	
	O_3	1.015 (0.983-1.047)	1.014 (0.982-1.047)		1.018 (0.986-1.051)
	NO_2	0.985 (0.951-1.020)		0.981 (0.947-1.017)	0.981 (0.947-1.016)
≥65 year	SO_2	1.122 (0.967-1.303)	1.120 (0.964-1.300)	1.125 (0.966-1.311)	
	O_3	1.013 (0.978-1.049)	1.011 (0.976-1.048)		1.013 (0.977-1.050)
	NO_2	1.003 (0.965-1.042)		0.997 (0.958-1.037)	1.000 (0.962-1.040)
Respiratory					
all ages	SO_2	1.054 (0.907-1.224)	1.060 (0.913-1.232)	1.052 (0.903-1.226)	
	O_3	0.973 (0.939-1.009)	0.973 (0.938-1.009)		0.972 (0.936-1.008)
	NO_2	1.008 (0.976-1.041)		1.002 (0.963-1.042)	1.010 (0.971-1.051)
≥65 year	SO_2	1.157 (0.871-1.537)	1.148 (0.864-1.526)	1.116 (0.836-1.491)	
	O_3	1.034 (0.963-1.111)	1.032 (0.961-1.109)		1.024 (0.952-1.103)
	NO_2	1.054 (0.978-1.135)		1.048 (0.971-1.130)	1.048 (0.971-1.131)
Circulatory					
all ages	SO_2	1.147 (0.922-1.428)	1.139 (0.914-1.418)	1.034 (0.981-1.090)	
	O_3	1.036 (0.983-1.092)	1.034 (0.981-1.090)		1.040 (0.986-1.098)
	NO_2	0.986 (0.931-1.043)		0.977 (0.921-1.035)	0.977 (0.922-1.036)
≥65 year	SO_2	1.174 (0.908-1.519)	1.169 (0.904-1.512)	1.195 (0.918-1.556)	
	O_3	1.024 (0.962-1.091)	1.022 (0.960-1.089)		1.027 (0.964-1.095)
	NO_2	0.990 (0.926-1.059)		0.980 (0.915-1.050)	0.985 (0.920-1.054)
Diabetic					
all ages	SO_2	1.379 (0.983-1.933)	1.385 (0.988-1.942)	1.364 (0.966-1.926)	
	O_3	0.975 (0.899-1.058)	0.972 (0.896-1.054)		0.969 (0.892-1.052)
	NO_2	1.030 (0.945-1.124)		1.014 (0.928-1.108)	1.038 (0.950-1.134)
≥65	SO_2	1.114 (0.727-1.707)	1.135 (0.741-1.738)	1.105 (0.715-1.709)	
	O_3	0.900 (0.811-0.998)	0.899 (0.810-0.997)		0.893 (0.804-0.993)
	NO_2	1.015 (0.909-1.134)		1.010 (0.902-1.131)	1.040 (0.929-1.164)
Intestinal infectious*					
all ages	SO_2	0.988 (0.719-1.357)	0.989 (0.720-1.359)	0.988 (0.715-1.367)	
	O_3	0.982 (0.914-1.056)	0.982 (0.914-1.056)		0.982 (0.912-1.057)
	NO_2	0.999 (0.923-1.081)		1.000 (0.922-1.084)	1.003 (0.925-1.087)
Other					
all ages	SO_2	1.029 (0.900-1.178)	1.024 (0.895-1.172)	1.054 (0.919-1.210)	1.027 (0.995-1.060)
	O_3	1.021 (0.990-1.054)	1.021 (0.989-1.053)		0.968 (0.935-1.003)
	NO_2	0.974 (0.941-1.008)		0.971 (0.938-1.006)	
≥65	SO_2	1.073 (0.934-1.232)	1.070 (0.932-1.230)	1.076 (0.934-1.240)	1.012 (0.978-1.047)
	O_3	1.011 (0.978-1.046)	1.010 (0.977-1.045)		0.998 (0.962-1.035)
	NO_2	1.000 (0.965-1.037)		0.997 (0.960-1.034)	

*There were insufficient intestinal infectious visits among the elderly (≥65 year) for the analysis.

Table 6. 8 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily all-cause visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	943.20	845.58	1.094	1.028	1.165	0.005	N/A
Age							
0-14 years	114.23	83.88	1.066	0.975	1.165	0.158	
15- 64 years	636.41	605.70	1.098	1.027	1.173	0.006	
≥ 65 years	186.34	154.77	1.108	1.030	1.193	0.006	0.798
Sex							
Male	397.95	329.88	1.116	1.047	1.190	0.001	
Female	543.29	515.64	1.063	0.994	1.137	0.074	0.304
Occupation							
Unemployed & economically inactive	193.70	159.69	1.119	1.041	1.203	0.002	
Non-manual workers	189.46	123.49	1.083	1.005	1.166	0.036	
Manual workers	50.73	56.27	1.073	0.964	1.194	0.198	0.753

[a] Mean daily count of all-cause visits when T > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.

Table 6. 9 Relative risk estimates distributed lag models (0-1 day) for temperature effects (linear) on daily respiratory visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	95.32	53.40	0.991	0.981	1.000	0.053	N/A
Age							
0-14 years	38.28	20.58	0.993	0.980	1.006	0.295	
15- 64 years	46.83	28.65	0.990	0.979	1.001	0.070	
≥ 65 years	9.67	6.92	0.998	0.978	1.018	0.810	0.782
Sex							
Male	44.40	24.40	1.005	0.994	1.017	0.344	
Female	50.45	29.86	0.980	0.969	0.991	0.000	0.002
Occupation							
Unemployed & economically inactive	18.02	10.74	0.985	0.970	0.999	0.042	
Non-manual workers	23.02	15.30	0.991	0.976	1.006	0.216	
Manual workers	3.55	3.30	1.015	0.983	1.048	0.370	0.249

[a] Mean daily count of respiratory visits when there was no temperature threshold (n = 1387 days).
[b] p-value of the test for heterogeneity between groups.

Table 6. 10 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily circulatory visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI		p-value	p-value [b]
				Lower	Upper		
All people	77.19	60.91	1.192	1.070	1.328	0.001	N/A
Age [c]							
0-14 years	0.75	1.37	-	-	-	-	
15- 64 years	46.96	37.72	1.204	1.082	1.340	0.001	
≥ 65 years	29.28	23.58	1.175	1.032	1.339	0.015	0.777
Sex							
Male	32.20	25.15	1.227	1.098	1.371	0.000	
Female	44.91	36.44	1.173	1.045	1.317	0.007	0.582
Occupation							
Unemployed & economically inactive	20.21	17.37	1.245	1.084	1.429	0.002	
Non-manual workers	20.36	15.86	1.124	0.989	1.277	0.074	
Manual workers	5.00	5.98	1.187	0.971	1.450	0.094	0.564

[a] Mean daily count of circulatory visits when T >29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.
[c] There were limited daily counts of circulatory visits among age 0-14 years for the analysis.

Table 6. 11 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily diabetic visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI		p-value	p-value [b]
				Lower	Upper		
All people	29.16	23.44	1.263	1.071	1.490	0.006	N/A
Age [c]							
0-14 years	0.27	0.70	-	-	-	-	
15- 64 years	19.71	16.16	1.259	1.068	1.485	0.006	
≥ 65 years	9.07	7.82	1.175	0.955	1.446	0.128	0.609
Sex							
Male	12.02	9.38	1.286	1.077	1.536	0.006	
Female	17.13	14.79	1.233	1.030	1.477	0.023	0.744
Occupation							
Unemployed & economically inactive	9.49	8.36	1.197	0.983	1.458	0.074	
Non-manual workers	8.27	7.24	1.374	1.120	1.685	0.002	
Manual workers	1.65	2.03	0.901	0.647	1.255	0.539	0.104

[a] Mean daily count of diabetic visits when T >29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.
[c] There were limited daily counts of diabetic visits among age 0-14 years for the analysis.

Table 6. 12 Relative risk estimates for distributed lag models (0-1 day) for temperature effects (linear) on daily intestinal infectious visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	9.21	5.56	1.026	1.004	1.048	0.018	N/A
Age							
0-14 years	3.89	2.74	1.002	0.973	1.032	0.895	
15- 64 years	4.50	3.28	1.038	1.008	1.069	0.013	
≥ 65 years	0.77	0.99	1.077	1.002	1.156	0.043	0.090
Sex							
Male	4.25	2.97	1.042	1.011	1.074	0.008	
Female	4.91	3.42	1.009	0.982	1.038	0.508	0.124
Occupation [c]							
Unemployed & economically inactive	1.96	1.74	1.016	0.973	1.061	0.462	
Non-manual workers	2.06	1.89	1.023	0.979	1.070	0.310	0.833
Manual workers	0.31	0.62	-	-	-	-	

[a] Mean daily count of intestinal infectious visits when there was no temperature threshold (n = 1387 days).
[b] p-value of the test for heterogeneity between groups.
[c] There was too limited counts of intestinal infectious visits to analyze for manual workers.

Table 6. 13 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (linear) on daily other visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	422.44	252.86	1.037	1.015	1.059	0.001	N/A
Age							
0-14 years	49.53	31.80	1.055	1.012	1.101	0.012	
15- 64 years	286.86	184.75	1.046	1.022	1.070	0.000	
≥ 65 years	84.39	43.37	1.007	0.986	1.030	0.502	0.029
Sex							
Male	181.58	104.49	1.046	1.022	1.070	0.000	
Female	237.73	150.65	1.028	1.006	1.052	0.015	0.288
Occupation							
Unemployed & economically inactive	114.74	79.47	1.034	1.008	1.060	0.010	
Non-manual workers	127.35	78.99	1.051	1.022	1.080	0.000	
Manual workers	28.73	28.53	1.006	0.966	1.048	0.765	0.222

[a] Mean daily count of other visits when there is no temperature threshold (n = 1387 days).
[b] p-value of the test for heterogeneity between groups.

Table 6. 14 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily neoplasm visits in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI		p-value	p-value [b]
				Lower	Upper		
All people	15.13	30.59	1.283	1.042	1.581	0.019	N/A
Age							
0-14 years [c]	0.57	1.07	-	-	-	-	
15- 64 years	11.54	24.00	1.298	1.041	1.619	0.021	
≥ 65 years	2.98	6.12	0.846	0.626	1.144	0.278	0.025
Sex							
Male	4.49	8.94	1.223	0.940	1.590	0.134	
Female	10.63	21.96	1.143	0.918	1.424	0.232	0.699
Occupation							
Unemployed & economically inactive	6.635	15.301	1.218	0.933	1.591	0.147	
Non-manual	1.211	1.510	1.169	0.807	1.695	0.409	
Manual workers	2.835	7.280	0.951	0.665	1.361	0.784	0.542

[a] Mean daily count of all-cause admissions when T > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.
[c] There were limited count of neoplasm visits in children for the analysis.

Table 6. 15 Risk estimates of daily out-patient visits per one degree Celsius increase in temperature in different seasons in Maung, Chiang Mai, from October 2002 to September 2006.

Outcome [c]	Season [a]	Mean	SD	RR	95%CI		p-value	p-value [b]
					Lower	Upper		
All-cause	Winter	989.74	600.47	1.021	0.978	1.065	0.349	
	Summer	1025.04	841.30	1.175	1.076	1.284	0.000	
	Rainy	890.67	624.05	1.030	0.924	1.148	0.592	0.019
Respiratory	Winter	122.17	59.86	0.992	0.977	1.008	0.318	
	Summer	78.40	43.81	0.992	0.970	1.014	0.463	
	Rainy	84.38	44.56	1.016	0.986	1.046	0.305	0.346
Circulatory	Winter	94.717	67.158	0.996	0.923	1.075	0.918	
	Summer	84.196	62.572	1.023	0.883	1.186	0.761	
	Rainy	74.565	53.404	1.019	0.854	1.217	0.832	0.936
Diabetic	Winter	33.01	24.08	1.045	0.912	1.198	0.523	
	Summer	32.43	25.67	1.171	0.942	1.455	0.155	
	Rainy	28.15	21.88	1.061	0.808	1.393	0.669	0.681
Intestinal infectious	Winter	10.01	5.74	1.036	0.998	1.075	0.061	
	Summer	9.69	5.24	1.028	0.978	1.079	0.280	
	Rainy	8.19	5.39	1.045	0.975	1.120	0.217	0.928
Other	Winter	478.43	271.95	1.090	1.036	1.146	0.001	
	Summer	414.55	242.87	1.074	1.000	1.153	0.049	
	Rainy	383.18	234.96	1.035	0.931	1.149	0.527	0.680

[a] A linear relationship was assumed for all seasons, winter: n = 481 days, summer: n = 368 days, and rainy: n = 612 days.

[b] p-value for test for heterogeneity between seasons.

[c] Quantifying temperature effects at a long lag (0-13 days) for all diseases, except respiratory and intestinal infectious admissions, which was done for the effects at a short lag (0-1 day).

Table 6. 16 Risk estimates of daily out-patient visits in distributed lag models (0-4 days) for a 10-unit increase of a pollutant between using negative binomial regression (NB) and using overdispersed Poisson regression (OP).

		Negative binomial regression			Overdispersed Poisson regression		
			95%CI			95%CI	
Pollutant	Outcome	RR	Lower	Upper	RR	Lower	Upper
SO_2							
	All-cause	1.047	0.909	1.205	0.995	0.881	1.125
	Respiratory	1.044	0.891	1.224	1.029	0.882	1.201
	Circulatory	1.222	0.972	1.536	1.155	0.939	1.42
	Diabetic	1.255	0.879	1.792	1.307	0.938	1.822
	Intestinal infectious	0.876	0.616	1.247	0.870	0.603	1.254
	Other	1.013	0.880	1.166	1.009	0.889	1.146
O_3							
	All-cause	1.001	0.969	1.033	0.985	0.957	1.014
	Respiratory	0.966	0.93	1.004	0.965	0.929	1.002
	Circulatory	1.017	0.964	1.073	1.015	0.967	1.066
	Diabetic	0.985	0.906	1.071	0.983	0.908	1.063
	Intestinal infectious	0.963	0.891	1.041	0.964	0.891	1.044
	Other	1.025	0.993	1.058	1.004	0.974	1.035
NO_2							
	All-cause	0.988	0.953	1.024	0.977	0.947	1.008
	Respiratory	1.007	0.966	1.049	1.005	0.966	1.046
	Circulatory	0.995	0.938	1.055	1.016	0.965	1.069
	Diabetic	0.99	0.903	1.086	1.019	0.935	1.11
	Intestinal infectious	0.996	0.913	1.086	0.993	0.908	1.085
	Other	0.978	0.943	1.014	0.970	0.939	1.002

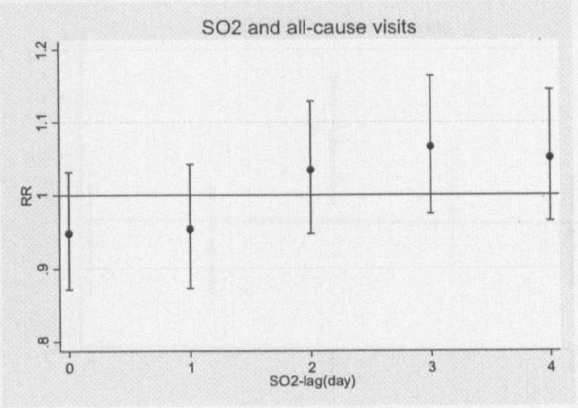
Table 6. 17 Risk estimates of daily out-patient visits per one degree Celsius increase in temperature (lag 0-13 days) between using negative binomial regression (NB) and using Overdispersed Poisson regression (OP).

	Negative binomial regression						Overdispersed Poisson regression					
				95%CI						95%CI		
Outcome (temperature terms)	Coef.	SE	RR	Lower	Upper	p-value	Coef.	SE	RR	Lower	Upper	p-value
All-cause (>29°C)	0.090	0.032	1.094	1.028	1.165	0.005	0.052	0.032	1.053	0.989	1.121	0.108
Respiratory* (linear)	-0.009	0.005	0.991	0.981	1.000	0.053	-0.007	0.005	0.993	0.984	1.002	0.147
Circulatory (>29°C)	0.175	0.055	1.192	1.070	1.328	0.001	0.160	0.053	1.173	1.059	1.301	0.002
Diabetic (>29°C)	0.234	0.084	1.263	1.071	1.490	0.006	0.195	0.082	1.215	1.035	1.426	0.017
Intestinal infectious* (linear)	0.025	0.011	1.026	1.004	1.048	0.018	0.026	0.011	1.026	1.004	1.049	0.021
Other (linear)	0.036	0.011	1.037	1.015	1.059	0.001	0.036	0.010	1.036	1.016	1.057	0.001

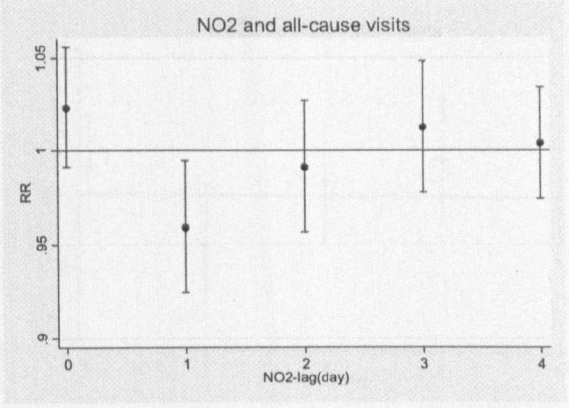
*Temperature effects at short lag (0-1day) were examined for these two diseases.

Figure 6. 1 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily all-cause visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

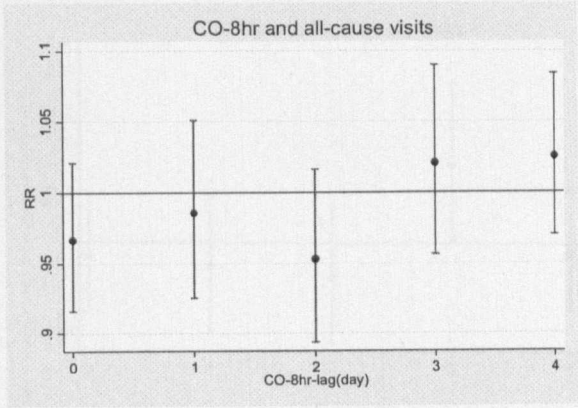
6.1a) SO_2



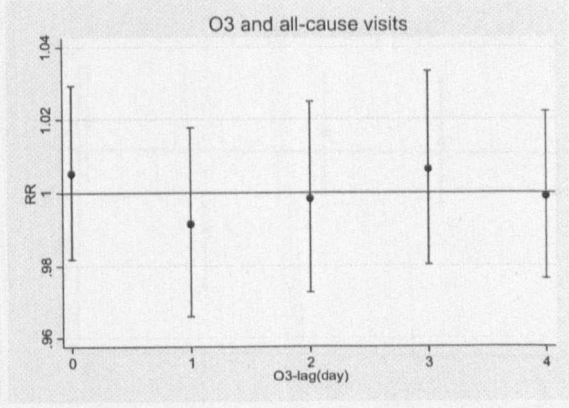
6.1b) NO_2



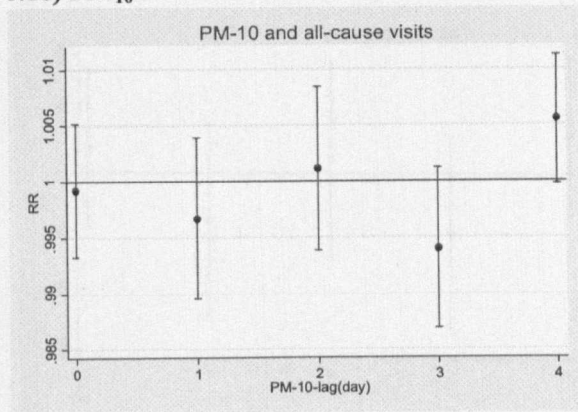
6.1c) CO



6.1d) O_3



6.1e) PM_{10}



6.1f) $PM_{2.5}$

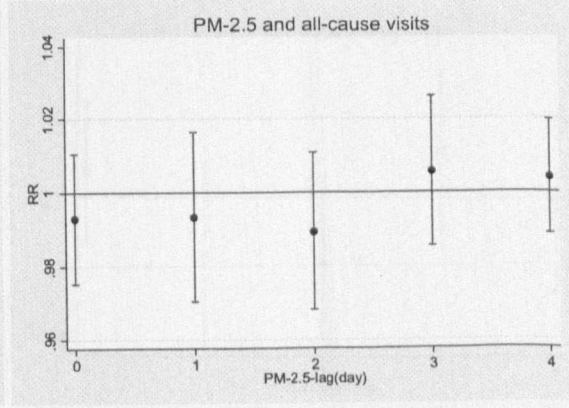
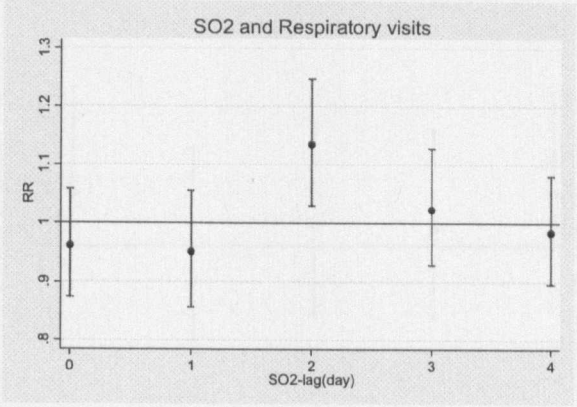
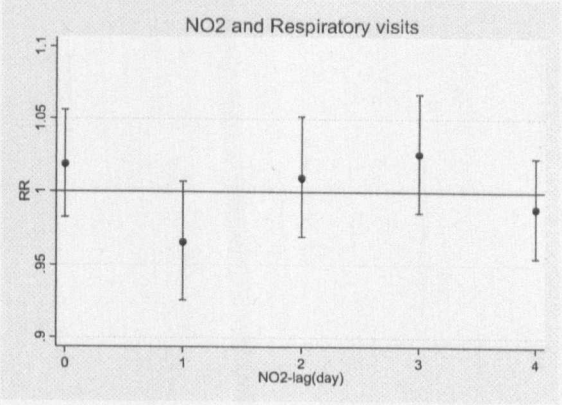


Figure 6. 2 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily respiratory visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

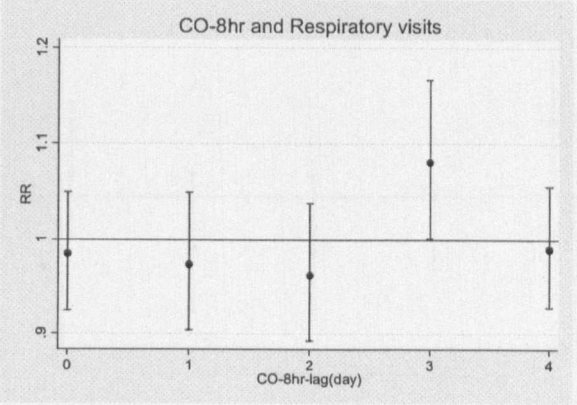
6.2a) SO_2



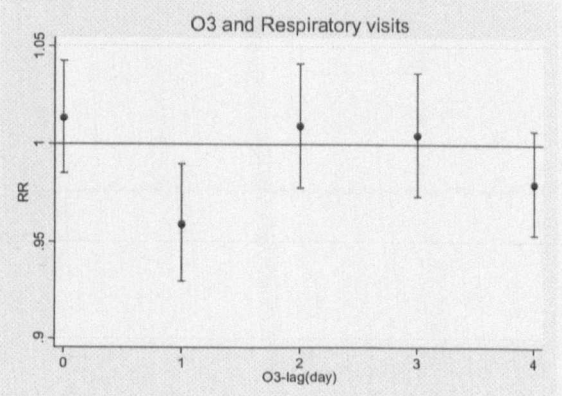
6.2b) NO_2



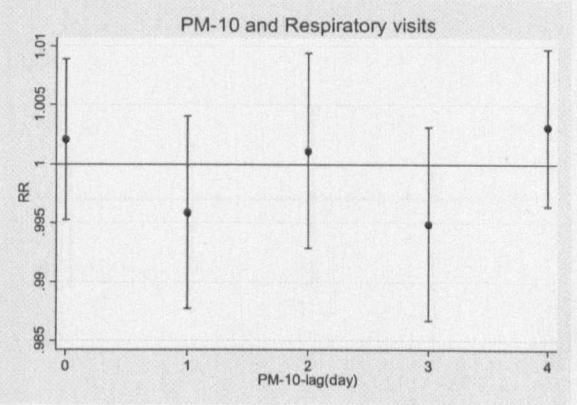
6.2c) CO



6.2d) O_3



6.2e) PM_{10}



6.2f) $PM_{2.5}$

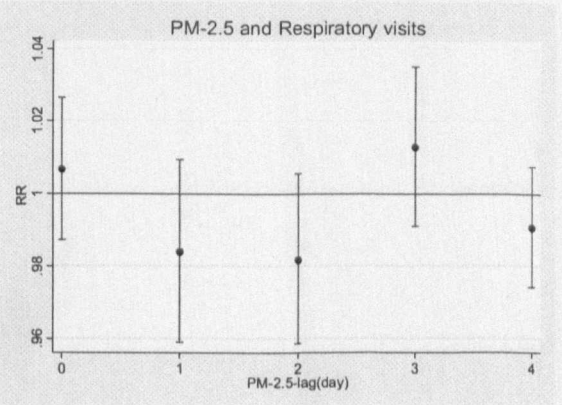
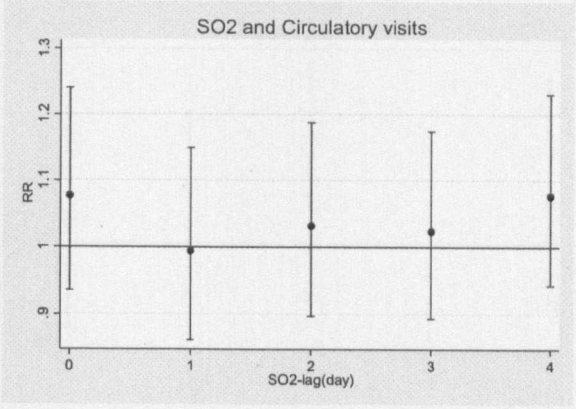
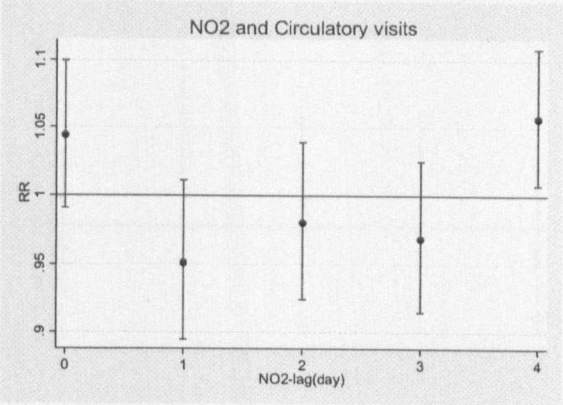


Figure 6. 3 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily circulatory visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

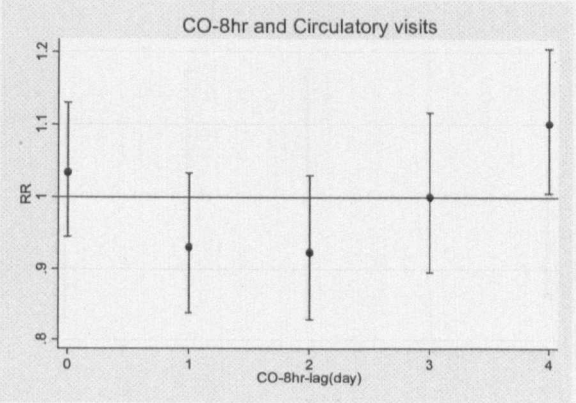
6.3a) SO_2



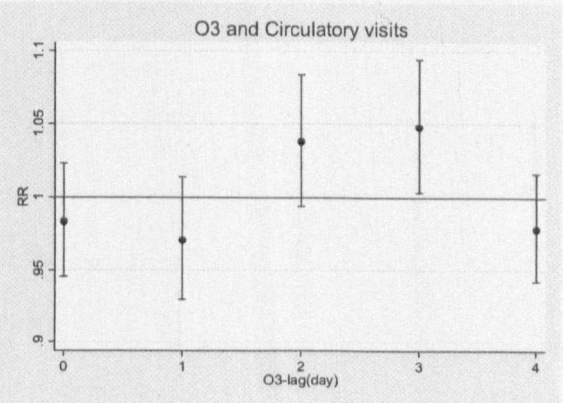
6.3b) NO_2



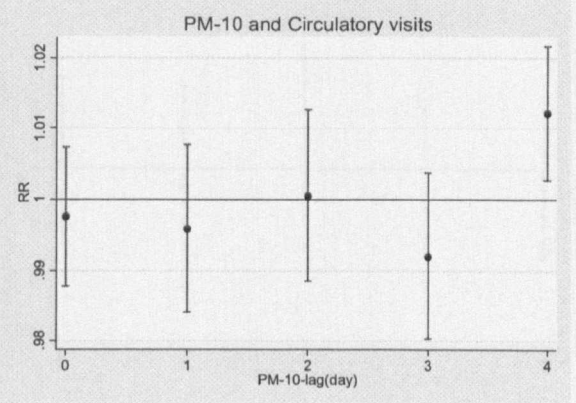
6.3c) CO



6.3d) O_3



6.3e) PM_{10}



6.3f) $PM_{2.5}$

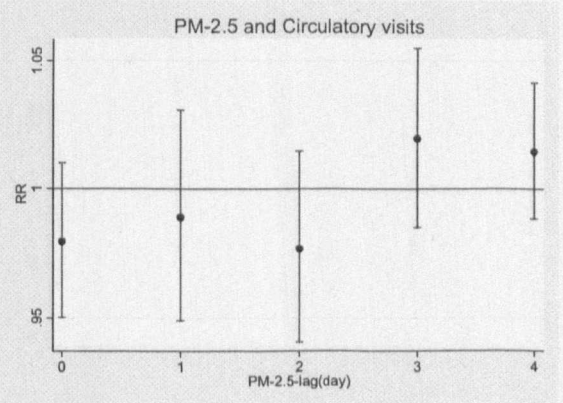
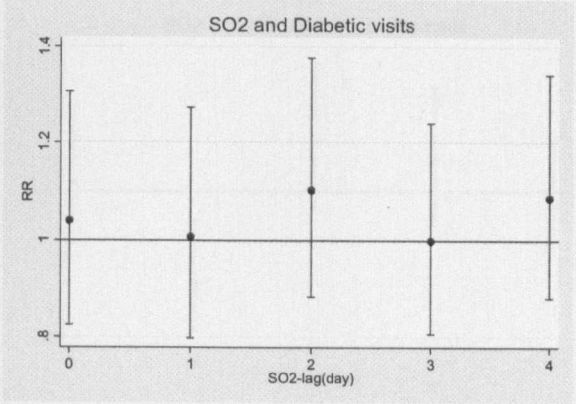
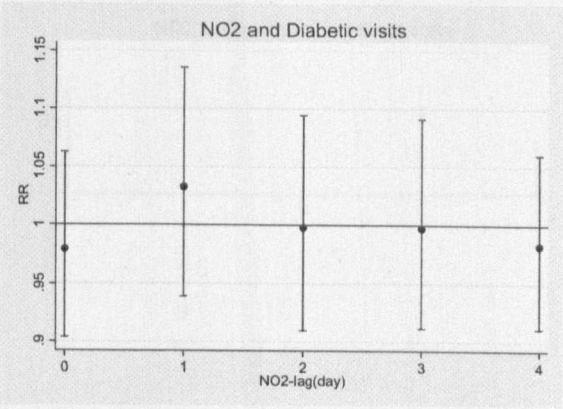


Figure 6. 4 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily diabetic visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

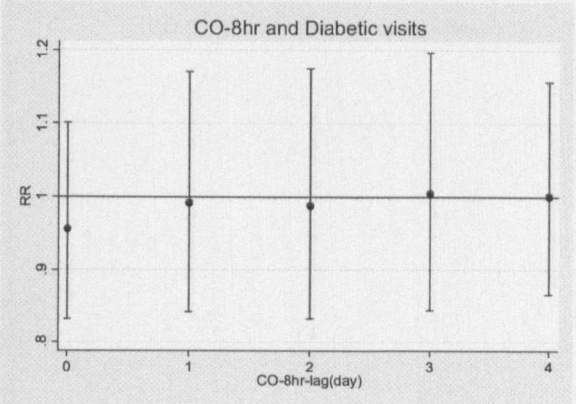
6.4a) SO_2



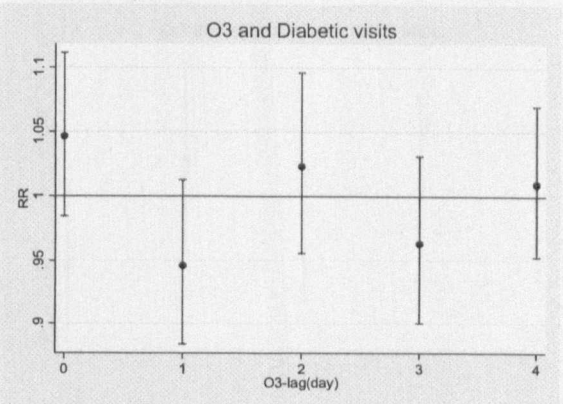
6.4b) NO_2



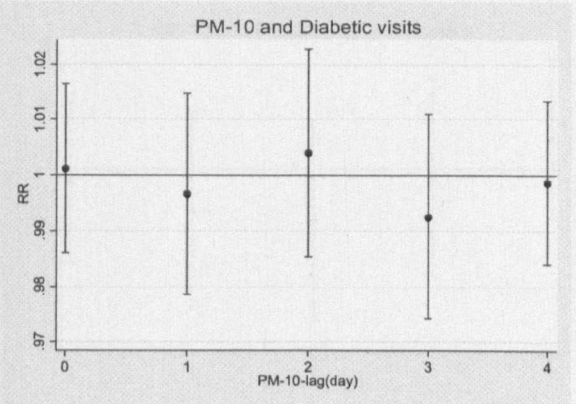
6.4c) CO



6.4d) O_3



6.4e) PM_{10}



6.4f) $PM_{2.5}$

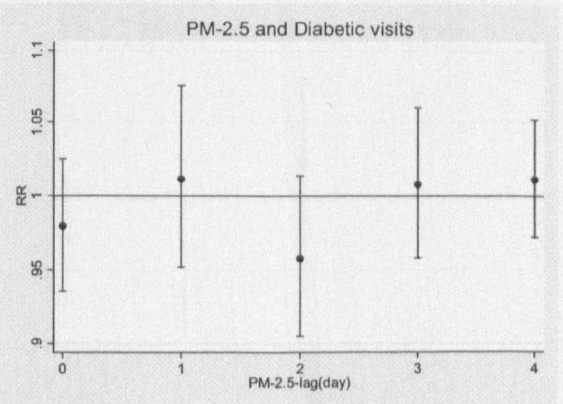
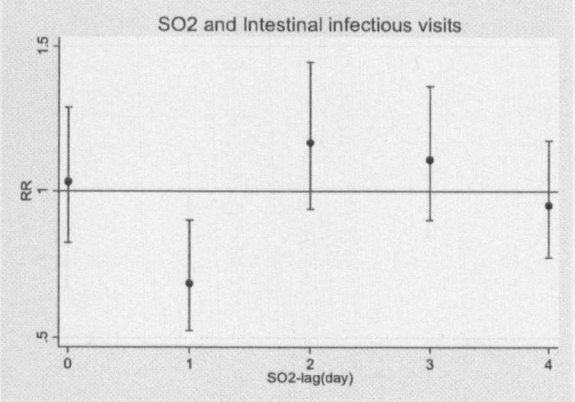
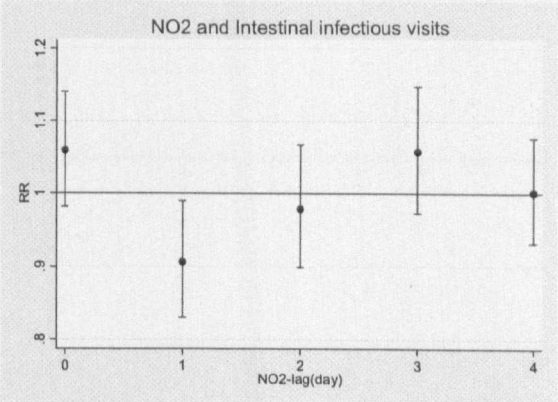


Figure 6. 5 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily intestinal infectious visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

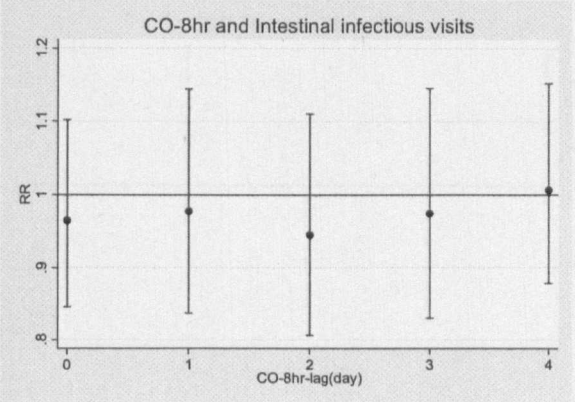
6.5a) SO_2



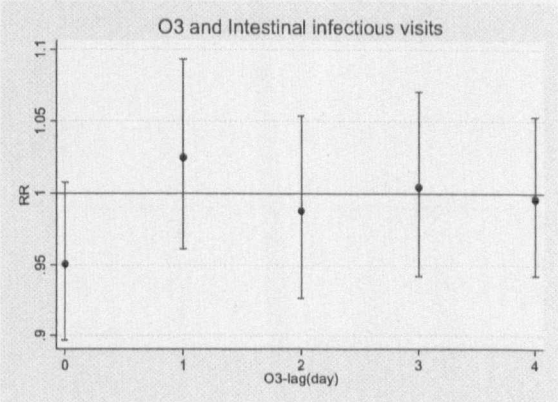
6.5b) NO_2



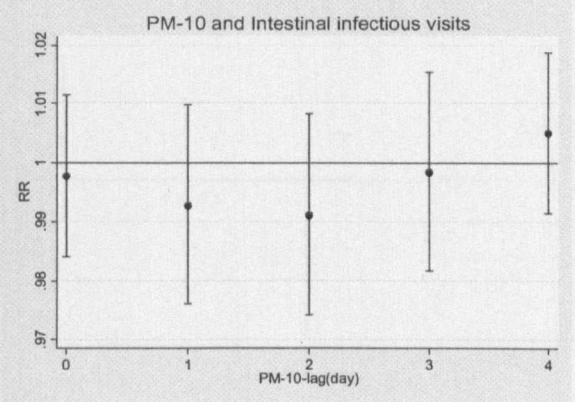
6.5c) CO



6.5d) O_3



6.5e) PM_{10}



6.5f) $PM_{2.5}$

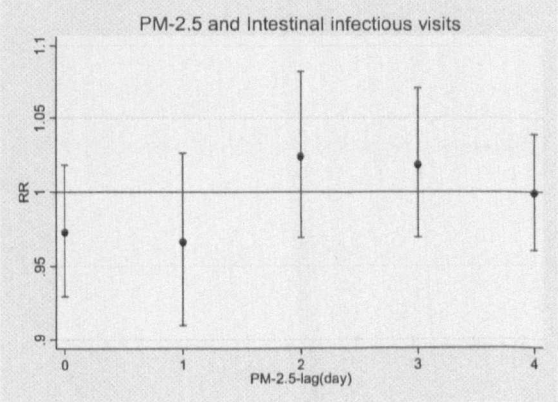
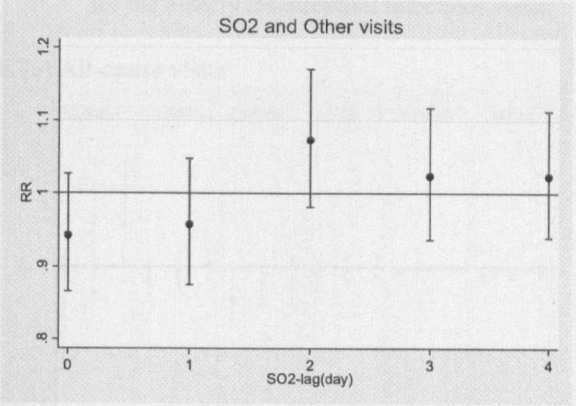
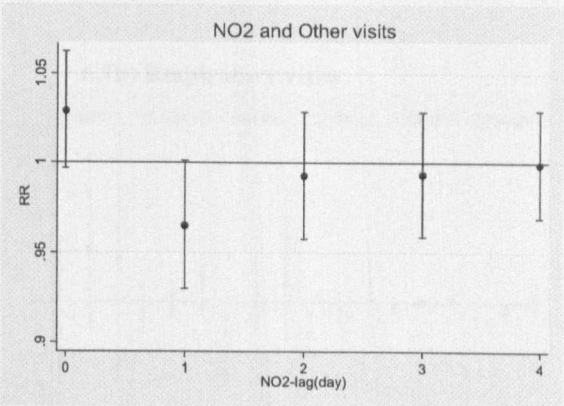


Figure 6. 6 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily other visits among all people in Muang, Chiang Mai, from October 2002 to September 2006.

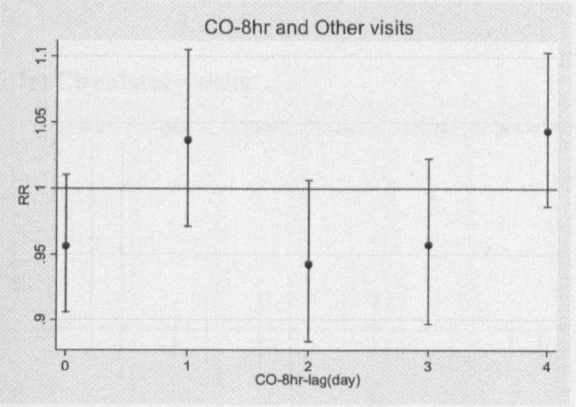
6.6a) SO_2



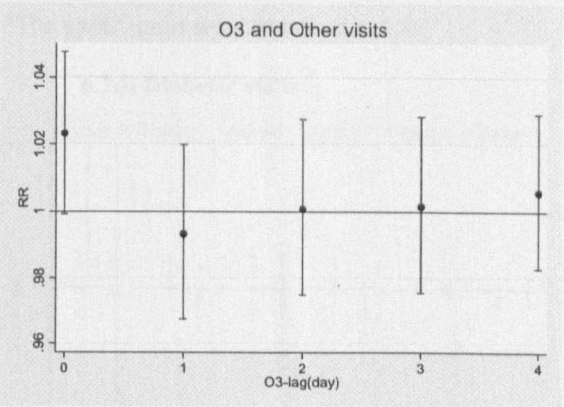
6.6b) NO_2



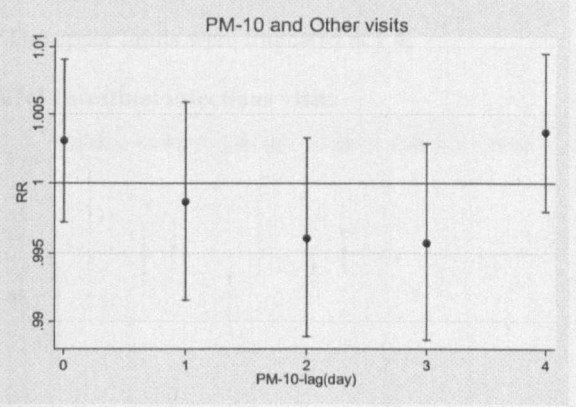
6.6c) CO



6.6d) O_3



6.6e) PM_{10}



6.6f) $PM_{2.5}$

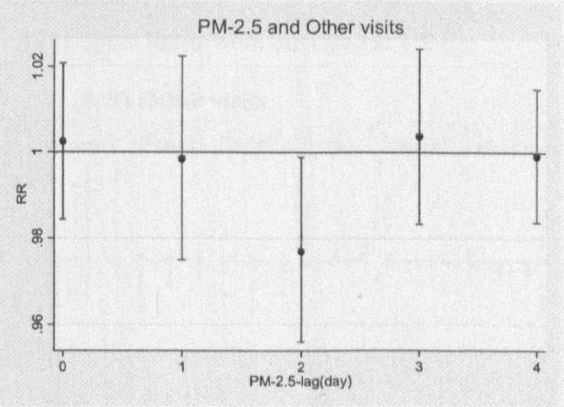
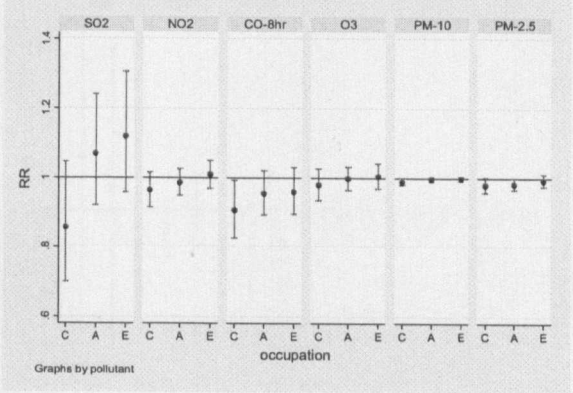


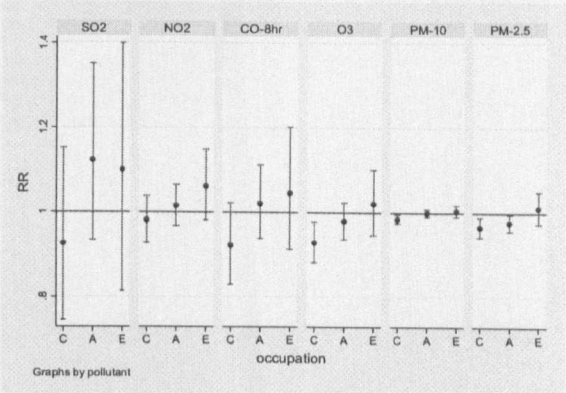
Figure 6. 7 Risk estimates for single pollutant, distributed lag models (0-4 days) for a10-unit increase of a pollutant (one unit increase for CO) on daily out-patient visits in different age groups in Muang, Chiang Mai, from October 2002 to September 2006.

Note: 1. **C** = Children (0-14 years), **A** = Adult (15-64 years), **E** = Elderly (≥ 65years).
2. There were limited counts to analyze for children for circulatory and diabetic visits, and for the elderly for intestinal infectious visits.

6.7a) All-cause visits

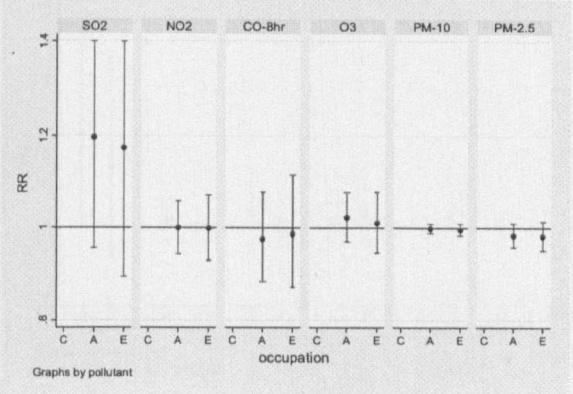


6.7b) Respiratory visits



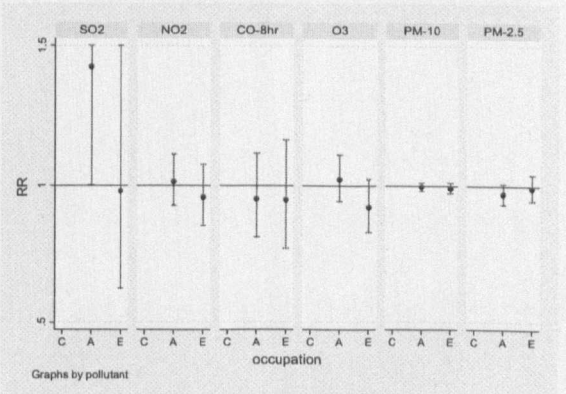
*The upper limits were truncated at 1.4.

6.7c) Circulatory visits



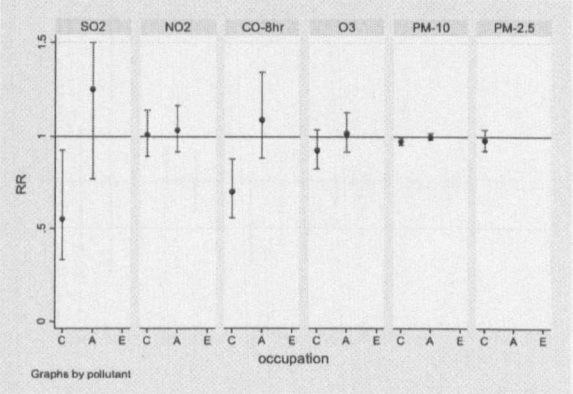
*The upper limits were truncated at 1.4.

6.7d) Diabetic visits



*The upper limits were truncated at 1.5.

6.7e) Intestinal infectious visits



*The upper limits were truncated at 1.5, limited counts to analyze for $PM_{2.5}$ effects in adults and the elderly.

6.7f) Other visits

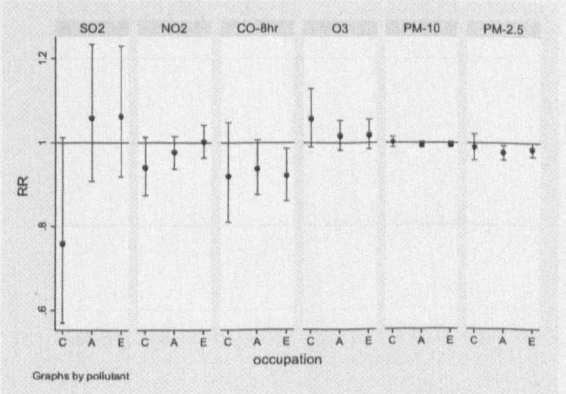
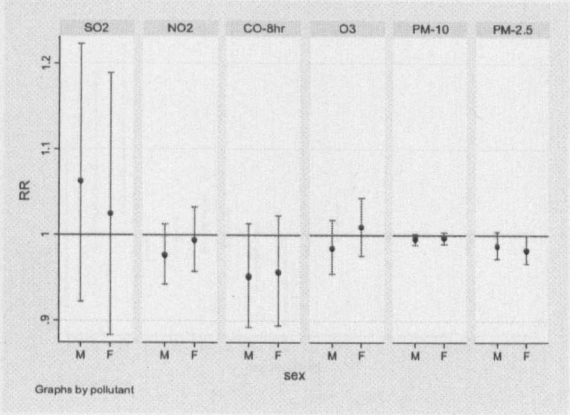


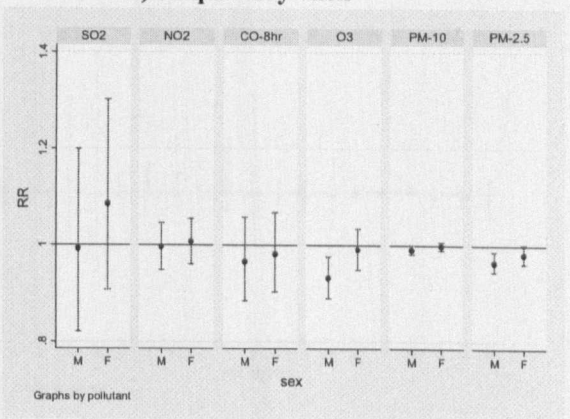
Figure 6. 8 Risk estimates for single pollutant, distributed lag models (0-4 days) for a10-unit increase of a pollutant (one unit increase for CO) on daily out-patient visits in males and females in Muang, Chiang Mai, from October 2002 to September 2006.

Note: M = Male, **F** = Female.

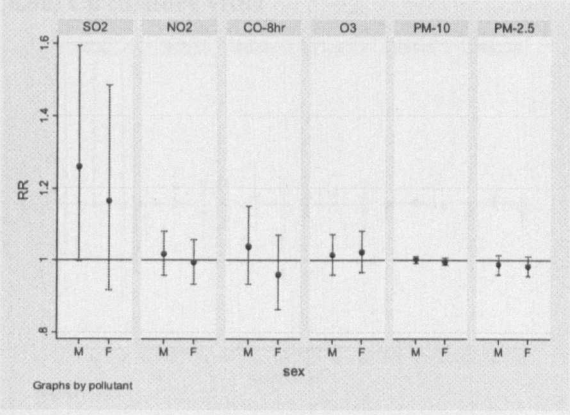
6.8a) All-cause visits



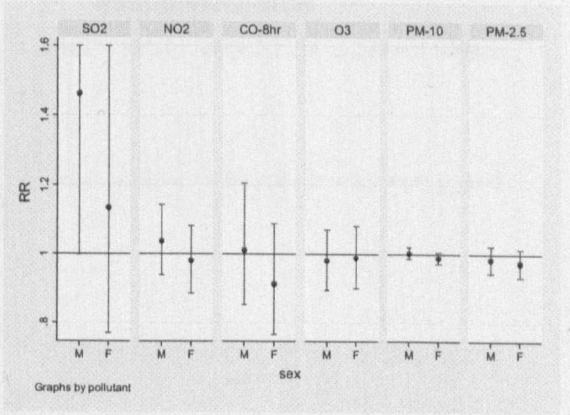
6.8b) Respiratory visits



6.8c) Circulatory visits

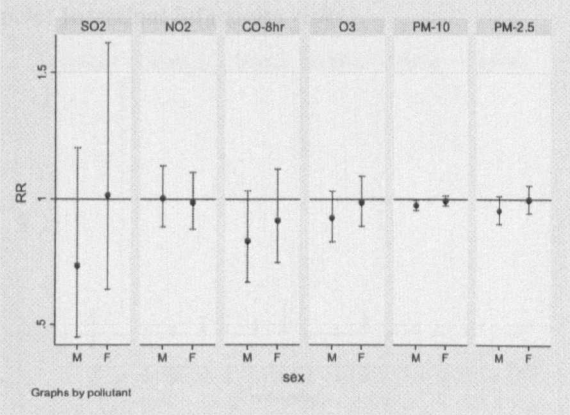


6.8d) Diabetic visits



*The upper limits were truncated at 1.6.

6.8e) Intestinal infectious visits



6.8f) Other visits

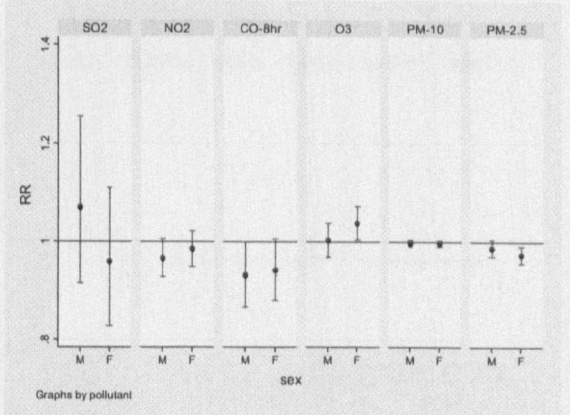
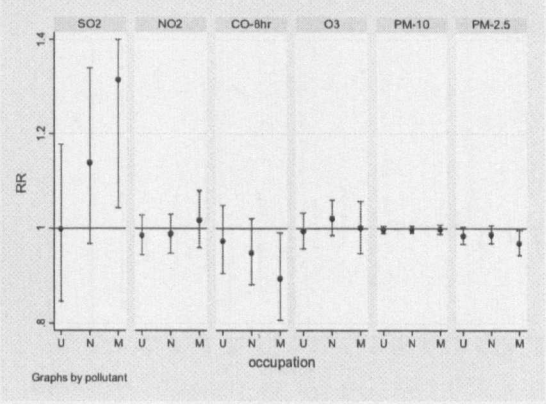


Figure 6. 9 Risk estimates for single pollutant, distributed lag models (0-4 days) for a10-unit increase of a pollutant (one unit increase for CO) on daily out-patient visits in different occupational groups in Muang, Chiang Mai, from October 2002 to September 2006.

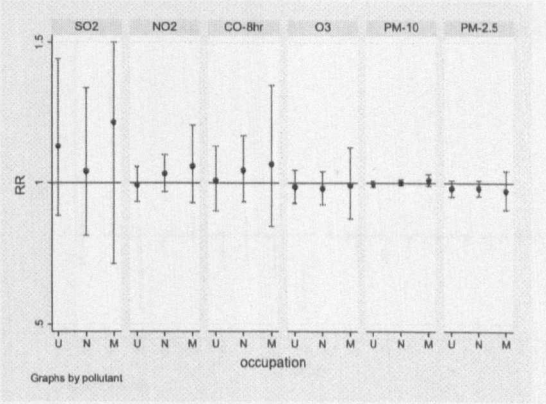
Note: U = unemployed & economically inactive people, **N** = non-manual workers, **M** = manual workers.

6.9a) All-cause visits



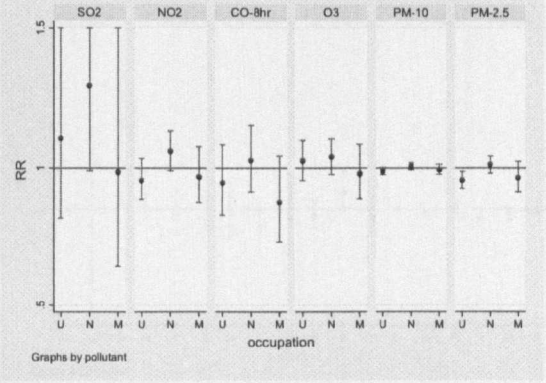
*The upper limits were truncated at 1.4.

6.9b) Respiratory visits



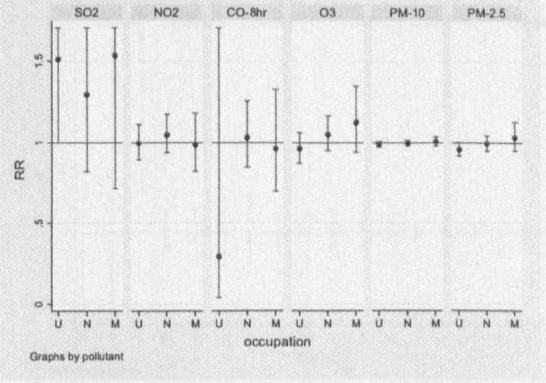
*The upper limits were truncated at 1.5.

6.9c) Circulatory visits



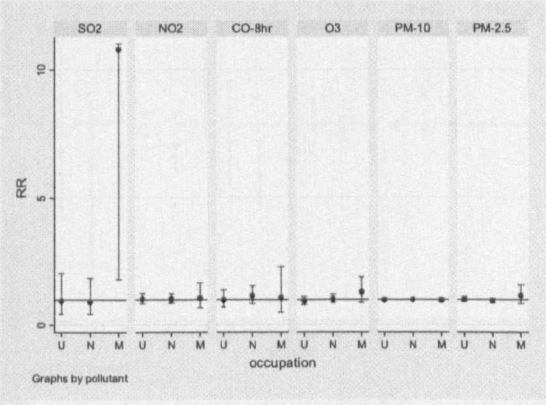
*The upper limits were truncated at 1.5.

6.9d) Diabetic visits



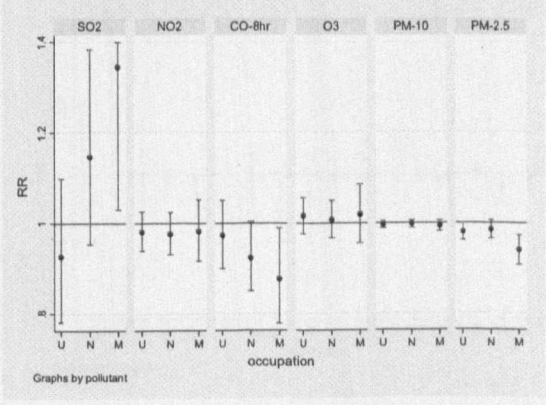
*The upper limits were truncated at 1.7.

6.9e) Intestinal infectious visits



*The upper limit were truncated at 11.0.

6.9f) Other visits

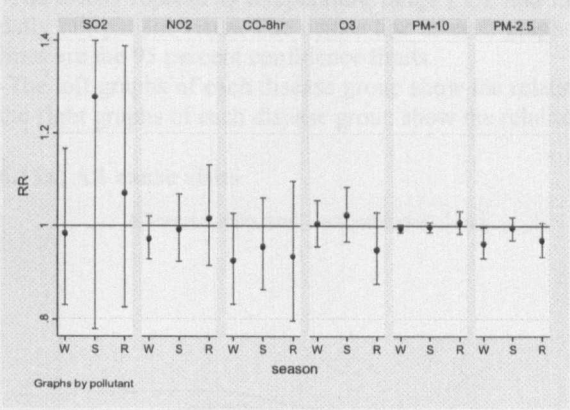


*The upper limits were truncated at 1.4.

Figure 6. 10 Risk estimates for single pollutant, distributed lag models (0-4 days) for a10-unit increase of a pollutant (one unit increase for CO) on daily out-patient visits in different seasons in Muang, Chiang Mai, from October 2002 to September 2006.

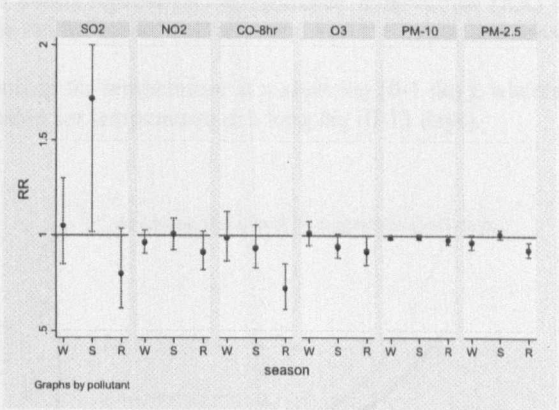
Note: W = Winter, **S** = Summer, **R** = Rainy.

6.10a) All-cause visits



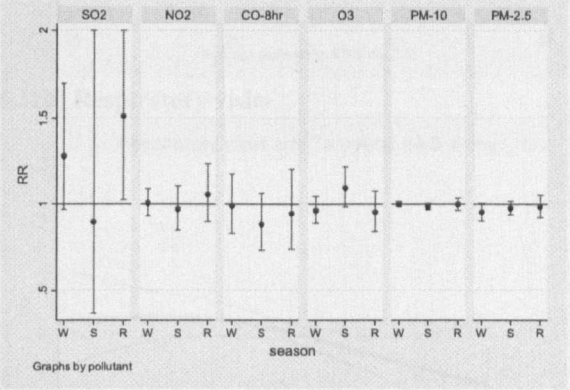
*The upper limits were truncated at 1.4.

6.10b) Respiratory visits



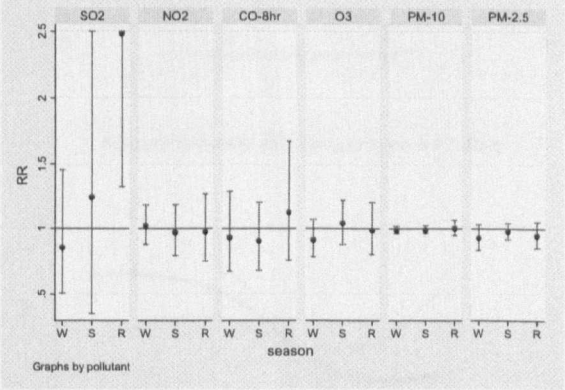
*The upper limit was truncated at 2.0.

6.10c) Circulatory visits



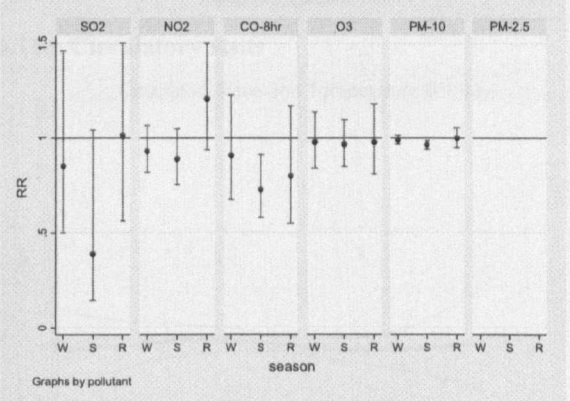
*The upper limits were truncated at 2.0.

6.10d) Diabetic visits



*The upper limits were truncated at 2.5.

6.10e) Intestinal infectious visits



*The upper limits were truncated at 1.5, limited counts to analyze for $PM_{2.5}$ effects in all seasons.

6.10f) Other visits

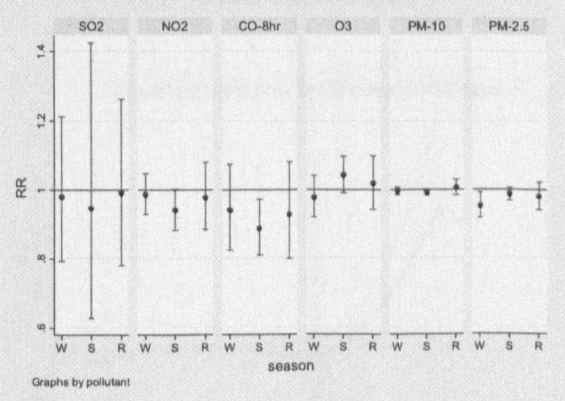
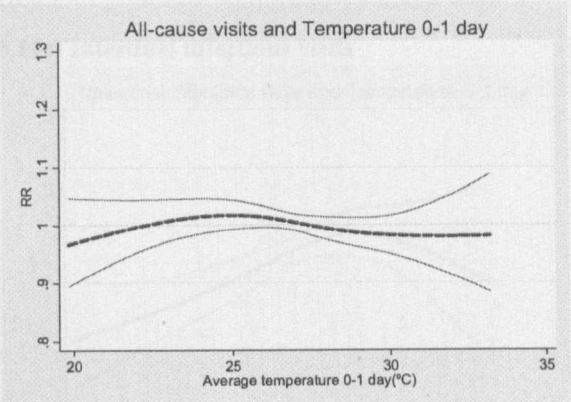
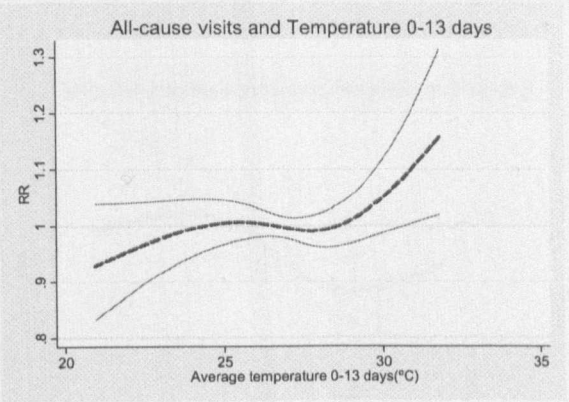


Figure 6. 11 General relationships between daily out-patient visits and temperature at both short lag (0-1 day) and long lag (0-13 days) in Muang, Chiang Mai, from October 2002 to September 2006.

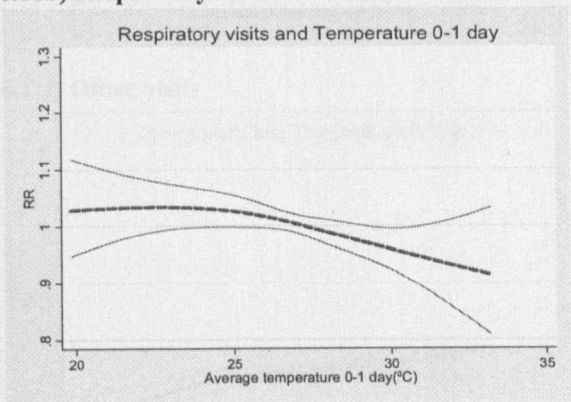
Note:
-Relationship between temperature and daily out-patient visits, adjusting for day of the week, holidays, month of the study (1-48), Thai new year, International new year, influenza, AR term at lag 1,7,14,21, 28, humidity, rain, SO_2, and O_3.
-The x-axis represents temperature range (°C), and the y-axis represents the estimated relative risk (RR) of daily out-patient visits. The centre line in each graph is the estimated spline curve, and the upper and lower lines are the 95 percent confidence limits.
-The left graphs of each disease group show the relationship for temperature at a short lag (0-1 day), whereas the right graphs of each disease group show the relationship for temperature at a long lag (0-13 days).

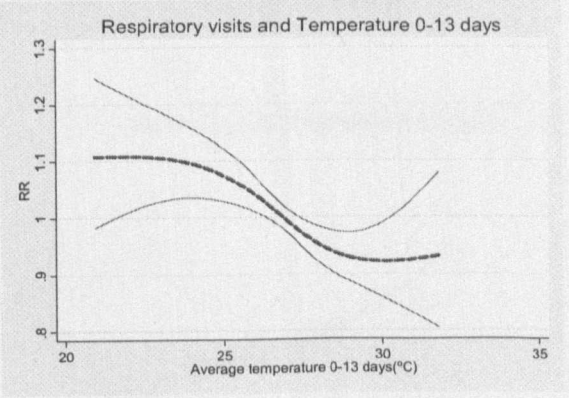
6.11a) All-cause visits



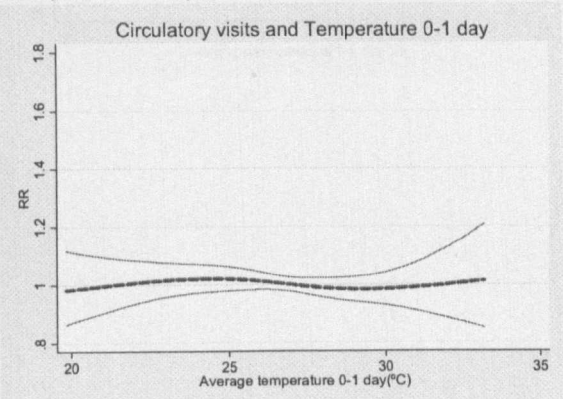


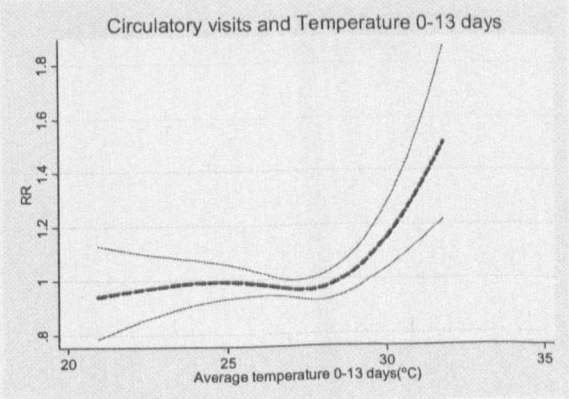
6.11b) Respiratory visits



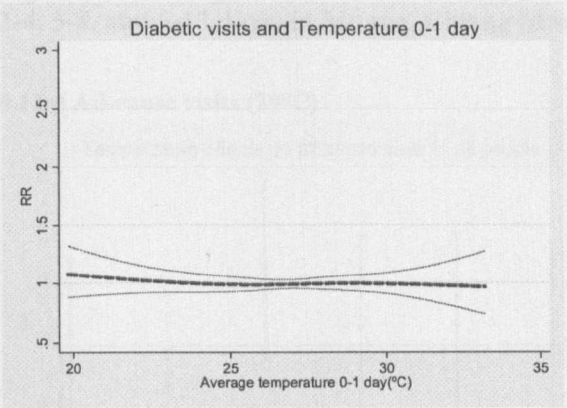


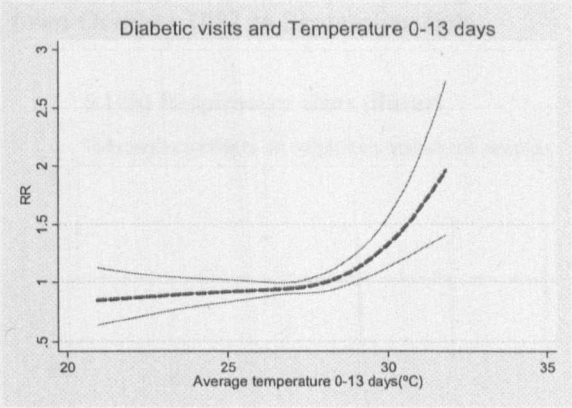
6.11c) Circulatory visits



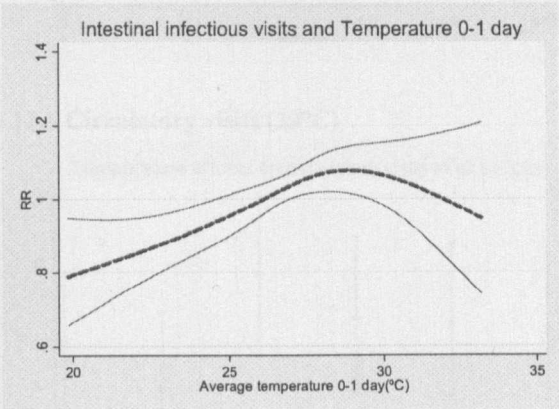


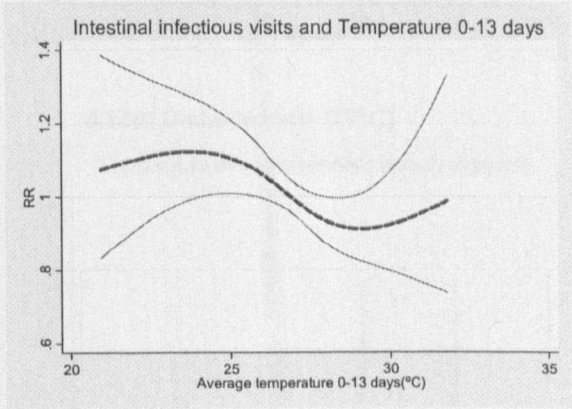
6.11d) Diabetic visits



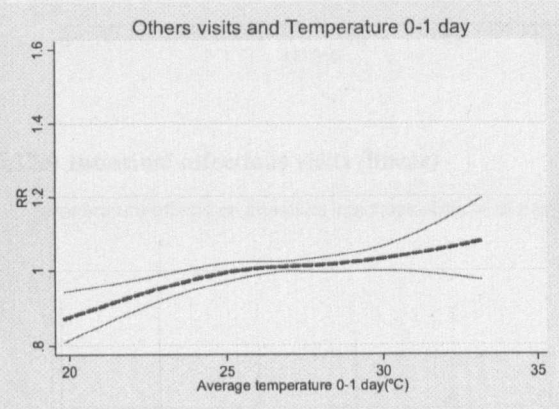


6.11e) Intestinal infectious visits





6.11f) Other visits



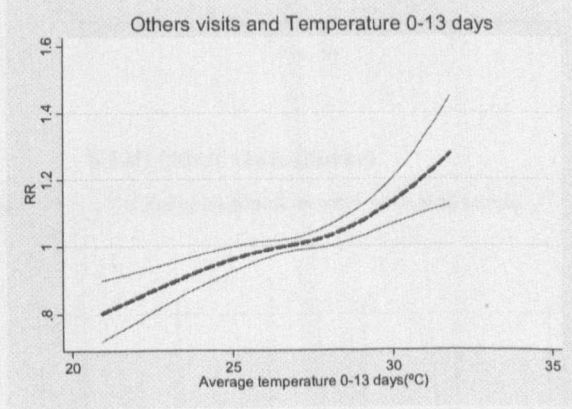
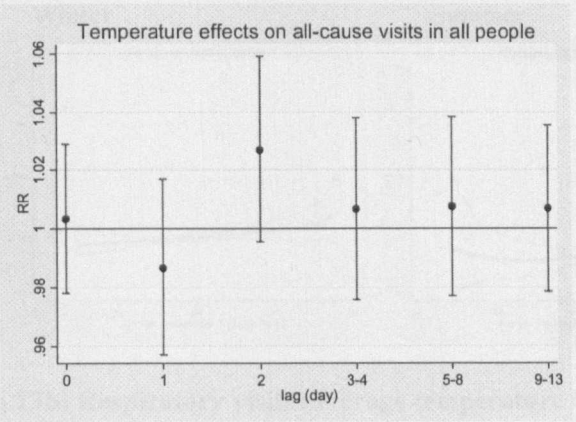
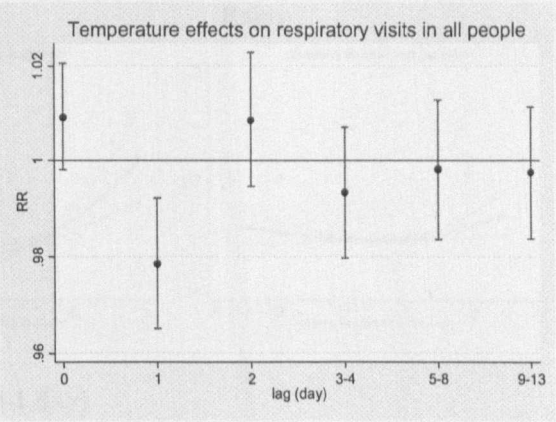


Figure 6. 12 Temperature effects on daily out-patient visits in different specified lags (0, 1, 2, 3-4, 5-8, and 9-13 days) in Muang, Chiang Mai, from October 2002 to September 2006.

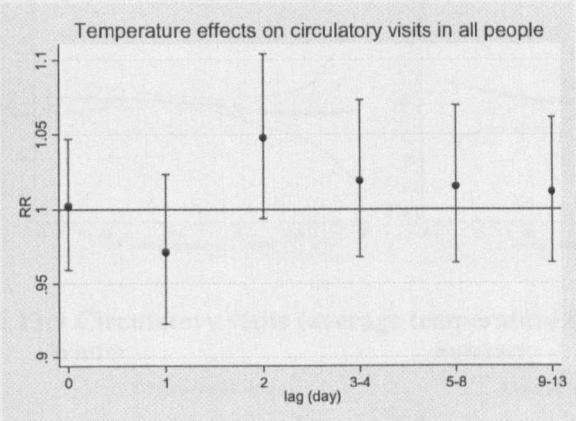
6.12a) All-cause visits (29°C)



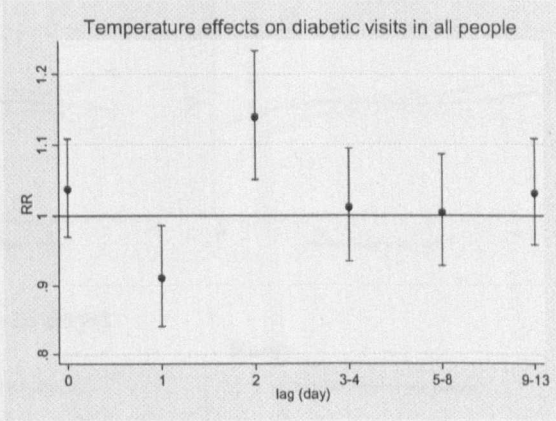
6.12b) Respiratory visits (linear)



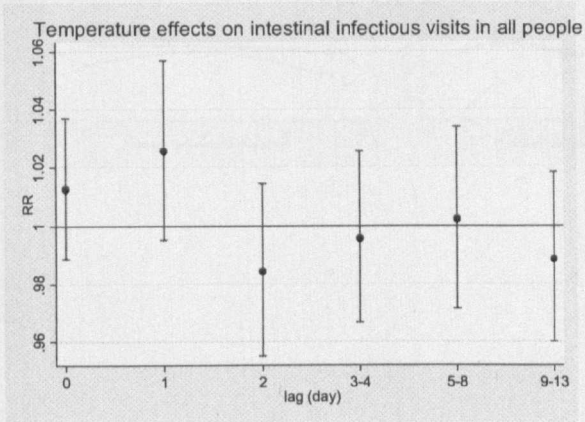
6.12c) Circulatory visits (29°C)



6.12d) Diabetic visits (29°C)



6.12e) Intestinal infectious visits (linear)



6.12f) Other visits (linear)

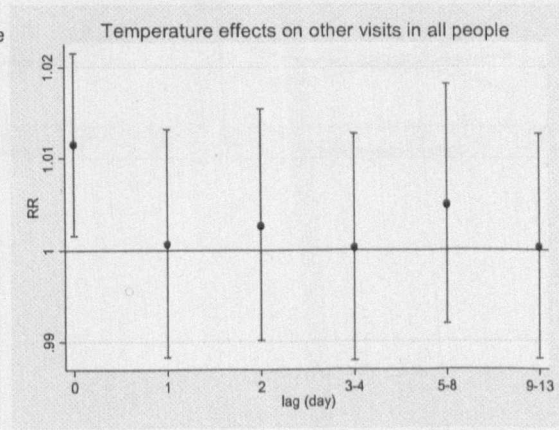
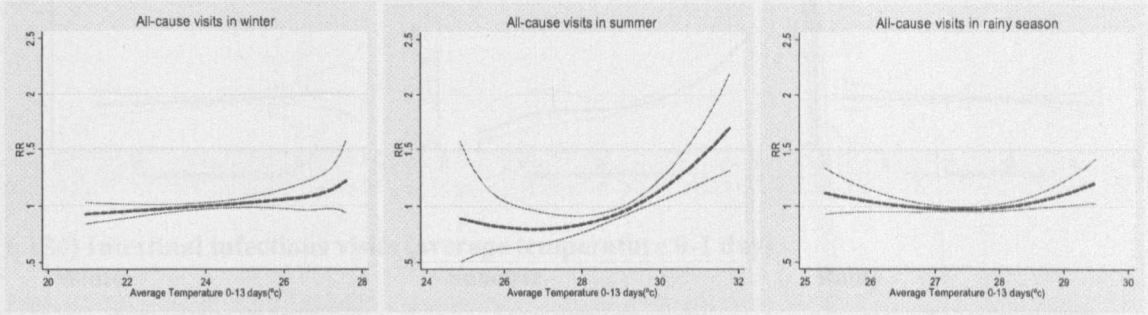


Figure 6. 13 General relationships between daily out-patient visits and temperature in different seasons in Muang, Chiang Mai, from October 2002 to September 2006.

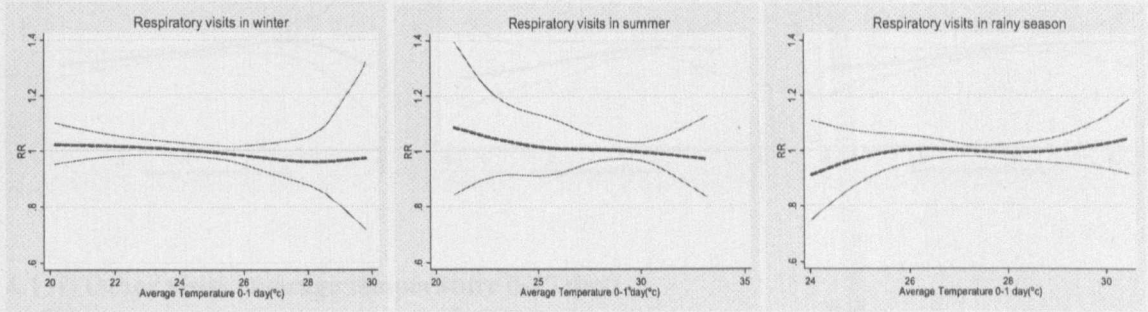
6.13a) All-cause visits (average temperature 0-13 days)

Winter **Summer** **Rainy**



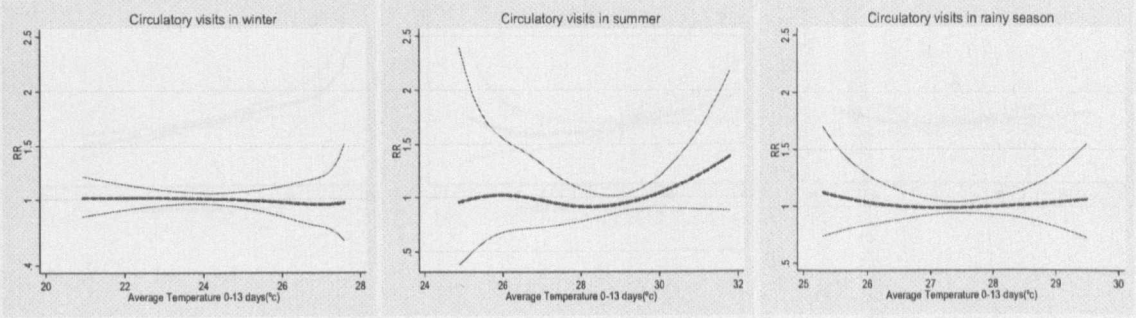
6.13b) Respiratory visits (average temperature 0-1 day)

Winter **Summer** **Rainy**



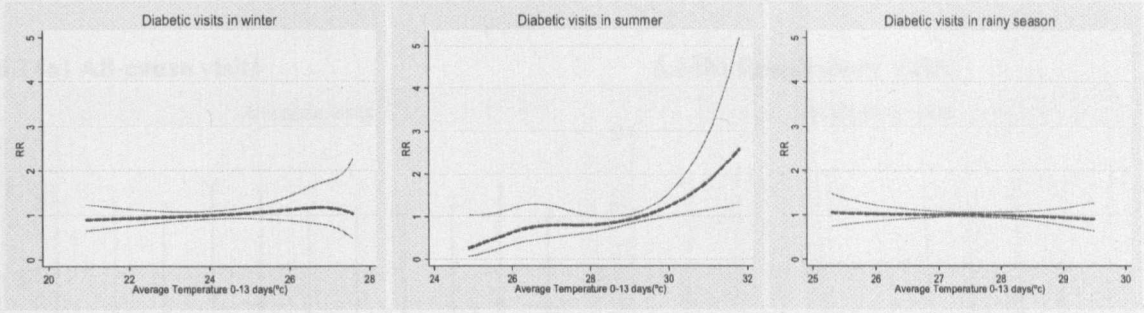
6.13c) Circulatory visits (average temperature 0-13 days)

Winter **Summer** **Rainy**



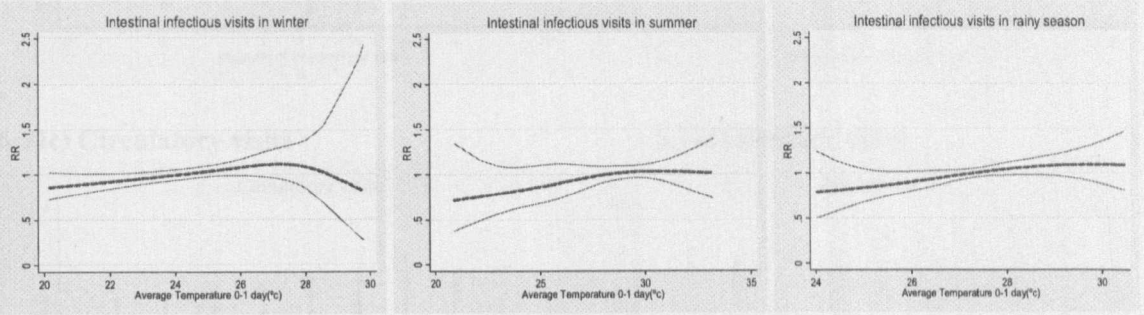
6.13d) Diabetic visits (average temperature 0-13 days)

Winter **Summer** **Rainy**



6.13e) Intestinal infectious visits (average temperature 0-1 day)

Winter **Summer** **Rainy**



6.13f) Other visits (average temperature 0-13 day)

Winter **Summer** **Rainy**

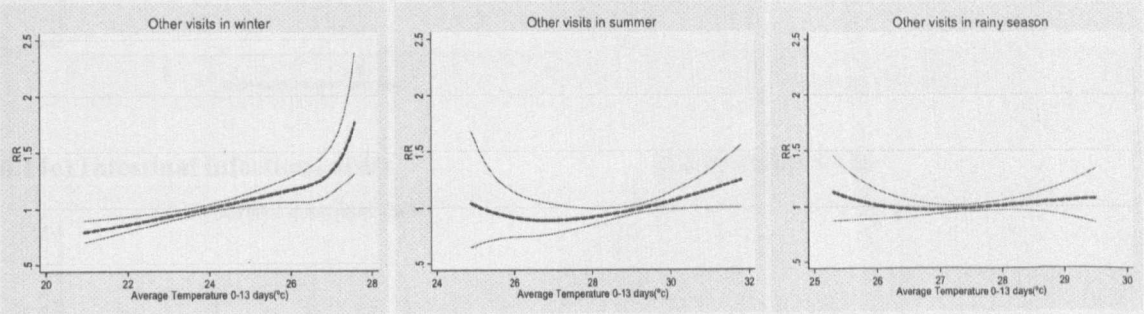
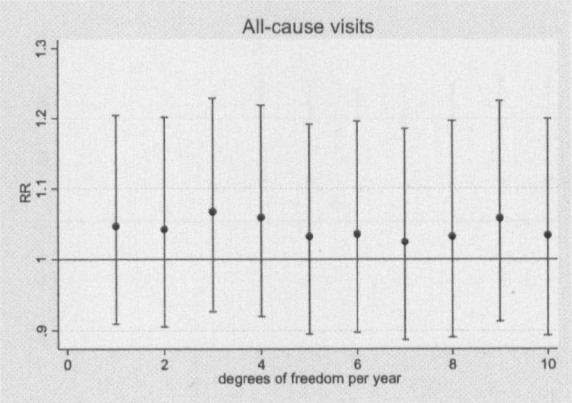
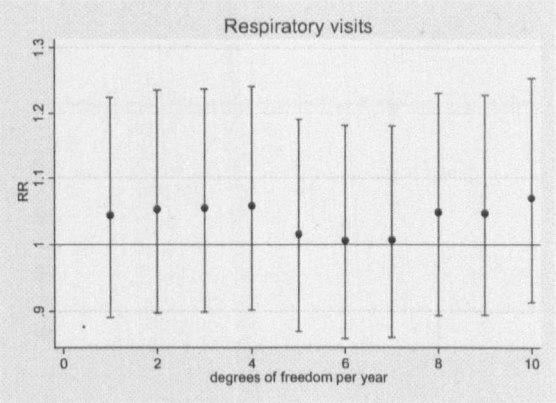


Figure 6. 14 Risk estimates of daily out-patient visits using different degrees of freedom per year for a 10-unit increase of SO_2 at lag 0-4 days.

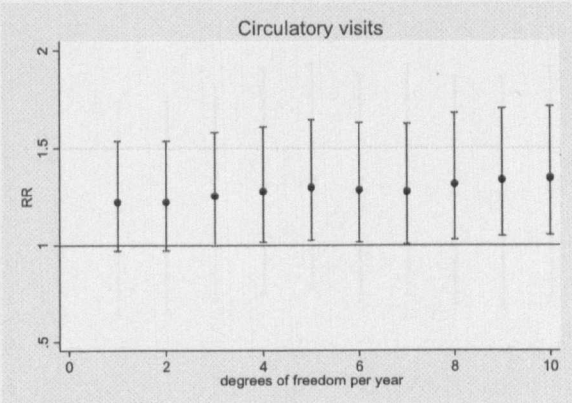
6.14a) All-cause visits



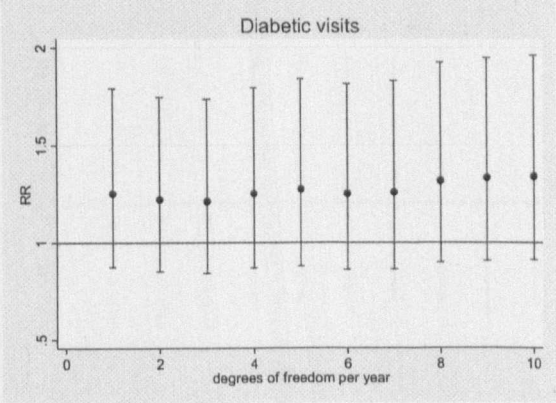
6.14b) Respiratory visits



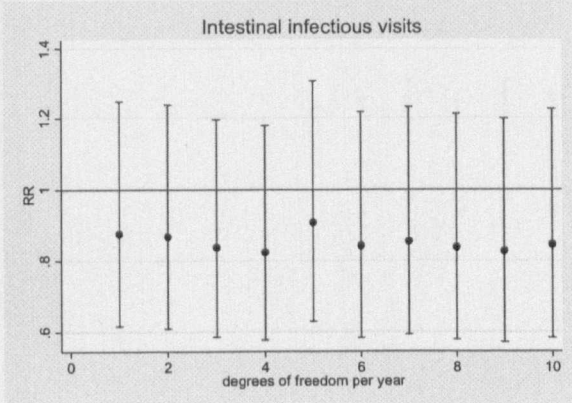
6.14c) Circulatory visits



6.14d) Diabetic visits



6.14e) Intestinal infectious visits



6.14f) Other visits

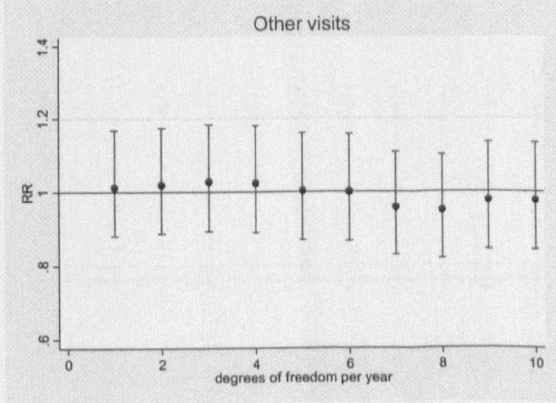
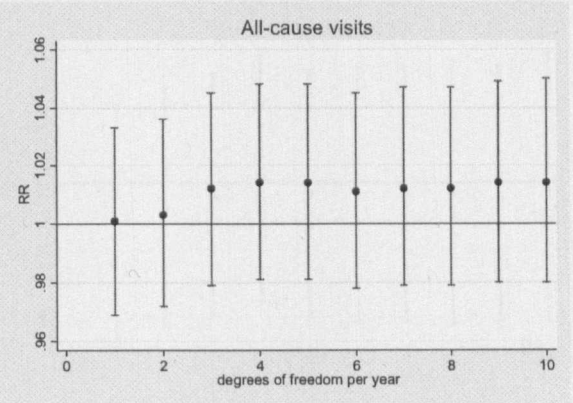
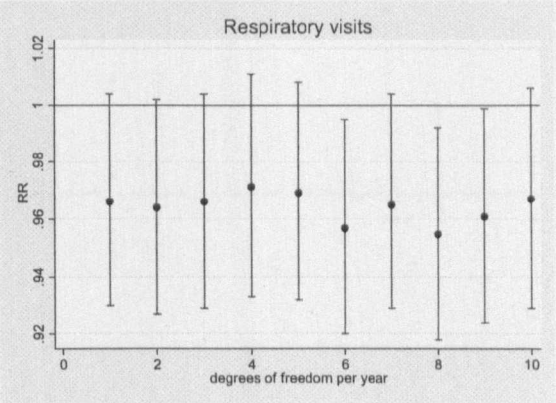


Figure 6. 15 Risk estimates of daily out-patient visits using different degrees of freedom per year for a 10-unit increase of O_3 at lag 0-4 days.

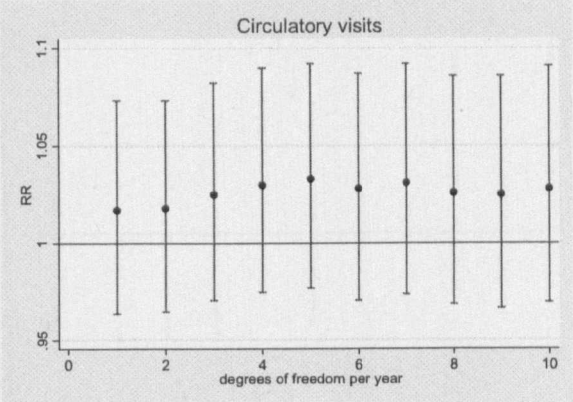
6.15a) All-causé visits



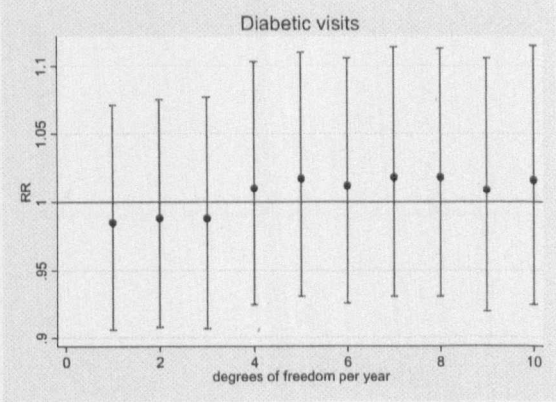
6.15b) Respiratory visits



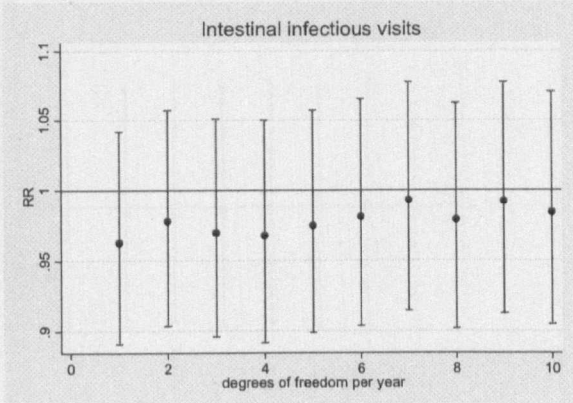
6.15c) Circulatory visits



6.15d) Diabetic visits



6.15e) Intestinal infectious visits



6.15f) Other visits

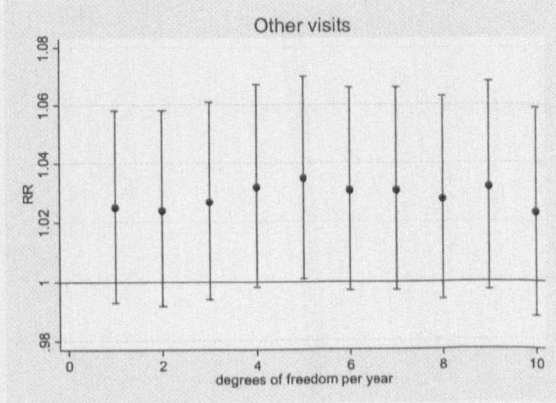
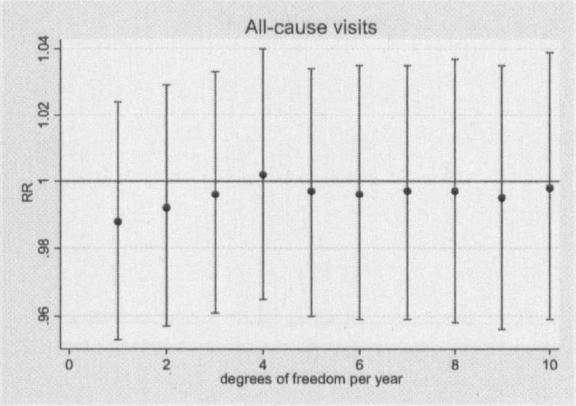
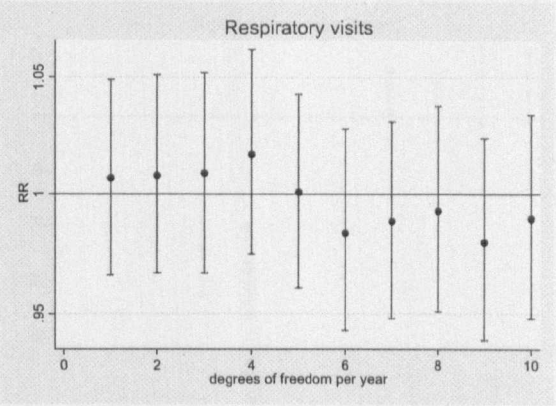


Figure 6. 16 Risk estimates of daily out-patient visits using different degrees of freedom per year for a 10-unit increase of NO_2 at lag 0-4 days.

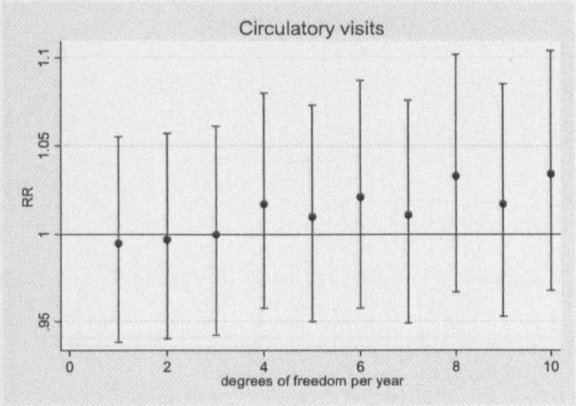
6.16a) All-cause visits



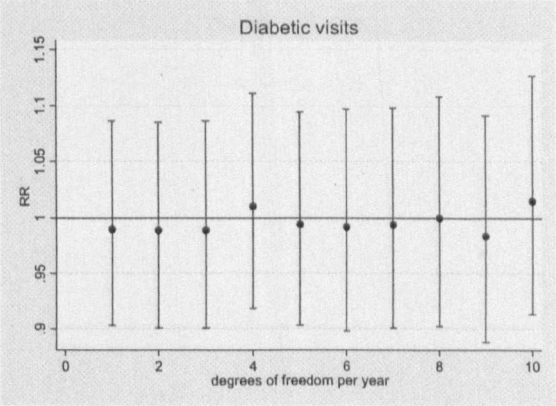
6.16b) Respiratory visits



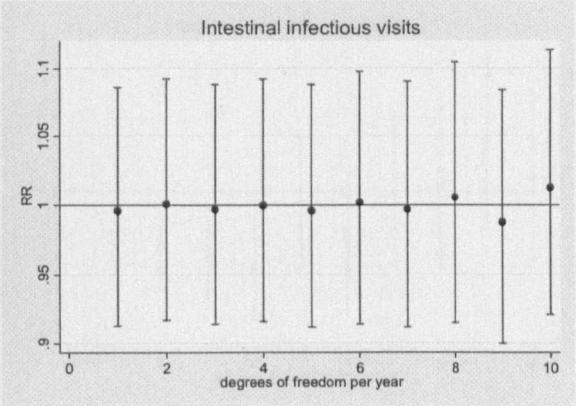
6.16c) Circulatory visits



6.16d) Diabetic visits



6.16e) Intestinal infectious visits



6.16f) Other visits

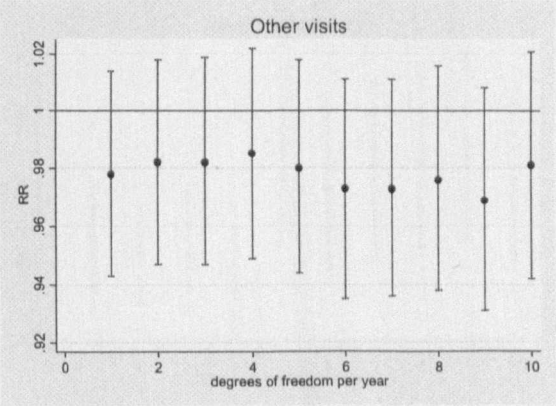
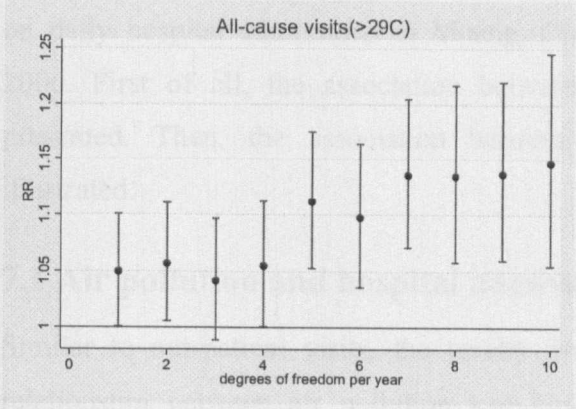
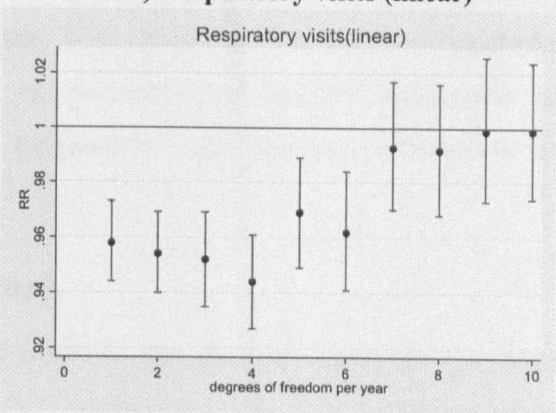


Figure 6. 17 Risk estimates of daily out-patient visits per one degree Celsius increase in temperature in Muang, Chiang Mai, from October 2002 to September 2006.

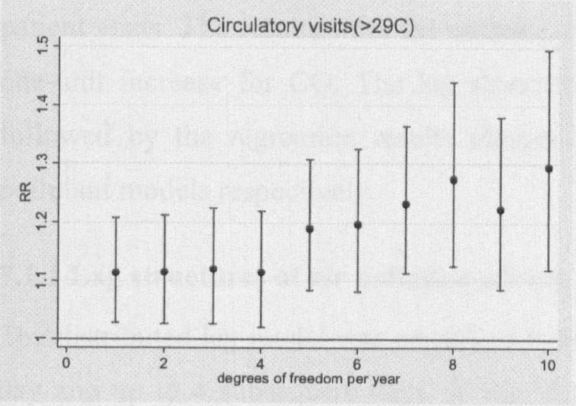
6.17a) All-cause visits (>29°C)



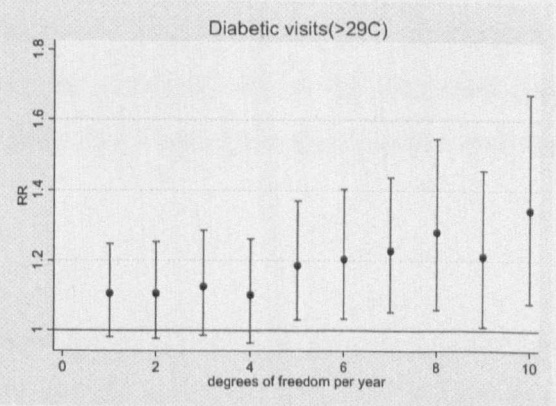
6.17b) Respiratory visits (linear)



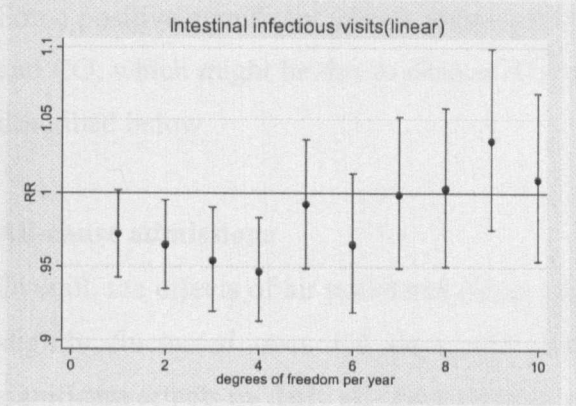
6.17c) Circulatory visits (>29°C)



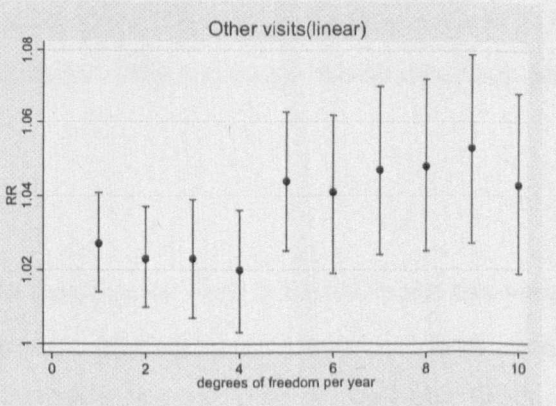
6.17d) Diabetic visits (>29°C)



6.17e) Intestinal infectious visits (linear)



6.17f) Other visits (linear)



Chapter 7 Regression results: Hospital admissions

This chapter provides the regression analysis results of air pollution and temperature effects on daily hospital admissions in Muang, Chiang Mai, from October 2002 to September 2006. First of all, the association between air pollution and hospital admissions are presented. Then, the association between temperature and hospital admissions are illustrated.

7.1 Air pollution and hospital admissions

Similar to out-patient visits, the results described in this chapter suggested the linear relationship between air pollution and hospital admissions. The risk estimates of air pollution on hospital admissions were also employed the same method used for the out-patient visits. The results were the estimate effects of a 10-unit increase of a pollutant, but one-unit increase for CO. The lag structure of air pollution effects are presented first, followed by the regression results obtained from the single pollutant models and two pollutant models respectively.

7.1.1 Lag structures of air pollution effects

The distributed lag model was employed to determine air pollution effects on the exposure day and up to 4 subsequent days. It was found that the estimated effects of air pollution were generally fluctuated over lag 0-4 day period, and were not statistically significant. Some positive significant effects were occasionally found for some pollutants such as SO_2 and CO, which might be due to chance. The estimated effects on main health outcomes are described below.

All-cause admissions

Overall, the effects of air pollutants on all-cause admissions were non-significant and were slightly fluctuated over 1-4 days after exposure (**Figure 7.1**). However, there were significant effects on daily all-cause admissions at lag 2 days for SO_2, and lag 0 day for O_3.

Respiratory admissions

The effects of air pollutants on respiratory admissions were found to be non-significant and reverted to RR = 1 over 2-4 days after exposure, except only SO_2 effects that tended to

increase slightly (**Figure 7.2**). A significant, positive effect of CO was found at lag 1 day, while the significant effect of O_3 was found to be positive at lag 0 day, but negative at lag 1 day.

Circulatory admissions

In general, the effects of air pollutants on circulatory admissions were not significant, with little fluctuations over lag 0-4 days (**Figure 7.3**). However, while the effects of most pollutants were relatively stable, the effects of O_3 gradually declined with time. The positive significant effects of CO on daily circulatory admissions were found at lag 1 day, while the negative significant effects PM_{10} were found at lag 2 days.

Diabetic admissions

There was no significant effect of air pollution on daily diabetic admissions over lag 0-4 days (**Figure 7.4**). Generally, the estimated effects of all pollutants slightly fluctuated over the period, with greater estimated effects at lag 2 days.

Intestinal infectious admissions

The overall estimated effects of air pollution on daily intestinal infectious admissions were found to be non-significant (**Figure 7.5**). However, some significant effects were occasionally found. The only one significant, positive effect was found at lag 3 days for $PM_{2.5}$, whereas the significant, negative effects were found at lag 1 day for CO and at lag 2 days for O_3.

Other admissions

Generally, there was no significant effect of air pollution on daily other admissions (**Figure 7.6**). One positive effect on other admissions was found on lag 1 day, while the rest of the estimated effects were negative or centred around one.

7.1.2 Air pollution effects on daily hospital admissions

The estimated effects presented in this section were the sum of all lags, which were lag 0-1 day and lag 0-4 days. In general, the overall estimated effects were found to be non-statistically significant. The greater estimates were found for SO_2, O_3, and CO than for other pollutants. The effects of air pollution on each selected health outcome are detailed as follows.

All-cause admissions

There were two pollutants: SO_2 and O_3 that provided positive effects on daily all-cause admissions, but none of the estimates were not statistically significant (**Table 7.1**). At lag 0-4 days, a 10-unit increase of SO_2 was associated with a 2.6% (95% CI, -9.9% to 16.9%) increase in all-cause admissions and of O_3 was associated with a 0.4% (95% CI, -2.4% to 3.4%) increase in all-cause admissions. In contrast, the rest of selected pollutants (NO_2, CO, PM_{10} and $PM_{2.5}$) provided negative (with some significant) effects on all-cause admissions.

Respiratory admissions

Although imprecisely estimated, the larger effects on daily respiratory admissions were found for SO_2, followed by CO and O_3, respectively (**Table 7.2**). For example, at lag 0-4 days, there was an increase in respiratory admissions of 41.0% (95% CI, 1.0% to 97.0%) per 10-unit increase of SO_2, of 5.9% (95% CI, -8.8% to 22.9%) per one-unit increase of CO, and of 1.5% (95% CI, -5.6% to 9.2%) per 10-unit increase of O_3. The negative, estimated effects were found for NO_2, PM_{10} and $PM_{2.5}$, but none of them was significant.

Circulatory admissions

The non-significant, positive effects of SO_2 and CO on daily circulatory admissions were found for both lag 0-1 day and lag 0-4 days (**Table 7.3**). For instance, the circulatory admissions increased by 5.0% (95% CI, -14.9% to 29.5%) at lag 0-1 day, and by 8.2% (95% CI, -18.8% to 44.1%) per 10-unit increase of SO_2. there were negative effects for both lags for NO_2 and $PM_{2.5}$, whereas there were positive effects at lag 0-1 day and negative effects at lag 0-4 days for O_3 and PM_{10}. However, all of the estimates effects were not statistically significant.

Diabetic admissions

The overall estimated effects of air pollution on daily diabetic admissions were not significant, and mostly negative (**Table 7.4**). There were only two positive effects, which were found for SO_2 and CO at lag 0-4 days. The large estimates of 40.1% (95% CI, -50.5% to 96.5%) increase in diabetic admissions were found to be associated with a 10-unit increase of SO_2, while the small estimates of 0.5% (95% CI, -38.0% to 62.9%) were found to be associated with one-unit increase of CO, but these estimates were imprecise as the CIs were considerably wide.

Intestinal infectious admissions

Generally, there were negative effects of air pollution on daily intestinal infectious admissions (**Table 7.5**). As can be seen, the negative effects of PM_{10} were statistically significant for both lags, with RR of 0.976 (95% CI, 0.959 to 0.993) at lag 0-1 day, and of 0.977 (95% CI, 0.955-0.999) at lag 0-4 days. The significant, negative effect was also found for CO at lag 0-1 day, with RR of 0.815 (95% CI, 0.685 to 0.970). There was only one positive effects found for NO_2 at lag 0-4 days, with RR of 1.052 (95% CI, 0.920 to 1.202).

Other admissions

Similar to intestinal infectious admissions, the estimated effects of air pollution on daily 'other' admissions were mainly found to be negative, which were statistically significant for some pollutants, such as NO_2 and PM_{10} (**Table 7.6**). O_3 was the only one pollutant that provided positive effects on 'other' admissions. It was found that a 10-unit increase in O_3 was in association with 2.0% (95% CI, -0.6% to 4.6%) increase in 'other' admissions at lag 0-1 days, and with 0.9% (95% CI, -2.2% to 4.2%) increase in 'other' admissions at lag 0-4 days.

Neoplasm admissions

As mentioned in previous chapter, due to the finding of some positive effects of air pollution on 'other' visits and admissions, this raised a concern about which particular sub-disease groups were the contribution of this pollution signal, though not significant. The diagnoses in 'other' diseases vary enormously with several kinds of diseases, but there were

relatively larger numbers of the visits/ admissions due to cancers or neoplasms (ICD-10: C00-D48), with 6.1% for the visits and 28.4% for the admissions. Since previous literature has shown evidence of the association between air pollution and cancers [163-165], this study explored further to see whether there was any effect of air pollution on neoplasm visits and admissions. While there was no significant effect on neoplasm visits (not shown), there was a significant effect of O_3 (lag 0-1 day) on neoplasm admissions (**Table 7.7**), with an increase in the admissions of 6.8% per 10-ppb increase in O_3 level. When the data were stratified by age and sex, the effects of O_3 (lag 0-1 day) remained significant for all subgroups, but no statistically significant differences between subgroups (see **Appendix 7A,** p. 325-6).

7.1.3 Air pollution and effect modification

As mentioned previously in the descriptive chapter, there were considerable missing values of occupation for hospital admissions data. Therefore, the occupation variable was excluded for the analysis with regard to effect modification. There were three variables: sex, age and season, to be examined whether they had modified air pollution effects in the hospital admissions data.

I. Effect modification by age

Overall, there was no evidence of effect modification by age on the association between air pollution and daily hospital admissions in this study (**Figure 7.7**). However, the estimated effects of air pollution in children and the elderly were relatively larger than those in adults, as can be seen from the respiratory admissions. None of the estimated effects in each age group were statistically significant at 5% level.

II. Effect modification by sex

There was also no significant difference in the estimated effects of air pollution between males and females in the present study (**Figure 7.8**). Although there was no significant difference between sex groups, the air pollution effects on respiratory admissions in females were slightly greater than those in males. However, there was a contradictory result of air pollution effects between sex groups for circulatory admissions, which was found that the CO effects were positive and larger in males, whereas the SO_2 effects were positive and larger in females.

III. Effect modification by season

No evidence of interaction between season and air pollution effects on daily hospital admissions was found in this study (**Figure 7.9**). For circulatory admissions, the effects of CO and SO_2 were found to be greater in winter than other seasons, but no significant difference in the effects between seasons.

7.1.4 Air pollution effects for two-pollutant models

By considering the results from single pollutant models, there were three pollutants: SO_2, O_3, and CO that provided more positive effects on daily hospital admissions than other pollutants. Therefore, these three pollutants were chosen to be included in the two pollutant models. The same methods used for the out-patient visits series were employed for determining the effects of the three pollutants in the two-pollutant models for the hospital admissions series. The results obtained from the two-pollutant models are illustrated in **Table 7.8**. As shown in the Table, the overall estimated effects of each pollutant on daily hospital admissions obtained by the two-pollutant models were relatively higher than those obtained by single pollutant models. However, the increased estimates in the two-pollutant models were not very consistent.

For example, when there were SO_2 and CO in the models, SO_2 effects were found to be larger than those in the single pollutant models for all disease groups among people in all ages. But, when looking at the elderly people ($\geq$ 65 year), it was found that SO_2 effects (when CO were included in the models) were smaller than those in the single pollutant models (i.e. respiratory disease). For O_3, the estimated effects among both all ages and the elderly found in the two-pollutant models (either with SO_2 or with CO) were generally higher than those found in the single pollutant models for all-cause, respiratory, and other admissions, but not for circulatory, diabetic, and intestinal infectious admissions. The estimated effects of CO when included O_3 in models were relatively larger than those obtained in the single pollutant models for all disease groups and for both all ages and the elderly, but its effects when having SO_2 in the models, instead of CO, were not consistently larger than those observed in the single pollutant models.

7.2 Temperature and hospital admissions

The results of investigating the effects of temperature on daily hospital admissions are presented in this section. It begins with the description of the general relationships between temperature and hospital admissions. This is followed by the lag structure of the temperature effects and their estimated effects on all selected health outcomes. The investigation of effect modification by age, sex, and season was also included.

7.2.1 General relationships between temperature and hospital admissions

By adopting the same procedure used for out-patient visits series, the plots of general relationship between temperature and hospital admissions are shown in **Figure 7.10**.

As can be seen, the use of temperature average at longer lag (0-13 days) better captured short-term effects of temperature on daily hospital admissions than the use of temperature average at a short lag (0-1 day) for most outcomes, except for respiratory and intestinal infectious admissions. An obvious linear increase with increasing temperature was seen for these two diseases. Similar to out-patient visit data, there was no cold effect found for hospital admission data, but heat effects only.

Based on graphical visualization for temperature at a long lag (0-13 days), the temperature threshold of 29°C was used for quantifying the short-term effects of temperature on all-cause, circulatory, and other admissions, whereas a linear term of temperature was used for diabetic admissions. Due to apparent linear increase of respiratory and infectious admissions with increasing temperature at a short lag (0-1 day), a linear term of temperature was used for quantifying temperature effects for these two diseases.

7.2.2 Lag structure of temperature effects

Temperature effects on daily hospital admissions for specified lag period are shown in **Figure 7.11**. Overall, there were no significant effects of temperature over 0-13 day period. The temperature effects were generally found to be larger at lag 1 and lag 2 days and relatively stable from lag 3 to 13 days. There was no significant increase or decrease of the temperature effects beyond lag 13 days in this study (not shown). Thus, the quantification of temperature effects for long lag up to 13 days should suffice for the study.

7.2.3 Temperature effects on hospital admissions

To quantify temperature effects, the distributed lag models were used, with adjustment for all possible potential confounders like the out-patient visit series. As mentioned earlier, for all-cause, circulatory, and other admissions, the linear relationship between temperature and these three outcomes were assumed when temperature were above 29°C. For respiratory, diabetic, and intestinal infectious admissions, the linear terms of temperature was employed for quantifying temperature effects. The distributed lag model from the exposure day and up to 13 previous days were carried out for most health outcomes, except for respiratory and intestinal infectious admissions (short lag, 0-1day). Thus, the estimated effects presented here were the sum of all lags from 0 to 13 days for long lag and from 0 to 1 day for short lag. Generally, for each 1°C increase in temperature, there were positive effects of temperature on most health outcomes, but not consistently significant across subgroups studied. The effects of temperature on each health outcome are described separately as the followings.

All-cause admissions

Overall, there were positive effects of temperature on all-cause admissions, with only one exception – the effects in children (**Table 7.9**). For each 1 °C increase in temperature above 29°C, there was an increase in all-cause admissions of about 4-12%. It was found that the all-cause admissions in all people increased by 5.3% (95% CI, -0.2% to 11.1%) per 1°C increase in temperature above this threshold. The effects of hot temperature were found to be largest and significant in the elderly, and slightly greater in males than in females.

Respiratory admissions

Generally, there was a small, positive increase in respiratory admissions in association with 1 °C increase in temperature (no threshold) (**Table 7.10**). The respiratory admissions in all people significantly increased by 2.8% (95%CI, 0.6% to 5.0%) per 1°C increase in temperature. The estimated effects of respiratory admissions were slightly greater in the elderly than in other age groups, and also slightly greater in females than in males.

Circulatory admissions

There was no evidence of hot temperature effects on daily circulatory admissions in the present study (**Table 7.11**). When temperature above 29°C, there was a decrease in circulatory admissions in most subgroups, and none of the estimates was significant. The only one positive increase was found in the elderly, but the estimate was small and also non-significant.

Diabetic admissions

Due to limited daily counts of daily diabetic admissions, the temperature effects could be estimated for all people only (**Table 7.12**). The imprecise estimate was found for diabetic admissions with very wide confidence interval. For each 1 °C increase in temperature, the diabetic admissions were found to increase about 4.2% (95% CI, -11.6% to 22.9%).

Intestinal infectious admissions

There were significant, positive effects of temperature on intestinal infectious admissions in all people, children, and male people, while there were non-significant, positive effects on the admissions in adult, the elderly and female people (**Table 7.13**). Among all people, it was anticipated that the intestinal infectious admissions significantly rose by 5.8% (95% CI, 2.3% to 9.3%) per 1 °C increase in temperature. The increase in intestinal infectious admission with increasing temperature admissions was found to be significantly larger in children (13.1% increase, 95% CI, 6.4% to 20.3%) and male people (10.6% increase, 95% CI, 4.8% to 16.6%) in comparison to other subgroups.

Other admissions

Overall, there were positive effects of hot temperature on 'other' admissions, but most of the effects were not statistically significant (**Table 7.14**). The stronger estimated effects were found for the elderly and male people, while the overall estimated effects on all people were not significant at 5% level.

Neoplasm admissions

Similar to the visits series, hot temperature effects on neoplasm admissions were also examined, although not the main outcome of interest. There were generally positive, but not

significant effects of hot temperature on neoplasm admissions (**Table 7.15**). The effects were found much stronger in children and male people, but no statistically significant differences between subgroups.

7.2.4 Temperature and effect modification by age and sex

Based on the results shown in **Table 7.9-7.14**, there was little evidence of effect modification by age and sex on the association between temperature and daily hospital admissions in this study. Overall, the estimated effects of temperature for most outcomes seemed to be larger in the elderly and male people. However, the significant differences between subgroups were found for intestinal infectious admissions only, with strongest estimates in children and male people.

7.2.5 Effect modification by season

The effect modification by season for hospital admission series was investigated by the same method used for out-patient visit series. The investigation of temperature effects was undertaken by looking at the relationships between temperature and hospital admissions in each season separately. The plots of the general relationships between them are illustrated in **Figure 7.12**. As shown in the figure, there was generally no visible apparent temperature threshold for all seasons. Therefore, a linear association was assumed for quantification temperature effects for all seasons. The estimated effects in each season are illustrated in **Table 7.15**. Overall, the positive, larger estimated effects of temperature were found in summer than other seasons for most outcomes. However, there were no significant differences in the estimated effects between seasons.

7.3 Sensitivity analyses of hospital admissions series

For hospital admissions series, the effect of re-admissions on the estimated risks is of most concern. It was speculated that even a small number of re-admissions could lead to the distortions in the data, which might result in false conclusions [208]. Since literature review has suggested that temperature effects, such as cold effects, may delay for more than two weeks after exposure [13, 188], the hospital admissions within 30 days could possibly due to the same episode. Because the present study investigated not only air pollution effects, but also temperature effects, it was decided to exclude the re-admissions within 30 days due to with the same diagnosis from the data set for the hospital admission series. Therefore, investigations of air pollution and temperature effects on the main outcomes of interest, using different types of admission data: all admissions, single admissions only, and the one used in the present study (with exclusions of re-admissions by the same diagnosis within 30 days), were undertaken. The risk estimates of air pollution effects and temperature effects are presented in **Table 7.16** and **7.17**, respectively.

As can be seen, although different types of admission data were used for the analysis, the estimated effects of selected air pollutants on hospital admissions were relatively similar, except for SO_2 and CO effects. The estimated effects of SO_2 obtained from the data used in the present study were higher than those obtained from the data with all admissions or single admissions in all disease groups, with only one exception, diabetic admissions, that the estimated effects were higher when using data with single admissions. Also, the estimated effects of CO on most health outcomes, using the data with single admissions, were slightly higher than those using the data with all admissions and with some exclusion employed by this study. For temperature, overall, the risk estimates of temperature effects on daily hospital admissions obtained by all types of admissions data were found to be similar. Even though the estimated effects of temperature were slightly lower when using single admissions data for diabetic admissions, the overall estimates were broadly the same for the rest of the outcomes.

Summary of hospital admissions series:

Air pollution effects

- There was some evidence of the association between air pollution and hospital admissions. Although the findings were non-significant at 5% level, the estimated effects were larger, particularly for SO_2, CO, and O_3.
- Since the effects of air pollution were generally found during 1-2 days after exposure, the use of lag 0-4 days for the investigation was sufficient to capture the short-term effects of air pollution in this study.
- There was no evidence of effect modification by age, sex, and season.
- The effects of the three selected air pollutants: SO_2, CO, and O_3 in the two-pollutant models were larger than those in the single pollutant models. But this finding was not consistent across all disease groups.

Temperature effects

- The positive effects of hot temperature were found for most diseases, but not consistently significant across subgroups. Most of the significant effects were found for respiratory and intestinal infectious admissions.
- There were some findings, which were contradictory to out-patient visits series. When temperature above 29°C, there was an increase in circulatory visits, while there was a decline in circulatory admissions.
- The investigation of temperature effects up to lag 13 days was sufficient since the effects did not increase or decrease beyond this period.
- There was little evidence of effect modification by age and sex.
- The temperature effects on hospital admissions were partially modified by season.

Sensitivity analyses:

- In the present study, the re-admissions in the data did not greatly affect the estimated effects of temperature, but had some impacts on the estimated effects of SO_2 and CO. That was, the SO_2 effects in this study (exclusion of re-admissions by the same diagnosis within 30 days) were slightly larger than those used the data, comprising all re-admissions or single admissions, while the CO effects in this study were slightly smaller than those used other two types of admissions.

Table 7. 1 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily all-cause admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	1.002	0.913	1.101	0.959
	0-4 days	1.026	0.901	1.169	0.699
NO_2(ppb)	0-1 day	0.969	0.944	0.995	0.020
	0-4 days	0.977	0.944	1.010	0.164
CO-8hr(ppm)	0-1 day	0.956	0.916	0.997	0.038
	0-4 days	0.977	0.922	1.034	0.421
O_3(ppb)	0-1 day	1.018	0.996	1.040	0.115
	0-4 days	1.004	0.976	1.032	0.793
$PM_{10}(\mu g/m^3)$	0-1 day	0.994	0.990	0.999	0.009
	0-4 days	0.993	0.987	0.998	0.012
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.990	0.981	1.000	0.053
	0-4 days	0.987	0.975	1.000	0.044

*The estimates are the sum of all lags.

Table 7. 2 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily respiratory admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	1.128	0.889	1.430	0.322
	0-4 days	1.410	1.010	1.970	0.044
NO_2(ppb)	0-1 day	0.998	0.933	1.068	0.956
	0-4 days	0.976	0.894	1.064	0.578
CO-8hr(ppm)	0-1 day	1.064	0.953	1.189	0.269
	0-4 days	1.059	0.912	1.229	0.456
O_3(ppb)	0-1 day	1.012	0.956	1.071	0.685
	0-4 days	1.015	0.944	1.092	0.681
$PM_{10}(\mu g/m^3)$	0-1 day	0.998	0.987	1.010	0.733
	0-4 days	0.995	0.980	1.009	0.475
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.991	0.966	1.016	0.460
	0-4 days	0.978	0.947	1.009	0.167

*The estimates are the sum of all lags.

Table 7. 3 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily circulatory admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	1.050	0.851	1.295	0.649
	0-4 days	1.082	0.812	1.441	0.591
NO_2(ppb)	0-1 day	0.991	0.937	1.049	0.764
	0-4 days	0.979	0.911	1.052	0.557
CO-8hr(ppm)	0-1 day	1.001	0.911	1.100	0.983
	0-4 days	1.009	0.889	1.144	0.893
O_3(ppb)	0-1 day	1.028	0.980	1.078	0.255
	0-4 days	0.990	0.932	1.052	0.741
$PM_{10}(\mu g/m^3)$	0-1 day	1.001	0.991	1.010	0.914
	0-4 days	0.999	0.986	1.011	0.811
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.993	0.973	1.014	0.533
	0-4 days	0.996	0.970	1.023	0.772

*The estimates are the sum of all lags.

Table 7. 4 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily diabetic admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.821	0.384	1.758	0.612
	0-4 days	1.401	0.495	3.965	0.525
NO_2(ppb)	0-1 day	0.823	0.660	1.025	0.082
	0-4 days	0.934	0.708	1.231	0.626
CO-8hr(ppm)	0-1 day	0.891	0.623	1.272	0.524
	0-4 days	1.005	0.620	1.629	0.984
O_3(ppb)	0-1 day	0.998	0.834	1.195	0.985
	0-4 days	0.990	0.792	1.237	0.928
$PM_{10}(\mu g/m^3)$	0-1 day	0.948	0.912	0.985	0.006
	0-4 days	0.955	0.910	1.003	0.067
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.956	0.889	1.028	0.221
	0-4 days	0.947	0.863	1.039	0.246

*The estimates the sum of all lags.

Table 7. 5 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily intestinal infectious admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.663	0.433	1.014	0.058
	0-4 days	0.718	0.400	1.287	0.265
NO_2(ppb)	0-1 day	0.953	0.860	1.057	0.366
	0-4 days	1.052	0.920	1.202	0.459
CO-8hr(ppm)	0-1 day	0.815	0.685	0.970	0.021
	0-4 days	0.853	0.676	1.076	0.179
O_3(ppb)	0-1 day	0.988	0.908	1.075	0.782
	0-4 days	0.944	0.847	1.052	0.295
$PM_{10}(\mu g/m^3)$	0-1 day	0.976	0.959	0.993	0.006
	0-4 days	0.977	0.955	0.999	0.043
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.976	0.941	1.012	0.194
	0-4 days	0.987	0.942	1.035	0.592

*The estimates the sum of all lags.

Table 7. 6 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily other admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

			95% Confidence Interval		
Pollutant (unit)	**Lag**	**RR***	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0-1 day	0.996	0.893	1.111	0.942
	0-4 days	0.988	0.849	1.149	0.875
NO_2(ppb)	0-1 day	0.958	0.929	0.988	0.006
	0-4 days	0.957	0.920	0.995	0.027
CO-8hr(ppm)	0-1 day	0.943	0.898	0.991	0.021
	0-4 days	0.967	0.905	1.034	0.325
O_3(ppb)	0-1 day	1.020	0.994	1.046	0.129
	0-4 days	1.009	0.978	1.042	0.562
$PM_{10}(\mu g/m^3)$	0-1 day	0.993	0.988	0.998	0.007
	0-4 days	0.991	0.984	0.998	0.007
$PM_{2.5}(\mu g/m^3)$	0-1 day	0.991	0.980	1.002	0.116
	0-4 days	0.987	0.973	1.001	0.070

*The estimates the sum of all lags.

Table 7. 7 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily neoplasm admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

Pollutant (unit)	Lag	Coef.	SE	RR*	95% CI		p-value
					Lower	Upper	
SO_2 (ppb)	0-1 day	0.008	0.010	1.082	0.889	1.317	0.431
	0-4 days	0.017	0.014	1.190	0.913	1.551	0.199
NO_2(ppb)	0-1 day	-0.003	0.003	0.967	0.915	1.023	0.248
	0-4 days	-0.006	0.004	0.945	0.881	1.013	0.111
CO-8hr(ppm)	0-1 day	-0.111	0.047	0.895	0.817	0.981	0.017
	0-4 days	-0.093	0.061	0.911	0.809	1.027	0.127
O_3(ppb)	0-1 day	0.007	0.002	1.068	1.022	1.116	0.004
	0-4 days	0.005	0.003	1.047	0.992	1.105	0.098
$PM_{10}(\mu g/m^3)$	0-1 day	-0.000	0.000	0.996	0.986	1.005	0.370
	0-4 days	-0.001	0.001	0.992	0.981	1.004	0.206
$PM_{2.5}(\mu g/m^3)$	0-1 day	-0.002	0.001	0.985	0.966	1.005	0.139
	0-4 days	-0.002	0.001	0.979	0.955	1.003	0.084

*The estimates are the sum of all lags.

Table 7. 8 Risk estimates of single pollutant models and two-pollutant models for a 10-unit increase of a pollutant (one-unit increase of CO) at average lag 0-4 days on daily hospital admissions in all ages and in the elderly(≥ 65 year) in Mauang, Chiang Mai, from October 2002 to September 2006.

Outcome		Single pollutant RR (95%CI)	SO_2 & O_3 RR(95%CI)	SO_2 & CO RR(95%CI)	O_3 & CO RR(95%CI)
All-cause					
all ages	SO_2	1.024 (0.898-1.168)	1.023 (0.897-1.166)	1.038 (0.909-1.185)	
	O_3	1.002 (0.976-1.028)	1.004 (0.976-1.032)		1.004 (0.977-1.033)
	CO	0.977 (0.923-1.035)		0.972 (0.916-1.031)	0.984 (0.928-1.043)
≥65 year	SO_2	0.922 (0.741-1.147)	0.932 (0.748-1.161)	0.927 (0.743-1.157)	
	O_3	1.009 (0.967-1.053)	1.018 (0.971-1.066)		1.010 (0.964-1.058)
	CO	1.003 (0.913-1.103)		1.019 (0.925-1.124)	1.008 (0.915-1.111)
Respiratory					
all ages	SO_2	1.383 (0.987-1.937)	1.467 (1.045-2.058)	1.402 (0.998-1.969)	
	O_3	1.000 (0.934-1.071)	0.986 (0.915-1.061)		1.009 (0.936-1.087)
	CO	1.061 (0.914-1.232)		1.035 (0.890-1.203)	1.072 (0.920-1.249)
≥65 year	SO_2	1.432 (0.761-2.695)	1.402 (0.738-2.665)	1.362 (0.713-2.602)	
	O_3	1.009 (0.890-1.143)	1.029 (0.896-1.182)		1.045 (0.910-1.200)
	CO	1.231 (0.940-1.613)		1.208 (0.916-1.595)	1.205 (0.912-1.592)
Circulatory					
all ages	SO_2	1.078 (0.807-1.440)	1.048 (0.784-1.402)	1.080 (0.805-1.447)	
	O_3	0.994 (0.939-1.052)	0.989 (0.929-1.052)		0.983 (0.923-1.046)
	CO	1.006 (0.887-1.141)		1.005 (0.884-1.142)	1.028 (0.903-1.169)
≥65 year	SO_2	1.030 (0.659-1.609)	1.002 (0.639-1.574)	0.948 (0.602-1.495)	
	O_3	0.994 (0.910-1.085)	0.986 (0.895-1.086)		0.978 (0.887-1.077)
	CO	1.128 (0.928-1.370)		1.128 (0.924-1.378)	1.149 (0.941-1.404)
Diabetic*					
all ages	SO_2	1.543 (0.541-4.401)	1.355 (0.471-3.900)	1.559 (0.543-4.479)	
	O_3	1.050 (0.850-1.298)	1.008 (0.801-1.269)		1.005 (0.800-1.263)
	CO	0.967 (0.597-1.567)		0.959 (0.586-1.570)	0.993 (0.605-1.631
Intestinal infectious*					
all ages	SO_2	0.712 (0.393-1.290)	0.787 (0.437-1.417)	0.760 (0.419-1.380)	
	O_3	0.953 (0.860-1.057)	0.944 (0.846-1.054)		0.954 (0.854-1.065)
	CO	0.847 (0.672-1.066)		0.860 (0.678-1.090)	0.875 (0.691-1.108)
Other					
all ages	SO_2	0.987 (0.847-1.150)	0.981 (0.842-1.143)	1.001 (0.857-1.168)	
	O_3	1.006 (0.976-1.037)	1.012 (0.980-1.046)		1.012 (0.980-1.046)
	CO	0.969 (0.907-1.035)		0.965 (0.901-1.033)	0.971 (0.908-1.039)
≥65	SO_2	0.850 (0.647-1.117)	0.880 (0.669-1.158)	0.875 (0.664-1.153)	
	O_3	1.013 (0.960-1.068)	1.024 (0.966-1.085)		1.013 (0.956-1.072)
	CO	0.963 (0.856-1.083)		0.987 (0.874-1.115)	0.968 (0.858-1.093)

*There were limited counts of admissions among the elderly (≥65 year) for the analysis.

Table 7. 9 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily all-cause admissions in Muang, Chiang Mai. from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI		p-value	p-value [b]
				Lower	Upper		
All people	110.50	50.78	1.053	0.998	1.111	0.061	
Age							
0-14 years	15.35	8.69	0.972	0.868	1.088	0.618	
15- 64 years	71.47	32.46	1.046	0.984	1.113	0.151	
≥ 65 years	23.59	12.34	1.119	1.022	1.226	0.015	0.158
Sex							
Male	52.50	24.05	1.064	0.994	1.139	0.076	
Female	57.90	27.85	1.038	0.972	1.109	0.266	0.609

[a] Mean daily count of all-cause admissions when T > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.

Table 7. 10 Relative risk estimates for distributed lag models (0-1 day) for temperature effects (linear) on daily respiratory admissions in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI		p-value	p-value [b]
				Lower	Upper		
All people	7.81	4.26	1.028	1.006	1.050	0.011	
Age							
0-14 years	1.88	1.62	1.028	0.984	1.073	0.216	
15- 64 years	3.70	2.64	1.027	0.995	1.059	0.094	
≥ 65 years	2.21	1.70	1.037	0.997	1.078	0.070	0.925
Sex							
Male	4.06	2.69	1.029	0.999	1.060	0.055	
Female	3.73	2.47	1.034	1.003	1.066	0.034	0.823

[a] Mean daily count of respiratory admissions when no temperature threshold (n=1387 days).
[b] p-value of the test for heterogeneity between groups.

Table 7. 11 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily circulatory admissions in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	11.18	5.86	0.979	0.867	1.105	0.730	
Age [c]							
0-14 years	0.27	0.60	-	-	-	-	
15- 64 years	6.52	3.74	0.941	0.801	1.106	0.462	
≥ 65 years	4.39	2.72	1.021	0.844	1.234	0.832	0.521
Sex							
Male	5.53	3.51	0.952	0.801	1.132	0.579	
Female	5.64	3.28	0.999	0.842	1.184	0.988	0.697

[a] Mean daily count of circulatory admissions when T > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.
[c] There were limited daily counts of circulatory admissions among age 0-14 years for the analysis.

Table 7. 12 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (linear) on daily diabetic admissions in Muang, Chiang Mai, from October 2002 to September 2006.

Group [c]	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	0.77	0.95	1.042	0.884	1.229	0.623	N/A

[a] Mean daily count of diabetic admissions when no temperature threshold (n = 1387 days).
[b] p-value of the test for heterogeneity between groups.
[c] There were very limited daily counts of diabetic admissions among subgroups for the analysis.

Table 7. 13 Relative risk estimates for distributed lag models (0-1 day) for temperature effects (linear) on daily intestinal infectious admissions in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	3.31	2.49	1.058	1.023	1.093	0.001	
Age							
0-14 years	0.94	1.13	1.131	1.064	1.203	0.000	
15- 64 years	1.98	1.85	1.023	0.979	1.068	0.307	
≥ 65 years	0.37	0.63	1.044	0.942	1.156	0.415	0.032
Sex							
Male	1.34	1.34	1.106	1.048	1.166	0.000	
Female	1.96	1.73	1.027	0.984	1.072	0.228	0.034

[a] Mean daily count of intestinal infectious admissions when no temperature threshold (n = 1387 days).
[b] p-value of the test for heterogeneity between groups.

Table 7. 14 Relative risks for distributed lag models (0-13 days) for temperature effects (linear) on daily other admissions in Muang, Chiang Mai, from October 2002 to September 2006.

Group	Mean [a]	SD	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	86.01	42.99	1.053	0.990	1.119	0.100	
Age							
0-14 years	12.00	7.54	0.988	0.869	1.123	0.853	
15- 64 years	57.67	28.07	1.039	0.971	1.112	0.264	
≥ 65 years	16.27	9.83	1.130	1.010	1.266	0.033	0.275
Sex							
Male	40.46	19.99	1.087	1.005	1.175	0.036	
Female	45.47	24.10	1.011	0.939	1.089	0.769	0.187

[a] Mean daily count of other visits when temperature > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups

Table 7. 15 Relative risk estimates for distributed lag models (0-13 days) for temperature effects (>29°C) on daily neoplasm admissions in Muang, Chiang Mai from October 2002 to September 2006.

Group	Mean [a]	SD	Coef.	SE	RR	95% CI Lower	95% CI Upper	p-value	p-value [b]
All people	19.19	15.46	0.062	0.062	1.064	0.942	1.202	0.315	
Age									
0-14 years	1.40	1.76	0.256	0.209	1.291	0.858	1.944	0.221	
15- 64 years	13.47	11.28	0.048	0.069	1.049	0.917	1.201	0.487	
≥ 65 years	4.31	3.81	0.019	0.107	1.020	0.827	1.256	0.856	0.594
Sex									
Male	7.81	6.97	0.173	0.087	1.189	1.003	1.410	0.046	
Female	11.38	9.15	-0.036	0.073	0.965	0.836	1.113	0.622	0.064

[a] Mean daily count of all-cause admissions when T > 29°C (n = 266 days).
[b] p-value of the test for heterogeneity between groups.

Table 7. 16 Risk estimates of daily hospital admissions per one degree Celsius increase in temperature in different seasons in Maung, Chiang Mai, from October 2002 to September 2006.

					95%CI			
Outcome [c]	**Season** [a]	**Mean**	**SD**	**RR**	**Lower**	**Upper**	**p-value**	**p-value** [b]
All-cause	Winter	97.62	44.99	1.032	0.754	1.412	0.845	
	Summer	106.76	51.35	1.101	1.032	1.176	0.004	
	Rainy	107.12	47.51	0.991	0.911	1.078	0.837	0.151
Respiratory	Winter	7.78	4.53	1.039	1.001	1.078	0.043	
	Summer	7.60	4.22	1.052	1.003	1.104	0.037	
	Rainy	7.97	4.12	0.987	0.926	1.052	0.692	0.272
Circulatory	Winter	11.46	5.87	0.951	0.863	1.048	0.313	
	Summer	10.81	5.98	1.075	0.941	1.229	0.289	
	Rainy	10.88	5.88	0.860	0.688	1.077	0.188	0.173
Diabetic	Winter	0.68	0.86	1.032	0.689	1.545	0.880	
	Summer	0.84	1.00	0.913	0.564	1.480	0.712	
	Rainy	0.80	0.99	1.315	0.562	3.079	0.528	0.760
Intestinal infectious	Winter	2.62	2.37	1.052	0.986	1.122	0.126	
	Summer	3.87	2.44	1.093	1.024	1.167	0.008	
	Rainy	3.46	2.47	1.022	0.927	1.127	0.664	0.492
Other	Winter	73.70	37.65	1.059	1.010	1.109	0.017	
	Summer	83.42	43.18	1.115	1.036	1.200	0.004	
	Rainy	83.81	39.50	1.019	0.930	1.118	0.683	0.296

[a] A linear relationship was assumed for all seasons, winter: n = 481 days, summer: n= 368 days, and rainy: n= 612 days.

[b] p-value of test for heterogeneity between seasons.

[c] Quantifying temperature effects at a long lag (0-13 days), except respiratory and intestinal infectious admissions, which was done for the effects at a short lag (0-1 day).

Table 7. 17 Risk estimates of daily hospital admissions per 10-unit increase of a pollutant (one-unit increase for CO) for single, distributed lag models at lag 0-4 days, using different types of admission data in Muang, Chiang Mai, from September 2002 to October 2006.

Pollutant (unit)	All admissions	Single admissions	Excluded re-admissions within 30 days with the same diagnosis*
All-cause			
SO_2 (ppb)	0.997	0.999	1.026
	(0.876-1.134)	(0.876-1.139)	(0.901-1.169)
NO_2 (ppb)	0.971	0.980	0.977
	(0.940-1.004)	(0.948-1.014)	(0.944-1.010)
CO-8hr (ppm)	0.964	0.984	0.977
	(0.910-1.021)	(0.929-1.042)	(0.922-1.034)
O_3(ppb)	1.004	0.998	1.004
	(0.977-1.032)	(0.971-1.026)	(0.976-1.032)
PM_{10}($\mu g/m^3$)	0.993	0.993	0.993
	(0.987-0.998)	(0.987-0.999)	(0.987-0.998)
$PM_{2.5}$($\mu g/m^3$)	0.987	0.989	0.987
	(0.975-1.000)	(0.977-1.002)	(0.975-1.000)
Respiratory			
SO_2 (ppb)	1.327	1.323	1.410
	(0.958-1.840)	(0.924-1.894)	(1.010-1.970)
NO_2 (ppb)	0.980	0.967	0.976
	0.902-1.066)	(0.881-1.061)	(0.894-1.064)
CO-8hr (ppm)	1.047	1.075	1.059
	(0.906-1.210)	(0.917-1.260)	(0.912-1.229)
O_3(ppb)	1.029	1.008	1.015
	(0.959-1.103)	(0.933-1.089)	(0.944-1.092)
PM_{10}($\mu g/m^3$)	0.997	0.993	0.995
	(0.983-1.011)	(0.978-1.009)	(0.980-1.009)
$PM_{2.5}$($\mu g/m^3$)	0.987	0.976	0.978
	(0.957-1.017)	(0.943-1.010)	(0.947-1.009)
Circulatory			
SO_2 (ppb)	1.033	1.017	1.082
	(0.779-1.369)	(0.754-1.372)	(0.812-1.441)
NO_2 (ppb)	0.973	0.979	0.979
	(0.906-1.044)	(0.908-1.055)	(0.911-1.052)
CO-8hr (ppm)	0.993	1.026	1.009
	(0.878-1.123)	(0.900-1.170)	(0.889-1.144)
O_3(ppb)	0.980	0.983	0.990
	(0.923-1.040)	(0.923-1.047)	(0.932-1.052)
PM_{10}($\mu g/m^3$)	0.996	1.001	0.999
	(0.984-1.008)	(0.988-1.014)	(0.986-1.011)
$PM_{2.5}$($\mu g/m^3$)	0.991	0.998	0.996
	(0.966-1.017)	(0.971-1.026)	(0.970-1.023)

*Data used in the present study.

(Table 7.17 continues next page)

Table 7.17 Risk estimates of daily hospital admissions, using different types of admission data (continued).

Pollutant (unit)	All admissions	Single admissions	Excluded re-admissions with the same diagnosis within 30 days*
Diabetic			
SO_2 (ppb)	1.341 (0.489-3.682)	1.592 (0.538-4.709)	1.401 (0.495-3.965)
NO_2 (ppb)	0.965 (0.737-1.263)	0.891 (0.667-1.192)	0.934 (0.708-1.231)
CO-8hr (ppm)	1.012 (0.631-1.623)	1.033 (0.624-1.710)	1.005 (0.620-1.629)
O_3(ppb)	1.010 (0.813-1.254)	1.025 (0.813-1.291)	0.990 (0.792-1.237)
$PM_{10}(\mu g/m^3)$	0.959 (0.915-1.006)	0.953 (0.906-1.004)	0.955 (0.910-1.003)
$PM_{2.5}(\mu g/m^3)$	0.963 (0.881-1.054)	0.940 (0.851-1.039)	0.947 (0.863-1.039)
Intestinal infectious			
SO_2 (ppb)	0.731 (0.409-1.307)	0.677 (0.373-1.231)	0.718 (0.400-1.287)
NO_2 (ppb)	1.058 (0.926-1.209	1.057 (0.923-1.209)	1.052 (0.920-1.202)
CO-8hr (ppm)	0.997 (0.986-1.008)	0.866 (0.685-1.095)	0.853 (0.676-1.076)
O_3(ppb)	0.977 (0.955-0.999)	0.940 (0.842-1.049)	0.944 (0.847-1.052)
$PM_{10}(\mu g/m^3)$	0.977 (0.955-0.999)	0.978 (0.956-1.001)	0.977 (0.955-0.999)
$PM_{2.5}(\mu g/m^3)$	0.983 (0.938-1.029)	0.987 (0.941-1.035)	0.987 (0.942-1.035)
Other			
SO_2 (ppb)	0.970 (0.836-1.126)	0.962 (0.827-1.118)	0.988 (0.849-1.149)
NO_2 (ppb)	0.952 (0.916-0.989)	0.960 (0.924-0.998)	0.957 (0.920-0.995)
CO-8hr (ppm)	0.953 (0.892-1.018)	0.970 (0.908-1.036)	0.967 (0.905-1.034)
O_3(ppb)	1.008 (0.977-1.041	1.004 (0.972-1.036)	1.009 (0.978-1.042)
$PM_{10}(\mu g/m^3)$	0.991 (0.984-0.997)	0.991 (0.984-0.997)	0.991 (0.984-0.998)
$PM_{2.5}(\mu g/m^3)$	0.987 (0.973-1.001)	0.989 (0.973-1.001)	0.987 (0.973-1.001)

*Data used in the present study.

Table 7. 18 Relative risks of temperature effects on daily hospital admissions per one degree Celsius increase in temperature for distributed lag models (0-13 days), using different types of admission data in Muang, Chiang Mai, from September 2002 to October 2006.

Type of admission data	Mean [a]	SD	RR	95% CI		p-value
				Lower	Upper	
All-cause (>29°C)						
All	122.70	58.90	1.064	1.007	1.123	0.026
Single	98.89	42.77	1.051	0.996	1.110	0.072
Some excluded [b]	110.50	50.78	1.053	0.998	1.111	0.061
Respiratory (linear) [c]						
All	8.22	4.39	1.024	1.003	1.045	0.026
Single	7.12	3.90	1.025	1.003	1.048	0.025
Some excluded [b]	7.81	4.26	1.028	1.006	1.050	0.011
Circulatory (>29°C)						
All	11.65	6.04	0.991	0.880	1.117	0.884
Single	10.32	5.35	0.958	0.845	1.086	0.505
Some excluded [b]	11.18	5.86	0.979	0.867	1.105	0.730
Diabetic (linear)						
All	0.81	0.98	1.051	0.895	1.234	0.546
Single	0.71	0.89	1.022	0.860	1.214	0.805
Some excluded [b]	0.77	0.95	1.042	0.884	1.229	0.623
Intestinal infectious (linear) [c]						
All	3.35	2.53	1.056	1.021	1.091	0.001
Single	3.19	2.42	1.056	1.021	1.092	0.002
Some excluded [b]	3.31	2.49	1.058	1.023	1.093	0.001
Other (>29°C)						
All	97.21	50.92	1.066	1.002	1.133	0.042
Single	76.34	35.81	1.056	0.993	1.122	0.082
Some excluded [b]	86.01	42.99	1.053	0.990	1.119	0.100

[a] Mean daily count of the admissions when temperature > 29°C (n = 266 days), and when no temperature threshold (n = 1387 days).

[b] Re-admissions by the same diagnosis within 30 days were excluded, which were used in the present study.

[c] Temperature effects for short lag (0-1 day) were examined for these two diseases.

Figure 7. 1 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily all-cause admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

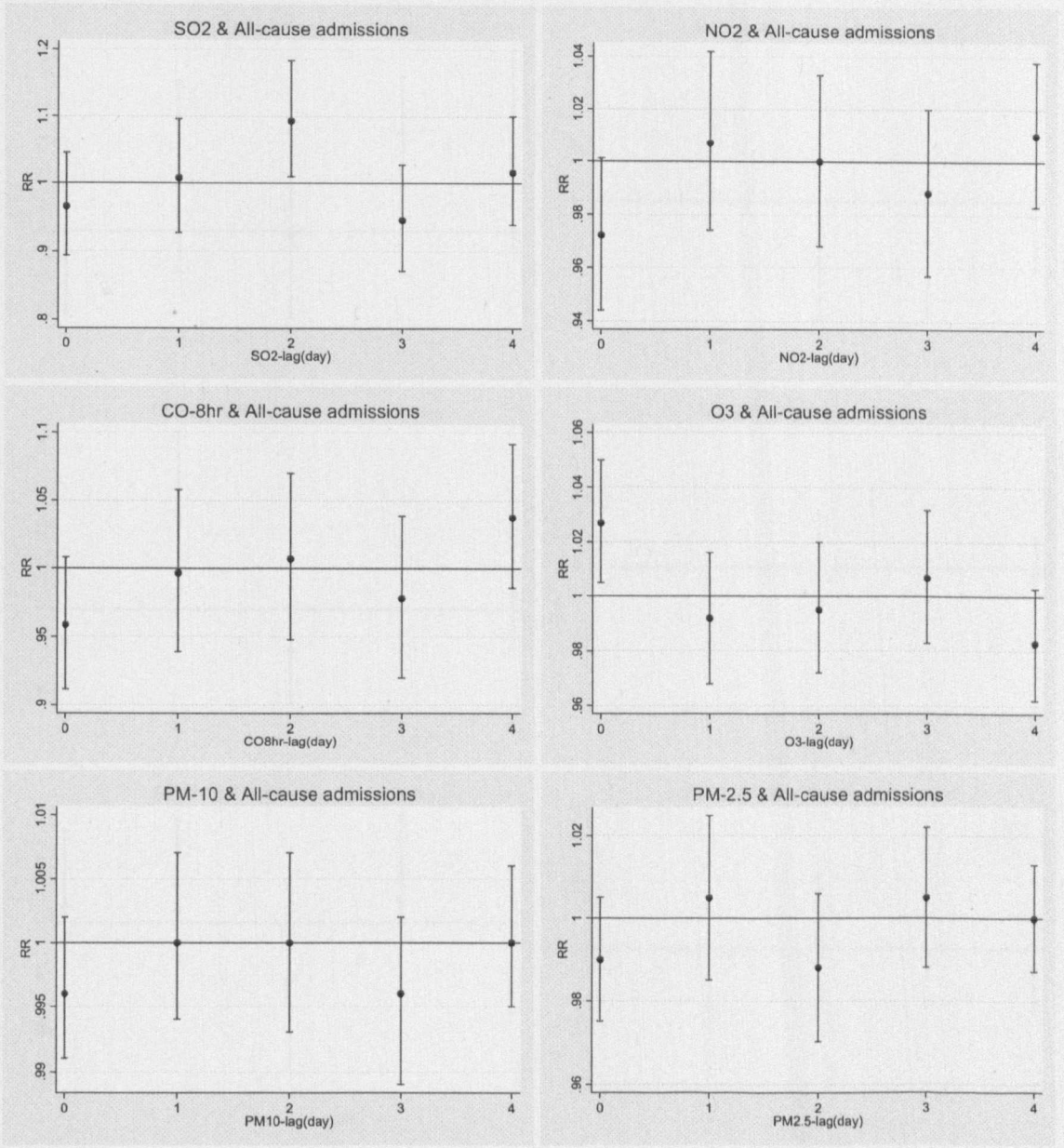


Figure 7. 2 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily respiratory admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

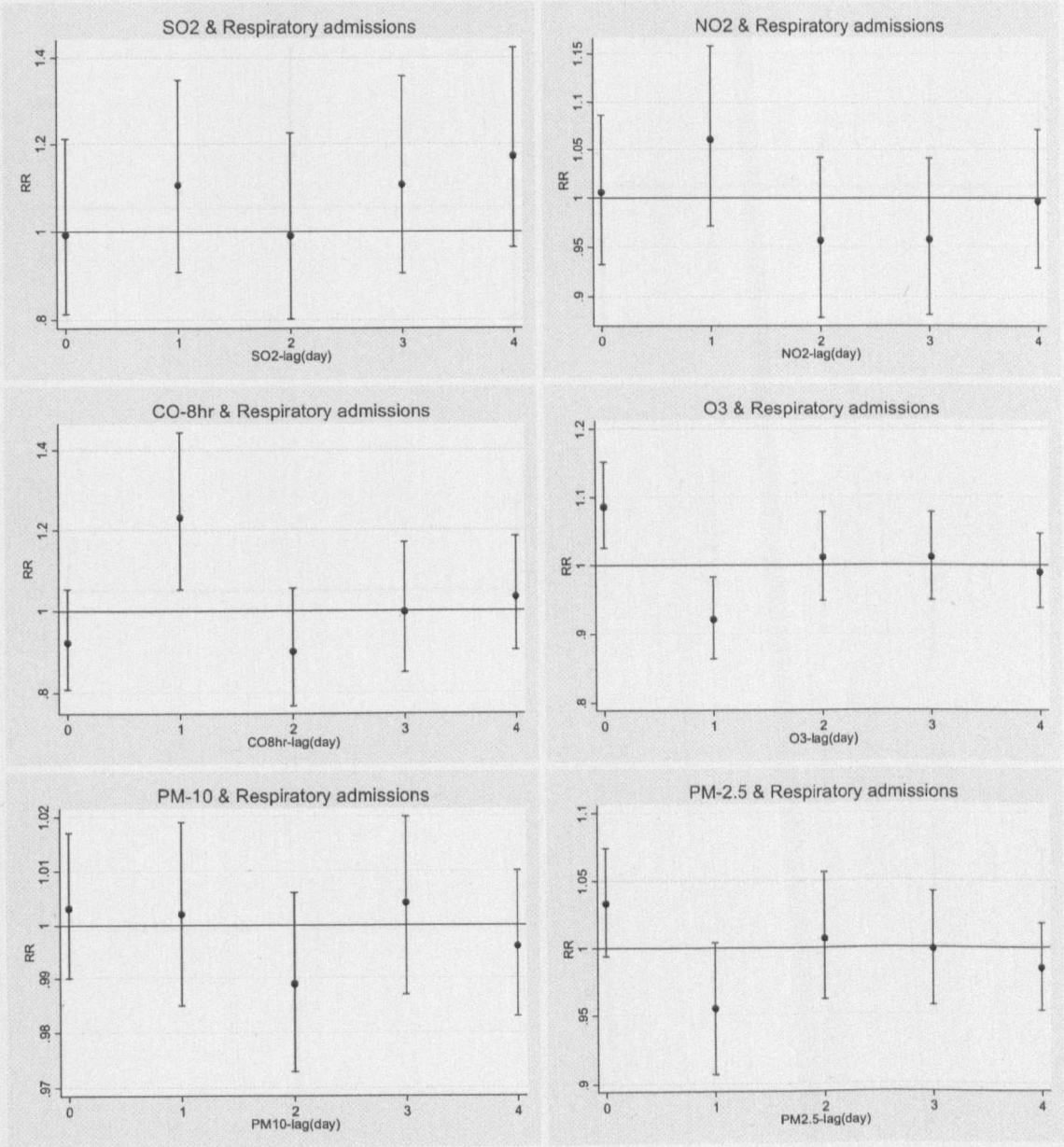


Figure 7. 3 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily circulatory admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

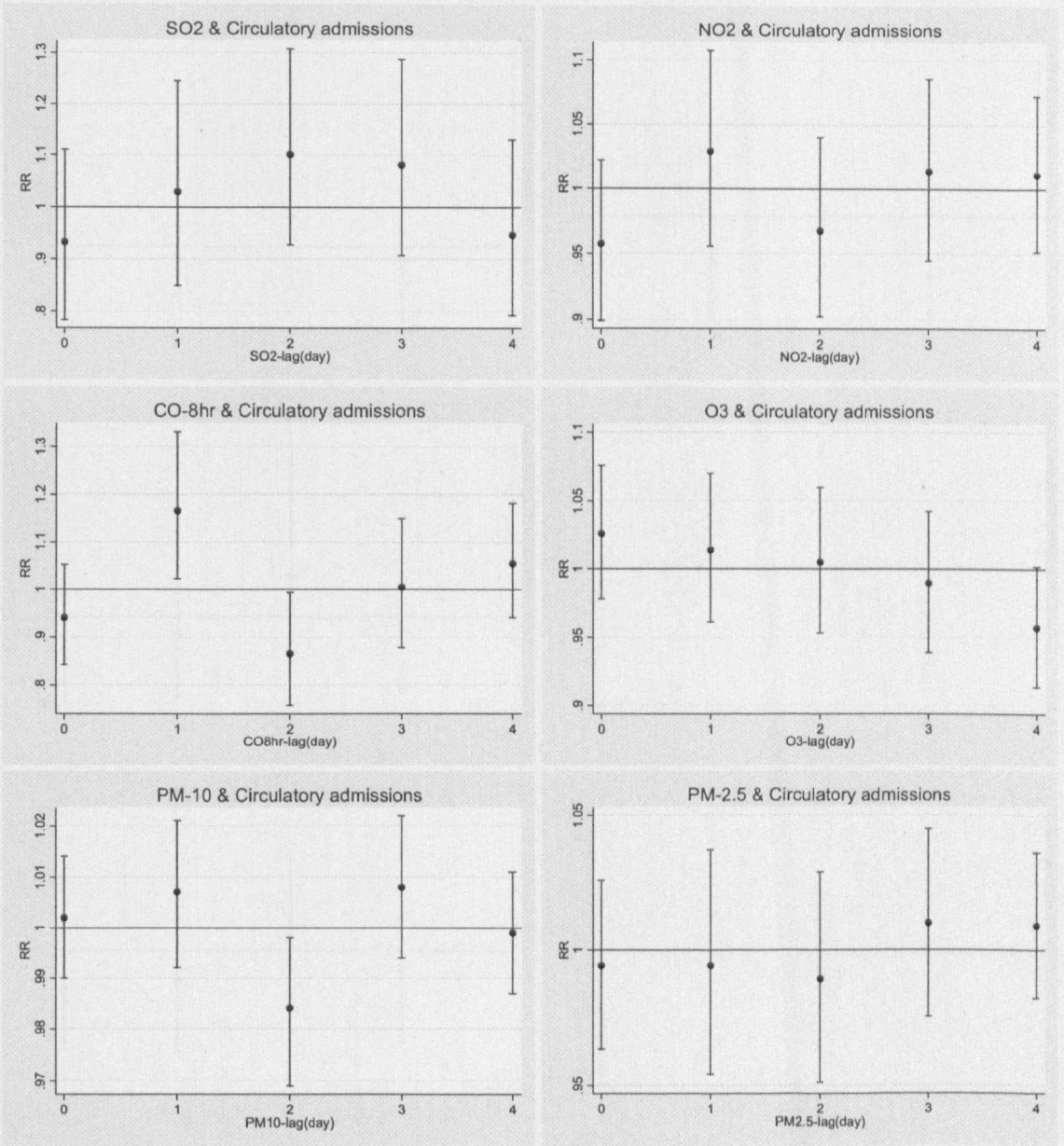


Figure 7. 4 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily diabetic admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

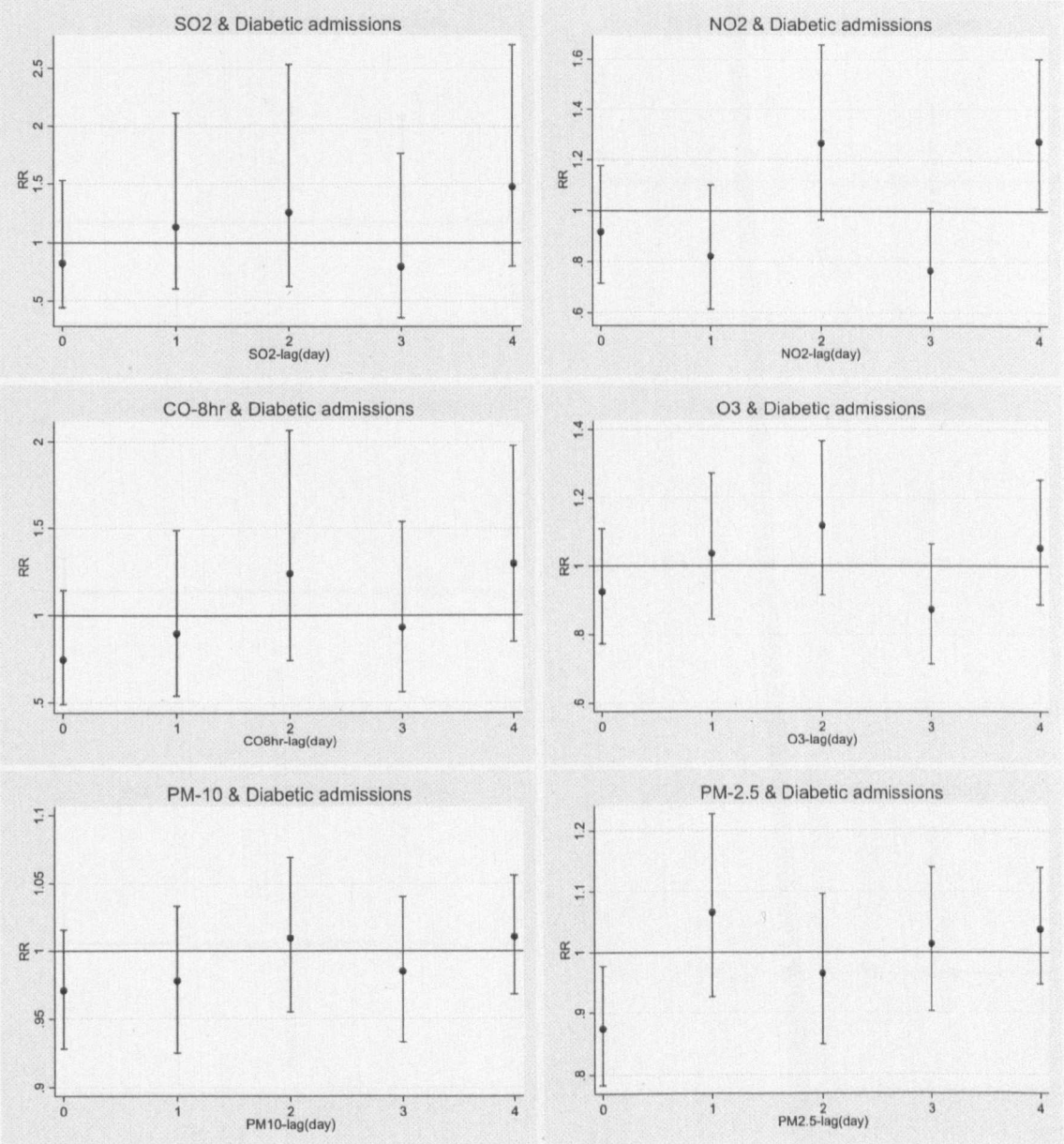


Figure 7. 5 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily intestinal infectious admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

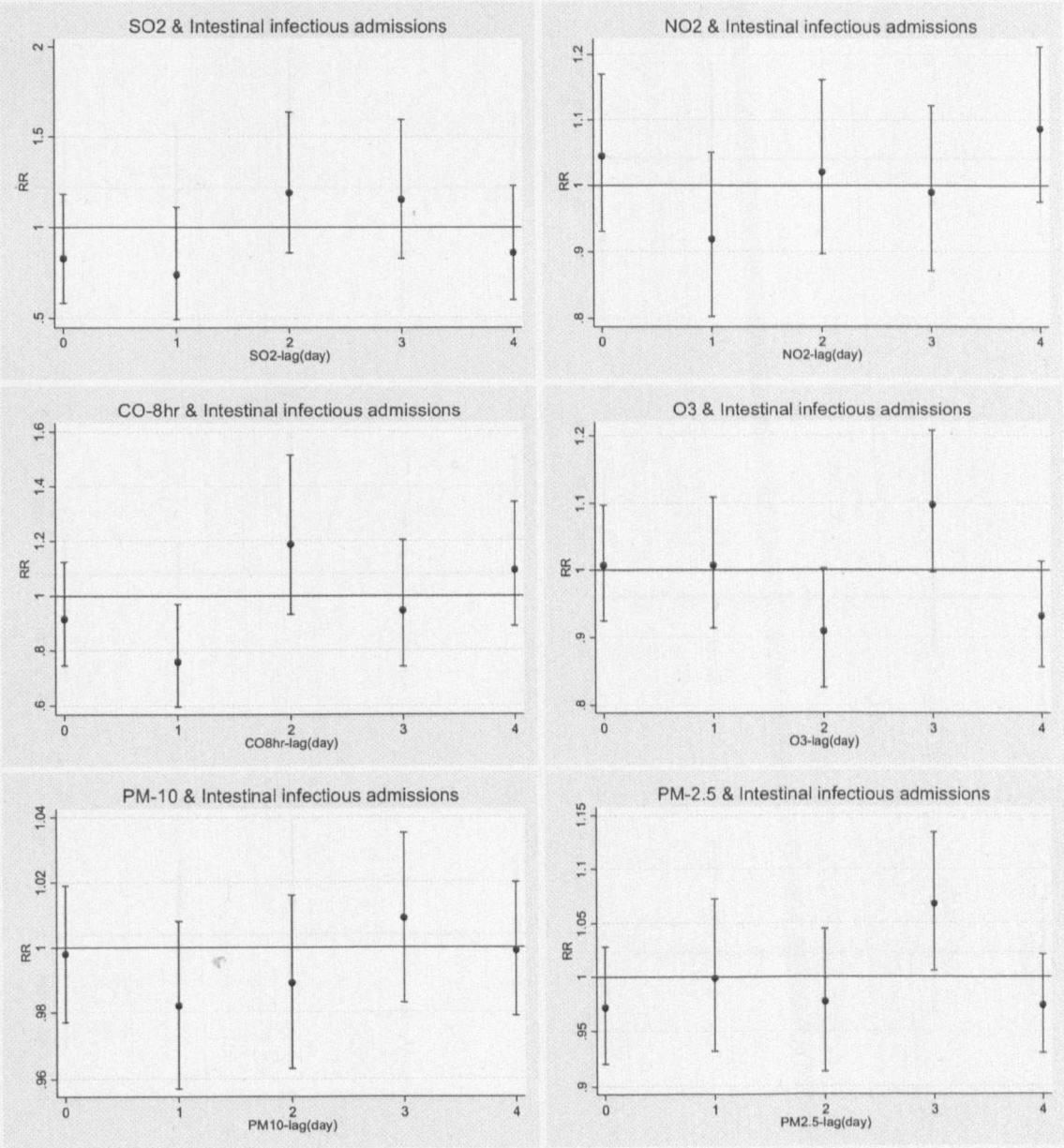


Figure 7. 6 Risk estimates for single pollutant models for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) in different lags (0-4 days) on daily other admissions among all people in Muang, Chiang Mai, from October 2002 to September 2006.

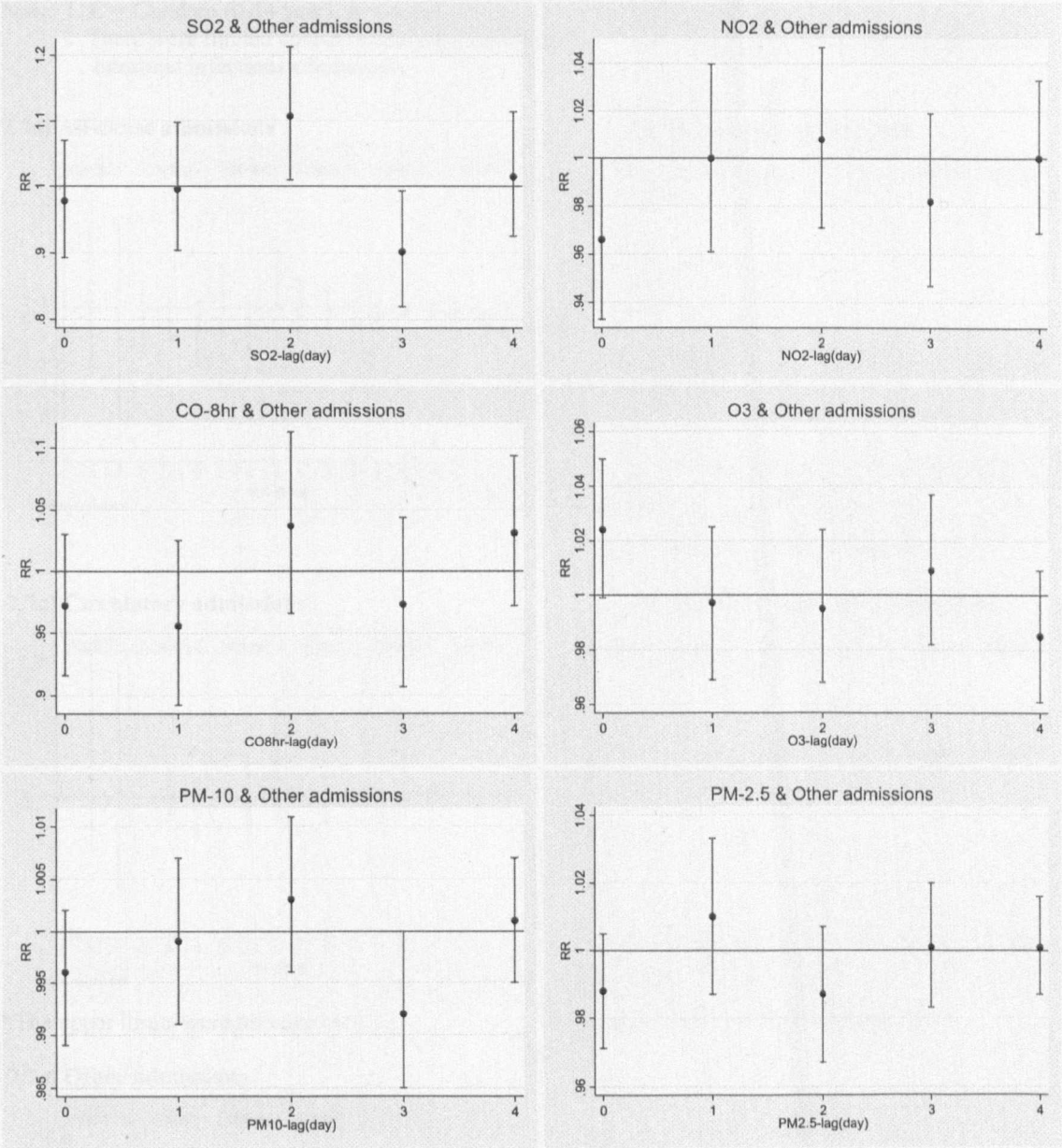
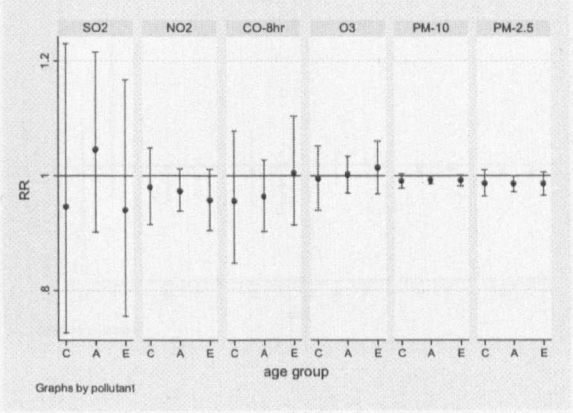


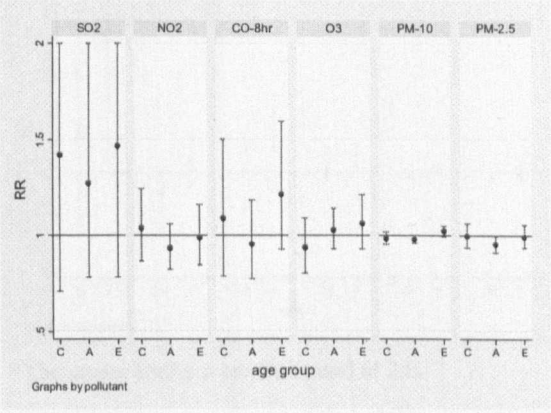
Figure 7. 7 Risk estimates of for single pollutant, distributed lag models (0-4days) for a 10-unit increase of a pollutant (one unit increase for CO) on daily hospital admissions in different age groups in Muang, Chiang Mai, from October 2002 to September 2006.

Note: 1. **C** = Children (0-14 year), **A** = Adult (15-64 year), **E** = Elderly (≥ 65 year)
2. There were limited counts to analyze in children for circulatory admissions, and in the elderly for intestinal infectious admissions.

7.7a) All-cause admissions

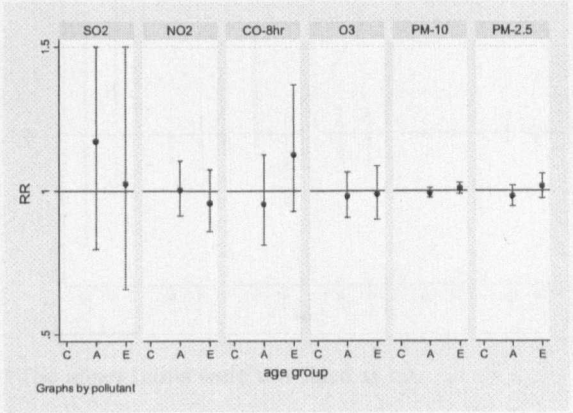


7.7b) Respiratory admissions



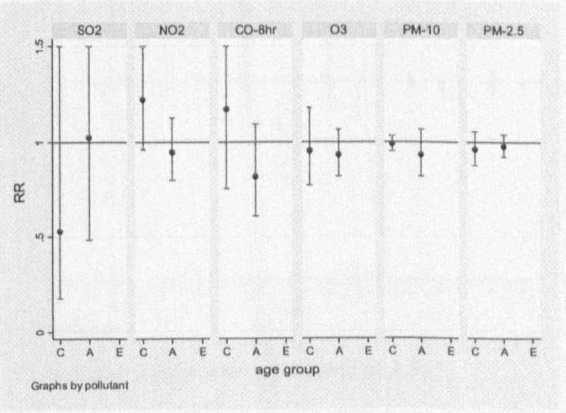
*The upper limits were truncated at 2.0.

7.7c) Circulatory admissions



*The upper limits were truncated at 1.5.

7.7d) Intestinal infectious admissions



*The upper limits were truncated at 1.5.

7.7e) Other admissions

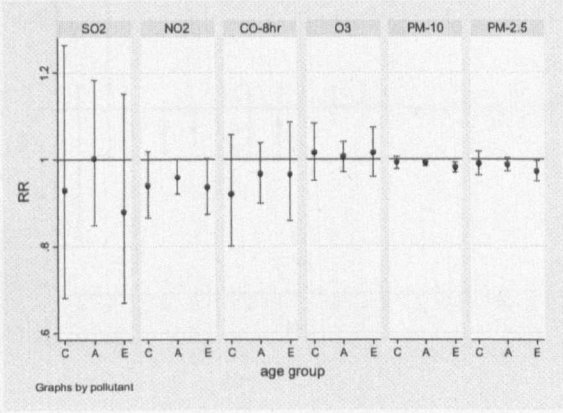
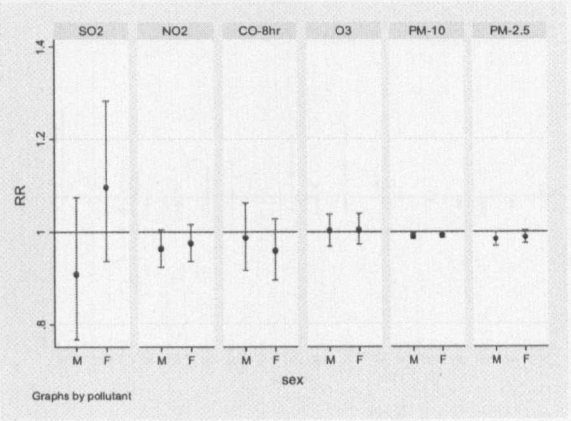


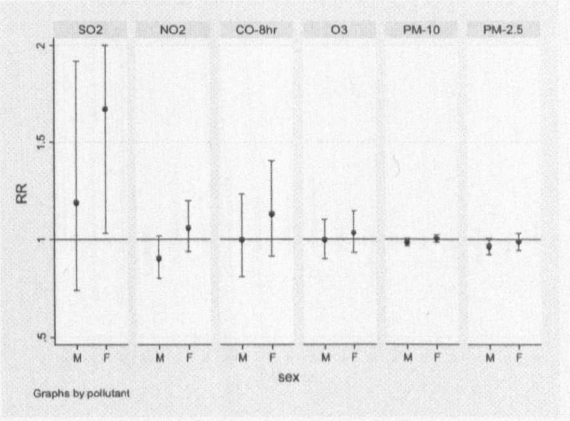
Figure 7. 8 Risk estimates of for single pollutant, distributed lag models (0-4days) for a 10-unit increase of a pollutant (one unit increase for CO) on daily hospital admissions in males and females in Muang, Chiang Mai, from October 2002 to September 2006.

Note: M = Male, **F** = Female

7.8a) All-cause admissions

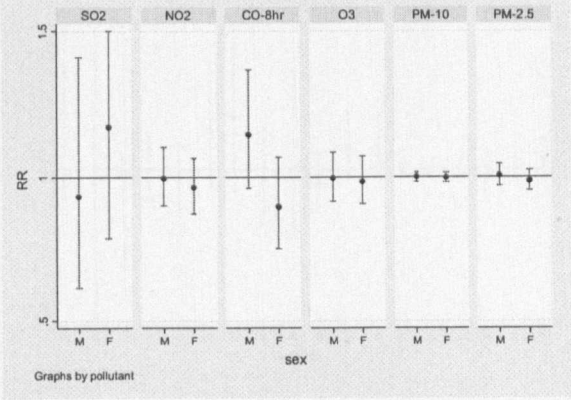


7.8b) Respiratory admissions



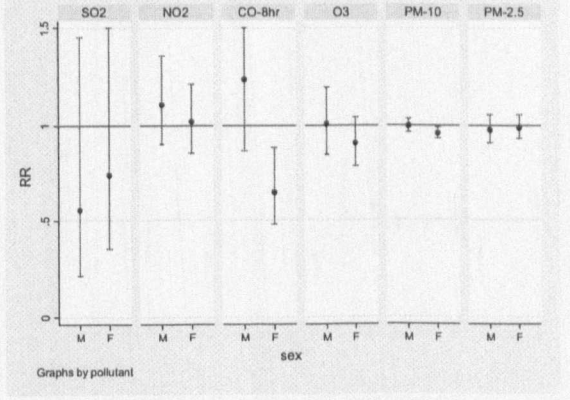
*The upper limits were truncated at 2.0.

7.8c) Circulatory admissions



*The upper limits were truncated at 1.5.

7.8d) Intestinal infectious admissions



*The upper limits were truncated at 1.5.

7.8e) Other admissions

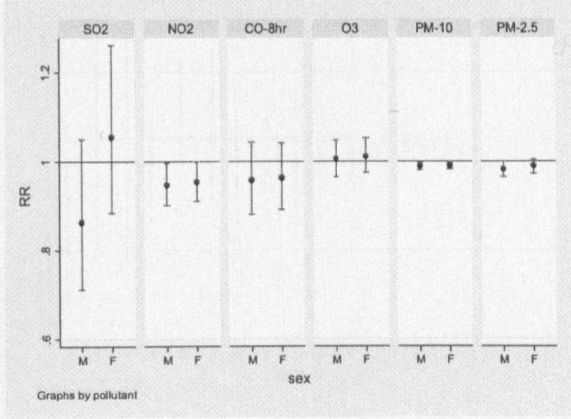
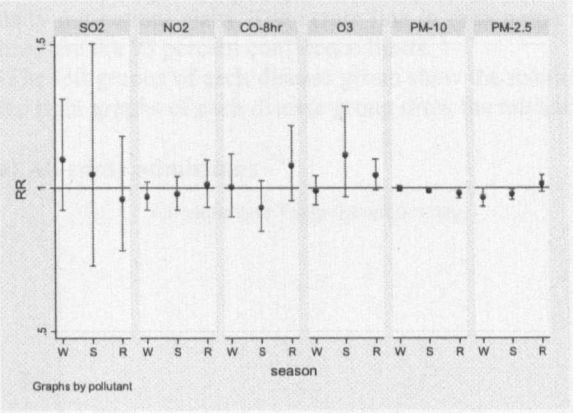


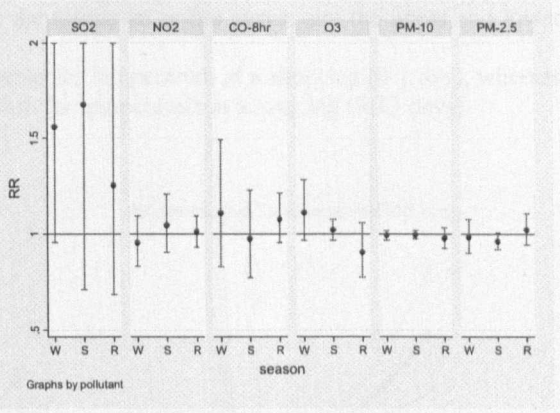
Figure 7. 9 Risk estimates of for single pollutant, distributed lag models (0-4days) for a 10-unit increase of a pollutant (one unit increase for CO) on daily hospital admissions in different seasons in Muang, Chiang Mai, from October 2002 to September 2006.

Note: W = Winter, **S** = Summer, **R** = Rainy season

7.9a) All-cause admissions

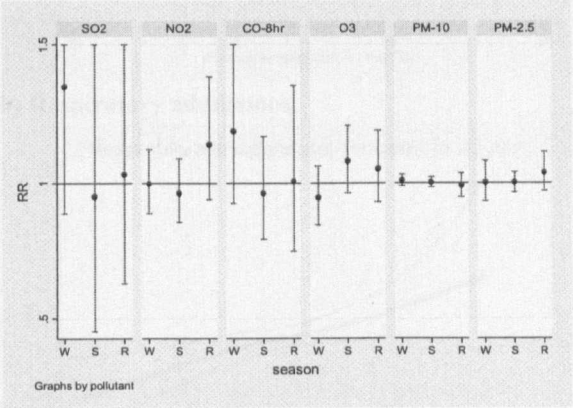


7.9b) Respiratory admissions



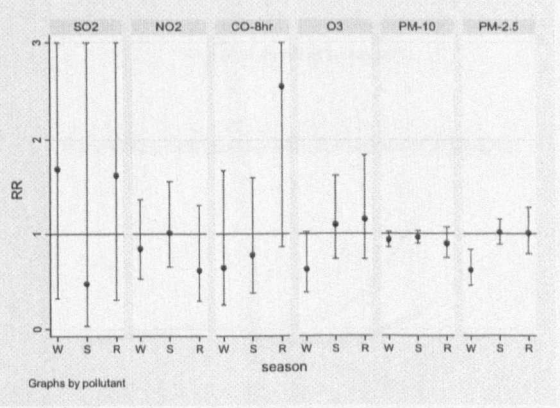
*The upper limits were truncated at 1.5.

7.9c) Circulatory admissions



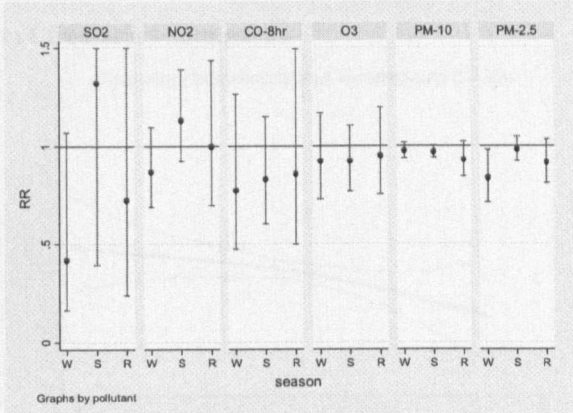
*The upper limits were truncated at 1.5.

7.9d) Diabetic admissions

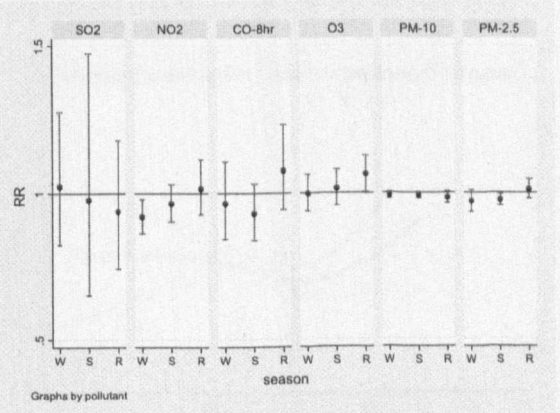


*The upper limits were truncated at 3.0.

7.9e) Intestinal infectious admissions



7.9f) Other admissions



*The upper limits were truncated at 1.5.

Figure 7. 10 General relationship between daily hospital admissions and temperature at both short lag (0-1 day) and long lag (0-13 days) in Muang, Chiang Mai, from October 2002 to September 2006.

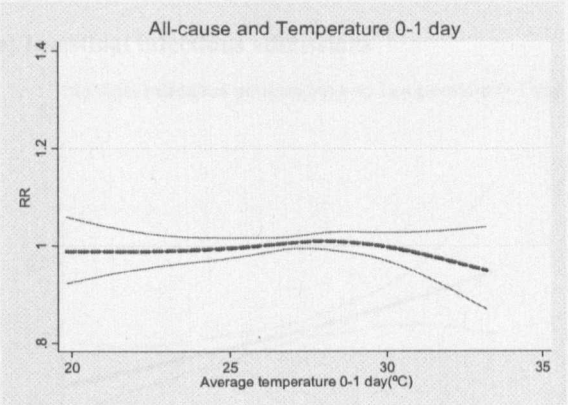
Note:

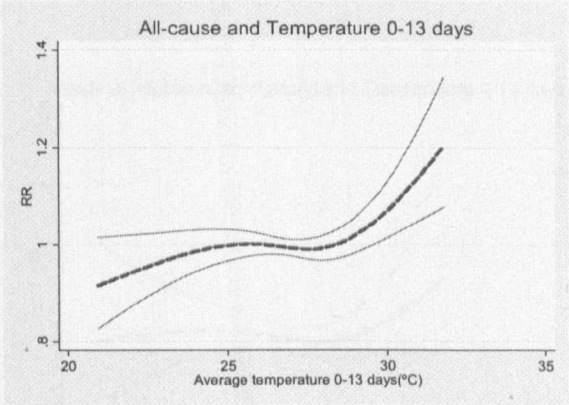
-Relationship between temperature and daily hospital admissions, adjusting for day of the week, holidays, month of the study (1-48), Thai new year, International new year, influenza, AR term at lag 1, humidity, rain, SO_2, and O_3.

-The x-axis represents temperature range (°C), and the y-axis represents the estimated relative risk (RR) of daily out-patient visits. The centre line in each graph is the estimated spline curve, and the upper and lower lines are the 95 percent confidence limits.

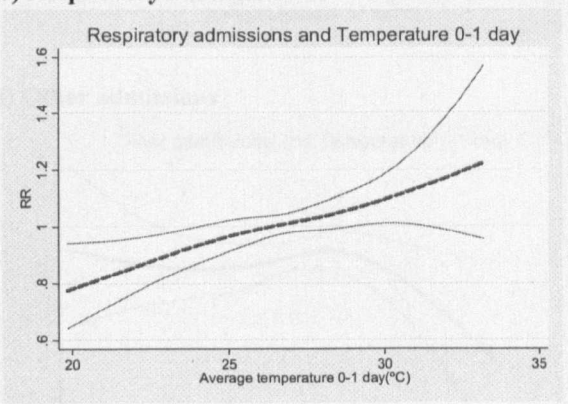
-The left graphs of each disease group show the relationship for temperature at a short lag (0-1 day), whereas the right graphs of each disease group show the relationship for temperature at a long lag (0-13 days).

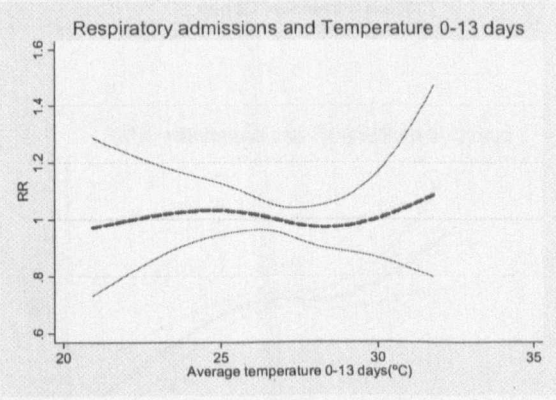
a) All-cause admissions



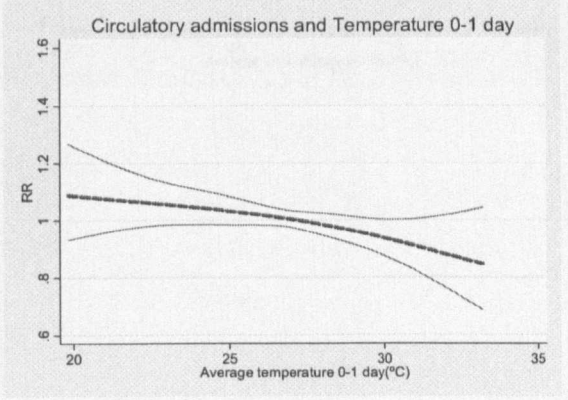


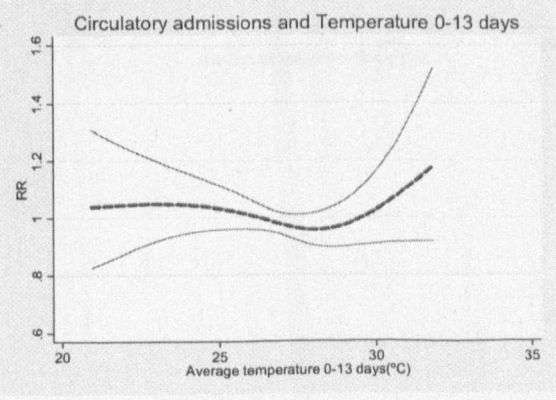
b) Respiratory admissions



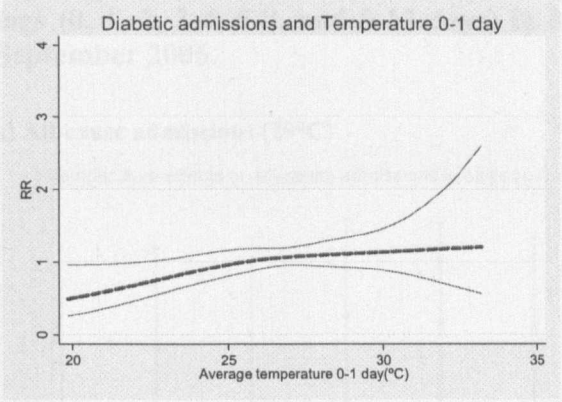


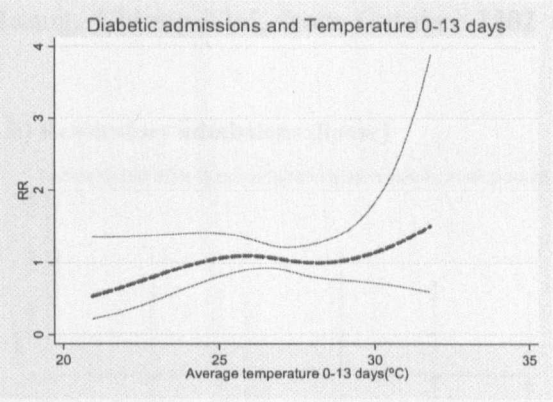
c) Circulatory admissions



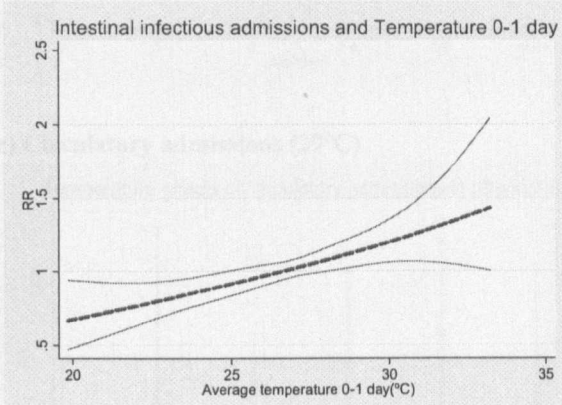


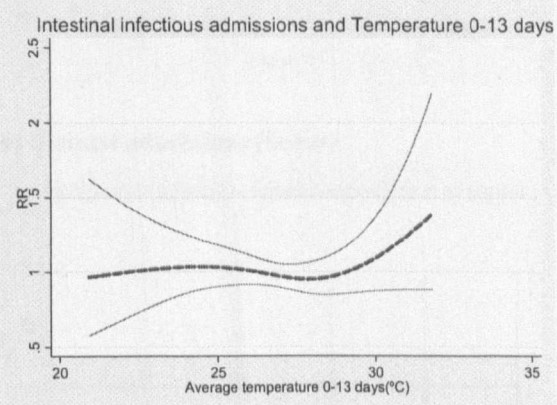
d) Diabetic admissions



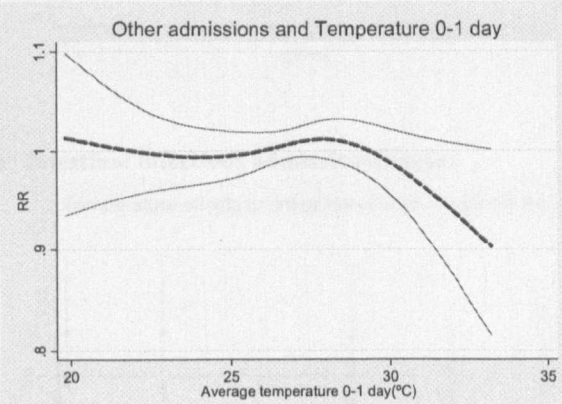


e) Intestinal infectious admissions





f) Other admissions



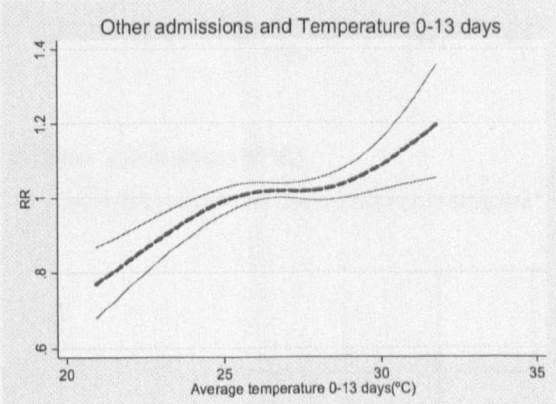
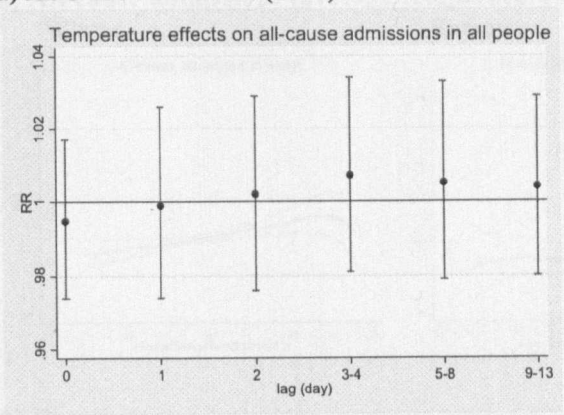
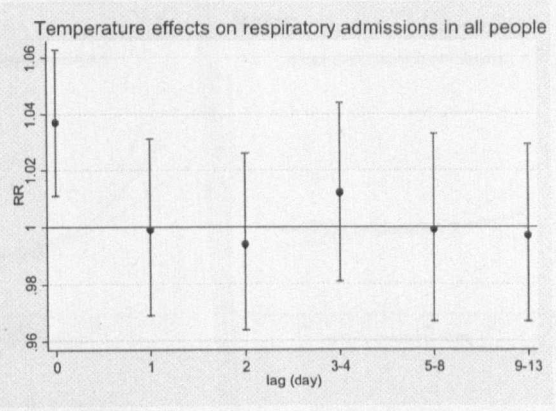


Figure 7. 11 Temperature effects on daily hospital admissions in different specified lags (0, 1, 2, 3-4, 5-8, and 9-13 days) in Muang, Chiang Mai, from October 2002 to September 2006.

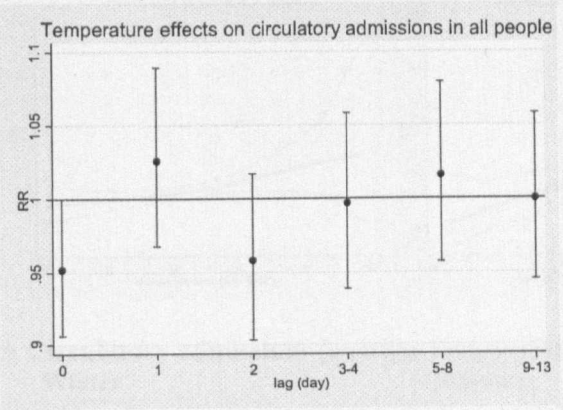
a) All-cause admissions (29°C)



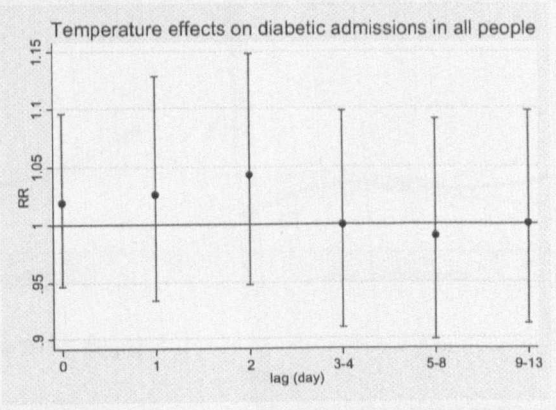
b) Respiratory admissions (linear)



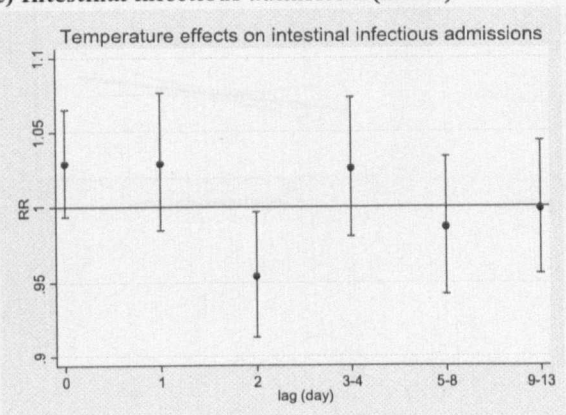
c) Circulatory admissions (29°C)



d) Diabetic admissions (linear)



e) Intestinal infectious admissions(linear)



f) Other admissions (29°C)

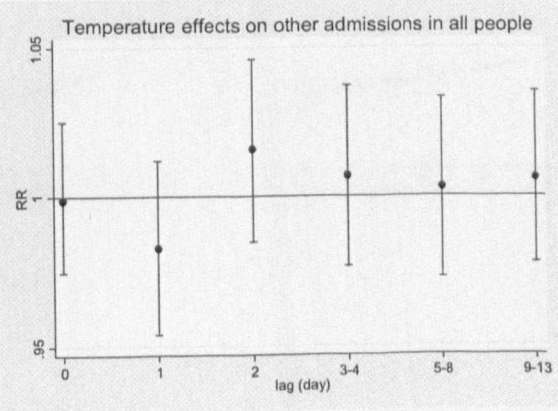
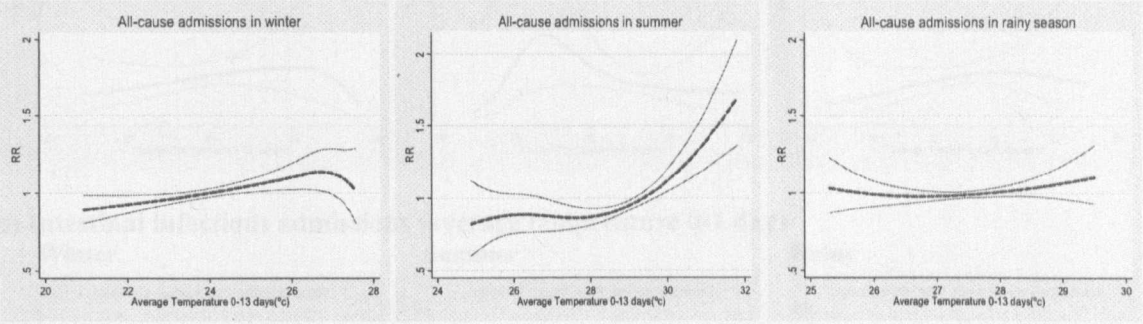


Figure 7. 12 Plots of the general relationships between daily hospital admissions and temperature in different seasons in Muang, Chiang Mai, from October 2002 to September 2006.

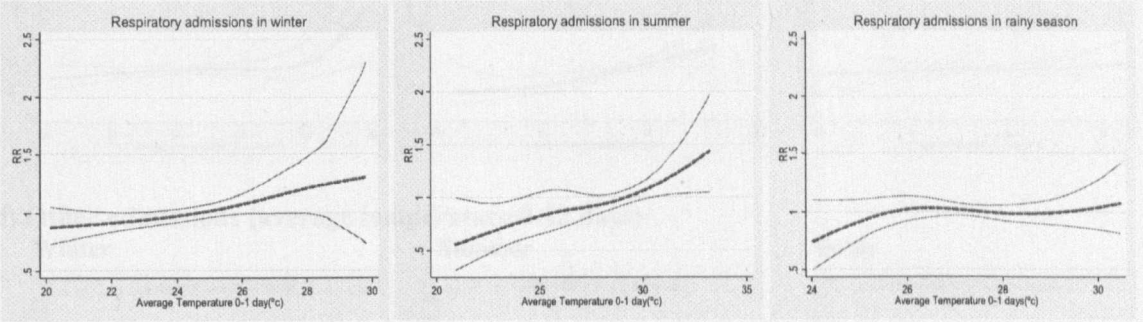
a) All-cause admissions (average temperature 0-13 days)

Winter **Summer** **Rainy**



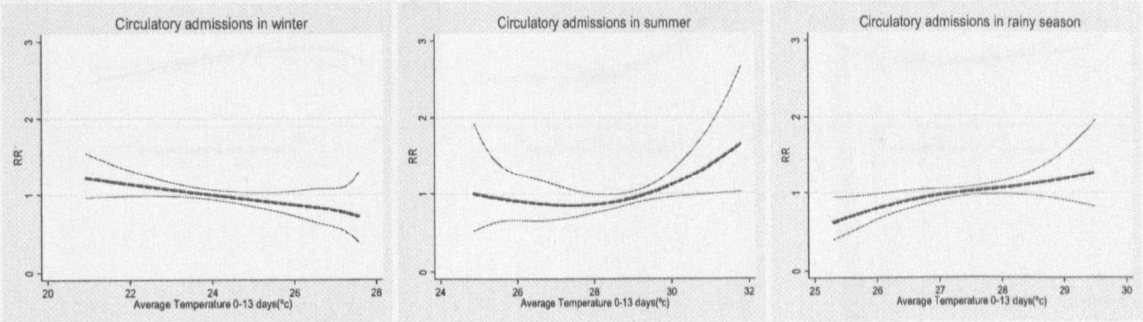
b) Respiratory admissions (average temperature 0-1 day)

Winter **Summer** **Rainy**



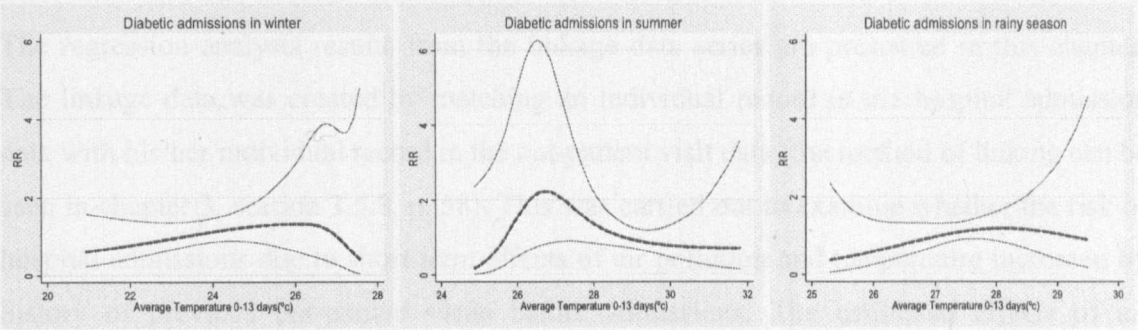
c) Circulatory admissions (average temperature 0-13 days)

Winter **Summer** **Rainy**



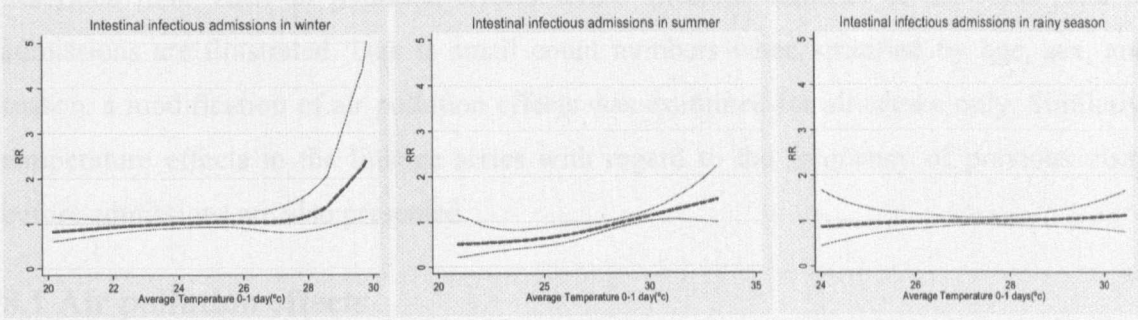
d) Diabetic admissions (average temperature 0-13 days)

Winter **Summer** **Rainy**



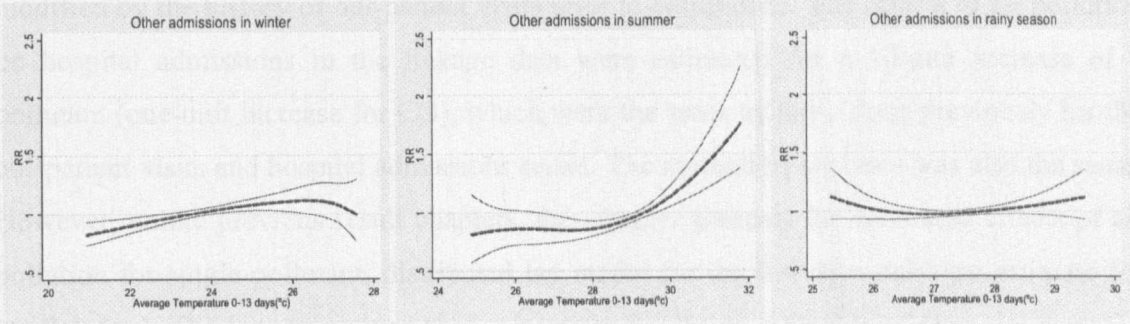
e) Intestinal infectious admissions (average temperature 0-1 day)

Winter **Summer** **Rainy**



f) Other admissions (average temperature 0-13 days)

Winter **Summer** **Rainy**



Chapter 8 Regression results: Linkage data

The regression analysis results from the linkage data series are presented in this chapter. The linkage data was created by matching an individual record in the hospital admission data with his/her individual record in the out-patient visit data (the method of linking can be seen in chapter 3, section 3.5.8, p. 58). This was carried out to examine whether the risk of hospital admissions due to short-term effects of air pollution and temperature increased by history of previous out-patient visits before admissions. The estimated effects of air pollution among people with and without history of previous visits before admissions are described first. Then air pollution effects across different numbers of the visits prior to admissions are illustrated. Due to small count numbers when stratified by age, sex, and season, a modification of air pollution effects was examined for all causes only. Similarly, temperature effects in the linkage series with regard to the frequency of previous visits before admissions are also presented.

8.1 Air pollution effects

The main focus of this section is whether air pollution effects on hospital admissions were modified by the history of out-patient visits prior to admissions. The effects of air pollution on hospital admissions in the linkage data were estimated for a 10-unit increase of a pollutant (one-unit increase for CO), which were the same as those done previously for the out-patient visits and hospital admissions series. The method of analyses was also the same. However, unlike previous result chapters, this chapter presents the estimated effects of air pollution for single pollutant, distributed lag model for lag 0-4 days only (no estimate for lag 0-1 day). The longer lag was chosen because the larger estimates of most pollutants in this study were predominantly found beyond lag 0-1 day (mostly at lag 2-3 days). Additionally, since the main interest was to see whether there was an increased risk with respect to history of previous visits, not about lag effects, looking at one lag period should be sufficient.

8.1.1 Air pollution effects among people with and without history of out-patient visits prior to hospital admissions

This section presents the comparison of the estimated effects of air pollution on hospital admissions among people with and without history of out-patient visits prior to their admissions. The risk of hospital admissions was estimated for all disease groups, except only diabetic admissions, for which numbers were very small (mean of total daily counts = 0.2, SD = 0.5). The risk estimates of air pollution effects on hospital admissions among people with and without history of the visits before admissions for specific disease groups are shown in **Table 8.1-8.5**. By comparison, the stronger effects of air pollution in people with history of the visits before admissions than those in people without history did not show consistently across all diseases. In addition, there were only some pollutants that exhibited significant differences between these two groups.

For all-cause admissions, the finding of more harmful or less protective effects in people with history than people without history was found for most pollutants, except NO_2 and O_3. But there were only SO_2 and CO that exhibited significant differences between the two groups. An increased risk of 25.5% (95% CI, -2.6% to 60.3%) was found in people with history of the visits prior to admissions, while a decreased risk of 49.8% (95% CI, -78.1% to 14.6%) was found in people without history in association with a 10-unit increase in SO_2 (ppb). According to the test for interaction, this difference was significant (p-value = 0.039). Although the negative effects of CO were found for both groups, people without history of the visits had higher protective effects (35.1% decrease, 95% CI, -52.5% to -11.4%) than people with history (8.7% decrease, 95% CI, -18.0% to 1.6%) per one-unit increase of CO (ppm). This difference was also significant (p-value = 0.042).

For respiratory admissions, the finding of more harmful effects in people with history than people without history was found for all pollutants, although the differences between the two groups were not statistically significant at 5% level. Similar finding was seen for circulatory admissions, with only one exception – O_3 effects (which were positive in people without history, but negative in people with history). There was a borderline significance between the two groups found for $PM_{2.5}$ effects on circulatory admissions (p-value = 0.057).

In contrast to other disease groups, for intestinal infectious admissions, there were harmful effects in people without history, but protective effects in people with history found for SO_2 and CO, whereas there was an opposite direction of this pattern found for the rest of the pollutants. However, none of the estimated effects were significant, and also no significant differences in the estimated effects between the two groups were observed.

For 'other' admissions, the patterns of air pollution effects were found to be similar to all-cause admissions, particularly for SO_2 and CO effects, which exhibited more harmful or less protective effects in people with history than in people without history. The differences in SO_2 and CO effects between the two groups were also significant. However, the opposite direction of the effects (less harmful or more protective) was observed for some other pollutants. However, there was only one borderline significance between the two groups, which was found for NO_2 effects (p-value = 0.059).

To sum up, there was no evidence of an increased effect of air pollution in people with history of out-patient visits prior to admissions compared to that in people without history as this pattern was not consistent across the studied pollutants or diseases. Approximately, there were about half of the estimates followed this pattern, while there were about half of the estimates showed the opposite direction of this pattern.

8.1.2 Do air pollution effects differ in accordance with the numbers of out-patient visits prior to hospital admissions?

Besides looking at the overall effects of air pollution on hospital admissions in people with and without history of the visits prior to admissions, the visits were also broken down into different group numbers (1, 2-5, and >5 visits) in order to see whether there were any changes of air pollution effects across these subgroups. The '0 visit' group, representing the admissions without history of the visits prior to admissions, was kept as a baseline for comparison. The effects of air pollution in each subgroup were examined first. Then, test for trends of air pollution effects across the numbers of previous visits before admissions was undertaken (see analytical methods in chapter 3, p. 64). Like all previous analyses, the quantification of air pollution effects in each subgroup as well as the test for trends of air pollution effects were done for a 10-unit increase of all pollutants, but one-unit increase of CO.

Figure 8.1 presents the plots of the estimated effects of each pollutant on hospital admissions across different group numbers of previous visits before admissions. As can be seen, SO_2 exhibited an increasing pattern of the effects with increasing number of the out-patient visits prior to admissions for most diseases, except for respiratory and intestinal infectious admissions. The relative risk of this increasing trend (though not significant) is shown in **Table 8.7.** For example, there was an increase in all-cause admissions of 13.0% (95% CI, -9.0% to 42.0%) for a 10- unit increase in SO_2 (ppb) per visit-category.

The somewhat increase in air pollution effects across the history of the visits was also found for some other pollutants, such as the effects of CO and PM_{10} on all-cause, respiratory, and 'other' admissions, but the effects did not always increase steadily with increasing number of previous visits. The results of tests for trends (**Table 8.7**) showed an increased risk of 2.0% (all-cause), 7.0% (respiratory), and 4.0% (other) for one-unit increase of CO (ppm) per visit-category, but no trend for PM_{10}. However, none of the tests were statistically significant.

As shown in **Figure 8.1**, a decrease in O_3 effects across the group numbers of previous visits was shown for circulatory admissions, whereas a somewhat increase in O_3 effects across the visit groups was seen for respiratory admissions. This corresponds to the estimated trends (**Table 8.7**). There was a reduction of 6.0% (95% CI, -17.0% to 8.0%) for circulatory admissions and a small increase of 2.0% (95% CI, -11.0% to 17.0%) for respiratory admissions in association with a 10-unit increase in O_3 (ppb) per visit-category, but not statistically significant.

In brief, when looking at air pollution effects across the numbers of out-patient visits before admissions, an increase in the effects with increasing numbers of the visits was more apparent for SO_2 than for other pollutants. On the contrary to SO_2, the apparent decreasing effects with increasing number of the visits were found for O_3, but for circulatory admissions only.

8.1.3 Are air pollution effects with respect to the history of out-patient visits before admissions modified by the factors like age, sex or season?

The effect modification of air pollution across the numbers of out-patient visits prior to admissions by age, sex, and season were also examined because it might be possible that these factors had some influence on the frequency of the visits of a patient (e.g. the elderly may visit a hospital more often than other age groups, the daily visits to a hospital may be inhibited by rain or too hot/cold weather in different season). Since there were large numbers of missing information of occupation (>30% missing), the modified effects by occupation were not undertaken for the linkage series. Due to the problem of very limited counts of most diseases across the group numbers of previous visits before admissions when stratified by age, sex, and season, resulting in very imprecise estimates, it was decided to present the analysis results for all-cause admissions only.

Effect modification by age

Overall, there was some evidence of effect modification by age, which can be seen in **Figure 8.2.** Even though, there is no apparent increase or decrease in estimated effects of most pollutants across the visit groups, the effects of some pollutants across the visits between age groups were found to be different. For example, there was a J-shaped pattern of NO_2 effects across the visit groups in children, with stronger, positive effects in '0 visit' and '>5 visits' groups, and a small negative effect in '1 visit' group. However, all of NO_2 effects across the visits in adults and the elderly were negative with a somewhat small decreasing trend with increasing numbers of previous visits.

According to tests for trends, some differences in air pollution effects across the visit groups between age groups were also observed. For examples, there was a somewhat increasing trend of SO_2 effects in all age groups, and the relative risk of this trend was also found in all age groups (**Table 8.7**). The risk associated with a 10-unit increase in SO_2 (ppb) per visit-category was greater in the elderly (28.0% increase) than in children (19.0% increase) and adults (11.0% increase). In contrast, the weakest increasing trend per one-unit increase in CO (ppm) for each visit-category was seen in adults (1.0% increase), compared to children (9.0% increase) and the elderly (6.0% increase). Notably, tests for heterogeneity

of the estimated trends across the visits between age groups were also undertaken, but none of the tests were significant at 5% levels (results not shown).

Effect modification by sex

The plots of estimated effects of air pollution across the numbers of the visits prior to admissions when stratified by sex are illustrated in **Figure 8.3**. Overall, there was no evidence of the effect modification by sex as the effects of most pollutants across the visit groups in males and females were broadly the same. There were also no significant differences in the estimated trends between males and females for all pollutants (**Table 8.7**).

Effect modification by season

Figure 8.4 presents the estimated effects of air pollution across the group numbers of the visits prior to the admissions for all seasons (winter, summer, and rainy). In general, there was some evidence of a modification of air pollution effects by season as the effects of each pollutant across the visit groups varied across seasons. For instance, there was a somewhat increase in the effects of SO_2 and CO across the visit groups in summer and rainy seasons, while there was no obvious increase or decrease in the effects of the two pollutants across the visit groups in winter. This corresponds to the estimated trends of these two pollutants across the visit groups illustrated in **Table 8.7**. There were however no significant differences in the estimated trends across the visit groups for all pollutants.

8.2 Temperature effects

This section describes temperature effects on hospital admissions in the linkage series. Similar to air pollution effects, the estimated effects of temperature were explored for hospital admissions in both people with and without history of out-patient visits prior to their admissions. Then, temperature effects across the group numbers of previous visits before admissions were investigated. To see whether temperature effects across the group numbers of previous visits were modified by age, sex, and season, the data analyses when stratified by these factors were also undertaken.

8.2.1 Temperature effects among people with and without history of out-patient visits prior to hospital admissions

According to graphical assessments (**Appendix 8A, Figure 8A-1**), the temperature threshold of 29°C was used for quantifying temperature effects (lag 0-13 days) on all-cause, circulatory and 'other' admissions, and a linear term of temperature was used for quantifying temperature effects (lag 0-1 day) on respiratory and intestinal infectious admissions. There was no investigation of temperature effects on diabetic admissions due to the very limited counts of diabetic admissions in the linkage data.

The risk estimates of temperature effects on hospital admissions in people with and without history of out-patient visits prior to admissions are shown in **Table 8.6**. Opposite to air pollution effects, the overall effects of temperature were found to be stronger in people without history of previous visits before admissions compared to people with history. There was only one exception, the estimated effects on circulatory admissions. However, none of the estimates reached the statistical significance at 5% level, and also no significant difference in the estimates between the two groups. For each 1°C increase in temperature, there was an increase in hospital admissions in people without history of the visits, ranging from 4.5% (respiratory) to 33.7% (other), while there was a smaller increase in people with history, ranging from 3.8% (all-cause) to 9.7% (intestinal infectious). In contrast to other disease groups, for circulatory admissions, the protective effect was found for people with no history (13.6% decrease), whereas the harmful effect was found for people with history (5.3% increase) per 1°C increase in temperature above 29°C.

8.2.2 Do temperature effects differ in accordance with the numbers of out-patient visits prior to hospital admissions?

Figure 8.5 presents the estimated effects of temperature across the numbers of previous out-patient visits before admissions. There was generally no apparent increase or decrease in temperature effects across the number of previous visits in association with each 1°C increase in temperature (relative to the identified temperature threshold) for all diseases. According to tests for trends shown in **Table 8.8**, there was no statistical significance in the estimated trends of temperature effects across the visit groups for all diseases.

8.2.3 Are temperature effects with respect to the history of out-patient visits prior to the admissions modified by factors like age sex, and season?

The effect modification of temperature effects by age, sex, and season with respect to the group numbers of out-patient visits prior to admissions are illustrated in this section for all-cause, respiratory, circulatory, and 'other' admissions. No stratified analysis for intestinal infectious admissions across the groups was carried out because of very small counts of this disease.

I. Effect modification by age

There was little evidence of effect modification by age across the numbers of previous visits before admissions as shown in **Figure 8.6**. Since the estimates could not be done for all visit categories in each age group, it is difficult to describe the effect modification by age here. Nevertheless, the pattern of temperature effects across the visits in children was seen to differ from those in adults and the elderly. For example, the temperature effects on 'other' admissions across the visits in children (0-14 years) were fluctuated and negative, while the effects across the visits in adults and the elderly were fairly stable and positive. There seemed to be an increasing pattern of temperature effects across the visits in children for respiratory admissions, but no clear pattern was observed in adults and the elderly due to inability to analyze for the estimated effects for these people in some visits groups.

When looking at the estimated trends of temperature effects across the visit groups (**Table 8.8**), there was only a small increase or decrease in the estimated trends across the visit

groups and none of them were significant. There were also no significant differences in the estimated trends between age groups.

II. Effect modification by sex

Figure 8.7 presents the estimated effects of temperature across the number of out-patient visits prior to admissions between males and females. Overall, there was no evidence of modification of temperature effects by sex as the effects across the visit groups in males and females were broadly similar for most diseases. This was consistent with the results from tests for trend (**Table 8.8**), which showed similar trends of the effects across the visit groups in males and females, except for circulatory admissions. For each 1°C increase in temperature per visit-category, there was a decrease in circulatory admissions of about 6.0% in males, whereas there was an increase in circulatory admissions of about 4.0% in females. These estimates were however very imprecise with very wide confidence intervals. There were also no significant differences in the estimated trends across the visit groups between males and females for all diseases.

III. Effect modification by season

Based on graphical visualization of the general relationships between temperature and the studied health outcomes (see **Appendix 8A, Figure 8A-2**), a linear association was assumed for all seasons. Therefore, linear terms of temperature were used for quantifying temperature effects across seasons for all diseases.

The estimated effects of temperature across the visit groups when stratified by season are presented in **Figure 8.8**. There were only two diseases (all-cause and 'other' admissions) that the effects across the visits group could be estimated for all seasons. Overall, there was little evidence of modification of temperature effects by season as the patterns of temperature effects across the visit groups in each season were slightly different. For example, for all-cause admissions, the somewhat downward patterns of the effects across the visit groups was visible in summer, but no clear patterns were shown in winter and rainy season. However, according to the estimated trends of temperature effects across the visit groups in different seasons shown in **Table 8.9**, there was a decreasing trend of the effects for all-cause admissions in all seasons (although a relatively large reduction was

shown in summer). In general, none of the estimated trends were statistically significant at 5% level, and no significant differences in the trends between seasons were found.

8.3 Sensitivity analyses for the linkage series

8.3.1 Linked period

In the present study, the 6-month period was chosen to assess whether the history of out-patient visits of a patient within a 6-month period prior to the admissions would have increased their vulnerability to air pollution and temperature exposure. Thus, the use of different time periods to obtain the count numbers of out-patient visits prior to admissions was explored to see whether it had different impacts on the findings. It was decided to choose 3 months for a shorter period and 12 months for a longer period to compare with the 6-month period already used in this study.

The overall time period used for the sensitivity analyses was restricted to be between October 2003 and January 2006. This was because the out-patient visit data began from October 2002, and therefore the history of out-patient visits for a 12-month period prior to admissions could be obtained for all patients (if they had the history) admitted from October 2003. Additionally, due to a dramatic drop of the linkage data from February to September 2006 (month 41th-48th, see descriptive result, section 5.3, p. 85), the linkage data created for the sensitivity tests for all time scales were also excluded month 41th-48th. The sensitivity analyses were undertaken for all-cause admissions only. The sensitivity tests showed that, when using different time period to obtain the linkage data, there were generally little changes in the patterns of air pollution and temperature effects across the number of the history of visits prior to the admissions, which can be seen in **Appendix 8B**.

For air pollution, according to the plots of estimated effects (**Figure 8B-1**), the differences in the patterns of air pollution effects across the visit groups when using different time period were visible for O_3 only. It was found that O_3 effects exhibited a decreasing pattern across the visit groups for the use of a shorter period (3 months), but no increasing or decreasing pattern for the use of longer periods (6 and 12 months). However, overall, there were no significant differences in the estimated trends of O_3 effects across the visit groups (**Table 8B-1**). The positive trend found for SO_2 effects was slightly larger when using a

shorter period to obtain the linkage data, while the trends found for other pollutants were the same for all time periods used to obtain the linkage data.

For temperature, no apparent upward or downward pattern was visible from the plots of the effects across the visit groups (**Figure 8B-2**). However, a positive trend of temperature effects was found when using a shorter period (3 months), whereas negative trends were found when using longer periods (6 and 12 months), which can be seen in **Table 8B-2**.

Based on this result, the use of a shorter period, which comprised more recent visits, seemed to provide stronger effects of both air pollution and temperature. These differences were however not statistically significant.

8.3.2 Inclusion of unmatched hospital admission cases in the linkage data

As mentioned previously, for Thai hospital system, all patients need to visit an out-patient department for preliminary investigations before admission to hospital. Therefore, health records of out-patient visits and hospital admissions on the same day generally presents in the two data sets. In other words, each hospital admission case should have at least one out-patient visit recorded on the same date of the admission (if there is no missing record).

In this study, it was decided that all out-patient visits recorded on the same day of the admission were not counted as a history of the visits prior to that admission. But the hospital admission that had only one record of out-patient visit, which occurred on the same day of the admission, was kept for the analysis in the linkage series as a hospitalized patient with no history of the visits prior to his/her admission (because this person had no previous visits before his/her admission date). Meanwhile, all hospital admissions that could not be matched with out-patient data or did not have any records in the out-patient visit data were excluded from the analysis.

Due to the problems with missing data and/or errors in inputting information in routine health records in both hospital admission and out-patient visit data sets, it was a concern whether all hospitalized people in this study truly had one out-patient visit when there was one record (occurring on the same date of admissions) presented the out-patient data set, or whether they actually had several out-patient visits before admissions (but those records

were missing and/or errors inputting information). This could result in unmatched cases when linking the two data sets for the linkage series. There was however nothing could be done to address this common problem of the data.

Nevertheless, for the '0 visit' group, it might be possible to assume that all hospital admissions, which could not be matched with the out-patient visit data, had their own "one previous out-patient visit" on the same date of their admissions in the out-patient visit data (but those records were just missing and/or errors). In this case, the unmatched hospital admission cases (which were excluded in this study) could also be counted as people with '0 visit' or no history of the visits prior to admissions and retained for the analyses.

To see whether an inclusion of the hospital admissions, which could not be matched with out-patient visit data, as people with '0' visits would have an impact on the linkage results, sensitivity tests were carried out to compare the patterns of air pollution and temperature effects across the group numbers of out-patient visits between two data sets:

1. the data used in this study – excluded all unmatched hospital admission cases and counted the matched cases that had only one record on the same date of admissions in out-patient data as people with no history of previous visits, and

2. the data that kept all unmatched hospital admissions cases by counting these admissions with no records presented in out-patient data, as people with no history of the visits – presumably, their out-patient records on the same date of admissions were missing.

Similar to the previous analyses, sensitivity tests for both air pollution and temperature effects in this section were undertaken for all-cause admissions only. The sensitivity analyses showed that the patterns of air pollution and temperature effects between the two data sets were broadly the same, which can be seen in **Appendix 8B**.

For air pollution, the plots of the patterns of air pollution effects across the visit groups were broadly similar for all pollutants (**Figure 8B-3**), but small differences were found from tests for trends (**Table 8B-3**). For example, there was a slightly larger positive trend for SO_2 effects for the 'matched cases only' data (13.0% increase for each 10-ppb increase

in SO_2 per visit-category, 95% CI, -10.0% to 42.0%) compared to 'both unmatched and matched cases' data (10.0% increase for each 10-ppb increase in SO_2 per visit-category, 95% CI, -5.0% to 27.0%).

For temperature, the plots of its patterns across the visit groups were similar for both data sets (**Figure 8B-4**). There was a contrasting pattern of the estimated trends across the visit groups between these two data sets (**Table 8B-4**). The small, decreasing trend of all-cause admissions of 0.7% (95% CI, -8.9% to 8.2%) for each 1°C increase in temperature (>29°C) per visit-category was found for the 'matched cases only' data, whereas the small, increasing trend of all-cause admissions of 0.8% (95% CI, -5.3% to7.3%) was found for the 'both unmatched and matched cases' data. This difference was however not significant.

Summary of the linkage series:

Air pollution effects

- There was no consistent evidence of an increased effect of air pollution in people with a history of out-patient visits before admissions in comparison to people without history.
- When looking at air pollution effects across the group numbers of out-patient visits prior to admissions, an increased effect of air pollution with increasing number of the visits was mostly found for SO_2, whereas no apparent increasing or decreasing effects across the visit groups was found for other pollutants. The tests for trends of air pollution effects across the visit groups were generally consistent with the estimated effects. However, none of the tests reached statistical significance at 5% level.
- There was little evidence of the effect modification of air pollution across the history of the visits by age, sex, and season. The different patterns of air pollution effects across the visit groups with respect to age, sex, and season were present for all pollutants, but the shape of the patterns varied from pollutant to pollutant. There were however no statistically significant differences in estimated trends across the visits between subgroups.

Temperature effects

- Unlike air pollution effects, a higher risk of hospital admissions in association with each 1°C increase in temperature was found in people with no history of the visits prior to their admissions compared to people with history. This was found for all diseases, except only circulatory admissions. However, none of the differences were significant.
- Overall, there was no apparent increase or decrease in temperature effects across the group numbers of the visits prior to admissions for all diseases. There was also no significant trend of temperature effects across the visit groups for all diseases.
- There was little evidence of effect modification of temperature effects across the visit groups by age, sex, and season. Generally, the estimated effects of temperature across the group numbers of the visits prior to admissions were slightly different in each subgroup. However, there was no obvious increase or decrease in the effects across the visit groups. There was also no statistically significant difference in the estimated trends across the visits between subgroups.

Sensitivity analyses

- There were no considerable changes in the estimated effects and trends of air pollution and temperature effects across the group numbers of previous visits before admissions when using different time periods for obtaining the linkage data. However, the estimated effects of air pollution (e.g. SO_2) and temperature effects were slightly larger when using a shorter time period in obtaining the previous visits before admissions than those when using longer periods.
- The different assumption in obtaining the '0 visit' groups or no history of the previous visits did not affect the estimated effects and trends of air pollution and temperature effects in the linkage series.

Table 8. 1 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily all-cause admissions in relation to the history of out-patient visits prior to their admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Pollutant (unit)	History of visits	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	0.502	0.219	1.146	0.102	
	With history	1.250	0.974	1.603	0.079	0.039
NO_2(ppb)	No history	1.010	0.836	1.220	0.919	
	With history	0.937	0.879	1.000	0.050	0.462
CO-8hr(ppm)	No history	0.649	0.475	0.886	0.007	
	With history	0.913	0.820	1.016	0.095	0.042
O_3(ppb)	No history	1.023	0.880	1.189	0.766	
	With history	1.003	0.953	1.055	0.922	0.808
PM_{10}($\mu g/m^3$)	No history	0.972	0.943	1.001	0.061	
	With history	0.995	0.984	1.005	0.306	0.148
$PM_{2.5}$($\mu g/m^3$)	No history	0.959	0.851	1.081	0.493	
	With history	0.977	0.937	1.018	0.272	0.773

[a] p-value for test for heterogeneity between groups.

Table 8. 2 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily respiratory admissions in relation to the history of out-patient visits prior to their admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Pollutant (unit)	History of visits	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	0.747	0.034	16.299	0.853	
	With history	1.356	0.574	3.202	0.487	0.715
NO_2(ppb)	No history	0.751	0.398	1.417	0.377	
	With history	1.214	0.972	1.517	0.087	0.162
CO-8hr(ppm)	No history	0.779	0.277	2.189	0.635	
	With history	1.120	0.770	1.629	0.552	0.517
O_3(ppb)	No history	0.755	0.436	1.309	0.317	
	With history	0.874	0.728	1.048	0.147	0.313
PM_{10}($\mu g/m^3$)	No history	0.956	0.864	1.057	0.379	
	With history	1.006	0.970	1.043	0.756	0.439
$PM_{2.5}$($\mu g/m^3$)	No history	0.962	0.630	1.470	0.859	
	With history	1.036	0.904	1.188	0.608	0.744

[a] p-value for test for heterogeneity between groups.

Table 8. 3 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily circulatory admissions in relation to the history of out-patient visits prior to their admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Pollutant (unit)	History of visits	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	0.454	0.045	4.609	0.504	
	With history	1.710	0.764	3.826	0.192	0.289
NO_2(ppb)	No history	0.660	0.359	1.214	0.181	
	With history	0.976	0.802	1.188	0.808	0.231
CO-8hr(ppm)	No history	0.668	0.248	1.801	0.425	
	With history	0.919	0.660	1.281	0.618	0.550
O_3(ppb)	No history	1.475	0.934	2.329	0.095	
	With history	0.983	0.838	1.152	0.830	0.100
$PM_{10}(\mu g/m^3)$	No history	0.975	0.887	1.071	0.598	
	With history	1.010	0.979	1.042	0.545	0.486
$PM_{2.5}(\mu g/m^3)$	No history	0.699	0.480	1.017	0.061	
	With history	1.023	0.914	1.144	0.693	0.057

[a] p-value for test for heterogeneity between groups.

Table 8. 4 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily intestinal infectious admissions in relation to the history of out-patient visits prior to their admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Pollutant (unit)	History of visits	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	2.459	0.099	60.946	0.583	
	With history	0.474	0.103	2.190	0.339	0.364
NO_2(ppb)	No history	1.025	0.516	2.035	0.944	
	With history	1.116	0.789	1.579	0.536	0.828
CO-8hr(ppm)	No history	1.306	0.433	3.944	0.636	
	With history	1.079	0.605	1.925	0.797	0.764
O_3(ppb)	No history	0.843	0.477	1.490	0.557	
	With history	0.860	0.645	1.147	0.304	0.951
$PM_{10}(\mu g/m^3)$	No history	0.950	0.855	1.057	0.346	
	With history	1.002	0.948	1.059	0.942	0.383
$PM_{2.5}(\mu g/m^3)$	No history	0.806	0.496	1.311	0.385	
	With history	0.937	0.744	1.180	0.581	0.439

[a] p-value for test for heterogeneity between groups.

Table 8. 5 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily other admissions in relation to the history of out-patient visits prior to their admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Pollutant (unit)	History of visits	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	0.333	0.125	0.887	0.028	
	With history	1.234	0.929	1.639	0.147	0.012
NO_2(ppb)	No history	1.131	0.905	1.413	0.279	
	With history	0.902	0.838	0.972	0.006	0.059
CO-8hr(ppm)	No history	0.595	0.410	0.864	0.006	
	With history	0.891	0.787	1.008	0.066	0.044
O_3(ppb)	No history	1.027	0.861	1.226	0.766	
	With history	1.026	0.968	1.087	0.393	0.992
PM_{10}($\mu g/m^3$)	No history	0.976	0.941	1.011	0.177	
	With history	0.992	0.980	1.004	0.197	0.400
$PM_{2.5}$($\mu g/m^3$)	No history	1.007	0.876	1.158	0.924	
	With history	0.968	0.923	1.016	0.190	0.600

[a] p-value for test for heterogeneity between groups.

Table 8. 6 Relative risk estimates for temperature effects (for each 1°C increase in temperature) on daily hospital admissions in relation to history of previous visits in Muang, Chiang Mai, from April 2003 to January 2006.

Outcome	n (day)	Mean [a]	SD	RR [b]	95%CI		p-value	Test for interaction [c]
					Lower	Upper		
All-cause (29°C)	173							
No history		3.08	2.09	1.217	0.883	1.678	0.230	
With history		26.34	13.83	1.038	0.922	1.168	0.541	0.362
Respiratory (linear)	974							
No history		0.22	0.49	1.045	0.868	1.260	0.641	
With history		1.92	1.51	1.040	0.979	1.104	0.206	0.962
Circulatory (29°C)	173							
No history		0.31	0.57	0.864	0.267	2.799	0.808	
With history		2.28	1.91	1.053	0.734	1.510	0.778	0.752
Intestinal infectious (linear)	974							
No history		0.17	0.43	1.171	0.945	1.450	0.150	
With history		0.74	0.90	1.097	0.992	1.212	0.071	0.588
Other (29°C)	173							
No history		2.24	1.72	1.337	0.922	1.938	0.126	
With history		21.26	12.17	1.059	0.924	1.213	0.410	0.248

[a] Mean daily count of hospital admissions relative to the identified temperature threshold.

[b] Temperature effects at short lag (0-1day) for respiratory and intestinal infectious admissions, and at a long lag (0-13 days) for all-cause, circulatory, and other admissions.

[c] p-value for test for heterogeneity between groups.

Table 8. 7 Estimated trends of air pollution effects across the group numbers of out-patient visits (0, 1, 2-5, and >5 visits) prior to hospital admissions in Muang, Chiang Mai, from January 2003 to April 2006.

Note: The estimated trends = a relative risk ratio for 10-unit increase of a pollutant (one-unit increase of CO) per visit-category.

	RR (95% Confidence Interval)					
Cause	**SO_2**	**NO_2**	**CO**	**O_3**	**PM_{10}**	**$PM_{2.5}$**
All-cause	1.13 (0.91-1.42)	0.99 (0.94-1.04)	1.02 (0.92-1.14)	0.98 (0.95-1.02)	1.00 (0.99-1.01)	1.00 (0.97-1.03)
Respiratory	1.19 (0.61-2.30)	1.01 (0.82-1.25)	1.07 (0.82-1.41)	1.02 (0.89-1.17)	1.00 (0.98-1.03)	0.98 (0.89-1.09)
Circulatory	1.25 (0.61-2.53)	0.96 (0.79-1.17)	0.91 (0.63-1.31)	0.94 (0.83-1.08)	0.99 (0.97-1.02)	1.01 (0.86-1.18)
Intestinal infectious	0.98 (0.32-2.99)	1.00 (0.78-1.28)	1.00 (0.66-1.50)	1.00 (0.81-1.24)	1.00 (0.96-1.04)	1.00 (0.84-1.19)
Other	1.16 (0.83-1.63)	0.99 (0.92-1.08)	1.04 (0.94-1.15)	0.99 (0.94-1.03)	1.00 (1.00-1.01)	0.99 (0.96-1.03)
Stratified by age						
All-cause 0-14	1.19 (0.67-2.11)	1.03 (0.90-1.18)	1.09 (0.83-1.43	0.99 (0.89-1.11)	1.01 (0.99-1.03)	1.01 (0.93-1.10)
15-64	1.11 (0.77-1.61)	0.99 (0.93-1.05)	1.01 (0.87-1.18)	0.95 (0.94-1.03)	1.00 (0.99-1.01)	0.93 (0.96-1.03)
≥ 65	1.28 (0.84-1.94)	0.98 (0.88-1.09)	1.06 (0.83-1.35)	0.98 (0.88-0.93)	1.00 (0.99-1.02)	1.01 (0.91-1.01)
Stratified by sex						
All-cause Male	1.20 (0.90-1.60)	0.99 (0.92-1.07)	1.02 (0.91-1.15)	0.98 (0.93-1.04)	1.00 (0.99-1.01)	0.99 (0.95-1.04)
Female	1.08 (0.82-1.41)	0.99 (0.93-1.06)	1.02 (0.92-1.14)	0.99 (0.93-1.04)	1.00 (1.00-1.01)	1.00 (0.96-1.04)
Stratified by season (day)						
All-cause Winter (333)	1.00 (0.66-1.54)	0.99 (0.93-1.05)	0.98 (0.78-1.23)	0.98 (0.90-1.07)	1.00 (0.99-1.01)	0.99 (0.94-1.03)
Summer (245)	1.10 (0.71-1.69)	0.99 (0.91-1.09)	1.03 (0.87-1.22)	0.98 (0.92-1.06)	1.00 (0.99-1.02)	1.01 (0.94-1.08)
Rainy (459)	1.21 (0.92-1.59)	0.99 (0.87-1.12)	1.03 (0.86-1.25)	1.00 (0.92-1.09)	1.03 (0.97-1.03)	0.97 (0.88-1.07)

Table 8. 8 Estimated trends of temperature effects across the group numbers of out-patient visits (0, 1, 2-5, and >5 visits) prior to hospital admissions in Muang, Chiang Mai, from January 2003 to April 2006.

Note: 1. The estimated trends = a relative risk ratio for 1°C increase in temperature per visit-category.
2. Temperature effects at a long lag (0-13 days) for all-cause, circulatory and other admissions, and at a short lag (0-1 day) for respiratory and intestinal infectious admissions.
3. p-value for the test for heterogeneity of the estimated trends between subgroups.

	RR (95% Confidence Interval)									
Group	**All-cause (29°C)**	**p-value**	**Respiratory (linear)**	**p-value**	**Circulatory (29°C)**	**p-value**	**Intestinal infectious (linear)**	**p-value**	**Other (29°C)**	**p-value**
All people	0.99 (0.91-1.08)	N/A	1.00 (0.96-1.05)	N/A	1.00 (0.75-1.34)	N/A	0.99 (0.92-1.07)	N/A	1.00 (0.91-1.10)	N/A
Stratified by age										
0-14 year	0.97 (0.28-3.40)		1.01 (0.78-1.31)		-		-		1.02 (0.31-3.41)	
15-64 year	1.00 (0.90-1.11)		1.01 (0.57-1.78)	0.997	1.03 (0.71-1.49)		-		1.00 (0.89-1.12)	
≥65 year	1.03 (0.51-2.09)	0.995	-	-	-	N/A	-	N/A	0.98 (0.20-4.85)	0.999
Stratified by sex										
Male	0.99 (0.87-1.13)		1.01 (0.95-1.07)		0.94 (0.21-4.14)		-		1.01 (0.87-4.75)	
Female	0.99 (0.84-1.17)	0.973	0.99 (0.93-1.06)	0.683	1.06 (0.29-3.84)	0.909	-	N/A	1.00 (0.85-1.18)	0.988

Table 8. 9 Estimated trends of temperature effects (lag 0-13 days) across the group numbers of out-patient visits (0, 1, 2-5, and >5 visits) prior to hospital admissions in different seasons in Muang, Chiang Mai, from January 2003 to April 2006.

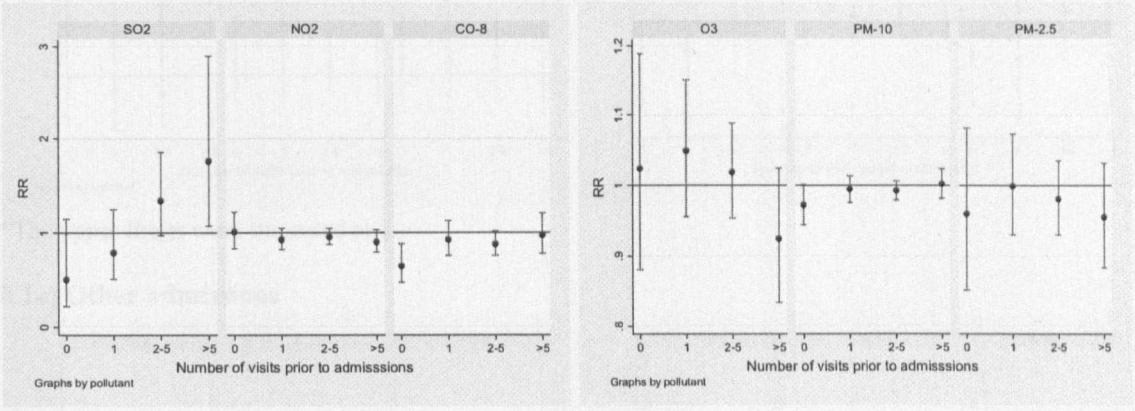
Note: The estimated trends = a relative risk ratio for 1°C increase in temperature per visit-category.

Outcome [a]	n(day)	Mean [b]	SD	RR	95% CI		p-value	p-value [c]
					Lower	Upper		
All-cause (>29°C)								
Winter	324	27.19	17.16	0.991	0.918	1.071	0.679	
Summer	232	29.93	18.33	0.965	0.861	1.081	0.307	
Rainy	418	29.37	17.39	0.985	0.840	1.156	0.730	0.930
Other (>29°C)								
Winter	324	21.18	14.96	0.990	0.902	1.088	0.698	
Summer	232	24.02	16.02	0.965	0.831	1.121	0.411	
Rainy	418	23.51	15.28	1.013	0.824	1.245	0.812	0.927

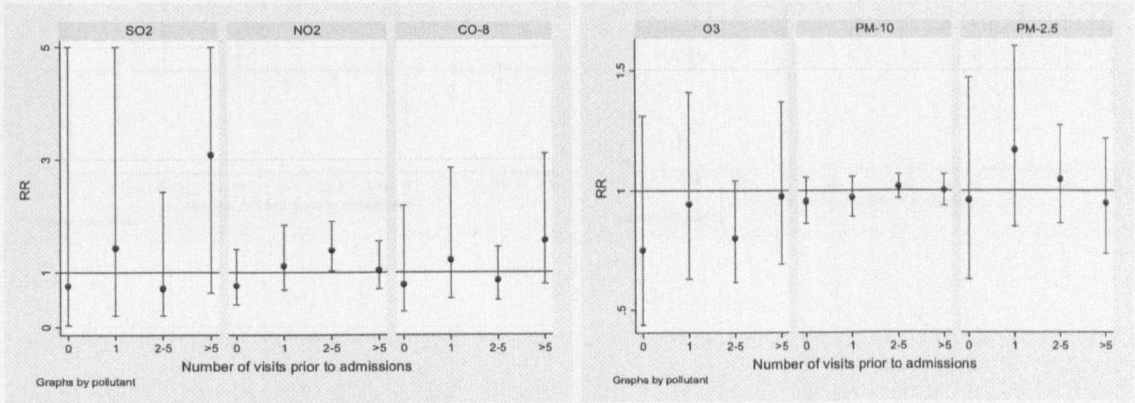
[a] Only these two diseases that the estimates could be done for all three seasons.
[b] Mean daily counts of hospital admissions in each season.
[c] p-value for test for heterogeneity of the estimated trends between seasons.

Figure 8. 1 Risk estimates for single pollutant, distributed lag models (0-4days) for a 10-unit increase of a pollutant (one unit increase for CO) on daily hospital admissions by history of the visits prior to admissions in Muang, Chiang Mai, from April 2003 to January 2006.

8.1a) All-cause admissions

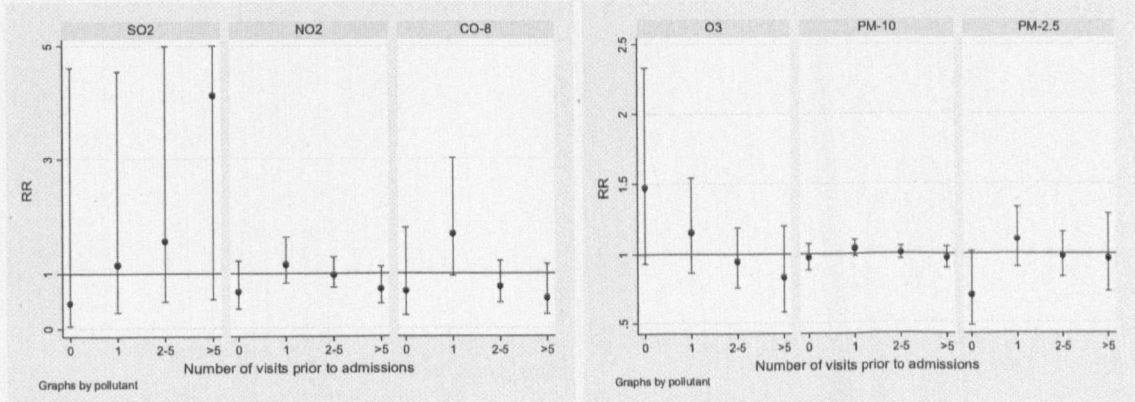


8.1b) Respiratory admissions



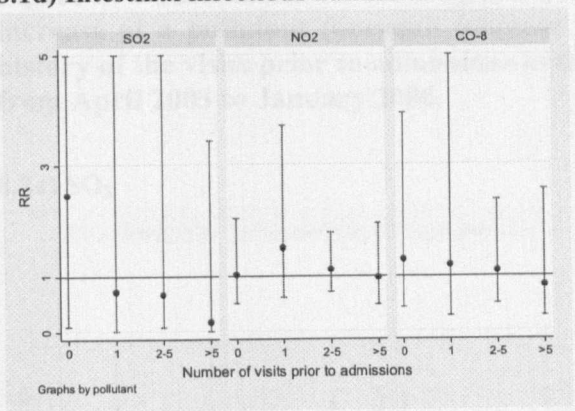
*The upper limits were truncated at 5.

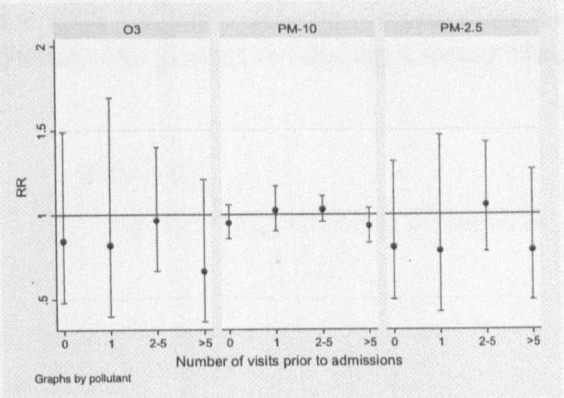
8.1c) Circulatory admissions



*The upper limits were truncated at 5.

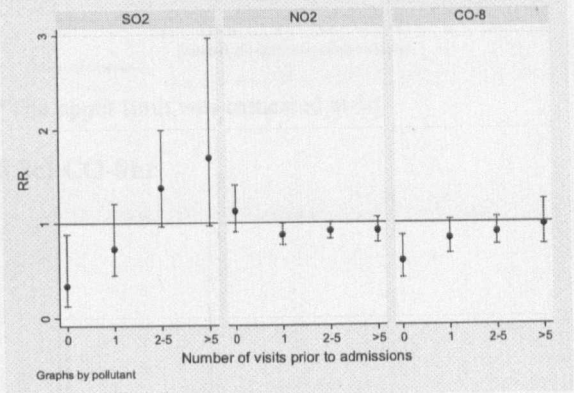
8.1d) Intestinal infectious admissions





*The upper limits were truncated at 5.

8.1e) Other admissions



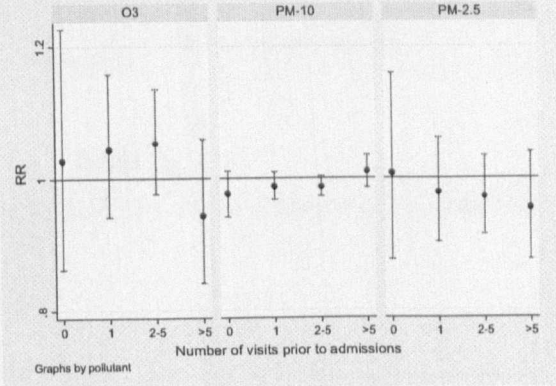
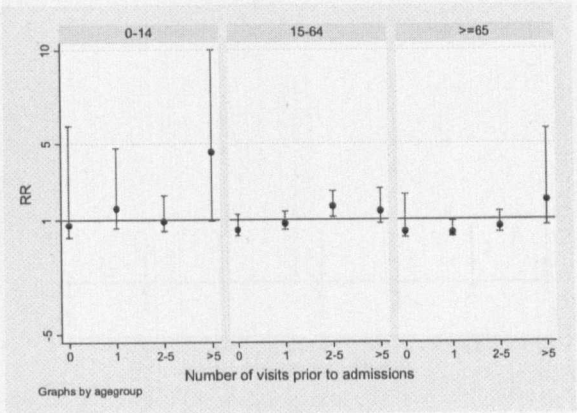
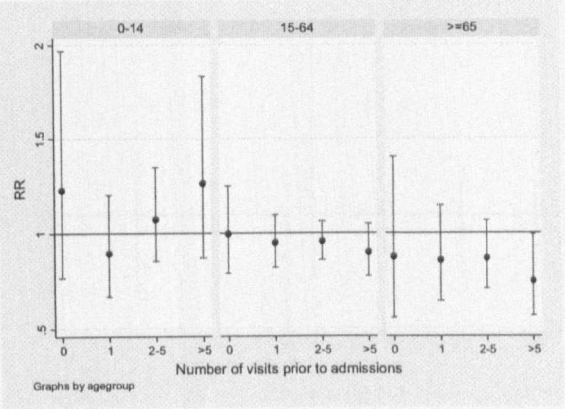


Figure 8. 2 Risk estimates for single, distributed lag models (0-4 days) for a 10-unit increase of a pollutant (one-unit increase for CO) on daily all-cause admissions by history of the visits prior to admissions in different age groups in Muang, Chiang Mai, from April 2003 to January 2006.

8.2a) SO_2

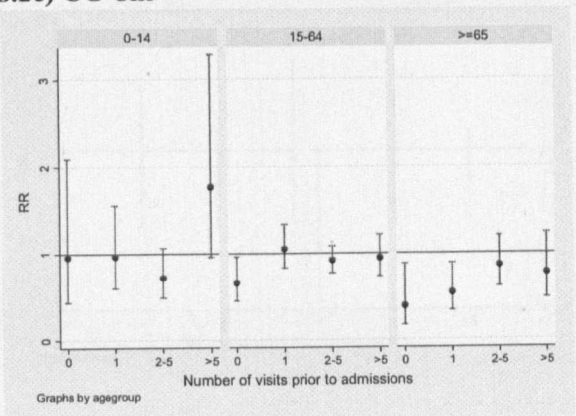


8.2b) NO_2

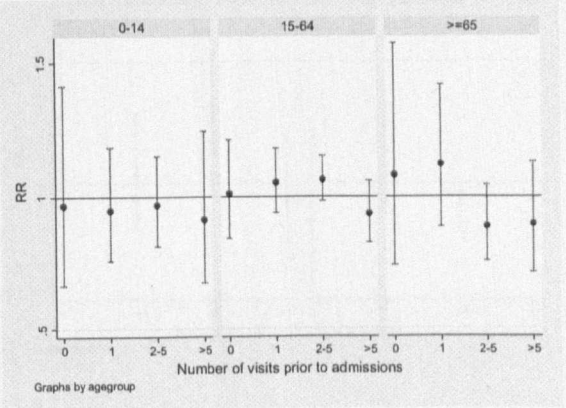


*The upper limit was truncated at 10.

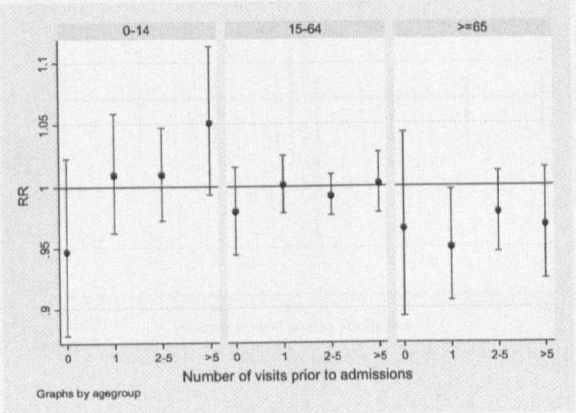
8.2c) CO-8hr



8.2d) O_3



8.2e) PM_{10}



8.2f) $PM_{2.5}$

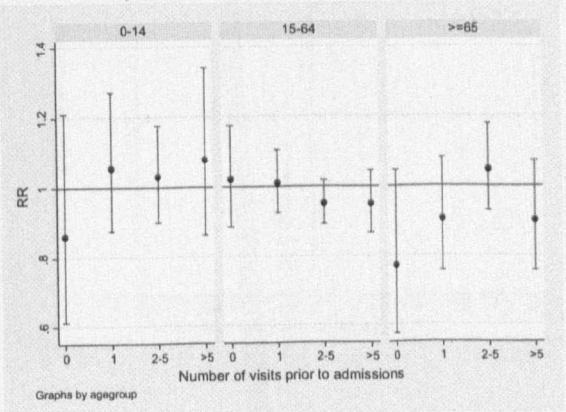
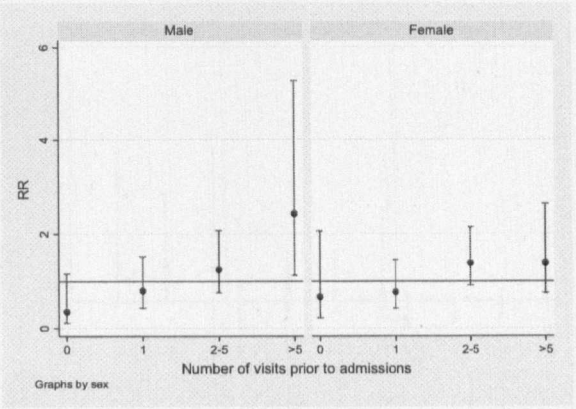
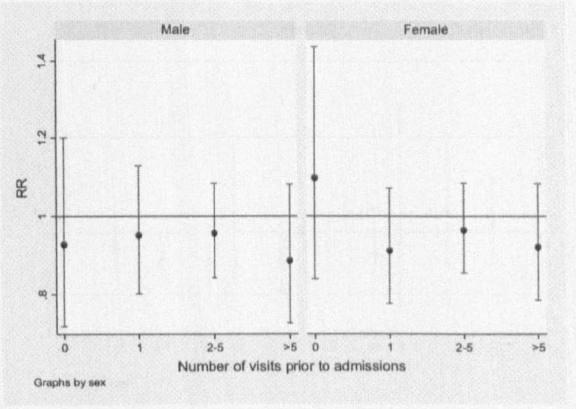


Figure 8. 3 Risk estimates for single, distributed lag models (0-4 days) for a 10-unit increase of a pollutant (one-unit increase of CO) on daily all-cause admissions by history of the visits prior to admissions in males and females in Muang, Chiang Mai, from April 2003 to January 2006.

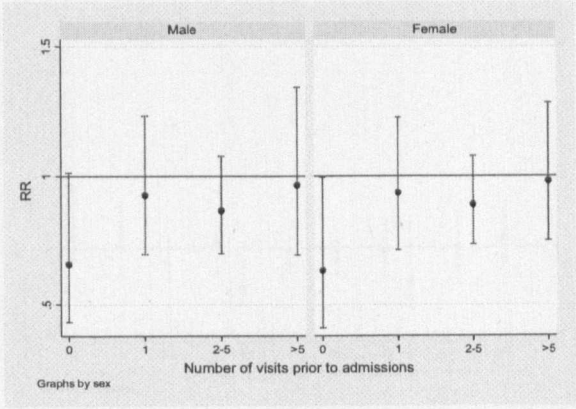
8.3a) SO_2



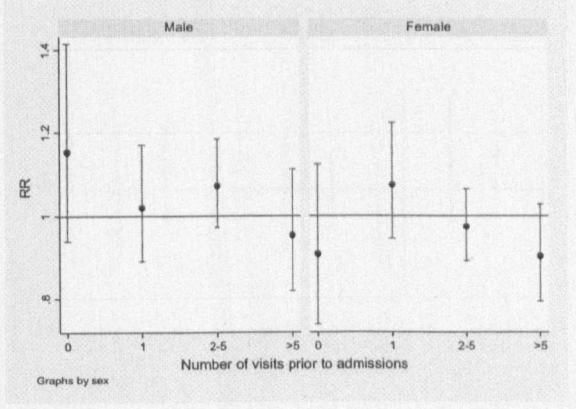
8.3b) NO_2



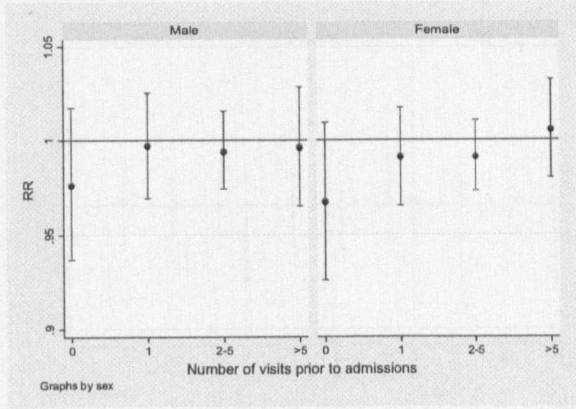
8.3c) CO-8hr



8.3d) O_3



8.3e) PM_{10}



8.3f) $PM_{2.5}$

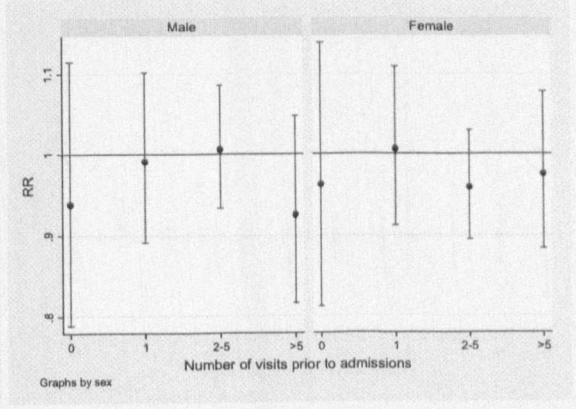
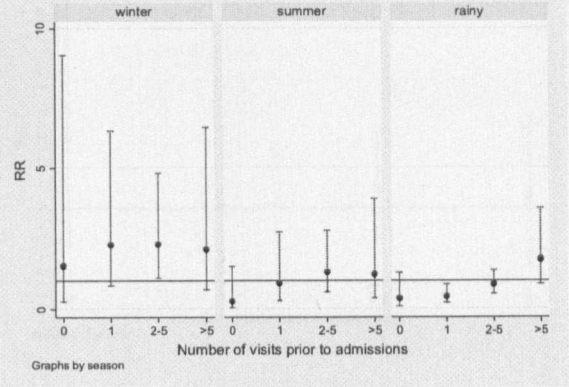
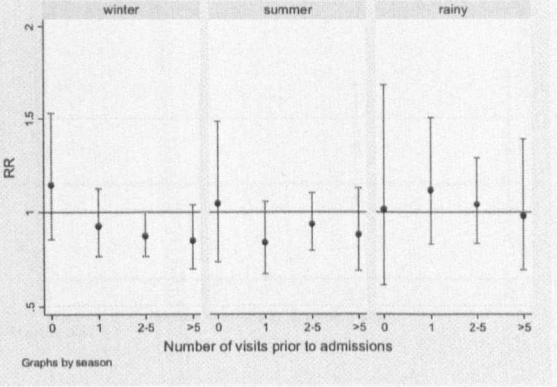


Figure 8. 4 Risk estimates for single, distributed lag models (0-4 days) for a 10-unit increase of a pollutant (one-unit increase of CO) on daily all-cause admissions by history of the visits prior to admissions in different seasons in Muang, Chiang Mai, from April 2003 to January 2006.

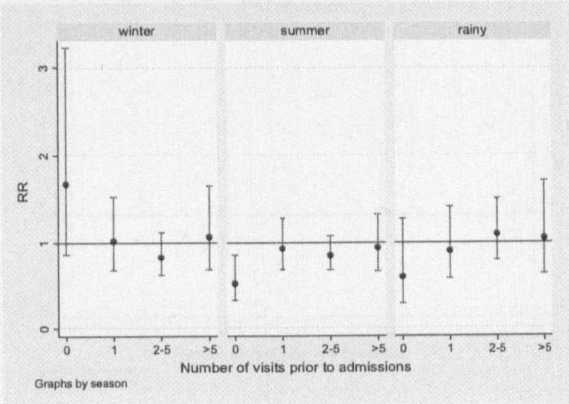
8.4a) SO_2



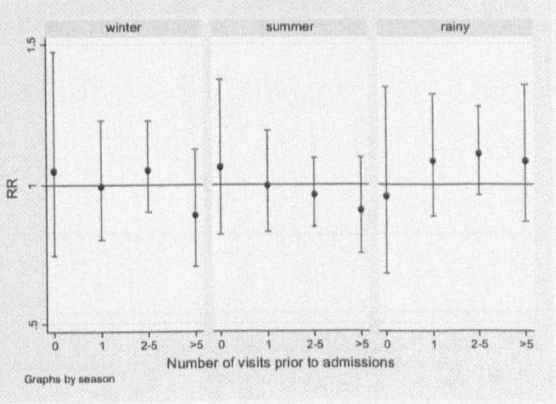
8.4b) NO_2



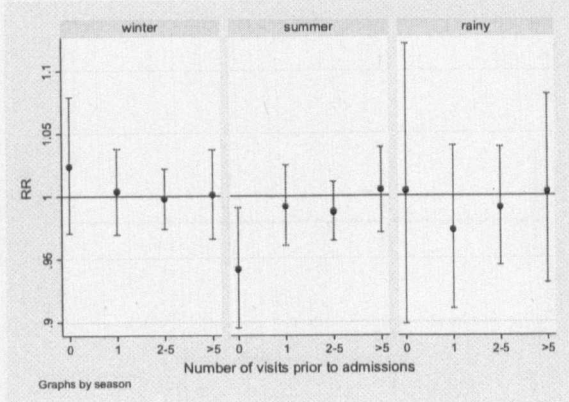
8.4c) CO-8hr



8.4d) O_3



8.4e) PM_{10}



8.4f) $PM_{2.5}$

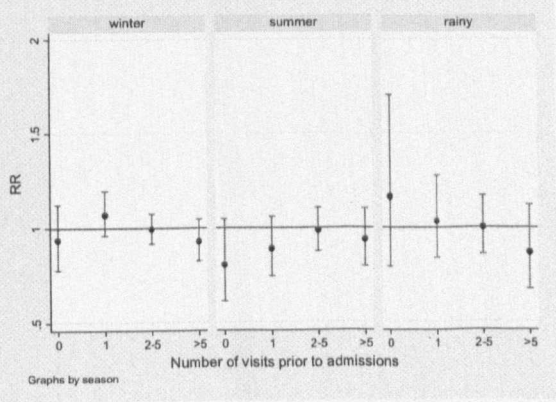
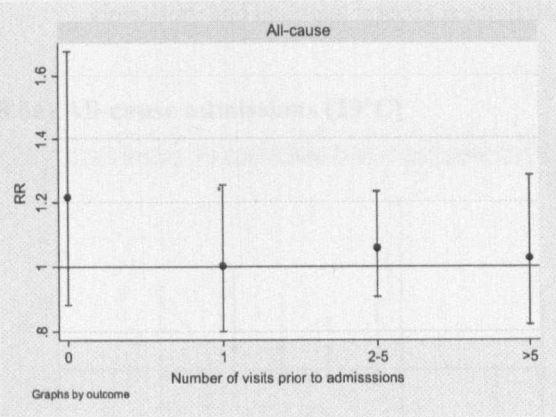
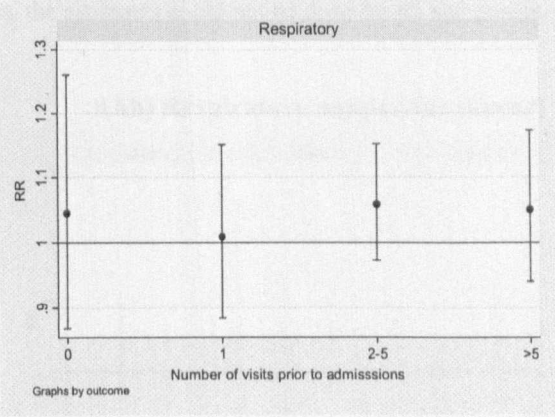


Figure 8. 5 Risk estimates of temperature effects for each 1°C increase in temperature on daily hospital admissions in all people by history of the visits prior to admissions in Muang, Chiang Mai, from April 2003 to January 2006.

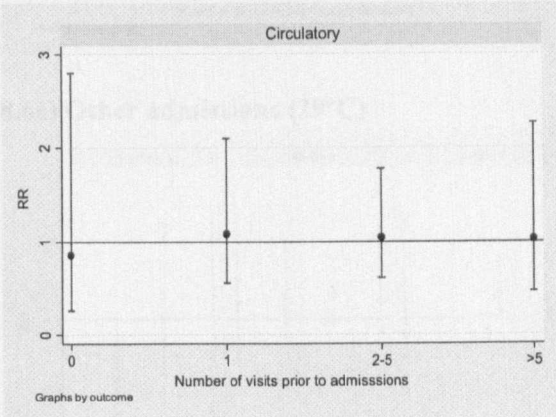
8.5a) All-cause (29°C)



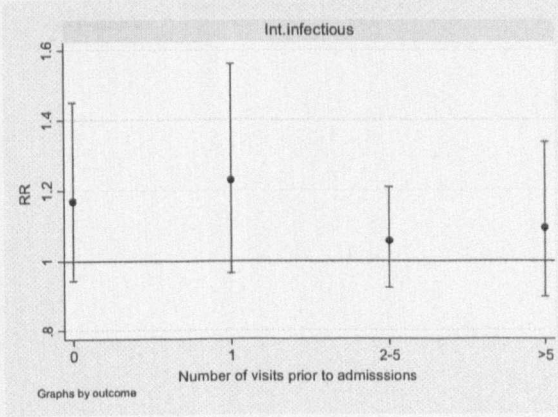
8.5b) Respiratory (linear)



8.5c) Circulatory (29°C)



8.5d) Intestinal infectious (linear)



8.5e) Other (29°C)

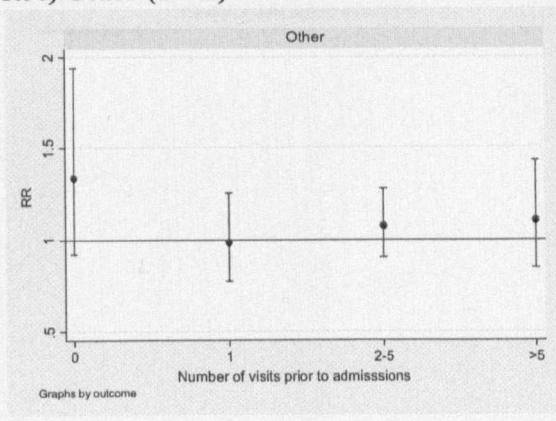
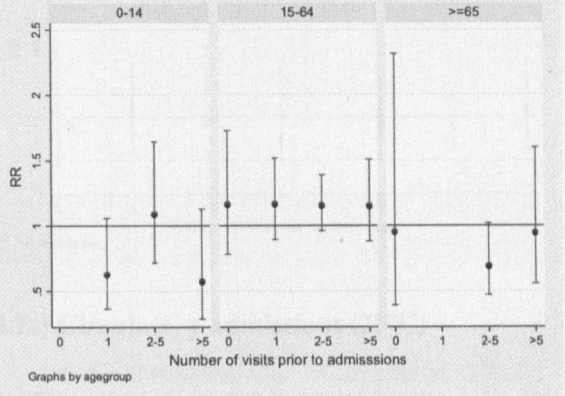


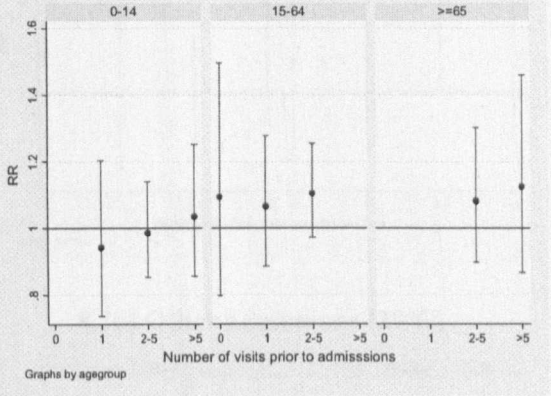
Figure 8. 6 Risk estimates of temperature effects for each 1°C increase in temperature on daily hospital admissions in different age groups by history of the visits prior to admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Note: The estimates relative to the number of the visits could not be done for some age groups, but for circulatory and intestinal infectious admissions, the estimates could not be done for all age groups.

8.6a) All-cause admissions (29°C)



8.6b) Respiratory admissions (linear)



8.6c) Other admissions (29°C)

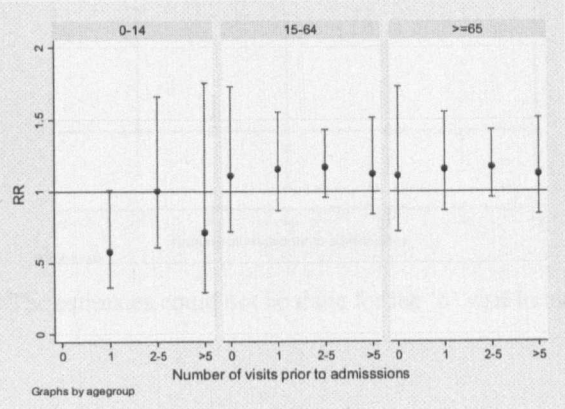
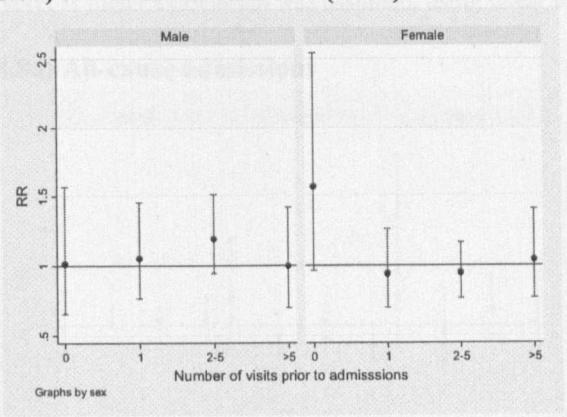
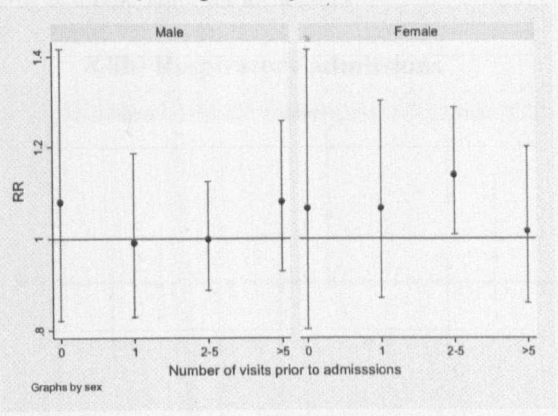


Figure 8. 7 Risk estimates of temperature effects for 1°C increase in temperature on daily hospital admissions in males and females by history of the visits prior to admissions in Muang, Chiang Mai, from April 2003 to January 2006.

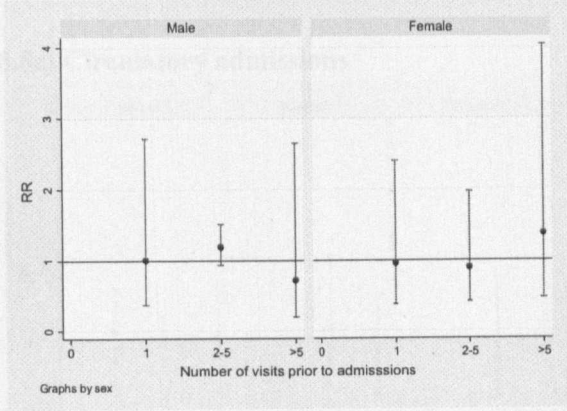
8.7a) All-cause admissions (29°C)



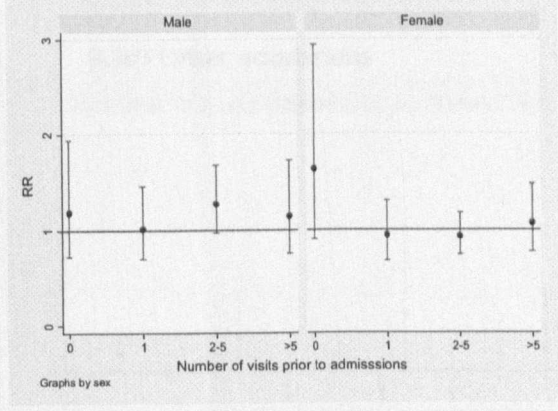
8.7b) Respiratory admissions (linear)



8.7c) Circulatory admissions (29°C)



8.7d) Other admissions (29°C)

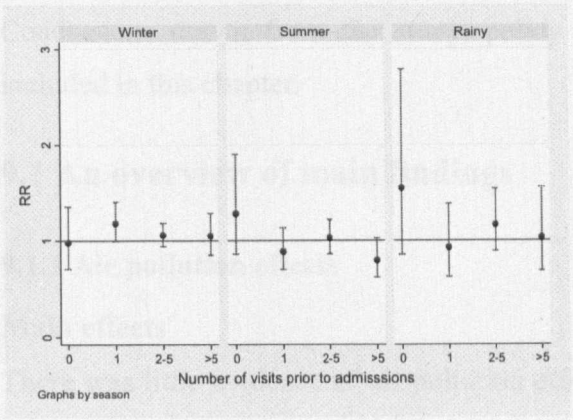


*The estimates could not be done for the 'o' visit in male.

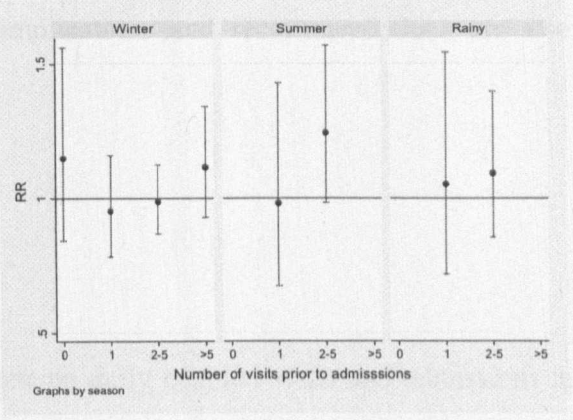
Figure 8. 8 Risk estimates of temperature effects for 1°C increase in temperature on daily hospital admissions in different seasons by history of the visits prior to admissions in Muang, Chiang Mai, from April 2003 to January 2006.

Note: A linear association was assumed, using linear terms of temperature for all seasons.

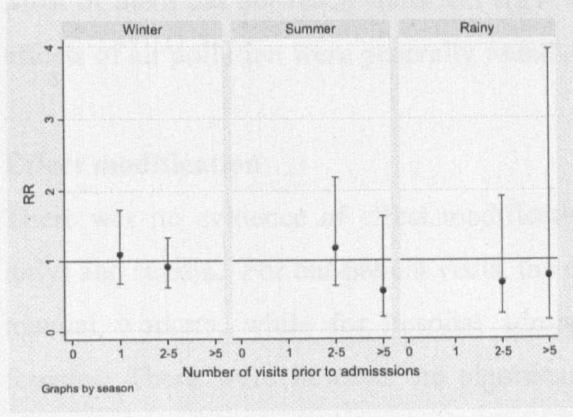
8.8a) All-cause admissions



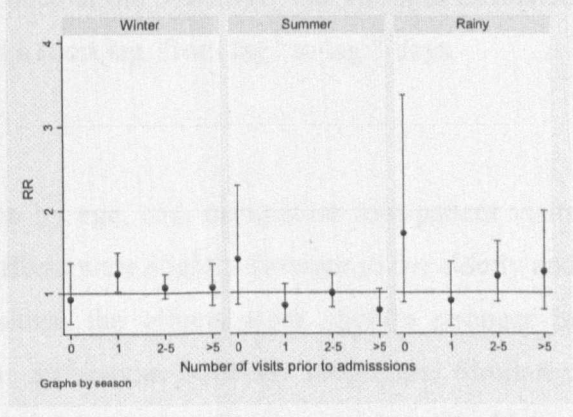
8.8b) Respiratory admissions



8.8c) Circulatory admissions



8.8d) Other admissions



Chapter 9: Discussion and Conclusion

This chapter provides an overview of the main findings, followed by a discussion of the findings in the context of existing literature. Some important issues of concern related to the findings are described. The strengths and limitations of the study are also discussed. Conclusions drawn from the study, policy implications and recommendations are also included in this chapter.

9.1 An overview of main findings

9.1.1 Air pollution effects

Main effects

There was little evidence of air pollution effects on daily hospital visits and admissions in Chiang Mai. Positive effects were found for some pollutants only, namely SO_2 and O_3. Most of them did not reach statistical significance at the 5% level. The stronger estimated effects of air pollution were generally found at a short lag, from lag1 to lag 3 days.

Effect modification

There was no evidence of effect modification by age, sex, occupation (out-patient visits only) and season. For out-patient visits, the effects were slightly stronger in the elderly and manual workers, while for hospital admissions, the effects were slightly stronger in females. There were however no significant differences between subgroups. Similarly, there was no consistent evidence of an increased risk of admissions in people with a history of out-patient visits prior to admissions, compared to those with no history. There were also no apparent trends (increasing or decreasing) of the effects across numbers of previous visits before admissions.

9.1.2 Temperature effects

Main effects

There was evidence of hot temperature effects on hospital visits and admissions, which was found for temperature above 29°C at a longer lag (0-13 day) for most diseases. The effects of hot temperature (with no threshold) at a short lag (0-1 day) were also found for respiratory and intestinal infectious diseases only.

Effect modification

There was no consistent evidence of a modification of temperature effects. The temperature effects on most disease outcomes were stronger in the elderly, male, and unemployed and economically inactive people. However, there were no differences between subgroups for all diseases, except for intestinal infectious admissions. The effects on this disease were significantly stronger in children and in males. Temperature effects seemed to be stronger in people without a history of previous visits than those with a history, though the differences were not statistically significant. There was no apparent pattern (either increase or decrease) of temperature effects across the numbers of previous visits before admissions.

9.1.3 Sensitivity analyses

- No difference in the estimated effects of air pollution and temperature between overdispersed Poisson (OP) models and negative binomial (NB) models.
- No significant impacts of the changes in degrees of freedom of time on air pollution effects. However, the changes in degrees of freedom (df) of time from 5df upward had caused an increase in temperature effects (but stable after that), suggesting that the core model was uncontrollable when using df of time below 5 df.
- For the hospital admissions series, the re-admissions did not greatly affect the estimates of temperature effects, but caused some changes in the estimates of SO_2 and CO effects.
- For the linkage series, there were no substantial changes in the patterns of air pollution and temperature effects across the number of visits before admissions when using different time period to obtain the linkage data or when using different inclusion and exclusion criteria of hospital admission cases. However, the positive trends (though non-significant) of air pollution (SO_2 in particular), and temperature effects were slightly larger when using a shorter time period to obtain history of the visits than those when using a longer time period (See **Appendix 8B, Table 8B-1 and 8B-2**).

9.2 The research findings and the existing knowledge

9.2.1 Air pollution and daily morbidity in Chiang Mai.

Are there any associations between air pollution and daily morbidity in Chiang Mai?

Overall, there was no significant association between air pollution and daily morbidity in Chiang Mai in the present study as most estimated effects did not reach statistical significance at the 5 % level. The lone exception was the significant association between O_3 and neoplasm admissions. However, the lack of a statistically significant association is not conclusive evidence that an association does not exist. The inability to achieve statistical significance may be hampered by factors, such as the limitations of the data used for the analyses as previously discussed in Chapter 4 and/or the nature of morbidity data itself. In general, as suggested by the literature, one would expect to see air pollution effects on emergency visits/ admissions. However, the data in the present study consisted of both elective and emergency visits/ admissions, which might contribute to the reduction of any true association (if there was). In addition, time series studies of short-term effects of air pollution and morbidity (hospital visits/ admissions) have shown less consistent findings in comparison to mortality studies. Unlike deaths, the visits and admissions to a hospital are usually affected by several circumstances, such as the perceived needs of individuals and the differences in ability to access health services of individuals [209]. These circumstances may affect the visits and admissions of each individual differently, which might result in the distortion and/or attenuation of the association between the exposure (air pollution) and health outcomes (hospital visits/ admissions).

Among all studied pollutants, SO_2 exhibited the largest positive estimated effects on the visits and admissions, though not statistically significant. SO_2 is a chemical compound produced by fuel combustion and is usually found more prevalent in industrial areas. Although there is no major industry in Chiang Mai, SO_2 may be emitted as a by product of the production processes of small factories around the city (e.g. agricultural, transportation, and food factories). The study found that there were relatively large estimated effects of SO_2, with an increase in respiratory admissions of 41.0% (95% CI, 1.0% to 97.0%), circulatory visits of 22.2% (95% CI, -2.8% to 53.6%), and diabetic visits of 25.5% (95% CI, -12.1% to 79.2%) in association with a 10-ppb increase in SO_2.

The finding of large estimated effects of SO_2 is in agreement with several time series studies of air pollution in Asia [84]. For example, in Beijing, it was found that an increase in non-surgery out-patient visits of 20.2% was significantly associated with an increase in SO_2 levels (6 $\mu g/m^3$ - 106 $\mu g/m^3$) [75]. In Seoul, a rise of hospital admissions for ischemic heart disease in the elderly of 32.0% (95% CI, 8.0% to 62.0%) associated with an interquartile increase in SO_2 (4.4 ppb) was observed [83]. The effect sizes of SO_2 found in this study were relatively larger than those found in Europe and America [16, 24, 80, 199, 210]. For example, the APHEA study in West European cities found a 6.0% (95% CI, 1.0% to11.0%) increase in respiratory admissions in the elderly (≥ 65year) for each 50 $\mu g/m^3$ increase in SO_2 levels [80]. A study in Denver, USA, observed a 9% increase in a risk of hospital admissions for dysrhythmias associated with a 25-75th percentile change in SO_2 levels (3.8 - 7.2 ppb) [24].

Besides SO_2 effects, the study also found positive effects of O_3, NO_2 and CO. The only positive significant effect of O_3 in the study was found for neoplasm admissions (which will be discussed later in the next section about health outcomes). The finding of positive effects (though not significant) of O_3 on the visits and admissions corresponds to previous findings in many regions [19, 79-81, 111, 211-215], which were predominantly found for respiratory disease. It has been postulated that O_3 may act as an irritant that induces defensive responses in the airways, such as increased mucus secretion and increased bronchial hyperactivity, and may also produce free radicals and oxidative stress on lung cells [111]. Besides respiratory disease, a recent study in Bangkok also showed a positive effect of O_3 on hospital visits for CVD among the elderly (≥ 65 years) [95]. However, there were some studies that did not find positive, significant associations between O_3 and hospitalizations [199, 216, 217].

The effects of NO_2 and CO on hospital visits/ admissions have also been observed in several settings [5, 33, 76, 77, 81, 82, 86]. These two pollutants are mainly generated by the combustion of fossil fuels, and therefore their concentrations are highly related with traffic and domestic combustions (e.g. heating, cooking and smoking) [54]. Chiang Mai is a growing city with rapid developments to serves an increasing population and large number of tourists. Problems with traffic congestion and domestic combustion in the city are likely

to be increasing. This might contribute to the small, positive effects of NO_2 and CO in the study.

The failure to detect the effects of PM_{10} and $PM_{2.5}$ in this study was not expected since particulate matter is the pollutant that shows consistent evidence of adverse health effects worldwide, even at low levels. Time series studies conducted in America (NMMPS), Europe (APHEA), and Canada have shown consistent evidence of acute effects of particulate matter on daily mortality and morbidity [26, 27, 106, 203]. The review of time series studies in Asia and the recent publication of the Public Health and Air Pollution in Asia (PAPA) project have also confirmed adverse effects of PM_{10} on both mortality and morbidity in several Asian countries [84, 94]. Moreover, another recent study in Bangkok demonstrated a positive effect of PM_{10} on hospital visits for CVDs among the elderly ($\geq$ 65 years) [95]. However, the failure to establish positive associations between particulate matter and health outcomes has occasionally occurred in some places. For example, a study in Denver, U.S.A., did not find any association between particulate matter and hospitalization for any CVDs [24]. Another study in the UK also found inconsistent associations between particulate matters ($PM_{2.5-10}$) and hospital admissions, and even found several large negative associations [107].

In this study, the inability to capture the positive effects of PM_{10} and $PM_{2.5}$ is difficult to explain. There was no reason to think that the unusual results were due to the statistical techniques since most techniques used in the study were adopted from those previously employed by several studies, such as the APHEA project, which were acknowledged to be reasonably robust [62]. The behavioural adaptation of the local population might be a possible explanation. A smoke haze usually occurs in the northern part of Thailand in recent years, particularly during the dry season (February-March). It mainly originates from traditional agricultural burning, forest fires and wood-fired cooking in the local area of the northern provinces of Thailand (including Chiang Mai), and neighbouring countries (e.g. Loas and Mianmar). As a consequence, the warning system to prevent adverse health effects of the haze, which has been implemented (including health education e.g. wearing mask, staying in the home when there is dense smog), may have increased awareness among the Chiang Mai population. This may have reduced the impacts of particulate matter

in the city due to the fact that particle is the fine product of the dust in the air (that people learn to avoid being exposed to).

What health outcomes were greatly affected by air pollution in the study?

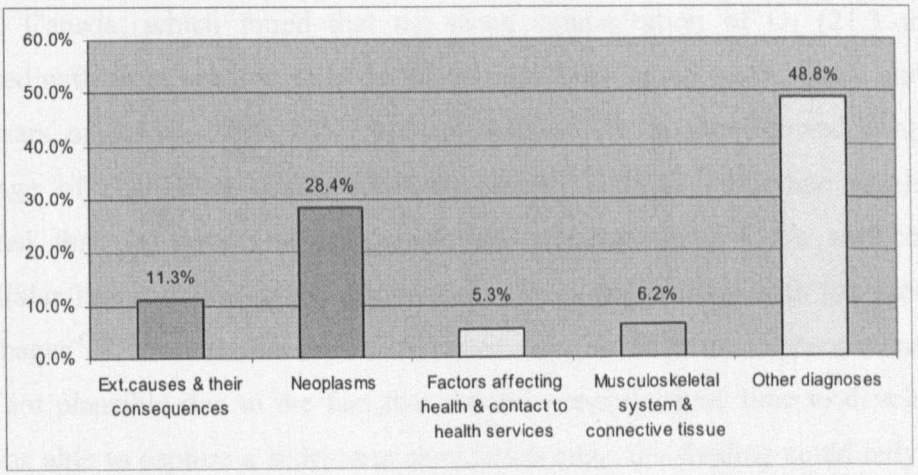
There were greater estimated effects of air pollution on respiratory and circulatory visits/ admissions than those on other disease groups in this study. This finding corresponds with the literature, although the effect sizes vary considerably among the published literature. The effects of SO_2 have been described for respiratory diseases [5, 77, 79, 107, 210, 212, 213, 218], and for CVDs [83, 212, 219]. The plausible mechanisms of SO_2 effects on these diseases has also been suggested by experimental studies as exposure to air pollutants could lead to an increase in broncho-constriction [146] and acute episodes of CVDs (e.g. myocardial infarction and cardiac arrhythmia), which may be due to the impairments of lung functions, inflammation of alveolar, increased coagulability of the blood, alterations of the nervous system control of the heart, and decrease of heart rate variability [151-153].

The study also found relatively large, positive effects of SO_2 on diabetic visits/ admissions (though not significant). This finding is supported by a study in Sao Paulo, Brazil, which showed a higher risk of CVDs emergency visits among diabetic patients than non-diabetic patients in association with SO_2 levels [157]. It has been pointed out that diabetic patients are at higher risks of deaths and illnesses associated with air pollution (particles, in particular). This may be related to cardiac functions, such as an increased plasma fibrinogen levels and other makers of systemic inflammation, increased C reactive protein levels, reduced heart rate variability and impairment in vascular reactivity and endothelial function [28, 29, 32]. Since there are still limited investigations of air pollution effects on diabetic morbidity compared to other diseases, more research determining the effects of air pollution on diabetic visits/ admissions is needed to confirm this finding.

As expected, there were generally no significant effects of air pollution on intestinal infectious visits and admissions. Most of these effects were negative. Since there is no plausible biological reason to expect that there is an association between air pollution and intestinal infectious disease, the finding of non-significant effects of air pollution on this disease group was intuitive.

For all-cause and 'other' visits/ admissions, the estimated effects found were broadly similar, with small positive effects for SO_2 and O_3, but negative effects for the rest of the studied pollutants. However, none of the estimates were significant. The 'other' visits/ admissions refer to visits/ admissions by other diseases apart from those previously discussed. To give a clearer idea about 'other' diseases, the percentage of the disease subgroups among this group were explored (for hospital admissions only) and shown in **Figure 9.1**.

Figure 9. 1 Percentage of subgroups of diseases among the 'other' diseases of hospital admissions in Muang, Chiang Mai, from September 2002 to October 2006.



As shown in the figure, the four largest subgroups of diseases represented in this category were admissions by neoplasms or cancers (28.4%), external causes and their consequences (11.3%), musculoskeletal system and connective tissue (6.2%), and factors affecting health and contact to health services (5.3%), respectively. Approximately half (48.8%) of the total admissions were accounted for by several diseases. Thus, the finding of positive effects of SO_2 and O_3 on 'other' admissions may partially be explained by the admissions due to cancers, which held almost 30% of the total. The association between ambient air pollution, particularly in industrialized countries, and cancer mortality (e.g. lung cancer) has been observed [163, 164, 166]. Although cancers were not the health outcome of interest in this study initially, the analysis for neoplasm admissions (ICD-10 code: C00-D48) was carried out according to evidence from the literature and the high percentage of neoplasms in the 'other' disease group. It was found that there were, indeed, positive effects of both SO_2 and O_3 on neoplasm admissions. The SO_2 effects were however not significant, but relatively

large, with a 19.0% (95% CI, -8.7% to 55.1%) increase in neoplasm admissions among all people per 10-ppb increase of SO_2 (0-4 days).

For O_3, a significant association between O_3 and neoplasm admissions was found, with a 6.8% (95% CI, 2.2% to 11.6%) increase in the admissions among all people per 10-ppb increase of O_3 (0-1 day). When the data were stratified by age and sex, the effects of O_3 (0-1 day) on neoplasm admissions remained significant, with stronger estimates in children and males. However, the differences between subgroups were not statistically significant. The finding of O_3 effects on neoplasm admissions in this study corresponds to a study in Quebec, Canada, which found that the mean concentration of O_3 (21.3 $\mu g/m^3$) was associated with an increase in daily deaths by neoplasms in the warm season among people $\geq$ 65 years of 3.93% (95% CI, 1.01% to 6.93%) [70]. It also showed a higher mean percentage of change in deaths for lung cancers (though borderline significant) and postulated that O_3 might be responsible for an alteration of the surfactant or the extracellular lining of the lungs, and that also have interactions with the functioning of macrophages [70]. Since the association between acute air pollution exposures and cancers is clearly not plausible due to the fact that cancers generally take time to develop and this study was able to capture a short-term association only, this finding could only be viewed as reflective of greater vulnerability among cancer patients due to their improper physiological functions compared to the general population [220]. This, therefore, could make them prone to be admitted to hospital in association with daily changes of air pollution.

Two pollutant model

Since there are several air pollutants mixtures in the air and most pollutants are highly correlated, this makes it difficult to separate the effects of one pollutant from other pollutants [59]. The issue of collinearity is one common problem in epidemiological studies due to the difficulty in determining the actual, single contribution of an exposure on health outcomes [60]. For two pollutant models, the interpretation of the results was done under the consideration that if one pollutant was acting only on its own without any contribution of one another pollutant, we would expect that the estimated effects of the pollutant would remain unchanged in a two-pollutant model compared to a single pollutant model [221].

That is, if one pollutant was not acting independently, its effects would become larger in the two-pollutant model due to synergistic action with one another pollutant, or would become smaller due to antagonistic effects.

In this study, for out-patient visits, the two-pollutant models for SO_2, O_3, and NO_2 showed that there was little change in the effects of these three pollutants obtained from the two-pollutant models compared to those obtained from the single pollutant models. This suggested that each pollutant might have acted mainly on its own. Therefore, its effects remained the same even when including another pollutant in the same models. While the results obtained from a two-pollutant model could vary from study to study, this finding is in agreement with a study in London that suggested that SO_2 and O_3 appeared to have independent effects on general practitioner consultations for allergic rhinitis [213].

For hospital admissions, the two-pollutant models for SO_2, CO, and O_3 provided relatively larger effects than those obtained from single pollutant models. There was however no consistency of the finding across all disease groups. In this case, it might be possible that two of the three pollutants had acted synergistically, resulting in the stronger estimated effects for the two-pollutant models than those for single pollutant models. However, we were unable to make a strong conclusion about the synergistic effects of two pollutants here because the results were not consistent across all diseases and none of the estimates were statistically significant.

What factors modified air pollution effects in Chiang Mai?

Overall, there was little evidence of effect modification by the studied factors. Only small differences in the estimated effects between subgroups were found. Even so, the differences were not statistically significant.

Age

The finding of somewhat stronger effects in the elderly in this study may be attributed to the consistently suggested vulnerability of the elderly to air pollutants noted in many previous studies, either in Europe or America [16, 19, 24, 36, 80, 106, 108, 114, 216] or in the Asia Pacific region [33, 81, 83, 215, 222, 223]. The susceptibility to air pollution among older people

may be due to the general deterioration of their physiological functions, especially the heart and lungs. Compared to younger people, older people are prone to have higher frequencies of both pre-existing pulmonary diseases and clinically severe infections of respiratory diseases [19]. Moreover, older people also have a higher risk of suffering from air pollution effects due to a decline of antioxidant defences [170].

Sex

Despite the finding of no statistically significant difference in air pollution effects between sexes, there was a suggestion of higher effects in females than in males, especially for respiratory admissions for all pollutants studied. According to the literature, the role of sex differences in environmental exposure-related health outcomes remains unclear. Some studies showed stronger estimated effects of air pollution in females compared to males [5, 18, 28, 89, 173, 175, 176], whereas others found a higher risk in males than in females [24, 174].

Occupation

This study found that air pollution effects were stronger among manual workers than other occupational groups (details of the 3-digit code of each group can be seen in **Appendix 3C**). The finding of stronger estimates in manual workers may be explained by relatively higher exposure to outdoor air pollution compared to other groups. In this study, the manual workers were blue-collar workers and those who worked outdoors (e.g. farmers, gardeners, and construction labourers). Therefore, this group was more likely to be exposed to outdoor air pollution than other occupational groups, resulting in the stronger estimated effects among them. In addition, it might also be possible that the manual workers in this population represented the low SES groups, which were more susceptible to air pollution as suggested by previous studies [181-183].

Season

The effects of air pollution on the visits and admissions in this study were found to vary from season to season (winter, summer, and rainy), but the differences were neither significant nor consistent across pollutants and health outcomes. In general, one would expect different effects of air pollution in different seasons, but this largely depends on geographical locations, metrological conditions, and population characteristics of each

research study. Most previous studies generally found stronger O_3 effects in the warm season as its formation requires the presence of sunlight [70, 111, 214]. This study also found that the O_3 effects were stronger in summer for most causes of out-patient visits (all-cause, circulatory, diabetic, and 'other' visits).

Previous out-patient visits

Previous research has investigated the linkage between hospital admissions and subsequent deaths [27]. However, to date, no research investigates whether the effects on hospital admissions are modified by history of out-patient visits before admissions. Accordingly, the linkage between out-patient visits and subsequent hospital admissions was established in this study. It is important to note that the insignificant findings for the linkage series may be partly because of small counts in the linkage data. Therefore, the discussion in this section was done with respect to stronger estimates (though not significant) observed from the series. It was found that there was no consistent evidence of an increased risk of admissions associated with air pollution in people with history of out-patient visits prior to admissions in comparison to people with no history. There were also no obvious trends (increasing or decreasing) of the effects across the numbers of previous visits before admissions. This may be explained by two possible reasons as follows:

First, people who make several visits to hospitals may not be very ill. These people may seek health care when starting to feel unwell. The health care treatments from their visits may be good enough to make them feel better and go home. In addition, the data in this study included not only emergency visits, but also scheduled visits to receive continuing care, such as drug treatments (e.g. HT cases). Hence, people with many counts of out-patient visits may not necessarily be admitted in later days.

Secondly, SES may partly play a role in effect modification by previous visits. It might be possible that people who were able to access health care services frequently were those who were of higher SES. These people may not need to worry too much about work or income. They may seek for health care by visiting a hospital whenever they feel unwell, leading to high count numbers of their out-patient visits. However, they may not be very sick or need admissions to hospital. Lower SES people, on the other hand, may be very worried about

their work and income. To stop working and go to hospital may mean losing their daily income. Thus, these people may not visit hospitals unless they are very ill, and require specialised care and admissions. As a consequence, lower SES people may have no history of out-patient visits or have relatively fewer visits prior to admissions, compared to higher SES people.

Since this is the only study, which has explored effect modification of air pollution on hospital admissions by previous visits, and the study was not able to examine the role of SES due to data limitations, more research should be undertaken to increase more understanding about this. In addition, sensitivity tests showed slightly larger estimated effects when using a shorter time period for obtaining previous history of out-patient visits before admissions, this raises the question of whether more recent visits would be a marker of greater vulnerability to air pollution exposure. It might be possible that the physiological functions (e.g. immune or blood circulation system) of a patient were not fully recovered within a few months after their visit, which could make them more vulnerable. However, this finding was not significant and was also found for SO_2 effects only. Hence, further research should also consider using a shorter time period for assessing effect modification by previous visits to see whether there is a consistency of the increased risk among more recent visits, and whether this could occur for other pollutants, not just SO_2.

If previous history of out-patient visits could modify the short-term effects of air pollution, one would expect that there might also be a possible effect modification by previous history of admissions on subsequent admissions. Moreover, it might be possible that previous admissions would provide greater modified effects than previous visits since admission cases generally have higher disease severity compared to out-patient visits. Hence, we also explored whether previous admissions had any influence on air pollution and temperature (which will be presented later in the temperature effects section) effects. Because previous admissions were not the main interest of the study at the beginning, it was decided to investigate the effect modification by previous admissions for discussion purposes and this was undertaken for all-cause admissions only.

For analysis purposes, previous admissions within a 6-month period (180 days) before each admission of a patient were counted. Then the latest admission of a patient was kept for the analysis by looking at the total counts of hospital admissions (within 180 days) prior to that latest admission. The same method of analysis employed for the linkage series was used, but not stratified analysis. The descriptive statistics and analysis results can be seen in **Appendix 9B (Table 9B-1 to 9B-4 and Figure 9B-1)**. Almost 80% of people in this data set had no history of admissions before their last admissions ('0' admission), followed by 1 admission (13.3%), 2-5 admissions (7.4%), and >5 admissions (1.1%) respectively.

It was found that there were no significant differences in air pollution effects between people with and without a previous history of admissions. Interestingly, when looking at air pollution effects across the group numbers of previous admissions, there was a somewhat decreasing pattern of the effects with increasing numbers of previous admissions for all pollutants (except O_3). The higher risk of subsequent admissions associated with air pollution among people with fewer numbers of previous admissions may be partially explained by the hospital admission data used in this study was health insurance claim data. It might be possible that hospital admissions were given to patients easily as this could guarantee the hospitals' income from reimbursement. Since there is also no constraints on hospital bed capacity in Thai hospitals, the increased admissions could occur in any groups, not necessarily those who were very ill and were admitted to hospital many times before.

9.2.2 Temperature and daily morbidity in Chiang Mai.

Effects of temperature on out-patient visits and hospital admissions

The study found significant effects of hot temperature on circulatory visits (all people), with an increase of 19.2% (95% CI, 2.3% to 32.8%) for each 1°C increase in temperature above 29°C. This finding is in agreement with a study conducted in 12 US cities that observed an association between hot temperatures and an increase in hospital admissions for heart disease in people ≥ 65 years [121]. This finding is also consistent with a study conducted in Denver, Colorado, and New York that demonstrated an association between high temperature and hospital admissions for CVDs [24, 134]. An increase in hospitalization during high temperature may be because the body of vulnerable people cannot establish appropriate compensatory measures, such as increasing cardiac output (required during heat

stress) or having chronic heart insufficiency due to inability to increase cutaneous circulation (which can impede dissipation of heat) [119].

However, this result is in contradiction with studies undertaken in London, Madrid, California, and 12 European cities, which suggested no association between high temperature and heart disease admissions [10, 135-137]. It has been posited that the lower heat effects on admissions than on mortality and/or no association between hot temperature and admissions may be because people die rapidly before receiving medical treatments or admissions to hospitals. The contradictory results between colder countries and a warmer country, like Thailand, may be explained by the possibility of having a higher temperature threshold among Thai people. Literature suggests that people tend to be able to adapt to their local climate through physiological acclimatisation, behaviour patterns, and adaptive mechanisms [158]. Since Thai people are generally accustomed to hot temperatures, their bodies may tolerate small increases in temperature better than people in colder countries, resulting in less severity of diseases (just getting ill, instead of dying). In addition, their illnesses may require only primary care services at out-patient visits, leading to negative and non-significant effects of hot temperature on hospital admissions for circulatory disease in this study.

The study also found significant effects of high temperatures on diabetic visits. For each 1°C increase in temperature above 29°C, there was an increase in diabetic visits of 26.3% (95%CI, 7.1% to 49.0%). This finding corresponds to a study in Chicago, which showed an increased numbers of diabetic admissions during a heat wave [119]. Similarly, studies on the impacts of extreme temperature in 50 US cities and in Wayne County, Michigan, observed a higher risk of dying on hot days among diabetic patients than other subjects [14, 158]. A recent study in California, U.S.A., also showed significant effects of high temperature on diabetic admissions [137]. This may be because diabetic patients have an impaired autonomic control and endothelial function, which could affect their responses to extreme thermal stress [14].

In this study, increasing temperature seemed to have a protective effect on respiratory visits, but not respiratory admissions. It was found that, among all people, there was a small

decrease in respiratory visits of 0.9% (95% CI, -1.9% to 0.0%), whereas there was a slightly larger and significant increase in respiratory admissions of 2.8% (95% CI, 0.6% to 5.0%) in association with each 1°C increase in temperature (no threshold). In general, the common cold or upper respiratory tract infection (URI) is a common respiratory problem during winter or cold period. Thus, it is possible that warmer temperature help reduce hospital visits due to cold or URI, which is usually a majority of daily counts of respiratory visits in Thailand. However, high temperatures may have induced more respiratory admissions, which may be explained by disease severity. Generally, we would expect more severe respiratory illness for admissions than for out-patient visits. While out-patient visits may be higher with less severe health problems (such as cold or URI), hospital admissions may be higher with more severe diseases (such as bronchitis, asthma, pneumonia or COPD). This is supported by the finding of a study in EU cities, which observed an increase in hospital admissions for respiratory illness with increasing temperature, particularly in the elderly [136].

The study found that an increase in intestinal infectious visits and admissions were significantly related to increasing temperature. For each 1°C increase in temperature without an identified threshold, there was a 2.6% (95% CI, 0.4% to 4.8%) increase in intestinal infectious visits, and a 5.8% (95% CI, 2.3% to 9.3%) increase in admissions. This finding corresponds to previous studies in Peru, Canada, EU countries, and Bangladesh, which suggested an increase in hospital visits and admissions due to diarrhoeal diseases, food poisoning, and bacterial enteric infections in association with an increase in temperature [159-162]. This may be because higher temperature promotes the growth of bacteria, and the transmission of infections [160, 162]. Generally, most intestinal infections have longer lag effects (e.g. 0-2 days or up to 1-2 weeks). However, approximately 81% of infectious diseases in this study (either out-patient visits or hospital admissions) fell into diarrhoea and gastroenteritis of presumed infectious origin (ICD-10 code: A09). Additionally, the surveillance of diarrhoeal diseases in Thailand also reported that 77.4% of total diarrhoea cases were classified as acute diarrhoea [224]. This suggests that the nature of intestinal infectious diseases in Thailand may be more acute compared to other places, which supports the finding of this study that the hot temperature effects were shown over a short lag period (0-1 day) for this disease group.

There were also positive effects of temperature on both all-cause and 'other' visits and admissions (all people), but the effects were found to be significant for out-patient visits, not for admissions. The positive effects of hot temperature on 'other' visits and admissions might be partially explained by the visits or admissions due to external causes and their consequences (e.g. injuries, accidents, suicide), and cancers. Both groups held almost 40% of total 'other' admissions (see **Figure 9.1**, p. 222). An increase in accidental events, such as traffic accidents and suicide, has also been reported to be associated with hot temperature [167-169]. However, it is important to note that the accidental events that could support the results of this study would have been non-fatal cases as there was an increase in hospital admissions, not deaths.

Compared to the general population, patients suffering from cancers (such as lung cancer) may be more vulnerable to temperature exposure because of the dysfunction of their physical organs, which could make them less able to tolerate hot temperatures. For instance, lung cancer patients would possibly have been affected by high temperatures in the similar way to patients with lung problems, such as chronic obstructive pulmonary disease (COPD), one of the most common causes of admissions for respiratory disease among the elderly. The patient with COPD may hyperventilate during hot temperature, which may increase dynamic hyperinflation leading to dyspnea and mechanical cardiovascular effects [136].

As mentioned previously, although cancers were not the disease of interest in this study, the analysis of temperature effects on neoplasm admissions was also undertaken because neoplasm held the largest proportion in 'other' visit/ admissions. There were positive effects of high temperature (>29°C) on neoplasm both visits and admissions in this study, though not consistently significant for all subgroups. The larger estimates were found for out-patient visits rather than for hospital admissions. However, the finding did not support the above hypothesis because the effects were larger in children (the admissions) and adults (the visits) than in the elderly. This suggested that there might not be only lung cancer (which mostly shown in the elderly) that made people more vulnerable to hot temperature, but other kinds of cancers found in children or adults might also make people more prone to hot temperature effects than the general population (because of their impaired physiological

functions). Health care seeking behaviour could be another explanation for this. More visits/ admissions among children suffering from cancers may be largely due to their parents' worries and eagerness in seeking health care when their children get ill. On the other hand, the elderly suffering from cancers may prefer to stay home and wait for dying as they are old and probably tired of seeking for health care.

Temperature effects on morbidity in Chiang Mai in comparison with previous study of temperature effects on mortality.

Previously, there was a study on heat- and cold-related mortality in 12 urban populations in low-and middle income countries [225]. Chiang Mai was one of the cities included in that study. Because the previous study and the present study were conducted at different time periods, and some analytical methods and the outcomes are also different, it may not be appropriate to make a comparison between them. However, one interesting point is that although the mortality study (1995-1997) was conducted earlier than this morbidity study (2002-2006), the temperature threshold of that study at which all-cause mortality rises (28°C) was very similar to the threshold obtained for an increase in all-cause visits and admissions (29°C) in the present study. The similarity of the thresholds between the two studies is therefore logical and reflects the high possibility of illnesses or deaths among the Chiang Mai population at temperatures above these identified thresholds (28-29°C). Hence, this is an important message for public health personnel to establish a warning system for high temperatures to prevent illnesses and deaths among the Chiang Mai population.

Lag effects of temperature

Most previous studies suggest that the effects of hot temperatures are immediate with short lag from 0 to 3-5 days, while the effects of cold temperatures are more delayed with a longer lag from 0 to at least 13 days [23, 187, 188]. This study found hot temperature effects (no threshold) at a short lag (0-1 day) for respiratory and intestinal infectious diseases, but the effects (>29°C) occurred at a longer lag (0-13 days) for the rest of the disease groups. The finding of hot temperature effects at a longer lag is corresponding to a study in Santiago (Chile) and Palermo (Italy), which suggests that the persistence of heat effects on respiratory deaths may be up to 20 days after exposure [189].

The difference in local climate may be a possible explanation for this. Most previous studies that found acute effects of hot temperature were conducted in colder countries [127], while the present study was undertaken in a tropical climate with more hot days over a year than cool days. Thus, the long period of hot days could have prolonged temperature effects on daily morbidity among the study population. Another explanation may be the adaptation and the tolerance of the population to their local climate as mentioned earlier. Because Thai people get used to hot weather, it might be take times for the effects of hot temperature to manifest and then lead to people seeking health care services.

What factors modified temperature effects in Chiang Mai?

There was little evidence of effect modification by age, sex, occupation (for out-patient visits only), and season since there were no significant differences in the effects of temperature between subgroups for most diseases.

Age

The study found that the effects of high temperature were stronger in the elderly in most disease groups for both out-patient visits and admissions, except only intestinal infectious admissions, which were significantly stronger in children. Research evidence shows that children are particularly vulnerable to increasing temperature, resulting in the visits and admissions due to infectious diseases (such as diarrhoea) [159, 197]. In this study, the stronger and significant effects found for hospital admissions, not for out-patient visits, among children may be explained by the greater severity of illnesses, which required admissions to hospitals for close observations than just received out-patient treatments and went home.

This finding of slightly larger effects in the elderly is consistent with most previous studies of high temperature effects on hospital visits and admissions, which have demonstrated that the elderly are more vulnerable compared to the general population [24, 118, 119, 121, 135, 136]. The greater susceptibility of the elderly may be because of a reduced thermoregulatory capacity together with a decline in ability to detect changes in their body temperature [14, 22, 25, 123, 126, 158, 226]. Furthermore, the cognitive impairment and diminished mobility may also limit their ability to perform behavioural defences, resulting in a delay in access to health care services [117, 118].

Sex

The study found slightly stronger effects of hot temperature in males than in females for most diseases. According to the literature, there was an inconsistency of temperature effects on sex as some studies showed an increased risk in females [8, 18, 128-130, 172], while some studies showed a higher risk in males [24, 132]. However, by comparison, females appear to be more vulnerable to high temperature than males as indicated by the majority of published literature [127]. In this study, the greater effects in males than in females may broadly be explained by higher outdoor activities among males, which led them to be more exposed to hot ambient temperatures than females. Traditionally, Thai females are more likely to be housewives, working at home than going out. Although this tradition is gradually changing (as more women work outside the home), it might still be possible that the old tradition still continues in the northern part of the country, particularly in Chiang Mai.

Occupation

There was inconsistency of temperature effects on occupation as the effects on all-cause, and circulatory visits were larger in unemployed and economically inactive people, whereas the effects on diabetic, intestinal infectious and 'other' visits were larger in non-manual workers. Unemployment is a surrogate for low SES, which has been suggested to have a greater susceptibility to temperature effects [158]. Thus, the larger estimated effects found for this group were possible. However, the stronger estimated effects found in non-manual workers are difficult to explain because these people usually work indoors and therefore should be less exposed to ambient temperature.

Season

When stratified by season, there were generally significant, positive effects of temperature (linear) on the visits and admissions in summer compared to other seasons. Despite no statistically significant differences in temperature effects between seasons for all diseases (except only all-cause visits), the stronger effects in summer highlighted the greater impacts of increasing temperature on daily morbidity in Chiang Mai.

Previous out-patient visits

The study found that people with no history of out-patient visits seemed to have an increased risk of hospital admissions compared to people without such a history. This may be explained by perception of temperature changes. In everyday life, people may not be aware of air pollution changes because the changes are generally invisible, except only during a heavy smoke period. Unlike air pollution, people could feel hot or cold when temperature increase or decrease [227, 228]. It may be possible that people who have many counts of out-patient visits may be more exposed to health education messages when visiting hospitals, and they therefore, may become more concerned about taking care of themselves than the less exposed population. Thus, these people may avoid going outdoor when it is very sunny and/or hot weather, or wear appropriate clothes for sun protection, which mean less exposure to hot temperature. This could result in a reduction of the effects among them compared to those without a history.

When looking at different numbers of out-patient visits prior to admissions, there was no increasing or decreasing trends of temperature effects across the group numbers of out-patient visits. The same explanations discussed previously for air pollution effects could be applied here. That is, having many counts of out-patient visits does not necessarily mean that these people will eventually have hospital admissions at later days. First, people with many visits may not be unhealthy. These people may instead be health conscious and always seek health care when feeling unwell, leading to many records of out-patient visits. Second, it might also be possible that hospital visits were affected by SES. The higher SES may visit hospitals often when not very ill or needing admission, while the lower SES may be worried about the need to work and therefore only visit hospitals when they have very serious illness that requires admission. Replication of the studies looking at modification of temperature effects by previous visits should consider including SES factors to ascertain the finding.

Similar to air pollution effects, the sensitivity analysis suggested stronger estimated trends of temperature effects across the visit groups when using a shorter time period for obtaining a previous history of out-patient visits (See **Appendix 8B, Table 8B-2**). The positive increasing trend of 1.8% was found when using a 3-month period, while the small

decreasing trends were found when using a longer period, with a decrease of 0.1% when using a 6-month period and of 0.3% when a using 12-month period. Although these changes were very small and non-significant, it raised an additional concern whether more recent visits would be a maker of greater vulnerability. If more recent visits could lead to admissions rather than later visits, the short time period (such as 3 months) would be an important period in which people should be aware of their susceptibility and avoid doing outdoor activities, which could lead them to be highly exposed to high temperatures (as well as air pollution).

With respect to possible effect modification by previous admissions, the investigation on modification of temperature effects by history of admissions was also done (for all-cause only and no stratified analysis). These are presented in **Appendix 9B (Table 9B-5 and Figure 9B-2)**. It was found that both groups of people, with and without a history of previous admissions, were affected by high temperature (>29°C). The effects were however much larger and significant in people with a previous history of hospital admissions (14.5% increase, 95% CI, 2.5% to 28.0%) than that in people with no history (4.4% increase, 95% CI, -2.0% to 11.2%). Although this difference was not statistically significant, previous admissions seemed to be a marker of vulnerability to temperature exposure, leading to subsequent admissions. The plot of estimated effects across the group number of previous admissions showed that there was a somewhat, small increase in the temperature effects with increasing number of previous admissions. There was also an estimated increase (though not significant) in all-cause admissions of 4.0% (95% CI, -6.9% to 16.3%) for each 1°C increase in temperature per admission-category.

9.2 Issues relating to the findings

9.2.1 Analytical issues

There were two main issues of concern relating to analytical methods used when developing the core models that might influence the study results. These are the model distribution assumption and the model seasonality with respect to the choice of degree of freedom (df) for time.

First, the negative binomial distribution was assumed for the modelling, instead of the Poisson distribution as commonly done in most time series studies. In general, time series analysis has a distinct assumption that daily counts of deaths or hospital admissions usually follow a Poisson distribution. However, because of the heavy overdispersion of the data as previously mentioned in Chapter 3 (Methods), this study employed negative binomial regression models to estimate the effects of air pollution and temperature instead. At the beginning, the Poisson regression was used for the analysis but it did not handle the overdispersion very well compared to the use of negative binomial regression as indicated by overdispersed parameters and residual plots (not shown). Thus, the sensitivity tests to compare the estimated effects obtained between negative binomial (NB) models and overdispersed Poisson (OP) models were undertaken. It was found that there were no differences in the estimates obtained between the two models. This suggests that the use of model distribution assumption different from the conventional methods did not affect the findings of the present study.

The choice of degree of freedom (df) for time was the second analytical issue in the study. To account for seasonal and long-term trends, smooth function of time was incorporated into the model. As indicated in the methods chapter, it was decided to start with using the small number of df (1 df first) of the spline for time when developing the core model. Since there are no absolute degrees of smoothing to be used for the modelling, evaluating various numbers of df used to ensure adequacy of adjustment for seasonality is important [203]. Oversmoothing may lead to confounding bias, whereas undersmoothing may result in attenuation of a true effect of the studies [202]. Therefore, the choice of smoothing in time series studies could vary from study to study. For example, the APHEA project used 3-4 df/year, the NMMAPS study used 7df/year, and the recent PAPA studies used 4-6df/year [62, 94, 203]. The sensitivity analysis to explore an impact of changing number of df for time in the study was undertaken, and the results showed that there were no substantial changes in air pollution effects in relation to the changes of number of df, while there was an increase in temperature effects when using 5 df upward (but the effects were fairly stable after that). This suggests that the use of 1df for time in the core model for investigating air pollution effects, and the use of 6 df for time in the original model for investigating temperature effects could provide reasonable results for the study.

9.2.2 Data quality issues

I. Health data

First, daily out-patient visit data were obtained from several district health centres and hospitals of various sizes (indicated by hospital beds) in Muang district of Chiang Mai. Thus, variations in diagnostic practices and different proportions in the degree of disease severity across health centres and hospitals would have occurred. For example, diagnostic accuracy from bigger hospitals with medical doctors may be more reliable than that from district health centres with no medical doctors (in health centres, nurses or public health personnel take this role, instead of doctors). However, all practitioners (e.g. doctors, nurses, and district health personnel) were formally trained to use the same coding system [206]; there is no change of the system during the study period; and the diagnostic practices were unlikely to change on a daily basis and/or in association with high and low air pollution days. Moreover, the misclassified diseases and missing diagnoses in this study were likely to occur randomly or to be non-differential. Therefore, it is possible to assume that the variations of diagnostic accuracy across data providers would not cause enormous changes in the estimated effects, and this non-differential misclassification would produce an underestimate of the short-term association in this study only [229]. Additionally, with the use of broad categories of diseases instead of finer specific disease codes, it was expected that the underestimation of the effects due to misclassification of disease outcomes would have been minimised.

Second, the large numbers of missing ID numbers in the out-patient visit data, which was used for linking between out-patient visits and hospital admissions, might also affect the estimations in the linkage series. Because of large amount of missing ID numbers in the out-patient data set, there were small count numbers in the linkage data, resulting in very imprecisely estimated effects. This made it difficult for interpretations and conclusions for the series. However, because the linkage data were created by the original data sets of out-patient visits and hospital admissions, the impacts of any missing information on the effects observed in the linkage series would occur in similar manners to those that occurred in the out-patient visits and hospital admissions series. Hence, it is reasonable to believe that the patterns of air pollution and temperature effects across the group numbers of out-patient visits before admissions obtained in the linkage series were likely to be non-differential.

Third, the mix of both elective and emergency cases in the health data is also an important issue of concern. Since it was impossible to distinguish between these two proportions in the health data, any true effects in this study might have been affected. If the proportion of emergency cases were bigger than elective cases, the estimated effects were likely to represent the short-term association among the study population. This is because we would expect to see the acute effects of exposures on emergency cases as suggested by previous air pollution studies [19, 78, 199, 207]. Conversely, if the proportion of elective cases were bigger than emergency cases, it could result in a dilution of the true effects in this study.

II. Air pollution data

In this study, air pollution data were obtained from the only two air monitoring stations located in Muang district of Chiang Mai. The total area of Muang district is approximately 152 sq km, with a population density of about 1,947 per sq km. For air pollution studies, the use of air pollution data from central monitoring stations could lead to misclassification of exposures for individuals living in the study area because exposure levels may not be the same for each individual. It have been accepted that the measurement error due to using exposure data from fixed air monitoring sites is likely to result in an underestimation of the effects [190, 230]. According to the summary of statistics of air pollution data from the two stations in this study (see **Appendix 4B**), levels of all pollutants (except only O_3) from the city central station (Yaparaj College station) were higher than the outskirt station (Chiang Mai City Hall station). Therefore, it was believed that the bias due to either over or under estimation of exposure levels of the study population would have been reduced by using the average levels between the two stations, instead of using exposure data from one station only. In any case, air pollution data from the fixed monitoring stations were only used as a proxy for actual air pollution exposure, and the main interest of this study design was the day-to-day changes in air pollution effects. A great variation in air pollution values over a daily basis was very unlikely. Hence, the use of exposure data from any of the two stations would not cause substantial changes in the estimated effects, even though the absolute values of air pollution from both stations are different. Nevertheless, it was acknowledged that measurement error of exposure in this study could not be ruled out because information from the two fixed stations may not truly represent the actual personal exposure of the entire population in the city.

9.2.3 Multiple testing

Multiple testing becomes an issue of concern in the present study since we analysed several exposure variables (6 pollutants and one temperature term), several health outcomes (e.g. 6 disease groups for out-patient visits series), and several lags (up to 4 days for air pollution and up to 13 days for temperature). We did not adopt a conservative method, such as Bonferroni's corrections, to adjust the findings because this method would imply an equal adjustment of all results in accordance with the total number of the tests performed, ignoring that there might be some differences in an importance or a plausibility of the results [231, 232]. Furthermore, the several lags studied are highly correlated. Thus, to use the Bonferroni adjustments in the present study by considering that all results are equal and independent may not be appropriate. We also did not adopt a more recent approach, such as the 'false discovery rate (FDR)' approach, to make comparison of the study results. The term FDR refers to the expected proportion of errors committed by falsely rejecting null hypotheses [233]. This is because this study is relatively simple, while the FDR approach is a complex method, which is more suitable for studies with considerable numbers of tests and comparisons (e.g. laboratory experiments) [233, 234].

For simplicity, it was decided to interpret the study results in an informal way by considering that the statistically significant results would occur by chance, and therefore, they would be compared to the actual number of the tests in the same set of the analyses [232]. This means that, in this study, emphasis was put on consistency of the results across the exposures and outcomes by looking at overall results rather than singling out only significant results from particular exposures or outcomes.

Concerning about multiple testing, all significant results of air pollution effects in this study were informally compared to the total number of the tests done in the same set of analyses (see **Appendix 9A**). It was found that the number of the statistical association seemed to be more than would be expected by chance. For example, of 36 tests of air pollution effects (lag 0-4 days) on out-patient visits, there were 4 statistically significant associations, and all of them were protective effects, which accounted for 11.1% of the total observations in this set. For hospital admissions, there were 5 statistically significant effects of air pollution (lag 0-4 days) out of 36 tests (13.8%), and all results were also protective effects. Furthermore,

the significant, protective effects appeared to be clustered at particles (PM_{10} and $PM_{2.5}$). The finding of protective effects of particles is really difficult to explain due to the large body of consistent evidence of adverse health effects of particulate matters (either PM_{10} or $PM_{2.5}$) worldwide [77, 103-108, 110-116, 235].

9.2.4 Harvesting

Harvesting effect refers to the assumption that air pollution and temperature effects may occur among people who would die or enter the hospital within a few days or weeks, anyway [73, 74]. This generally implies that there would be a depletion of the pool of vulnerable individuals, which would lead to subsequently fewer cases following a period with a relatively large number of cases. In other words, there would be subsequent negative effects following the large, positive effects (a rebound effect) during the episode. In general, this phenomenon is usually found in mortality studies rather than morbidity studies. Since the present study is a morbidity study, we would expect that harvesting effect is unlikely to be a major threat here. Moreover, the plots of the estimated effects did not obviously show any sign of harvesting effects. Therefore, we did not attempt to profoundly explore this phenomenon for the study.

9.3 Strengths of the study

Although most study results, particularly for air pollution effects, did not achieve statistical significance, there are some important contributions of the study to environmental health.

Firstly, the study has added to the epidemiological research of air pollution and temperature effects on morbidity, particularly in Asia and in a tropical country. To date, although there are many air pollution and temperature studies worldwide, there are fewer studies looking at morbidity effects compared to mortality effects, which is obviously seen for temperature studies. Moreover, the majority of research studies have been conducted in developed countries, especially in Europe and America, where their climate and economies are different from Thailand and other Asian countries. For Thailand, there are very few time-series studies of air pollution, which were conducted in the capital city, Bangkok, only. To date, in Chiang Mai, there are only three air pollution studies and none of them are time-series studies. Two of them are the International Study of Asthma and Allergies in Childhood (ISACC) [44, 236], and another one is a cohort study looking at the association

between air pollution and the peak expiratory flow rates among asthmatic children [237]. Additionally, there is only one previous time-series study of temperature effects on mortality in the city (ISOTHURM project) [225]. Therefore, this study is the first time series study of air pollution that investigated the effects on different age groups (not only children) and different disease groups (not only asthma) , and also the first morbidity study of temperature effects in Chiang Mai. Consequently, this study has increased understanding of the morbidity effects of acute exposure to air pollution and temperature and also contributed to identification of subpopulations that might have a greater vulnerability to these effects in the Asian region, and particularly in Thailand.

Secondly, the study has demonstrated that existing routinely collected health and meteorological data in Thailand can be a useful tool in conducting an epidemiological research study. However, the investigation needs to be undertaken with careful considerations to analytical methods in order to minimise possible bias and confounding due to limitations and nature of data quality in the country. This study has also suggested that, with more improvement of data quality, there will be a greater chance to further explore and/or replicate studies to accurately detect stronger associations, which could in turn, encourage researchers to establish more environmental, epidemiological research in Thailand.

Thirdly, the study has highlighted the possible impacts of hot temperature in Thailand. Since Thailand is a tropical country with moderate to high temperatures, one would expect that local people would be accustomed to a hot climate and be able to adapt to this environment very well. Additionally, in Thailand, more attention has been paid to dealing with public health risks in the cold season than in the warm season. This is due to annual reports of deaths that usually occur during winter among the poor who live in remote areas of the country (which may be partly because of insufficient warm clothing for winter). Thus, this study could raise awareness that Thailand might also encounter the negative impacts of hot weather on health, which are predicted to increase all over the world.

9.4 Limitations of the study

9.4.1 Confounding

For time series studies of short-term effects of air pollution and temperature, potential confounding refers to time-dependent variables, including slow time-varying factors (such as long-term time trends and seasonality) and short-term time varying factors (such as weather variables e.g. temperature may confound air pollution effects, and humidity may confound temperature effects). These variables associate with day-to-day changes in air pollution and temperature, and also associate with day-to-day changes in health outcomes (hospital visits/ admissions).

In the present study, possible potential confounders were taken into account. For example, natural splines of time and month of the study were incorporated into the core models (for both air pollution and temperature models) in order to control for factors that change slowly or seasonally over time, such as seasonal and between-month differences. Weather variables, including temperature (for modelling air pollution effects), humidity, and rain, were also controlled for. The residual plots as well as PACF plots were checked each time when including more variables into the models to see whether there were any significant residuals shown from the plots. Although the use of statistical modelling techniques to control for potential confounding may not guarantee the complete elimination of residual confounding due to unmeasured, poorly measured, or unknown risk factors [238], the residual confounding in terms of time varying factors were minimized and should not be considered a major issue of this study.

9.4.2 Bias

a) Information bias

Measurement error of exposures

It has been acknowledged that time series studies that employ exposure data from fixed monitoring stations may experience some degrees of measurement error in estimating daily exposure of the study population [190]. This is because exposure data from fixed sampling sites may not truly represent the actual exposure of large mobile populations. Individuals may not experience the same period and levels of exposure. In this study, one monitoring station is located in the inner city alongside a busy road and another one is located in the

outskirts of the city about 50 metres far from the nearest road (the stations are approximately 10 kilometres apart).

For air pollution, the daily average levels of air pollutants from the two stations were used for examining air pollution effects. If we used the data from only one station in the inner city alongside a busy road, we might overestimate exposure levels of the population due to the fact that not all people live in the city centre and are highly exposed to traffic air pollution. On the other hand, if we used the data from only the outskirt station, we might underestimate exposure levels of the entire population as well. Thus, it was expected that the use of daily average levels of air pollutants calculated from the two stations would best describe exposure levels of individuals living in the city of Chiang Mai.

For temperature, the daily mean temperature from one station (the inner city station), was used for examining temperature effects. This was because this station provided more complete data (fewer missing records compared to another station). With the use of records from the inner city station, one might say that the urban temperature might represent the exposure levels of people experiencing temperature effects as a result of 'urban heat island effects', not the levels that the general population were exposed to. However, there were no substantial differences in temperature levels between the two stations. Thus, the temperature levels from this station should be a reasonable estimate of the exposure for the study population as people, either those living in urban or suburban areas, had experienced similar temperatures.

Although air pollution and temperature levels were chosen with careful considerations for ensuring a representative sample of exposure levels of the study population, the measurement error of exposures would still be an issue in this study. This was due to the fact that the exposure data used was the population-average exposure, not the actual personal measurements. However, because the same daily average levels were used for all available health records on the same day, the measurement error would be the non-differential misclassification. In addition, this error is known as the Berkson type and is likely to cause an underestimation of the true association (bias toward the null) of the study only [190, 230, 239].

Measurement error of outcomes

Although hospital visits and admissions can be used as health endpoints for investigating air pollution and temperature effects, quality of the information with regard to the accuracy and the completeness of the information are of great concern.

The first concern is about diagnostic accuracy. Because out-patient visit and hospital admission data in this study were used for administrative control and payment for health care services, there might be some bias regarding the information on diagnosis, favouring diseases that receive more expensive treatments. In addition, although all involved health centres and hospitals utilized the same diagnostic tool (DRG system in accordance with ICD-10 diagnostic manual), there might still be variability in diagnostic records across the health centres and hospitals. However, as mentioned previously in chapter 4 (data quality), Thailand had employed the DRG system for about a 10-year period before officially adopting this system in 1998. Moreover, quality audits and surveys about health records have also been conducted. There was also no change in the health record system during the study period. This should indicate a reasonable quality of the health data used in this study.

Furthermore, it is also reasonable to believe that the misclassification of diagnosis would not have changed enormously over time or vary greatly from day-to-day basis. Since the study was designed for determining short-term effects of the exposures, misclassification of diagnosis should not cause a considerable bias of the study. With concern that the misclassification of diagnosis would vary by season (e.g. the high respiratory visits/ admissions during cold weather may lead to diagnosing some people with respiratory diseases when they are actually ill with some other diseases), the study analysed for air pollution and temperature effects in each season separately. Additionally, in order to address the possibility of misclassification of diagnosis, the broad categories of diseases (respiratory, cardiovascular, diabetic, and intestinal infectious diseases) were used, instead of specific diseases (e.g. pneumonia, asthma, stroke, and CHF). Taking into account the above concerns and explanations, misclassification of the outcomes in regard to diagnostic accuracy should not be substantial in the present study.

The second concern is about missing information e.g. missing data in some months at some health centres and hospitals, and missing individual information, such as age, sex, and occupation. For the problem of missing data in some months, the month of the study (1-48) was incorporated into the core models to control for between-month differences. With respect to missing individual information, the stratification by age, sex, and occupation, was done in broad categories. The variables with high percentages of missing data (e.g. missing occupation information >30% for hospital admission data) were also excluded from the analyses. In addition, caution was taken when interpreting the study findings. Thus, despite an existence of missing data, the influence of the problem was minimised in the present study.

b) Selection bias

Hospital bed capacity

When analysing and interpreting data on hospital admissions, bed capacity of a hospital is one important issue of concern. This is because the availability of beds may affect the rates of admissions to a hospital, which influence the timing of the admissions [208]. If there is a limitation in the supply of beds, a patient may not be admitted when there is a manifestation of the health problem. In general, hospital admissions are highest during winter (Nov-Feb) of each year due to an increase in respiratory infection cases during cold weather. However, as mentioned previously in chapter 4 (data quality), Thai hospitals generally provide extra beds for admissions when necessary. That is, under the Thai hospital system, a patient will be admitted to hospital when needed in accordance with medical indications of disease severity that need close observations and/or advance treatments. Thus, the constraint of bed capacity is very unlikely to cause selection bias in this study.

Under-representation of study population

The main concern in regard to the limitations of the health data in terms of inability to distinguish between emergency and elective cases, variability in health care seeking behaviours, and the possibility of an influx of a neighbouring population into the study area were already discussed in chapter 4 (data quality). These factors could cause the spurious association of the study results.

In addition to those previously mentioned, there is also a concern about whether there is an under-representation of some portions of the study population. In general, people who visit or are admitted to private hospitals are thought to be from the wealthier portion of the population, while people who visit or are admitted to government hospitals are thought to be from the poorer portion. If this assumption is true, when we use the data from only government sectors, it may be possible that there is an under-representation of the wealthier portion of the population.

On the other hand, if we use the data from only private sectors, there might be an under-representation of the poorer portion of the population. However, the under-representation of poorer or wealthier subjects can only pose limitations on inferences about socioeconomic differences in the vulnerability to air pollution and temperature exposure. Since this study did not attempt to explore the socioeconomic impacts on air pollution and temperature effects in Chiang Mai, and the health data used in this study was not only derived from government hospitals, but also from some private hospitals in Chiang Mai (those registered to the government with respect to health insurance claim system), the selection bias in relation to socioeconomic differences should not be a major threat to the study.

Nevertheless, it is important to acknowledge that some degree of selection bias for hospital admissions in the study might occur due to the fact that the data were health insurance claim data. As previously discussed about effect modification of previous out-patient visits, it might be possible that, in some cases, even though a patient was not severely ill, he/she might still be admitted to hospital because he/she had health insurance that guaranteed the hospital income received from the reimbursement. However, it is possible to assume that this could occur randomly over time on a regular basis, which should not cause substantial bias in the study.

c) Ecological bias

Ecological bias refers to uncontrolled confounding that occurs when rates of exposure relative to rates of outcome are compared between geographical areas [240]. This bias could occur because exposure and health outcomes are measured at the aggregated level, it is impossible to link exposure with disease in particular individuals as we cannot be sure

whether those people who died or were admitted to hospital due to respiratory disease were the same people who experienced the air pollution exposure. Furthermore, we may not be able to control for potential confounding factors that are unmeasured at the individual level. Time series studies can be considered as ecological studies in the sense that exposure measurements are area-wide and the study subjects are not followed individually through time as in cohort studies [241]. Thus, time series studies that aim to combine information on the exposure and health outcome and make comparisons within and between multi-site studies from different countries and regions could be prone to ecological bias. However, the present study was a small-area study, and the data was collected in a homogeneous and restricted geographical area of the city of Chiang Mai only. The analyses were also restricted to only one study population. Therefore, it was very unlikely that the study was subjected to ecological bias.

9.4.3 Generalizability

In addition to differences in the nature of health data in different settings, regional differences in terms of population characteristics (e.g. physiology, behaviour, and culture) and geographical locations in different settings may also vary. This could lead to the differences in the vulnerability to the exposure and the variability of exposure levels and durations. Other factors, such as study period, measurement methods of air pollution and temperature, and patterns of medical practice are also different. Accordingly, results of the studies undertaken in different places could vary from study to study. In general, small-area studies or single-city studies are less generalizable to other locations than multi-cities studies. Single-city studies have been criticized for their findings not being consistent, and that even the re-analysis of the data in the same city could give inconsistent results [242]. Therefore, the multi-cities studies, such as NMMAPS, APHEA, and PAPA projects, have been conducted to overcome some of those criticisms and to make the studies comparable across different locations. The results of these projects can provide evidence of consistency and/or heterogeneity in air pollution effects and can also identify the potential effect modifiers of air pollution effects across different geographic locations [242, 243]. Because the present study was conducted in a single city of the north of Thailand with a tropical climate and 4-year time-series data used in the study was not very long, the findings may not be generalizable to other places.

9.4.4 Small daily counts of the investigations

The effects of air pollution are generally seen to be stronger for specific cardio-respiratory diseases (e.g. asthma, COPD, CHF, and MI) and specific subgroups of people (e.g. children and the elderly) [35, 112, 210]. Due to the relatively small daily counts of the visits/ admissions when the data were broken down into specific disease groups and subgroups of population (by age, sex, and occupation), the present study was unable to explore further for finer age, sex, and occupation within each disease groups and for finer specific diseases, but for broad categories only. The small daily counts provided limited statistical power, resulting in the often low precision of the estimates as shown by the wide confidence intervals.

The lack of statistical power was obviously presented in the results obtained for the linkage series, which were very imprecisely estimated as the confidence intervals were very wide. There were relatively small daily counts for the investigation of modified effects of previous visits on hospital admissions (total counts of 29,937). The limitation was due to too many missing patient ID numbers, which was the best variable to be used for linking the visits with the admissions due to uniqueness of this information at the individual level. We did try to link the two data sets (out-patient visits and hospital admissions) by using other variables, such as hospital number (HN) or dates of birth, but there was no big difference in the linkage data obtained. Because of the imprecise estimates obtained for the linkage data, this made it difficult to make specific interpretations and/or any strong conclusions about the findings. Since, to date, there is no investigation on modification of air pollution and temperature effects by previous hospital visits/ admissions on subsequent admissions, replication of the study is needed to confirm the findings.

9.4.5 Lack of some relevant information at the individual level

Although the study explored the modification of air pollution and temperature effects by factors at the individual levels, including age, sex, occupation, and history of previous visits, there were still some other relevant factors, such as SES (e.g. income and educational levels) and heat adaptations (e.g. air-conditioning use at home), which might play a role in the association. As discussed earlier, evidence suggests that people of lower SES may be more vulnerable to air pollution and temperature effects [181-183]. There were some previous studies using occupation as an indicator of SES to determine air pollution effects [182, 183].

Despite having information about occupation, the present study was not able to use it to identify SES of the study population because of the fact that there is no standard of income levels relative to occupation in Thailand. However, future improvements of data quality in the country by collecting direct information on individual income levels as well as educational levels may help to assess the role of SES on the association.

With regard to temperature effects, literature suggests that data at the individual levels in terms of heat adaptations, such as air-conditioning use, might also play a role in the association between hot temperature and health outcomes [244]. However, unlike the capital city, Bangkok, the use of air-conditioning is not very common in Thai people's homes, especially in the north, as the annual average temperature is relatively moderate. Moreover, traditionally, Thai people's homes are not tightly sealed, and opening windows for ventilation is commonly seen. Therefore, it is reasonable to believe that the lack of information on air-conditioning use should not cause any substantial change in the estimated effects of hot temperatures in the study.

9.5 Public health implications

- The finding of larger estimated effects of a classical pollutant, such as SO_2, in the present study reflects dissimilarities between developed world and less developed world. That is, while the problem of urban air pollution in developed countries has changed to be related to photochemical oxidants and acidic aerosols, the problem of urban air pollution in less developed countries, such as Thailand, is still related to a classical pollutant. This could also imply that environmental health policies and emission control measures that have been implemented in the country may not have been in place very long and/or not effective enough to cause substantial changes in air pollution problems. In general, SO_2 is usually found in industrial cities. Since there is no big industry in Chiang Mai and levels of SO_2 in the city are also well below the recommended standard, the larger estimated effects of SO_2 than of other pollutants is difficult to explain. Nevertheless, this result has confirmed that air pollution, even at low levels, could effects people's health. It also suggests that the Chiang Mai population may be particularly sensitive to SO_2 compared to other pollutants as a recent cohort study of air pollution in Chiang Mai also found

significant effects of SO_2 on the peak expiratory flow rate among asthmatic children [237]. Thus, further development and implementation of more advanced, rigorous, and consistent mitigation measures to identify sources of the pollutant and regularly monitor its levels in the city should be taken into consideration.

- The finding of hot temperature effects, instead of cold temperature effects, in this study is very important. Besides giving more attention on the impact of cold weather during winter that usually cause deaths in Thailand, there is also a need for public health interventions to educate people about the adverse consequences of increasing temperatures, and how to behave appropriately during hot periods in order to prevent serious illness. Traditionally, Thai people's homes are not tightly sealed, and opening windows for ventilation is commonly seen. Thus, air-conditioning use to reduce the impact of hot temperatures is economically and culturally inappropriate for introducing in the Thai community. Other interventions that have been introduced in European, American and Asian (e.g. Shanghai) cities, such as advising people to stay in cooler places, drink more water, avoid direct exposure to sunlight, and look after their more vulnerable neighbours, particularly the elderly (e.g. Buddy system) during hot days [245], would be more appropriate.

  Meanwhile, health care centres and hospitals should be notified in advance to prepare adequate, suitable medical treatments and staff for the possible increased morbidity during the hot days, particularly when the temperature rises above 29°C. Additionally, unlike previous studies, this study identified longer lag period (0-13 days) for heat effects. Therefore, health care providers should be made aware of adverse health consequences occurring up to 2 weeks following hot days. Attention should also be paid to the preparedness of health care facilities and staff in dealing HYPERLINK \l "_Toc247948233" ▯ hospital visits/ admissions for some specific diseases, such as diabetes, cardiovascular, and intestinal infectious diseases. It should be noted that hot temperature effects on intestinal infections in the city may be more acute than those observed in other places as this study found the effects over a short lag period (0-1 day) for this disease group.

- There was a greater vulnerability to an increasing temperature for intestinal infectious admissions in children. In addition, despite no statistically significant difference between subgroups, the larger estimates were found in the elderly, manual workers for air pollution effects, and in the elderly and unemployed and economically inactive people for temperature effects. Thus, it is noteworthy that the warning system in preventing adverse health effects should have been targeted to these potentially vulnerable people.

9.6 Conclusions and recommendations

This study was carried out to assess the short-term effects of air pollution and temperature on daily out-patient visits and hospital admissions in the Muang district in Chiang Mai, the second biggest province of Thailand. A time series approach was used for the investigation with careful considerations in selecting analytical methods to minimise possible bias and confounding. While there was little evidence of air pollution effects, there was significant evidence of hot temperature effects on daily morbidity in Chiang Mai. The higher risk of intestinal infectious admissions due to increasing temperature was found to be significant in children. A suggestion of larger effects of air pollution and temperature on the elderly, manual workers, and unemployed and economically inactive people was also observed. Some recommendations drawn from the study for future research are given below.

- Although this study has provided some evidence about air pollution and temperature effects on daily morbidity in Chiang Mai, replicated studies should be carried out in order to confirm the findings. Since it has been widely acknowledged that multi-cities studies could provide greater understanding of modifiers of air pollution and temperature effects than single-cities studies, it might be worth conducting time series studies on both morbidity and mortality in more cities in Thailand (e.g. in the biggest city of each region – north, north-eastern, east, west, central, and south) in order to provide deeper insight of air pollution and temperature effects specific to the country as a whole. However, it would be better to improve the quality of health data before conducting the research, such as having data that can differentiate emergency and elective cases, and the complete data with less missing information. Additionally, if diagnostic codes of the data are complete, it might be worth

exploring further specific disease codes, such as COPD, stroke and CHF, which could provide a deeper insight of the effects than using broad categories of diseases.

- With regard to the improvement of routinely collected data in the country, an improvement of both accuracy and completeness in collecting some additional information at the individual level, such as SES indicators (e.g. education, and income levels), should also be undertaken. The complete data at the individual level will provide a greater opportunity for researchers to further explore the impacts of air pollution and temperature on health and to indentify the vulnerable groups of people in the study population.

- Further investigations could also explore specific diseases, such as renal failure, and other infectious diseases (e.g. food poisoning, dengue hemorrhagic fever, and malaria) that may also increase in association with increasing temperature [46, 47, 137, 160, 161]. Future studies on the association between temperature and these particular diseases and on what kind of factors may influence the association would be helpful for establishing health promotion interventions to minimize the impacts of hot temperatures in the future.

- There was no evidence that people with many counts of previous visits would have a greater vulnerability to air pollution and temperature effects, leading to subsequent hospital admissions in the present study. This may be partly due to the possibility that the data comprised more health conscious people and/or those with high SES. More research studies are needed to increase the understanding of modified effects by previous visits (and previous admissions) as well as the role of SES on subsequent hospital admissions. In addition, since the sensitivity tests suggested that more recent visits could be a marker of greater vulnerability, a shorter time period (such as 3-month period, instead of 6-month period as used in this study) may be more appropriate for obtaining previous visits/ admissions. If the data in future studies allows, it may be more interesting to link individual records of the same person from the visits to admissions, and from the admissions to death, in order to see which specific diseases, and at which particular stage, would make an individual more susceptible to illness and death in relation to air pollution and temperature.

- Finally, to better inform health policy makers, further studies, which provide estimations of health care costs used for hospital visits/ admissions, and deaths in association with air pollution and temperature effects should also be conducted. This information will not only increase awareness of the impacts of air pollution and temperature among the public and policy makers, but can also be a useful guide for establishing appropriate public health policies and budgets to assist in providing sufficient health facilities and services to cope with an increase in daily morbidity and mortality, which is anticipated to increase as a result of global climate change and variability in the future.

In conclusion, despite having several limitations, the study has shown evidence of the short-term effects of hot temperature, but little evidence of air pollution effects on daily morbidity in Chiang Mai. Although the strength of the association was not very high, the study results were reasonably robust as suggested by a range of sensitivity tests and most of the study results were generally in good agreement with the existing knowledge. However, an identification of vulnerable groups of people is required more explorations from future research as this has not been clearly shown in this study. Replication studies, either in the same city or other cities in the country, should be undertaken to confirm the findings and to provide a greater opportunity for interpretations and comparisons. In addition, a wider range of research studies to determine air pollution and temperatures effects and other factors that may influence the association in less developed countries is still needed in order to implement the most appropriate public health policies and interventions specific to Thailand and the Asian region. This is because populations in different locations are different physically, behaviourally, culturally, and economically.

Collaboration

Collaboration was sought with two main sources of the data for the study.

1) The Chiang Mai Provincial Health Offices in Thailand for health data.

2) The Pollution Control Department (PCD), Bangkok, Thailand for air pollution and meteorological data.

Ethical consideration

The proposed study employed secondary data, which were the routinely collected health data of the Chiang Mai Provincial Health Office under the universal coverage (the 30 baht health insurance) scheme. Although the name of each patient was not shown on the data set, patients could be identified though their individual identification numbers (ID) and hospital number (HN). Thus, ethical approval was sought with the LSHTM Ethic Committee and the Ethic Committee of the Faculty of Medicine, Chiang Mai University, Thailand. In addition, the study results were presented as the effects of air pollution and temperature on groups of population without specific to any individual. There was no ID or HN of any patient shown in the study results.

Methods of keeping patients' personal information

To ensure that patients' personal information had been keeping secretly throughout the study, methods of covering patients' secrets was be done as follows.

- Health data was collected in a CD. Then, the principal investigator (PI) created confidential password of a CD. Thus, PI as the only one person who knew the password and was able to access the health data.
- All CDs of the health data was kept in the drawer of PI's personal cabinet at the study office. The drawer was locked and only the PI that had the key to open this drawer. After completion of the study, All CDs will also be kept in the same way at PI's workplace for 5-year period, and then will be destroyed.
- During the period of data analysis, the confidential password was also used for accessing the health data files in the computer. There was be only PI who knew the password and able to access the health data for analysis purposes.

References

1. Ponka A. Asthma and low level air pollution in Helsinki. Archives of Environmental Health. 1991;46(5):262-71.
2. Pope III CA. Respiratory Hospital Admissions Associated with PM 10 Pollution in Utah, Salt Lake, and Cache Valleys. Archives of Environmental Health. 1991;46(2):90-7.
3. Brunekreef B, Dockery DW, Krzyzanowski M. Epidemiology studies on short-term effects of low levels of major ambient air pollution components. Environmental Health Perspectives. 1995;103(Supplement 2):3-13.
4. Hong Y, Leem J, Ha E. Air pollution and daily mortality in Inchon, Korea. Journal of Korean Medical Science. 1999 June;14(3):239-44.
5. Luginaah IN, Fung KY, Gorey KM, Webster G, Wills C. Association of Ambient Air Pollution with Respiratory Hospitalization in a Government-Designated "Area of Concern": The Case of Windsor, Ontario. Environmental Health Perspectives. 2005;113(3):290-6.
6. Kunst AE, Looman CWN, Mackenbach JP. Outdoor air temperature and mortality in the Netherlands: a time-series analysis. American Journal of Epidemiology. 1993;137(3):331-41.
7. Keatinge WR, Donaldson GC, Cordioli E, Martinelli M, Kunst AE, Mackenbach JP, et al. Heat related mortality in warm and cold regions of Europe: observational study. BMJ. 2000 Sep 16;321(7262):670-3.
8. Basu R, Samet JM. Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence. Epidemiologic Reviews. 2002;24(2):190-202.
9. Hajat S, Kovats RS, Atkinson RW, Haines A. Impact of hot temperatures on death in London: a time series approach. Journal of Epidemiology and Community Health. 2002;56(367-372).
10. Kovats RS, Hajat S, Wilkinson P. Constrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. Occupational and Environmental Medicine. 2004;61:893-8.
11. Goodman PG, Dockery DW, Clancy L. Cause-Specific Mortality and the Extended Effects of Particulate Pollution and Temperature Exposure. Environmental Health Perspectives. 2004;112(2):179-85.
12. El-Zein A, Tewtel-Salem M. On the association between high temperature and mortality in warm climates. Science of the Total Environment. 2005 May 1;343(1-3):273-5.
13. Braga ALF, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology. 2001;12(662-667).
14. Schwartz J. Who is sensitive to extremes of temperature?: A case-only analysis. Epidemiology. 2005 Jan;16(1):67-72.
15. Utell MJ, Frampton MW. Who is susceptible to particulate matter and why? Inhalation Toxicology. 2000;12(Suppl 1):37-40.
16. Schwartz J. Short term fluctuations in air pollution and hospital admissions of the elderly for respiratory disease. Thorax. 1995 May;50(5):531-8.
17. Schwartz J. Air Pollution and Children's Health. Pediatrics. 2004;113(4):1037-43.
18. Annesi-Maesano I, Agabiti N, Pistelli R, Couilliot M-F, Forastiere F. Subpopulations at increased risk of adverse health outcomes from air pollution. European Respiratory Journal. 2003;21(Suppl. 40):57s-63s.

19. Delfino RJ, Murphy-Moulton AM, Becklake MR. Emergency room visits for respiratory illnesses among the elderly in Montreal: association with low level ozone exposure. Environmental Research. 1998 Feb;76(2):67-77.
20. Fischer P, Hoek G, Brunekreef B, Verhoeff A, van Wijnen J. Air pollution and mortality in The Netherlands: are the elderly more at risk? European Respiratory Journal 2003 May;40(Suppl):34s-8s.
21. Gouveia N, Fletcher T. Respiratory diseases in children and outdoor air pollution in Sao Paulo, Brazil: a time series analysis. Occupational and Environmental Medicine. 2000;57:477-83.
22. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE. The impact of heat waves and cold spells on mortality rates in the Dutch population. Environmental Health Perspectives. 2001 May;109(5):463-70.
23. Hajat S, Haines A. Associations of cold temperatures with GP consultations for respiratory and cardiovascular disease amongst the elderly in London. International Journal of Epidemiology. 2002;31:825-30.
24. Koken PJ, Piver WT, Ye F, Elixhauser A, Olsen LM, Portier CJ. Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. Environmental Health Perspectives. 2003 Aug;111(10):1312-7.
25. Basu R, Dominici F, Samet JM. Temperature and mortality among the elderly in the United States: a comparison of epidemiologic methods. Epidemiology. 2005 Jan;16(1):58-66.
26. Goldberg MS, Bailar JC, 3rd, Burnett RT, Brook JR, Tamblyn R, Bonvalot Y, et al. Identifying subgroups of the general population that may be susceptible to short-term increases in particulate air pollution: a time-series study in Montreal, Quebec. Research Report Health Effect Institute. 2000 Oct(97):7-113; discussion 5-20.
27. Goldberg MS, Burnett RT, Bailar JC, 3rd, Tamblyn R, Ernst P, Flegel K, et al. Identification of persons with cardiorespiratory conditions who are at risk of dying from the acute effects of ambient air particles. Environmental Health Perspectives. 2001 Aug;109 Suppl 4:487-94.
28. Bateson TF, Schwartz J. Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. Epidemiology. 2004 Mar;15(2):143-9.
29. Dubowsky SD, Suh H, Schwartz J, Coull BA, Gold DR. Diabetes, obestity, and hypertension may enhance associations between air pollution and markers of systemic inflammation. Environmental Health Perspectives. 2006;114(7):992-8.
30. Mann JK, Tager IB, Lurmann F, Segal M, Quesenberry CPJ, Lugg MM, et al. Air pollution and hospital admissions for ischemic heart disease in persons with congestive heart failure or arrhythmia. Environmental Health Perspectives. 2002 Dec;110(12):1247-52.
31. Morris RD, Naumova EN. Carbon monoxide and hospital admissions for congestive heart failure: evidence of an increased effect at low temperatures. Environmental Health Perspectives. 1998;106(10):649-53.
32. O'Neill MS, Veves A, Zanobetti A, Sarnat JA, Gold DR, Economides PA, et al. Diabetes enhances vulnerability to particulate air pollution-associated impairment in vascular reactivity and endothelial function. Circulation. 2005 Jun 7;111(22):2913-20.
33. Wong TW, Lau TS, Yu TS, Neller A, Wong SL, Tam W, et al. Air pollution and hospital admissions for respiratory and cardiovascular diseases in Hong Kong. Occupational and Environmental Medicine. 1999 October;56(10):679-83.

34. Zanobetti A, Schwartz J. Are diabetics more susceptible to the health effects of airborne particles? American Journal of Respiratory and Critical Care Medicine. 2001;164:831-3.
35. Zanobetti A, Schwartz J, Gold D. Are there sensitive subgroups for the effects of airborne particles? Environmental Health Perspectives. 2000;108(9):841-5.
36. Prescott GJ, Cohen GR, Elton RA, Fowkes FGR, Agius RM. Urban air pollution and cardiopulmonary ill health: a 14.5 year time series study. Occupational and Environmental Medicine. 1998;55:697-704.
37. Corey LM, Baker C, Luchtel DL. Heart-rate variability in the apolipoprotein E knockout transgenic mouse following exposure to Seattle particulate matter. Journal of Toxicology and Environmental Health Part A. 2006 May;69(10):953-65.
38. Wong CM, Ma S, Hedley AJ, Lam TH. Does ozone have any effect on daily hospital admissions for circulatory diseases? Journal of Epidemiology and Community Health. 1999 September;53(9):580-1.
39. General information of Chiang Mai Province. Chiang Mai: Chiang Mai Provincial Operation Centre2006.
40. The Pollution Control Department. Summary of state of Thailand's pollution. 2003 [cited 2005 February 21]; in Thai]. Available from: http://www.pcd.go.th.
41. The Pollution Control Department. Daily ambient air quality report. 2005 [cited 2005 February 21]; Available from: http://www.pcd.go.th.
42. Chiang Mai Mail. Chiang Mai air pollution critical2004; 2 No 52 (Saturday December 27, 2003 - January 2, 2004): Available from: http://www.chiangmai-mail.com/062/news.shtml#hd2.
43. Naewboonien V, Wongburanawatt J. Chiang Mai's Environmental Challenges. Chiang Mai: The International Network for Environmental Compliance and Enforcement (INECE); 1996 [cited 2006 June 21]; Available from: http://www.inece.org/4thvol1/4toc.htm.
44. Trakultivakorn M. Prevalence of asthma, rhinitis, and eczema in Northern Thai Children from Chiang Mai (International Study of Asthma and Allergies in Childhood, ISAAC). Asian Pacific Journal of Allergy Immumology. 1999;17(4):243-8.
45. McMichael AJ, Patz J, Kovats RS. Impacts of global environmental change on future health and health care in tropical countries. British Medical Bulletin. 1998;54(2):475-88.
46. Patz JA, Campbell-Lendrum D, Holloway T, Foley JA. Impact of regional climate change on human health. Nature. 2005 Nov 17;438(7066):310-7.
47. Haines A, Patz JA. Health effects of climate change. Jama. 2004 Jan 7;291(1):99-103.
48. Haines A, Kovats RS, Campbell-Lendrum D, Corvalan C. Climate change and human health: impacts, vulnerability and public health. Public Health. 2006 Jul;120(7):585-96.
49. Pope III CA, Schwartz J. Time series for the analysis of pulmonary health data. American Journal of Respiratory and Critical Care Medicince. 1996 Dec;154(6 Pt 2):S229-33.
50. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual Review of Public Health. 2006;27:57-79.
51. Brunekreef B, Holgate ST. Air pollution and health. The Lancet. 2002;360(1233-1242).

52. Dockery DW. Acute respiratory effects of particulate air pollution. In: Curtis CJ, Reed JM, Battarbee RW, Harrison RM, editors. Urban air pollution and Public Health. London: Ensis Publishing; 1994. p. 45-52.
53. Chan-Yeung MNW. Air pollution and health. Hong Kong Medical Journal. 2000;6(4):390-8.
54. Holgate ST, Samet JM, Koren HS, Maynard RL. Air pollution and health. London: Academic press; 1999.
55. Davalia JL, Davies RJ. Mechanisms underlying pollution-induced lung damage. In: Curtis CJ, Reed JM, Battarbee RW, Harrison RM, editors. Urban air pollution and public health. London: Ensis Publishing; 1996. p. 53-7.
56. WHO. Air quality guidelines for Europe 2nd ed. Copenhagen World Health Organization. Regional Office for Europe. ; 2000.
57. EPA Victoria. Particles. Victoria, Australia: EPA Victoria; 2003 [updated August 4, 2003; cited 2005 August 13]; Available from: http://www.epa.vic.gov.au/Air/Issues/air_part.asp.
58. Maroni M, Seifert B, Lindvall T. Indoor air quality: a comprehensive reference book. New York: Elsevier Science; 1995.
59. Greenland S. Basic problems in interaction assessment. Environmental Health Perspectives. 1993 Dec;101 Suppl 4:59-66.
60. Morgenstern H, Thomas D. Principles of study design in environmental epidemiology. Environmental Health Perspectives. 1993 Dec;101 Suppl 4:23-38.
61. Dockery DW, Pope III CA. Acute Respiratory Effects of Particulate Air Pollution. Annual Review of Public Health. 1994;15:107-32.
62. Katsouyanni K, Touloumi G, Samoli E, Gryparis A, Le Tertre A, Monopolis Y, et al. Confounding and effect modification in the short-term effects of ambient particles on total mortality: results from 29 European cities within the APHEA2 project. Epidemiology. 2001 Sep;12(5):521-31.
63. Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, et al. The National Morbidity, Mortality, and Air Pollution Study. Part II: Morbidity and mortality from air pollution in the United States. Research Report Health Effects Institute. 2000 Jun;94(Pt 2):5-70; discussion 1-9.
64. Bremner SA, Anderson HR, Atkinson RW, McMichael AJ, Strachan DP, Bland JM, et al. Short-term associations between outdoor air pollution and mortality in London 1992-4. Occupational and Environmental Medicine. 1999 Apr;56(4):237-44.
65. Morgan G, Corbett S, Wlodarczyk J, Lewis P. Air pollution and daily mortality in Sydney, Australia, 1989 through 1993. American Journal of Public Health. 1998 May;88(5):759-64.
66. Michelozzi P, Forastiere F, Fusco D, Perucci CA, Ostro B, Ancona C, et al. Air pollution and daily mortality in Rome, Italy. Occupational and Environmental Medicine. 1998 Sep;55(9):605-10.
67. Mar TF, Norris GA, Koenig JQ, Larson TV. Associations between air pollution and mortality in Phoenix, 1995-1997. Environmental Health Perspectives. 2000 Apr;108(4):347-53.
68. Moolgavkar SH. Air pollution and daily mortality in three U.S. counties. Environmental Health Perspectives. 2000 Aug;108(8):777-84.
69. Loomis DP, Borja-Aburto VH, Bangdiwala SI, Shy CM. Ozone exposure and daily mortality in Mexico City: a time-series analysis. Research Report Health Effects Institute. 1996 Oct(75):1-37; discussion 9-45.

70. Goldberg MS, Burnett RT, Brook J, Bailar JC, 3rd, Valois MF, Vincent R. Associations between daily cause-specific mortality and concentrations of ground-level ozone in Montreal, Quebec. American Journal of Epidemiology. 2001 Nov 1;154(9):817-26.
71. Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. Ozone and short-term mortality in 95 US urban communities, 1987-2000. Jama. 2004 Nov 17;292(19):2372-8.
72. Bell ML, Dominici F, Samet JM. A meta-analysis of time-series studies of ozone and mortality with comparison to the national morbidity, mortality, and air pollution study. Epidemiology. 2005 Jul;16(4):436-45.
73. Schwartz J. Is there harvesting in the association of airborne particles with daily deaths and hospital admissions? Epidemiology. 2001 Jan;12(1):55-61.
74. Zanobetti A, Schwartz J, Samoli E, Gryparis A, Touloumi G, Atkinson R, et al. The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement. Epidemiology. 2002 Jan;13(1):87-93.
75. Xu X, Dockery DW, Christiani DC, Li B, Huang H. Association of air pollution with hospital outpatient visits in Beijing. Archives of Environmental Health. 1995 May-June;50(3):214-20.
76. Sinclair AM, Tolsma D. Associations and Lags between Air Pollution and Acute Respiratory Visits in an Ambulatory Care Setting:25-Month Results from the Aerosol Research and Inhalation Epidemiological study. Journal of the Air and Waste Management Association. 2004;54:1212-8.
77. Wong TW, Tam W, Tak Sun Yu I, Wun YT, Wong AH, Wong CM. Association between air pollution and general practitioner visits for respiratory diseases in Hong Kong. Thorax. 2006 Jul;61(7):585-91.
78. Peel JL, Tolbert PE, Klein M, Metzger KB, Flanders WD, Todd K, et al. Ambient Air pollution and Respiratory Emergency Department Visits. Epidemiology. 2005;16:164-74.
79. Wilson AM, Wake CP, Kelly T, Salloway JC. Air pollution, weather, and respiratory emergency room visits in two northern New England cities: an ecological time-series study. Environmental Research. 2005 Mar;97(3):312-21.
80. Spix C, Anderson HR, Schwartz J, Vigotti MA, LeTertre A, Vonk JM, et al. Short-term effects of air pollution on hospital admissions of respiratory diseases in Europe: a quantitative summary of APHEA study results. Air Pollution and Health: a European Approach. Archives of Environmental Health. 1998 Jan-Feb;53(1):54-64.
81. Morgan G, Corbett S, Wlodarczyk J. Air pollution and hospital admissions in Sydney, Australia, 1990 to 1994. American Journal of Public Health. 1998 Dec;88(12):1761-6.
82. Fusco D, Forastiere F, Michelozzi P, Spadea T, Ostro B, Arca M, et al. Air pollution and hospital admissions for respiratory conditions in Rome, Italy. European Respiratory Journal. 2001;17:1143-50.
83. Lee JT, Kim H, Cho YS, Hong YC, Ha EH, Park H. Air pollution and hospital admissions for ischemic heart diseases among individuals 64+ years of age residing in Seoul, Korea. Archives of Environmental Health. 2003 Oct;58(10):617-23.
84. Health Effects Institute. Health Effects of Outdoor Air Pollution in Developing Countries of Asia: A Literature Review, Special report 15. Boston2004.
85. Wong CM, Ma S, Hedley AJ, Lam TH. Effect of air pollution on daily mortality in Hong Kong. Environmental Health Perspectives. 2001 April;109(4):335-40.

86. Wong GW, Ko FW, Lau TS, Li ST, Hui D, Pang SW, et al. Temporal relationship between air pollution and hospital admissions for asthmatic children in Hong Kong. Clinical and Experimental Allergy. 2001 April;31(4):565-9.
87. Wong TW, Tam WS, Yu TS, Wong AH. Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. Occupational and Environmental Medicine. 2002 Janurary;59(1):30-5.
88. Wong CM, Atkinson RW, Anderson HR, Hedley AJ, Ma S, Chau PY, et al. A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared. Environmental Health Perspectives. 2002;110(1):67-77.
89. Hong YC, Lee JT, Kim H, Ha EH, Schwartz J, Christiani DC. Effects of air pollutants on acute stroke mortality. Environmental Health Perspectives. 2002 February;110(2):187-91.
90. Hong Y, Lee J, Kim H, Kwon H. Air pollution: a new risk factor in ischemic stroke mortality. Stroke. 2002 September;33(9):2165-9.
91. Kwon HJ, Cho SH, Nyberg F, Pershagen G. Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. Epidemiology. 2001 July;12(4):413-9.
92. Lee J, Shin D, Chung Y. Air pollution and daily mortality in Seoul and Ulsan, Korea. Environmental Health Perspectives. 1999 February;107(2):149-54.
93. Cho B, Choi J, Yum Y-T. Air pollution and hospital admissions for respiratory disease in certain areas of Korea. Journal of Occupational Health. 2000;42:185-91.
94. Health Effects Institute. Public health and air pollution in Asia (PAPA): Key results from Bangkok, Hong Kong, Shanghai, and Wuhan. Communication 13. Boston, MA.2008.
95. Buadong D, Jinsart W, Funatagawa I, Karita K, Yano E. Association between PM10 and O3 levels and hospital visits for cardiovascular diseases in Bangkok, Thailand. Journal of Epidemiology. 2009;19(4):182-8.
96. Cao J, Li W, Tan J, Song W, Xu X, Jiang C, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. Science of the Total Environment. 2009 Oct 15;407(21):5531-6.
97. Chew F, Goh D, Ooi B, Saharam R, Hui J, Lee B. Association of ambient air-pollution levels with acute asthma exacerbation among children in Singapore. Allergy. 1999 April;54(4):320-9.
98. Lee JT, Kim H, Hong YC, Kwon HJ, Schwartz J, Christiani DC. Air pollution and daily mortality in seven major cities of Korea, 1991-1997. Environmental Research. 2000 November;84(3):247-54.
99. Venners SA, Wang B, Xu Z, Schlatter Y, Wang L, Xu X. Particulate matter, sulfur dioxide, and daily mortality in Chongqing, China. Environmental Health Perspectives. 2003;111(4):562-7.
100. Xu X, Gao J, Dockery DW, Chen Y. Air pollution and daily mortality in residential areas of Beijing, China. Archives of Environmental Health. 1994 July-August;49(4):216-22.
101. Xu Z, Yu D, Jing L, Xu X. Air pollution and daily mortality in Shenyang, China. Archives of Environmental Health. 2000 Mar-Apr;55(2):115-20.
102. Ha EH, Lee JT, Kim H, Hong YC, Lee BE, Park HS, et al. Infant susceptibility of mortality to air pollution in Seoul, South Korea. Pediatrics. 2003 February;111(2):284-90.
103. Schwartz J. Air pollution and hospital admissions for the elderly in Birmingham, Alabama. American Journal of Epidemiology. 1994 Mar 15;139(6):589-98.

104. Ostro B, Chestnut L, Vichit-Vadakan N, Laixuthai A. The impact of particulate matter on daily mortality in Bangkok, Thailand. Journal of the Air and Waste Management Association. 1999 September;19(9 spec No.):100-7.
105. Gwynn RC, Burnett RT, Thurston GD. A time-series analysis of acidic particulate matter and daily mortality and morbidity in the Buffalo, New York, region. Environmental Health Perspectives. 2000 Feb;108(2):125-33.
106. Atkinson RW, Anderson HR, Sunyer J, Ayres J, Baccini M, Vonk JM, et al. Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. Air Pollution and Health: a European Approach. American Journal of Respiratory and Critical Care Medicine. 2001 Nov 15;164(10 Pt 1):1860-6.
107. Anderson HR, Bremner SA, Atkinson RW, Harrison RM, Walters S. Particulate matter and daily mortality and hospital admissions in the west midlands conurbation of the United Kingdom: associations with fine and coarse particles, black smoke and sulphate. Occupational and Environmental Medicine. 2001 Aug;58(8):504-10.
108. Anderson HR, Atkinson RW, Bremner SA, Marston L. Particulate air pollution and hospital admissions for cardiorespiratory diseases: are the elderly at greater risk? European Respiratory Journal 2003 May;40(Supplement):39s-46s.
109. Morris RD. Airborne particulates and hospital admissions for cardiovascular disease: a quantitative review of the evidence. Environmental Health Perspectives. 2001 Aug;109 Suppl 4:495-500.
110. Chen Y, Yang Q, Krewski D, Shi Y, Burnett RT, McGrail K. Influence of relatively low level of particulate ar pollution on hospitalization for COPD in elderly people. Inhalation Toxicology. 2004 Jan;16(1):21-5.
111. Medina-Ramon M, Zanobetti A, Schwartz J. The effect of ozone and PM10 on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multicity study. American Journal of Epidemiology. 2006 Mar 15;163(6):579-88.
112. Arena VC, Mazumdar S, Zborowski JV, Talbott EO, He S, Chuang YH, et al. A retrospective investigation of PM10 in ambient air and cardiopulmonary hospital admissions in Allegheny County, Pennsylvania: 1995-2000. Journal of Occupational and Environmental Medicine. 2006 Jan;48(1):38-47.
113. Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA. 2006 Mar 8;295(10):1127-34.
114. Ulirsch GV, Ball LM, Kaye W, Shy CM, Lee CV, Crawford-Brown D, et al. Effect of particulate matter air pollution on hospital admissions and medical visits for lung and heart disease in two southeast Idaho cities. Journal of Exposure Science and Environmental Epidemiology. 2007 Aug;17(5):478-87.
115. Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, et al. Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. JAMA. 2008 May 14;299(18):2172-9.
116. Bell ML, Ebisu K, Peng RD, Walker J, Samet JM, Zeger SL, et al. Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999-2005. American Journal of Epidemiology. 2008 Dec 1;168(11):1301-10.
117. Keim SM, Guisto JA, Sullivan JB, Jr. Environmental thermal stress. Annals of Agricutural and Environmental Medicine. 2002;9(1):1-15.
118. Faunt JD, Wilkinson TJ, Aplin P, Henschke P, Webb M, Penhall RK. The effete in the heat: heat-related hospital presentations during a ten day heat wave. Australian and New Zealand Journal of Medicine. 1995 Apr;25(2):117-21.

119. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR. Excess hospital admissions during the July 1995 heat wave in Chicago. American Journal of Preventive Medicine. 1999 May;16(4):269-77.
120. Feigin VL, Nikitin YP, Bots ML, Vinogradova TE, Grobbee DE. A population-based study of the associations of stroke occurrence with weather parameters in Siberia, Russia (1982-92). European Journal of Neurology. 2000 Mar;7(2):171-8.
121. Schwartz J, Samet JM, Patz JA. Hospital admissions for heart disease: the effects of temperature and humidity. Epidemiology. 2004 Nov;15(6):755-61.
122. Martens WJM. Climate change, thermal stress and mortality changes. Social science and medicine. 1997;46(3):331-44.
123. Ballester F, Corella D, Perez-Hoyos S, Saez M, Hervas A. Mortality as a function of temperature. A study in Valencia, Spain, 1991-1993. International Journal of Epidemiology. 1997 Jun;26(3):551-61.
124. Pan WH, Li LA, Tsai MJ. Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese. Lancet. 1995 Feb 11;345(8946):353-5.
125. Mackenbach JP, Looman CWN, Kunst AE. Air pollution, lag effects of temperature, and mortality: the Netherlands 1979-87. Journal of Epidemiology and Community Health. 1993;47:121-6.
126. Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. American Journal of Epidemiology. 2002 Jan 1;155(1):80-7.
127. Basu R. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environmental Health. 2009;8:40.
128. Rooney C, McMichael AJ, Kovats RS, Coleman MP. Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave. Journal of Epidemiology and Community Health. 1998 Aug;52(8):482-6.
129. Vassallo M, Gera KN, Allen S. Factors associated with high risk of marginal hyperthermia in elderly patients living in an institution. Postgraduate Medical Journal. 1995 Apr;71(834):213-6.
130. Diaz J, Garcia R, Velazquez de Castro F, Hernandez E, Lopez C, Otero A. Effects of extremely hot days on people older than 65 years in Seville (Spain) from 1986 to 1997. International Journal of Biometeorology. 2002 Aug;46(3):145-9.
131. Heat-related mortality--Chicago, July 1995. MMWR Morbidity and Mortality Weekly Report. 1995 Aug 11;44(31):577-9.
132. Greenberg JH, Bromberg J, Reed CM, Gustafson TL, Beauchamp RA. The epidemiology of heat-related deaths, Texas--1950, 1970-79, and 1980. American Journal of Public Health. 1983 Jul;73(7):805-7.
133. Stephan F, Ghiglione S, Decailliot F, Yakhou L, Duvaldestin P, Legrand P. Effect of excessive environmental heat on core temperature in critically ill patients. An observational study during the 2003 European heat wave. British Journal of Anaesthesia. 2005 Jan;94(1):39-45.
134. Lin S, Luo M, Walker RJ, Liu X, Hwang SA, Chinery R. Extreme High Temperatures and Hospital Admissions for Respiratory and Cardiovascular Diseases. Epidemiology. 2009 Jul 10.
135. Linares C, Diaz J. Impact of high temperatures on hospital admissions: comparative analysis with previous studies about mortality (Madrid). European Journal of Public Health. 2008 Jun;18(3):317-22.
136. Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, et al. High temperature and hospitalizations for cardiovascular and respiratory causes in 12

European cities. American Journal of Respiratory and Critical Care Medicine. 2009 Mar 1;179(5):383-9.
137. Green RS, Basu R, Malig B, Broadwin R, Kim JJ, Ostro B. The effect of temperature on hospital admissions in nine California counties. International Journal of Public Health. 2009 Sep 22.
138. Rudge J, Gilchrist R. Excess winter morbidity among older people at risk of cold homes: a population-based study in a London borough. Journal of Public Health 2005 Dec;27(4):353-8.
139. Panagiotakos DB, Chrysohoou C, Pitsavos C, Nastos P, Anadiotis A, Tentolouris C, et al. Climatological variations in daily hospital admissions for acute coronary syndromes. International Journal of Cardiology. 2004 Apr;94(2-3):229-33.
140. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and Environmental Science. 2003 Jun;16(2):133-9.
141. Green MS, Harari G, Kristal-Boneh E. Excess winter mortality from ishaemic heart disease and stroke during colder and warmer years in Israel. European Journal of Public Health. 1994;4:3-11.
142. Nakaji S, Parodi S, Fontana V, Umeda T, Suzuki K, Sakamoto J, et al. Seasonal changes in mortality rates from main causes of death in Japan (1970--1999). European Journal of Epidemiology. 2004;19(10):905-13.
143. Hong YC, Rha JH, Lee JT, Ha EH, Kwon HJ, Kim H. Ischemic stroke associated with decrease in temperature. Epidemiology. 2003 Jul;14(4):473-8.
144. Ye F, Piver WT, Ando M, Portier CJ. Effects of temperature and air pollutants on cardiovascular and respiratory diseases for males and females older than 65 years of age in Tokyo, July to August Environmental Health Perspectives. 2001 April;109(4):355-9.
145. Liang WM, Liu WP, Chou SY, Kuo HW. Ambient temperature and emergency room admissions for acute coronary syndrome in Taiwan. International Journal of Biometeorology. 2008 Jan;52(3):223-9.
146. Sandstrom T. Respiratory effects of air pollutants: experimental studies in humans. European Respiratory Journal. 1995 Jun;8(6):976-95.
147. Gilmour MI, Park P, Selgrade MK. Ozone-enhanced pulmonary infection with Streptococcus zooepidemicus in mice. The role of alveolar macrophage function and capsular virulence factors. The American Review of Respiratory Disease. 1993 Mar;147(3):753-60.
148. Chitano P, Hosselet JJ, Mapp CE, Fabbri LM. Effect of oxidant air pollutants on the respiratory system: insights from experimental animal research. European Respiratory Journal. 1995 Aug;8(8):1357-71.
149. Tyrrell D, Barrow I, Arthur J. Local hyperthermia benefits natural and experimental common colds. BMJ. 1989 May 13;298(6683):1280-3, cited in Schwartz J. 2005.
150. Keatinge WR, Coleshaw SR, Easton JC, Cotter F, Mattock MB, Chelliah R. Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. American Journal of Medicine. 1986 Nov;81(5):795-800.
151. Goldberg MS, Burnett RT, Valois MF, Flegel K, Bailar JC, 3rd, Brook J, et al. Associations between ambient air pollution and daily mortality among persons with congestive heart failure. Environmental Research. 2003 Jan;91(1):8-20.
152. Hoek G, Brunekreef B, Fischer P, van Wijnen J. The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. Epidemiology. 2001;12:355-7.

153. Gold DR, Litonjua A, Schwartz J, Lovett E, Larson A, Nearing B, et al. Ambient pollution and heart rate variability. Circulation. 2000 Mar 21;101(11):1267-73.
154. Bates DV. Health indices of the adverse effects of air pollution: the question of coherence. Environmental Research. 1992 Dec;59(2):336-49.
155. Keatinge WR, Coleshaw SR, Easton JC, Cotter F, Mattock MB, Chelliah R. Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. American Journal of Medicine. 1986 Nov;81(5):795-800, cited in Schwartz et al 2004.
156. The Eurowinter Group. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. . Lancet. 1997 May 10;349(9062):1341-6.
157. Pereira Filho MA, Pereira LA, Arbex FF, Arbex M, Conceicao GM, Santos UP, et al. Effect of air pollution on diabetes and cardiovascular diseases in Sao Paulo, Brazil. Brazilian Journal of Medical and Biological Research. 2008 Jun;41(6):526-32.
158. Medina-Ramon M, Zanobetti A, Cavanagh DP, Schwartz J. Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. Environmental Health Perspectives. 2006 Sep;114(9):1331-6.
159. Checkley W, Epstein LD, Gilman RH, Figueroa D, Cama RI, Patz JA, et al. Effect of El Nino and ambient temperature on hospital admissions for diarrhoeal diseases in Peruvian children. Lancet. 2000 Feb 5;355(9202):442-50.
160. Kovats RS, Edwards SJ, Hajat S, Armstrong BG, Ebi KL, Menne B. The effect of temperature on food poisoning: a time-series analysis of salmonellosis in ten European countries. Epidemiology and Infection. 2004 Jun;132(3):443-53.
161. Fleury M, Charron DF, Holt JD, Allen OB, Maarouf AR. A time series analysis of the relationship of ambient temperature and common bacterial enteric infections in two Canadian provinces. Internaltional Journal of Biometeorology. 2006 Jul;50(6):385-91.
162. Hashizume M, Armstrong B, Hajat S, Wagatsuma Y, Faruque AS, Hayashi T, et al. Association between climate variability and hospital visits for non-cholera diarrhoea in Bangladesh: effects and vulnerable groups. International Journal of Epidemiology. 2007 Oct;36(5):1030-7.
163. Cohen AJ. Outdoor air pollution and lung cancer. Environmental Health Perspectives. 2000 Aug;108 Suppl 4:743-50.
164. Chen H, Goldberg MS, Villeneuve PJ. A systematic review of the relation between long-term exposure to ambient air pollution and chronic diseases. Reviews on Environmental Health. 2008 Oct-Dec;23(4):243-97.
165. Vineis P, Forastiere F, Hoek G, Lipsett M. Outdoor air pollution and lung cancer: recent epidemiologic evidence. International Journal of Cancer. 2004 Sep 20;111(5):647-52.
166. Lewtas J. Air pollution combustion emissions: characterization of causative agents and mechanisms associated with cancer, reproductive, and cardiovascular effects. Mutation Research. 2007 Nov-Dec;636(1-3):95-133.
167. Abe T, Tokuda Y, Ohde S, Ishimatsu S, Nakamura T, Birrer RB. The influence of meteorological factors on the occurrence of trauma and motor vehicle collisions in Tokyo. Emergency Medical Journal. 2008 Nov;25(11):769-72.
168. Nofal FH, Saeed AA. Seasonal variation and weather effects on road traffic accidents in Riyadh city. Public Health. 1997 Jan;111(1):51-5.
169. Page LA, Hajat S, Kovats RS. Relationship between daily suicide counts and temperature in England and Wales. British Journal of Psychiatry. 2007 Aug;191:106-12.

170. Kelly FJ, Dunster C, Mudway I. Air pollution and the elderly: oxidant/antioxidant issues worth consideration. European Respiratory Journal 2003 May;40(Suppl.):70s-5s.
171. Smolander J. Effect of cold exposure on older humans. International Journal of Sports Medicine. 2002 Feb;23(2):86-92.
172. Stafoggia M, Forastiere F, Agostini D, Biggeri A, Bisanti L, Cadum E, et al. Vulnerability to heat-related mortality: a multicity, population-based, case-crossover analysis. Epidemiology. 2006 May;17(3):315-23.
173. Martins LC, Pereira LA, Lin CA, Santos UP, Prioli G, Luiz Odo C, et al. The effects of air pollution on cardiovascular diseases: lag structures. Rev Saude Publica. 2006 Aug;40(4):677-83.
174. Granados-Canal DJ, Chardon B, Lefranc A, Gremy I. Air pollution and respiratory hospital admissions in greater Paris: exploring sex differences. Archives of Environmental and Occupational Health. 2005 Nov-Dec;60(6):307-13.
175. Sunyer J, Schwartz J, Tobias A, Macfarlane D, Garcia J, Anto JM. Patients with chronic obstructive pulmonary disease are at increased risk of death associated with urban particle air pollution: a case-crossover analysis. American Journal of Epidemiology. 2000 Jan 1;151(1):50-6.
176. Medina-Ramon M, Schwartz J. Who is more vulnerable to die from ozone air pollution? Epidemiology. 2008 Sep;19(5):672-9.
177. Jinsart W, Tamura K, Loetkamonwit S, Thepanondh S, Karita K, Yano E. Roadside particulate air pollution in Bangkok. Journal of the Air and Waste Management and Association. 2002 Sep;52(9):1102-10.
178. Ruchirawat M, Navasumrit P, Settachan D, Tuntaviroon J, Buthbumrung N, Sharma S. Measurement of genotoxic air pollutant exposures in street vendors and school children in and near Bangkok. Toxicology and Applied Pharmacology. 2005 Aug 7;206(2):207-14.
179. Rodahl K. Occupational health conditions in extreme environments. Annals of Occupational Hygiene. 2003 Apr;47(3):241-52.
180. Schwartz J. Assessing confounding, effect modification, and thresholds in the association between ambient particles and daily deaths. Environmental Health Perspectives. 2000 Jun;108(6):563-8.
181. Jerrett M, Burnett RT, Brook J, Kanaroglou P, Giovis C, Finkelstein N, et al. Do socioeconomic characteristics modify the short term association between air pollution and mortality? Evidence from a zonal time series in Hamilton, Canada. Journal of Epidemiology and Community Health. 2004 Jan;58(1):31-40.
182. Ou CQ, Hedley AJ, Chung RY, Thach TQ, Chau YK, Chan KP, et al. Socioeconomic disparities in air pollution-associated mortality. Environmental Research. 2008 Jun;107(2):237-44.
183. Wong CM, Ou CQ, Chan KP, Chau YK, Thach TQ, Yang L, et al. The effects of air pollution on mortality in socially deprived urban areas in Hong Kong, China. Environmental Health Perspectives. 2008 Sep;116(9):1189-94.
184. Ito K, Thurston GD, Silverman RA. Characterization of PM2.5, gaseous pollutants, and meteorological interactions in the context of time-series health effects models. Journal of Exposure Science and Environmental Epidemiology. 2007 Dec;17 Suppl 2:S45-60.
185. Moolgavkar SH, Luebeck EG. A critical review of the evidence on particulate air pollution and mortality. Epidemiology. 1996 Jul;7(4):420-8.
186. Kim H, Kim Y, Hong YC. The lag-effect pattern in the relationship of particulate air pollution to daily mortality in Seoul, Korea. International Journal of Biometeorology. 2003 Sep;48(1):25-30.

187. Diaz J, Alberdi JC, Pajares MS, Lopez C, Lopez R, Lage MB, et al. A model for forecasting emergency hospital admissions: effect of environmental variables. Journal of Environmental Health. 2001 Oct;64(3):9-15.
188. Pattenden S, Nikiforov B, Armstrong BG. Mortality and temperature in Sofia and London. Journal of Epidemiology and Community Health. 2003 Aug;57(8):628-33.
189. Muggeo V, Hajat S. Modelling the nonlinear multiple-lag effects of ambient temperature on mortality in Santiago and Palermo : a constrained segmented distributed lag approach. Occupational and Environmental Medicine. 2008 Dec 18.
190. Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environmental Health Perspectives. 2000 May;108(5):419-26.
191. WHO. International Statistical Classification of Diseases and Health Related Problems (The) ICD-10 Geneva: The World Health Organisation; 2006 [cited 2006 May 22]; Available from: http://www.who.int/classifications/icd/en/.
192. Katsouyanni K, Schwartz J, Spix C, Touloumi G, Zmirou D, Zanobetti A, et al. Short term effects of air pollution on health: a European approach using epidemiologic time series data: the APHEA protocal. Journal of Epidemiology and Community Health. 1996;50(Suppl 1):S12-S8.
193. Schwartz J, Spix C, Touloumi G, Bacharova L, Baramamdazadeh T, le Tertre A, et al. Methodological issues in studies of air pollution and daily counts of deaths or hospital admissions. Journal of Epidemiology and Community Health. 1996;50(Suppl 1):S3-S11.
194. Gardner W, Mulvey EP, Shaw EC. Regression analyses of counts and rates: Poisson, overdispersed Poisson, and negative binomial models. Psychological Bulletin. 1995;118(3):392-404.
195. McCullough P, Nelder JA. Generalized Linear Models. 2 ed. London: CHAPMAN& HALL/CRC; 1989.
196. O'Neill MS, Hajat S, Zanobetti A, Ramirez-Aguilar M, Schwartz J. Impact of control for air pollution and respiratory epidemics on the estimated associations of temperature and daily mortality. International Journal of Biometeorology. 2005;50(2):121-9.
197. Hashizume M. Time series study of the relationship between rainfall and diarrhoea in Bangladesh. London: London School of Hygiene and Tropical Medicine; 2007.
198. Braga AL, Zanobetti A, Schwartz J. The lag structure between particulate air pollution and respiratory and cardiovascular deaths in 10 US cities. Journal of Occupational and Environmental Medicine. 2001 Nov;43(11):927-33.
199. Atkinson RW, Bremner SA, Anderson HR, Strachan DP, Bland JM, de Leon AP. Short-term associations between emergency hospital admissions for respiratory and cardiovascular disease and outdoor air pollution in London. Archives of Environmental Health. 1999 Nov-Dec;54(6):398-411.
200. Chatfield C. The analysis of time series: an introduction. London: CHAPMAN & HALL/CRC; 2004.
201. Katsouyanni K, Anderson HR, Hoek G. Design and analysis of temporal studies in air pollution epidemiology.: Air Pollution Epidemiology Report series 10.1997, cited in Gouveia N. 1998.
202. Peng RD, Dominici F, Louis TA. Model choice in time series studies of air pollution and mortality. Journal of the Royal Statistical Society: Series A. 2006;162(2):179-203.
203. Health Effects Institute. Revised Analyses of the National Morbidity, Mortality, and Air Pollution Study, Part II. Boston MA.2003.

204. Vasavid C, Tangcharoensathien V, Tisayaticom K, Patcharanarumol W, Opanapun N. Health and welfare of Thai population after Universal Health Care Coverage (UC)-part 1: illness, utilisation compliance of health care services of UC members. Journal of Health Science. 2004;13:428-39.
205. Thamthatarree C, Rueangdej S. Quality indicators of administrative data and hospital characteristics. Nonthaburi, Thailand: Health Systems Research Institute; 2003.
206. Prasanwong C, Rueangdej S, Lokchareanlap S, Thatsaringkarnsakul W, Pantarassami C, Yeonyongsuwan M. Medical coding practices in Thailand. Nonthaburi, Thailand: Health System Research Institute; 2002.
207. Xu X, Li B, Huang H. Air pollution and unscheduled hospital outpatient and emergency room visits. Environmental Health Perspectives. 1995 March;103(3):286-9.
208. Bennett AE. Limitations of the use of hospital statistics as an index of morbidity in environmental studies. Journal of the Air Pollution Control Association. 1981 Dec;31(12):1276-8.
209. Lipfert FW. A critical review of studies of the association between demands for hospital services and air pollution. Environmental Health Perspectives. 1993 Jul;101 Suppl 2:229-68.
210. Sunyer J, Atkinson R, Ballester F, Le Tertre A, Ayres JG, Forastiere F, et al. Respiratory effects of sulphur dioxide: a hierarchical multicity analysis in the APHEA 2 study. Occupational and Environmental Medicine. 2003 Aug;60(8):e2.
211. Schwartz J. Air pollution and hospital admissions for respiratory disease. Epidemiology. 1996 Jan;7(1):20-8.
212. Ponce de Leon A, Anderson HR, Bland JM, Strachan DP, Bower J. Effects of air pollution on daily hospital admissions for respiratory disease in London between 1987-88 and 1991-92. Journal of Epidemiology and Community Health. 1996 Apr;50 Suppl 1:s63-70.
213. Hajat S, Haines A, Atkinson RW, Bremner SA, Anderson HR, Emberlin J. Association between air pollution and daily consultations with general practitioners for allergic rhinitis in London, United Kingdom. American Journal of Epidemiology. 2001 Apr 1;153(7):704-14.
214. Tenias JM, Ballester F, Perez-Hoyos S, Rivera ML. Air pollution and hospital emergency room admissions for chronic obstructive pulmonary disease in Valencia, Spain. Archives of Environmental Health. 2002 Jan-Feb;57(1):41-7.
215. Simpson R, Williams G, Petroeschevsky A, Best T, Morgan G, Denison L, et al. The short-term effects of air pollution on hospital admissions in four Australian cities. Australian and New Zealand Journal of Public Health. 2005 Jun;29(3):213-21.
216. Larrieu S, Jusot JF, Blanchard M, Prouvost H, Declercq C, Fabre P, et al. Short term effects of air pollution on hospitalizations for cardiovascular diseases in eight French cities: the PSAS program. Science of the Total Environment. 2007 Nov 15;387(1-3):105-12.
217. Linn WS, Szlachcic Y, Gong H, Jr., Kinney PL, Berhane KT. Air pollution and daily hospital admissions in metropolitan Los Angeles. Environmental Health Perspectives. 2000 May;108(5):427-34.
218. Atkinson RW, Anderson HR, Strachan DP, Bland JM, Bremner SA, Ponce de Leon A. Short-term associations between outdoor air pollution and visits to accident and emergency departments in London for respiratory complaints. European Respiratory Journal. 1999 Feb;13(2):257-65.

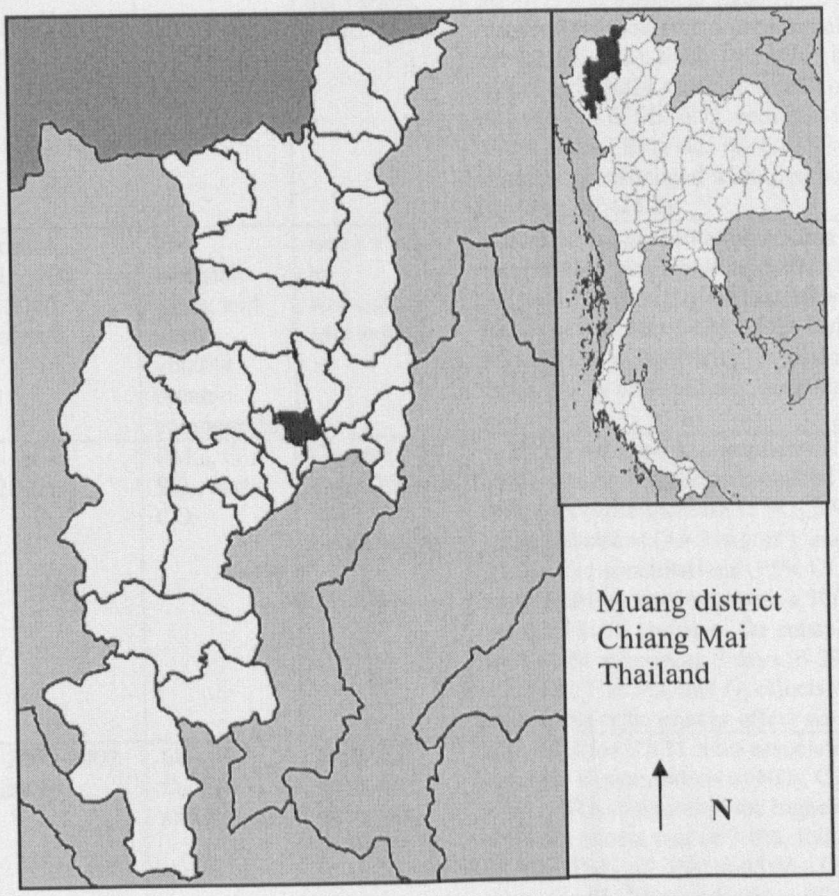
219. Poloniecki JD, Atkinson RW, de Leon AP, Anderson HR. Daily time series for cardiovascular hospital admissions and previous day's air pollution in London, UK. Occupational and Environmental Medicine. 1997 Aug;54(8):535-40.
220. Frank R, Tankersley C. The association between airborne particles and daily mortality rate: an explanatory hypothesis. Presented at the International Symposium on Health Effects of Particulate Matter in Ambient Air; April 23-25; Prague, Czechoslovakia.1997, cited in Goldberg et al 2001.
221. Katsouyanni K, Touloumi G, Spix C, Schwartz J, Balducci F, Medina S, et al. Short-term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. Air Pollution and Health: a European Approach. BMJ. 1997 Jun 7;314(7095):1658-63.
222. Hwong JS, Chan CC. Effects of air pollution on daily clinic visits for lower respiratory tract illness. American Journal of Epidemiology. 2002 Januray 1;155(1):1-10.
223. Barnett AG, Williams GM, Schwartz J, Best TL, Neller AH, Petroeschevsky AL, et al. The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in Australian and new zealand cities. Environmental Health Perspectives. 2006 Jul;114(7):1018-23.
224. Phonboon K, Kunasol P, Chayaniyayodhin T, Srisomporn D. Surveillance of diarrhoeal diseases in Thailand. Bulletin of the World Health Organization. 1986;64(5):715-20.
225. McMichael AJ, Wilkinson P, Kovats RS, Pattenden S, Hajat S, Armstrong B, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. International Journal of Epidemiology. 2008 Oct;37(5):1121-31.
226. Baccini M, Biggeri A, Accetta G, Kosatsky T, Katsouyanni K, Analitis A, et al. Heat effects on mortality in 15 European cities. Epidemiology. 2008 Sep;19(5):711-9.
227. Natsume K, Ogawa T, Sugenoya J, Ohnishi N, Imai K. Preferred ambient temperature for old and young men in summer and winter. International Journal of Biometeorology. 1992 Mar;36(1):1-4.
228. Thorsson S, Lindqvist M, Lindqvist S. Thermal bioclimatic conditions and patterns of behaviour in an urban park in Goteborg, Sweden. International Journal of Biometeorology. 2004 Feb;48(3):149-56.
229. Rothman K. Modern Epidemiology. 3rd ed. Philadelphia, PA Lippincott-Raven; 2008.
230. Armstrong BG. Effect of measurement error on epidemiological studies of environmental and occupational exposures. Occupational and Environmental Medicine. 1998 Oct;55(10):651-6.
231. Bland JM, Altman DG. Multiple significance tests: the Bonferroni method. BMJ. 1995 Jan 21;310(6973):170.
232. Perneger TV. What's wrong with Bonferroni adjustments. BMJ. 1998 Apr 18;316(7139):1236-8.
233. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. Jounal of Royal Statistical Society B. 1995;57(1):289-300.
234. Tsai CA, Hsueh HM, Chen JJ. Estimation of false discovery rates in multiple testing: application to gene microarray data. Biometrics. 2003 Dec;59(4):1071-81.
235. Morris RD. Airborne particulates and hospital admissions for cardiovascular disease: a quantitative review of the evidence. Environ Health Perspect. 2001 Aug;109 Suppl 4:495-500.

236. Sriyaraj K, Priest N, Shutes B. Environmental factors influencing the prevalence of respiratory diseases and allergies among schoolchildren in Chiang Mai, Thailand. International journal of environmental health research. 2008 Apr;18(2):129-48.
237. Wiwatanadate P, Trakultivakorn M. Air pollution-related peak expiratory flow rates among asthmatic children in Chiang Mai, Thailand. Inhalation Toxicology. 2010 Mar;22(4):301-8.
238. Pope CA, 3rd, Burnett RT. Confounding in air pollution epidemiology: the broader context. Epidemiology. 2007 Jul;18(4):424-6; discussion 7-8.
239. Zeka A, Schwartz J. Estimating the independent effects of multiple pollutants in the presence of measurement error: an application of a measurement-error-resistant technique. Environmental Health Perspectives. 2004 Dec;112(17):1686-90.
240. Morgenstern H. Ecological studies. In: Rothman KJ, Greenland S, editors. Modern Epidemiology 2nd edition. Philladephia: Lippincott-Raven; 1998. p. 459-80.
241. Goldberg MS, Burnett RT, Brook JR. Counterpoint: Time-series studies of acute health events and environmental conditions are not confounded by personal risk factors. Regulatory Toxicology Pharmacology. 2008 Jul;51(2):141-7; discussion 8-50.
242. Fisher G, Kjellstrom T, Kingham S, Hales S, Shrestha R. Health and Air Pollution in New Zealand: Final report. 2007. Available from: http://www.hapinz.org.nz/HAPINZ%20Report%20Final%20Clean%20June%202007%20v3.pdf.
243. Samet JM. Air pollution risk estimates: determinants of heterogeneity. Journal of Toxicology and Environmental Health Part A. 2008;71(9-10):578-82.
244. O'Neill MS, Zanobetti A, Schwartz J. Disparities by race in heat-related mortality in four US cities: the role of air conditioning prevalence. J Urban Health. 2005 Jun;82(2):191-7.
245. Sheridan SC, Kalkstein LS. Progress in heat watch-warning system technology. American Meteorological Society; 2004 [cited 2010, Feb 22]; Available from: http://www.climateknowledge.org:16080/heat_waves/Doc1005_Sheridan_Kalkstein_HWWS_%20BAMS_2004.pdf.

Appendices

Appendices for chapter 1

Appendix 1A: Map of study area.



Source: http://en.wikipedia.org/wiki/Chiang_Mai_Province

Appendices for chapter 2

Appendix 2A: Air pollution effects on morbidity.

Table 2A-1 Time series studies of air pollution effects on daily out-patient visits

Setting (reference)	Exposure	Outcome	Results
Beijing, China , 1990 (Xu et al, 1995)	SO_2 and TSP	Daily unscheduled out-patient visits	Each 100 $\mu g/m^3$ increase in TSP was significantly associated with total out-patient visits (β=21.1, SE=7.7) and pediatric visits (β=3.4, SE 1.3), but marginally associated with internal medicine visits (β=4.2, SE=2.2). Each 100 $\mu g/m^3$ increase in SO_2 was significantly associated with internal medicine visits (β=14.6, SE=6.7), pediatric visits (β=12.7, SE=3.7), and ER visits (β=6.8, SE=2.7), but marginally associated with total out-patient visits (β=41.5, SE=24.2).
Atlanta, 25 months, from August 1, 1998 to August 31, 2000 (Sinclair & Tolsma, 2004)	PM, inorganic gases, and polar volatile organic compounds	Daily visits to ambulatory care setting	A 22.3 % increase in adult asthma visits was significantly associated with PM (Risk ratio =1.23). PM was significantly associated with URI visits at 3-5 days lag (RR=1.021). Fine PM, course PM, and SO_2 were also significantly associated with LRI visits, but in different risk estimates and different lags.
London,1992-1994 (Hajat et al, 2002)	PM_{10}, O_3, SO_2, and CO	General practitioner (GP) consultations	A 24.5% increase in consultations (95% CI, 14.6, 35.2) was significantly associated with a 10th to 90th percentile increase in SO_2 levels 4 days prior to consultations (13-31$\mu g/m^3$), and a 37.6% increase in consultations (95% CI, 23.3, 53.5) was significantly associated with a 10th -90th percentile increase in O_3 levels on the consultation days as well as the preceding 3 days (6-29 ppb) among children. The SO_2 and O_3 effects were also found in adults, but with smaller effect sizes.
Hong Kong, 2000-2002 (Wong et al, 2006)	SO_2, NO_2, O_3, PM_{10}, and $PM_{2.5}$.	Daily GP visits for respiratory diseases	GP visits for URTI were associated with an increase concentration of NO_2, O_3, PM_{10}, and $PM_{2.5}$. NO_2 constituted the highest contribution with the excess risk of 3.0%, followed by O_3 (2.5%), $PM_{2.5}$ (2.1%) and PM_{10} (2.0%), respectively. Similar findings of association between these all pollutants and non-URTI were also found.
Atlanta, 1993-2000 *detailed measurements of PM were available for final 25 months (Peel et al, 2005)	PM_{10}, NO_2, O_3, CO, and SO_2,	Emergency room (ER) visits	1-3% increase in URI visits was associated with a standard deviation increase of O_3, NO_2, CO and PM_{10}, a 3% increase of pneumonia visits was associated with a 2 $\mu g/m^3$ increase of $PM_{2.5}$ and organic carbon, and a 2-3% of increases in chronic obstructive pulmonary disease (COPD) visits were associated with a standard deviation increase of NO_2 and CO.
Portland, Maine & Manchester, New Hampshire, 1998-2000 (Wilson et al, 2005)		Emergency room (ER) visits	A 5% (95% CI 2%, 7%) increase in all respiratory ER visits and a 6% (95% CI, 1%, 12%) increase in asthma visits were associated with an interquartile range (IQR, the 75th-25th) increase in SO_2. In addition, a 5% increase in asthmatic ER visits was found to be associated with an IQR increase in O_3.

Table 2A-2 Results of time series studies of air pollution effects on hospital admissions.

Setting	Exposure	Outcome	Results
Spokane county, USA., from January 1, 1988 to December 31 1990 (Schwartz, 1995)	SO_2, PM_{10} and O_3	Hospital admissions for respiratory disease	A 50 $\mu g/m^3$ increase in PM_{10} and in peak-hour O_3 was associated with the increased risk of respiratory hospital admissions, with RR=1.085 (95% CI 1.036, 1.136) for PM_{10} and RR=1.244 (95% CI 1.002, 1.544) for O_3.
Five West European cities (London, Amsterdam, Rotterdam, Paris, and Milano), APHEA study results (Spix et al, 1998)	SO_2, NO_2, O_3, BS, and TSP	Hospital admissions for all respiratory causes	A 50 $\mu g/m^3$ increase in SO_2 was associated with overall increase of 2% (95% CI 1, 5) hospital admissions among the elderly. A 50$\mu g/m^3$ increase in NO_2 was associated with an increase of 2% (95% CI 0, 3) hospital admissions. A 50 $\mu g/m^3$ increase in daily 8-hour average of O_3 was strongly associated with a risk estimate of 3% (95% CI 1, 5) for adult admissions and of 4% (95% CI 2, 6) for elderly admissions. The risk estimates appeared to be higher in warm season.
Sydney, Australia, 1990-1994 (Morgan et al, 1998)	O_3, NO_2 and PM_{10}	Hospital admissions for asthma, COPD and heart disease	An increase in daily maximum 1-hour NO_2 concentrations from the 10th to 90th percentile was associated with an increase of 5.29% (95% CI 1.07, 9.68) in childhood asthma admissions and 4.6% (95% CI -0.17, 9.61) in COPD admissions. An increase in daily maximum 1-hour particulate concentrations from the 10th to 90th percentile was associated with an increase of 3.01% (95% CI -0.38, 6.52) in COPD admissions. An increase in daily maximum 1-hour NO_2 concentrations, daily maximum 1-hour O_3 concentrations, and daily mean particulate from the 10th to 90th percentile was associated with an increase in heart disease admission among patients aged 65 and older of 6.71% (95% CI 4.25, 9.23) for NO_2, 2.45% (95% CI -0.37, 5.35) for O_3, and 2.82% (95% CI 0.90, 4.77) for particulate.
Rome, Italy, from January 1995 to October 1997 (Fusco et al, 2001)	PM_{10}, SO_2, NO_2, O_3, and CO	Hospital admissions for respiratory conditions	An increase IQR in NO_2 of 2.5% (22.3$\mu g/m^3$) and in CO of 2.8% (1.5mg/m^3) was significantly associated with total respiratory admissions. The NO_2 effects on hospital admissions, particularly acute respiratory infections, tended to be stronger (4.0% increase, lag 0) than other causes of admissions. A 5.5% increase in CO levels was associated with asthma admissions, whereas a 4.3% increase in CO levels was associated with COPD admissions.
Ontario, Canada, from April 1, 1995 to December 31, 2000 (Luginaah et al, 2005)	NO_2, SO_2, CO, O_3, PM_{10}, and total reduced sulphur (TRS)	Hospital admissions for respiratory disease	An elevated NO_2 levels (lag 2) were significantly associated with respiratory admissions among females aged 0-14 years, with an RR of 1.19 (95% CI 1.002, 1.411), but no significant association among females in other age groups or males in all age groups. Elevated CO levels (lag 2) were significantly associated with hospital admissions among females aged 0-14 years, with RR of 1.07(95% CI 1.001, 1.139). A significant effect of SO_2 (lag 0) on admissions among females aged 0-14 years was found, with RR of 1.11 (95% CI 1.011, 1.221). The effect of PM_{10} (lag 2) was found to be significantly associated with respiratory for males age 15-64 years.

Table 2A-2 Air pollution effects on hospital admissions (continued).

Setting	Exposure	Outcome	Results
Valencia, Spain, from Jan 1994-Dec1995 (Tenias et al, 2002)	NO_2, SO_2, CO, O_3,	ER admissions for COPD	Increases of 10 microg/m3 in ozone levels (lag 5) and of 1 mg/m3 in carbon monoxide (lag 1) were associated with increases of 6.1% (95% confidence interval [CI] = 2.2%, 10.1%) and of 3.9% (95% CI = 1.4%, 6.6%), respectively, in the expected chronic obstructive pulmonary disease cases. There was no significant association for the remainder of the pollutants.
204 US counties, from 1999 to 2002 (Dominici et al, 2006)	$PM_{2.5}$	Hospital admissions (from Medicare National Claims History files)	There was a short-term increase in hospital admission rates associated with PM2.5 for all of the health outcomes except injuries. The largest association was for heart failure, which had a 1.28% (95% confidence interval, 0.78%-1.78%) increase in risk per 10-microg/m3 increase in same-day PM2.5. Cardiovascular risks tended to be higher in counties located in the Eastern region of the United States, which included the Northeast, the Southeast, the Midwest, and the South.
Vancouver, from June 1995 to March 1999 (Chen et al, 2004)	$PM_{2.5}$, PM_{10}, $PM_{10\text{-}2.5}$ NO_2, SO_2, CO, O_3,	COPD admissions in the elderly (≥65 yr)	PM measures had a positive effect on COPD hospitalization, especially 0 to 2 days prior to the admissions, before copollutants were accounted for. For 3-day average levels of exposure the relative risk estimates were 1.13 (95% confidence interval: 1.05-1.21) for PM(10), 1.08 (1.02-1.15) for PM(2.5), 1.09 (1.03-1.16) for PM(10-2.5), and 1.05 (1.01-1.09) for COH. The associations were no longer significant when NO(2) was included in the models.
Denver, Colorado, in July and August between 1993 and 1997 (Koken, 2003)	NO_2, SO_2, CO, O_3,	Hospitalization for cardiovascular diseases (> 65yr)	O_3 is associated with an increase in the risk of hospitalization for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease. SO_2 appears to be related to increased hospital stays for cardiac dysrhythmias, and CO is significantly associated with congestive heart failure. No association was found between particulate matter or NO_2 and any of the health outcomes. Males tend to have higher numbers of hospital admissions than do females for all of the selected cardiovascular diseases, except for congestive heart failure. Higher temperatures appear to be an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure, and are associated with a decrease in the frequency of visits for coronary atherosclerosis and pulmonary heart disease.
Two southeast Idaho cities, from Nov 1994 to Mar 2000 (Ulirch et al, 2007)	PM_{10}, NO_2, SO_2,	Hospital admissions and medical visits for respiratory and cardiovascular disease	In single-pollutant models, respiratory disease admissions and visits increased (7.1-15.4% per 50 microg/m3 PM10) for each age group analyzed, with the highest increases in two groups, children and especially the elderly. Unexpectedly, evidence of an association between PM10 with cardiovascular disease was not found, possibly due to the lifestyles of the mostly Mormon study population.

Appendix 2B: Time series studies in Asian countries (Health Effect Institute, 2004).

China – 6

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
1. Gao et al 1993 Beijing	1 yr (1989) All deaths	TSP, SO_2	Total mortality, RespD mortality	The daily number of death was regressed on the logarithmic air levels of SO_2 and/or TSP on the same day with Poison regression method, adjusting for the influence of temperature and humidity.	Logarithmic levels of airborne SO_2 were significantly associated with daily number of deaths (especially from bronchitis, COPD, and cor pulmonale).
2. Venners et al 2003 Chongqing	1 yr (1995) 576,000 residents	SO_2, $PM_{2.5}$	Daily mortality (RespD, CVD, cancers, other)	A core model was generated using robust Poisson regression with allowance for overdispersion to control for gradual time trends due to environmental or population changes, periodic seasonal trends, meteorologic factors, and day-of-the-week effects. After testing the fit of cubic smoothing splines of values on the same day and at lags up to 3 days previous, cross-validation was used to add the best-fitting single terms for both temperature and humidity.	When SO_2 increased by $100\mu g/m^3$, relative risks of mortality(lag 3) as increased. The association of $PM_{2.5}$ and daily mortality was negative and nonsignificant. Rates of mortality due to cancer and other causes did not change. Estimated RespD and CVD mortality correlated with SO_2 even after control for $PM_{2.5}$.
3. Xu et al 1994 Beijing	1 yr (1989) 1.5 million residents in two areas	SO_2, TSP	Daily mortality (all causes, CVD, cardiopulmonary disease, cancer)	Poison regression with a Markov approach, controlling for the effects of temperature, humidity, and day of week. The regression coefficients (on the previous days' mortality) were estimated, using a quasi-likelihood approach, and the variances were estimated robustly.	SO_2 was significantly associated with total mortality (at levels below WHO recommendations) and with COPD, CHD, Cardiopulmonary, and CVD mortality. TSP was significantly associated only with COPD mortality. SO_2 and TSP were significant predictors of total mortality in summer, but in winter only SO_2 was a significant predictor.

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
4. Xu et al 1995 Beijing	1 yr (1990)	SO_2, TSP	Hospital out-patient visits	Linear regression models with a Markov correction for auto-correlation, adjusting for temperature, humidity, season, and day of the week. GAM technique was used to produce smoothing plots and then the regression coefficients (on the previous days' visits) were estimated by a quasi likelihood approach with robust estimates of variances.	The number of daily nonsurgical out-patient visits was significantly associated with SO_2 and TSP levels, especially in summer. This was true even though the mean SO_2 concentration in summer was only 17μg/m^3.
5. Xu et al 1995	1 yr (1990)	SO_2, TSP	Daily hospital out-patient and ER visits (unscheduled out-patient visit to internal medicine, pediatric, and ER visits)	GAM was used to produce smoothing plots to determine the functional dependence between daily hospital and ER visits and the covariates included air pollution concentration, temperature, and humidity. The regression coefficients (on the previous days' visits) were estimated by using a quasi-likelihood approach with robust estimates of variances.	Results suggested an exposure-response relation between TSP and SO_2 and hospital out-patient visits both at high air pollution levels and at levels well below WHO air quality standards.
6. Xu et al 2000 Shenyang	1 yr (1992) 3.1 million residents	SO_2, TSP	Daily mortality (all causes, CVD, cardiopulmonary disease, COPD, cancer)	Poison regression, with a Markov approach, was used to regress daily counts, controlling for temperature, humidity, day of week, and a time variables. *GAM techniques used was the same as the above study*	High mean TSP (430μg/m^3) and SO_2 (197μg/m^3) levels were each positively associated with total daily mortality. The risk of all-cause mortality increased by an estimated 1.7% and 2.4% with a 100μg/m^3 concomitant increase in TSP and SO2, respectively. TSP was also significantly associated with CVD mortality, and SO_2 was positively associated with COPD mortality.

Hong Kong - 6

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
7. Wong et al 1999	2 yr (1994-1995)	PM_{10}, NO_2, SO_3, O_3	Hospital admissions for RespD and CVD	Poison regression model (APHEA protocol), controlling for time trend, season, and other cyclical factors, temperature, and humidity. The terms included in the core model were: linear and quadratic time trends; year; trigonometric terms to control for seasonality; days of the week; holiday effect; mean temperature; and humidity.	Levels of NO_2, SO_2, O_3, and PM_{10} were significantly associated with admissions for RespD, CVD, COPD and heart failure. NO_2, O_3, and PM_{10} were significantly associated with admissions for asthma, pneumonia, and influenza. Significant positive interactions were found between NO_2, O_3, and PM_{10} and between O_3 and winter months. Patients aged $\geq$ 65 yrs were at greater risk.
8. Wong et al 1999	3 yr (1995-1997) 629,196 people $\geq$ 65yr	O_3	Hospital admissions for CVD or CBVD	Poison regression with adjustment for overdispersion and auto-correlation. The core model included mean daily temperature and relative humidity, day of week, holidays and days after holidays, and day with number of influenza admissions over 75 percentile, day (t=1 to 912), t^2, year, and seasonality variables.	Daily hospital admissions for all causes of circulatory disease were associated with increased ozone with the strongest effect on patients with arrhythmias and heart failure, with the relative risks markedly increased in the cool season.
9. Wong et al 2001 Hong Kong	2 yr (1993-1994) 1217 children < 15 yr	PM_{10},NO_2, SO_2	Hospital admissions for asthma	Poison regression (APHEA protocol), controlling for seasonal patterns and meteorological conditions (temperature and humidity).	Daily admissions for asthma increased significantly with increases in ambient NO_2 (RR=1.08 per 10 increase), SO_2 (RR=1.06), and inhalable particles (RR=1.03).
10. Wong et al 2001 Hong Kong	3 yr (1995-1997) All residents	NO_2, SO_2, PM_{10},O_3	Daily mortality (nonaccidental, CVD, RespD)	Poisson regression (APHEA protocol), trend on days (1-1,096), seasonality, temperature, humidity; and dummy variables for days of the week, holidays, and influenza epidemics (over 8/week).	Ambient concentrations of NO_2, SO_2, and O_3 were associated with mortality from all nonaccidental causes, CVD, and RespD during the cool season but not the warm season. PM_{10} was associated with RespD mortality only.

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
11. Wong et al 2002	3 yr (1995-1997, Hong Kong and 1992-1994, London)	NO_2, SO_2, PM_{10},O_3	Hospital admissions for asthma (15-64 yr), RespD (60 yr only), cardiac disease (all ages), IHD (all ages)	Poison regression, with nonparametric smoothing method to control for seasonality and nonlinear dependence to control for temperature, humidity, and influenza admissions.	For respiratory admissions (≥ 65yrs), both cities showed positive associations with PM_{10}, NO_2, SO_2, and O_3 with slightly different lags (shorter lags in Hong Kong and longer lags in London). For cardiac admissions, both cities showed positive associations with PM_{10}, NO_2, and SO_2 with similar lag patterns. Associations between NO_2 and O_3 were negative in London, but positive in Hong Kong.
2. Wong et al 2002	4 yr (1995-1998) Hong Kong residents	NO_2, SO_2, PM_{10},O_3	Daily mortality (RespD, CVD, and CBVD)	Poison regression (APHEA protocol), adjusting for time trend, seasonal variations, temperature, and humidity.	Levels of NO_2, SO_2, O_3, and PM_{10} (a 10μg/m^3 increase in the concentration of a pollutant) were significantly associated with mortality from RespD and from IHD. In multipollutant analyses, O_3 and SO_2 were significantly associated with all respiratory mortality, NO_2 was associated with mortality from IHD, and PM_{10} was not associated with RespD or CVD mortality.

Taiwan – 1

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
13. Hwang and Chan 2002 50 townships and city districts	1 yr (1998)	NO_2, CO, SO_2, O_3, PM_{10}	Daily clinic visits for lower respiratory tract illness	General linear regressions with seasonal autoregressive moving-average residual processes. Dummy variables included day of week (Sun, Mon, and Sat), special holidays, average temperature and dew point temperature for the previous 3 days. Another two temperature variables were added in the models to allow changes in the slope for temperature effects when the temperature was above 32°C.	The numbers of daily clinic visits were associated with current day levels of NO_2, CO, SO_2, and PM_{10}. People over 65 yr were most susceptible, and estimated pollution effects decreased as exposure lag increased.

India – 1

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
14. Cropper et al 1997 Delhi	4 yr (1991-1994)	TSP, SO_2, NO_x	Mortality (nonparametric dealths; RespD and CVD deaths)	Autoregressive Poisson models, controlling for seasonal/cyclical terms, a daily time trend, year, and weather variables (temperature and humidity).	Mortality for ages 5 to 64 yr was significantly associated with TSP. The authors not, however, that reducing TSP by 100 10μg/m^3 led to a 2.3% increase in deaths compared with a 6% increase reported for other countries. They attributed the difference to differences in expected life span.

Japan – 1

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
15. Ye et al 2001 Tokyo	Summer months of July- August from 1980 – 1995 Emergency transports >65yr	NO_2, O_3, PM_{10}, CO, SO_2	CVD (angina, cardiac insufficiency, hypertension, MI) and RespD (asthma, acute and chronic bronchitis, pneumonia)	Generalized linear models, adjusting for autocorrelations in the daily maximum temperature and daily average of air quality variables (lag times of 1–4 days).	Concentrations of NO_2 or PM_{10} were associated with daily hospital emergency transports for angina, cardiac insufficiency, MI, asthma, acute and chronic bronchitis, and pneumonia among men and women. Except for pneumonia, daily maximum temperatures were not associated with hospital emergency transports. Increasing daily maximum temperatures, however, were associated with decreased hospital emergency transport for hypertension.

Singapore – 1

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
16. Chew et al 1999	5 yr (1990-1994) Children (3-21 yr)	SO_2, NO_2, O_3, TSP	Morbidity: acute asthma, ER visits	Multivariate linear-regression models, controlling for meteorologic variables (temperature and daily rainfalls).	Although levels of air pollution were generally within WHO quality guidelines, higher levels of SO_2 and TSP were associated with more frequent ER visits for children 3-12 yr but not for those 13-21 yr. An adjusted increase in 2.9 ER visits for every 20μg/m^3 increase in SO_2 levels, lagged by 1 day, was observed on days when levels were above 68μg/m^3. With TSP, an adjusted increase of 5.8 ER visits for 20μg/m^3 every increase in its daily levels, lagged by 1 day, was observed on days with levels > 73μg/m^3.

South Korea – 11

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
17. Cho et al 2000 Ulsan, Daejeon, Suwon	1 yr (1996) 3.6 million people	TSP, CO, NO_2, SO_2, O_3	Morbidity: hospitalizations for RespD (bronchial asthma, COPD, bronchitis)	Poison regression - to analyze the number of daily-admitted respiratory disease patients. GAM- to control time (trends and seasonal fluctuations), weather (association between T and RH and respiratory diseases), and holidays. Loess's non-parametric method – to investigate the interaction between any two factors.	In a single-pollutant model, respiratory admissions were highly correlated with CO in a residential area and with NO_2 and CO in a mixed residential-industrial area. In a multipollutant model, TSP and CO were significantly associated in the residential area, but CO alone was significantly associated in the industrial area.
18. Ha et al 2003 Seoul	5 yr (1995-1999 Postneonates; 1mo-1yr (1045), 2-64yr (67,597), >65yr (100,316)	TSP, CO, NO_2, SO_2, O_3, PM_{10}	Daily total and respiratory mortality (excluding accidental deaths)	GAM and smoothing parameters with LOESS (locally- weighted smoother) function in S-PLUS to control for long-term trends, seasonality, meteorologic influences (temperature and relative humidity).	CO level was significantly associated with respiratory mortality, especially for postneonates. The total mortality for an interquartile change ($49\mu g/m^3$ in PM_{10}) was greatest among postneonates (RR=1.142; 95%CI, 1.096-1.190), followed by the elderly > 65yr (RR=1.023; 95%CI, 1.022-1.024). For respiratory mortality, RR for an interqualtile change of PM_{10} in postneonates (RR=2.108; 95%CI, 1.784-2.283) was also greater than those in other groups.
19. Hong et al 1999 Inchon	1 yr (1995)	TSP, PM_{10}, SO_2, NO_2, O_3, CO	Daily mortality (total)	GAM, which included Loess function of time trends season and meteorologic influences such as temperature and humidity.	Total daily mortality increased 1.2% for each $10\mu g/m^3$ increase in 6-moving average of TSP and 1.2% for each $10\mu g/m^3$ increase in 5-moving average of PM_{10}. Associations between gaseous pollutants and total mortality were not significant. The relative risk of death increased at particulate levels well below the Korean Air Quality Standard at that time.
20. Hong et al 1999 Inchon	2 yr (1995-1996) 2.4 million residents	TSP, PM_{10}, SO_2, NO_2, O_3, CO	Mortality: CVD, RespD, and total deaths not due to accidents of violence.	GAM, which included loess function of temperature, relative humidity, time trends, and indicator variables of the season.	PM_{10} was significantly associated with total, CVD and RespD mortality. SO_2 and CO were significantly associated with RespD mortality. O_3 was not significantly or linearly associated with mortality of any cause. The combined index of PM_{10}, NO_2, SO_2, and CO seemed to better explain exposure-response relation.

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
21.Hong et al 2002 Seoul	4 yr (1995-1998) 10.6 million people	PM_{10}, SO_2, NO_2, O_3, CO	Mortality: stroke	GAM, controlling for seasonal and long-term trends and meteorologic influences, such as temperature, relative humidity, and barometric pressure.	Estimated increase in stroke mortality was 1.5% for each interquartile increase in PM_{10} and O_3 in the same day. Stoke mortality increased 3.1% for NO_2, 2.9% for SO_2, and 1.4% for CO in a 2-day lag for each interquarile increase in single pollutant models. The elderly and women were more susceptible to particulate pollutants.
22. Hong et al 2002 Seoul	7 yr (1991-1997)	TSP, SO_2, NO_2, CO, O_3	Daily stroke mortality (both hemorrhagic and ischemic)	GAM, controlling for time trends, day of the week, and meteorological influences such as same-day and previous day temperature, relative humidity, and atmospheric pressure.	TSP, SO_2, NO_2, CO, and O_3 levels were significantly associated with ischemic, but not hemorrhagic, stroke mortality: the estimated RRs of 1.03 (95% CI, 1.00-1.06) and 1.04 (95% CI, 1.01-1.08) for ischemic stroke mortality for each IQR increase in TSP and SO_2 concentrations on the same day; and the significant increased RRs of 1.04 (95% CI, 1.01-1.07) for NO_2 with a 1-day lag, of 1.06 (95% CI, 1.02-1.09) for CO with 1-day lag, and of 1.06 (95% CI, 1.021.10) for O_3, a 3-day lag for each IQR increase.
23 Kwan et al 2001 Seoul	5 yr (1994-1998)	PM_{10}, CO, NO_2,SO_2, O_3	Mortality (nonaccidental)	Two methods: the GAM approach using Poisson log-linear regression and the case-crossover design using conditional logistic regression. The loess smoothing function was used to control for seasonal variations and T, RH, barometric pressure on the same day)	An increase in PM_{10} was associated with an increase in mortality from congestive heart failure (CHF). CO, NO_2, SO_2, and O_3 were also associated with mortality from CHF. The odds ratios and 95% CIs were estimated from GAMs in the general population for an IQR increase of PM_{10} (42.1 mg/m3), CO (0.59 ppm), NO_2 (14.6 ppb), SO_2 (9.9 ppb), and O_3 (20.5 ppb). The estimated effects (both methods) appeared larger among the CHF patients than among the general population (2.5 ~ 4.1 times higher depending on the pollutants).

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
24. Lee et al 1999 Seoul, Ulsan	6 yr (1991-1995)	SO_2, O_3, TSP	Mortality (nonaccidental)	Poison regression, controlling for variability in the weather and seasons. The regression coefficients were estimated, using generalized estimation equations (GEEs), and the variances were estimated robustly. After establishing the full model, TSP, SO_2, or O_3 was considered a main risk factor. Air pollution levels were generally treated as a continuous variable in the Poisson regression analysis.	Increase of 50 ppb of SO_2 significantly increased all cause mortality by 12-13%. A 50 ppb increase of O_3 increased all cause mortality by 14% and 15% in the two study cities.
25. Lee et al 2000 7 cities	7 yr (1991-1997) 22.8 million people	SO_2, O_3, TSP	Mortality (nonaccidental)	GAMs for highly flexible fitting of seasonal and long-term trends in air pollution and nonlinear associations with weather variables (temperature and relative humidity).	Increase of 50 ppb of SO_2 corresponded to 1-12% more deaths depending on the city assessed. Estimated risk of death by SO_2 was unaffected by adding TSP and O_3 to the model. All ambient levels were below Korea's standard at that time.
26. Lee et al 2002 Seoul	3 yr (1997-1999) 6436 children < 15 yr	PM_{10}, SO_2, NO_2, O_3, CO	Hospitalization due to asthma attack	GAM with a log link and Poisson error allowing for over-dispersion. LOESS, a moving regression smoother – to remove the long-term time trends of air pollution levels and weather variables (temperature and humidity). The effect of each pollutant was reported in units of its IQR in the daily averages (for PM_{10}, SO_2, and NO_2) and the maximum hourly levels (for O_3 and CO).	Estimated relative risk of asthma hospitalization was 1.07 for PM_{10}, 1.11-1.16 for SO_2, NO_2, O_3, and CO. In the multipollutant models, control for other pollutants did not change the estimated effect for O_3 or NO_2.
27. Park et al 2002 Seoul	5 yr (1996-1999) 1264 school children	PM_{10}, SO_2, NO_2, O_3, CO	Illness-related school absenteeism	Poison regression, controlling for long-term trends, seasonality, day of the week, holiday, and meteorologic variables.	Exposures to PM_{10}, SO_2, and O_3 but not NO_2 were associated with illness-related absenteeism from elementary school.

Thailand – 1

Citation, location	Period, sample	Exposure	Health outcome	Statistical method	Main results
28. Ostro et al 1999 Bangkok	3 yr (1992-1995) 6+ million people	PM_{10}	Mortality (all except accidental, homicidal, suicidal)	A multivariate Poison regression model, controlling for several covariates including temperature, humidity, day of week, season, and time.	PM10 was significantly associated with alternative measures of daily mortality. The results suggest relative risks consistent with or greater thatn those reported in most US studies: A 10μg/m^3 change in daily PM10 was associated with 1-2% increases in natural and CVD mortality and a 3-6% increase in RespD mortality.

List of the papers:

1. Gao J. Relationship between air pollution and mortality in Dongcheng and Xicheng Districts, Beijing. Zhonghua Yu Fang Yi Xue Za Zhi. 1993 November;27(6):340-3.Gao J. Relationship between air pollution and mortality in Dongcheng and Xicheng Districts, Beijing. Zhonghua Yu Fang Yi Xue Za Zhi. 1993 November;27(6):340-3.
2. Venners S, Wang B, Xu Z, Schlatter Y, Wang L, Xu X. Particulate matter, sulfur dioxide, and daily mortality in Chongqing, China. Environmental Health Perspectives. 2003;111(4):562-7.
3. Xu X, Gao J, Dockery D, Chen Y. Air pollution and daily mortality in residential areas of Beijing, China. Archives of Environmental Health. 1994 July-August;49(4):216-22.
4. Xu X, Dockery D, Christiani D, Li B, Huang H. Association of air pollution with hospital out-patient visits in Beijing. Archives of Environmental Health. 1995 May-June;50(3):214-20.
5. Xu X, Li B, Huang H. Air pollution and unscheduled hospital out-patient and emergency room visits. Environmental Health Perspectives. 1995 March;103(3):286-9.
6. Xu Z, Yu D, Jing L, Xu X. Air pollution and daily mortality in Shenyang, China. Archives of Environmental Health. 2000 Mar-Apr;55(2):115-20.
7. Wong T, Lau T, Yu T, Neller A, Wong S, Tam W, et al. Air pollution and hospital admissions for respiratory and cardiovascular diseases in Hong Kong. Occupational and Environmental Medicine. 1999 October;56(10):679-83.
8. Wong C, Ma S, Hedley A, Lam T. Does ozone have any effect on daily hospital admissions for circulatory diseases? Journal of Epidemiology and Community Health. 1999 September;53(9):580-1.
9. Wong G, Ko F, Lau T, Li S, Hui D, Pang S, et al. Temporal relationship between air pollution and hospital admissions for asthmatic children in Hong Kong. Clinical and Experimental Allergy. 2001 April;31(4):565-9.
10. Wong C, Ma S, Hedley A, Lam T. Effect of air pollution on daily mortality in Hong Kong. Environmental Health Perspectives. 2001 April;109(4):335-40.
11. Wong C, Atkinson R, Anderson H, Hedley A, Ma S, Chau P, et al. A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared. Environmental Health Perspectives. 2002;110(1):67-77.
12. Wong T, Tam W, Yu T, Wong A. Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. Occupational and Environmental Medicine. 2002 Janurary;59(1):30-5.
13. Hwong J, Chan C. Effects of air pollution on daily clinic visits for lower respiratory tract illness. American Journal of Epidemiology. 2002 Januray 1;155(1):1-10.

14. Cropper M, Simon N, Alberini A, Sharma P. The health effects of air pollution in Delhi, India: Policy Research Working Papers, World Bank 1997.
15. Ye F, Piver W, Ando M, Portier C. Effects of temperature and air pollutants on cardiovascular and respiratory diseases for males and females older than 65 years of age in Tokyo, July to August Environmental Health Perspectives. 2001 April;109(4):355-9.
16. Chew F, Goh D, Ooi B, Saharam R, Hui J, Lee B. Association of ambient air-pollution levels with acute asthma exacerbation among children in Singapore. Allergy. 1999 April;54(4):320-9.
17. Cho B, Choi J, Yum Y-T. Air pollution and hospital admissions for respiratory disease in certain areas of Korea. Journal of Occupational Health. 2000;42:185-91.
18. Ha E, Lee J, Kim H, Hong Y, Lee B, Park H, et al. Infant susceptibility of mortality to air pollution in Seoul, South Korea. Pediatrics. 2003 February;111(2):284-90.
19. Hong Y, Leem J, Ha E. Air pollution and daily mortality in Inchon, Korea. Journal of Korean Medical Science. 1999 June;14(3):239-44.
20. Hong Y, Leem J, Ha E, Christiani D. PM(10) exposure, gaseous pollutants, and daily mortality in Inchon, South Korea. Environmental Health Perspectives. 1999 November;107(11):873-8.
21. Hong Y, Lee J, Kim H, Ha E, Schwartz J, Christiani D. Effects of air pollutants on acute stroke mortality. Environmental Health Perspectives. 2002 February;110(2):187-91.
22. Hong Y, Lee J, Kim H, Kwon H. Air pollution: a new risk factor in ischemic stroke mortality. Stroke. 2002 September;33(9):2165-9.
23. Kwon H, Cho S, Nyberg F, Pershagen G. Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. Epidemiology. 2001 July;12(4):413-9.
24. Lee J, Shin D, Chung Y. Air pollution and daily mortality in Seoul and Ulsan, Korea. Environmental Health Perspectives. 1999 February;107(2):149-54.
25. Lee J, Kim H, Hong Y, Kwon H, Schwartz J, Christiani D. Air pollution and daily mortality in seven major cities of Korea, 1991-1997. Environmental Research. 2000 November;84(3):247-54.
26. Lee J, Kim H, Song H, Hong Y, Cho Y, Shin S, et al. Air pollution and asthma among children in Seoul, Korea. Epidemiology. 2002 July;13(4):481-4.
27. Park H, Lee B, Ha E, Lee J, Kim H, Hong Y. Association of air pollution with school absenteeism due to illness. Archives of Pediatrics and Adolescent Medicine. 2002 December;156(12):1235-9.
28. Ostro B, Chestnut L, Vichit-Vadakan N, Laixuthai A. The impact of particulate matter on daily mortality in Bangkok, Thailand. Journal of the Air and Waste Management Association. 1999 September;19(9 spec No.):100-7.

Appendices for chapter 3

Appendix 3A: The PAPA protocol

Revision on March 15, 2006

PROTOCOL FOR COORDINATED TIME-SERIES STUDIES OF

DAILY MORTALITY IN ASIAN CITIES

I. RATIONALE

The time-series studies of daily mortality in Asian countries are anticipated to produce a large international literature on air pollution and daily rates of mortality and hospital admissions, strengthening both that literature and the conclusions one could draw from the individual PAPA studies. Within Asia a wider breadth of such studies, especially if designed from the start to be comparable, would enhance region-specific combined analyses, providing more definitive estimates of local effects for decision makers.

Recent meta-analyses (Cohen AJ, Anderson HR, Ostro B, et al. 2004[1]; PAPA Review) suggest that proportional increases in daily mortality per $10\mu g/m^3$ increase in PM_{10} are similar among North America, Western Europe, and developing countries. However, there are relatively few meta-analysis studies in Asia. Most studies are not geographically representative, and have taken inconsistent approaches to the definition of health outcomes and data analyses that complicate comparisons with each other and with the broader literature. In addition, the worldwide data have not been appropriately analyzed to determine whether there are real differences in the magnitude of the effects of short-term exposure, and the reasons for these differences (e.g., differences in air pollution, population characteristics).

Efforts to bring the world's data together for such analyses are underway with funding from HEI and the EC in the APHENA project. These efforts would also be strengthened by the additional variability in air pollution, climate and population characteristics that Asian studies could contribute. The results of a coordinated set of time-series studies in Asia would also inform extrapolation to Asia of the results of US and European studies of the effects of long-term exposure on mortality from chronic cardiovascular and respiratory diseases.

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[1] Cohen AJ, Anderson HR, Ostro B, Pandey KD, Krzyzanowski M, Kuenzli N, Gutschmidt K, Pope CA, Romieu I, Samet JM, Smith KR. 2004. Mortality impacts of urban air pollution. In: Comparative Quantification of Health Risks: Global and Regional Burden of Disease Due to Selected Major Risk Factors (Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds), vol 2. World Health Organization, Geneva, Switzerland.

II. SPECIFIC OBJECTIVES

The specific objectives of a coordinated analysis of multi-city Asian data are to:

- Develop a protocol for the design and analysis of data from multiple Asian cities;
- Develop a management framework to conduct the coordinated analysis;
- Conduct coordinated analyses of common exposures and health endpoints according to the protocol, including meta-analyses to the extent possible;
- Contribute to the international scientific discussion on the conduct and interpretation of time-series studies of the effects of short-term exposure;
- Report the results of the coordinated analyses in an HEI final report and papers in the broader peer-reviewed literature.
- Stimulate the development of routine systems for recording daily deaths and admissions for the purpose of time-series analysis.

III. ELEMENTS OF A COORDINATED STUDY

The conduct of a coordinated set of time-series studies in Asia requires the development of a detailed protocol that describes the methodology. The methodology is described under the **Materials and Methods** section below, and includes a description of the participating centers, the design of the coordinated multi-city database, the design of the coordinated analyses, and the approach that will be taken by the participating investigators to the management of the coordinated analysis.

IV. MATERIALS AND METHODS

A. PARTICIPANTS

i. Participating Research Centers

- City selection includes rationale for selection, and description of city location (geographic, degree of urbanization, etc).
- Selection of cities has been governed by interests expressed by existing investigators through responses to RFIQs issued by HEI. The responses comprised cities with the current information and research capacity to conduct analyses in the cities to which they have access, and those who expressed interest but could not proceed without development of new databases or statistical capacity.
- Description of individual studies including population, available data, and personnel are as follows:

  - **Bangkok**

  Bangkok is proposing to examine the effects of PM_{10} and several gaseous pollutants, i.e. ozone, nitrogen dioxide, and sulfur dioxide, on daily mortality for the years 1997 through 2003 and for all 50 districts of Bangkok. With the population of six to ten million people, Bangkok has an average of about 100 deaths per day. Both mortality and air quality data are computerized and readily available from the Registrar Office and the Pollution Control Department, respectively.

  The team will test for gender- and age-stratified associations with mortality. It will also investigate disease-specific associations with mortality focusing on cardiovascular and pulmonary causes. In addition, during part of the period of the proposed study, Thailand experienced a serious recession. As a result, it will be able to assess whether an air pollution-mortality association existed during this period and also whether the likely reductions in traffic during the

recession were associated with lower mortality rates. The proposed research team of Thai and U.S. researchers has had considerable experience conducting time-series studies and in working in Thailand. The team composes of Dr. Nuntavarn Vichit-Vadakan (PI), Dr. Bart Ostro, Dr. Nitaya Vajanapoom, and Dr. Wichai Akeplakorn.

- **Hong Kong**

In Hong Kong, time-series studies will be performed for short-term effects of air pollution on mortality and hospital admissions. The confounding and modifying effects of influenza epidemics will also be assessed. The studies will include the whole Hong Kong population of 6.8 million with an age distribution: 23% < 20; 62% 20-59 and 15% 60+ years. The period of the study spans from the year 1996 to 2002. During this period, the health outcome data, air pollution data, and other covariates are available in electronic form. In addition, there are By-Census (5 yearly) and Census data (10 yearly) within the period, thus providing socioeconomic and demographic information of the population for better interpretation of the results of the study. The investigators from Hong Kong team include: Dr. CM Wong (PI), Prof. JSM Peiris, Prof. AJ Hedley, Dr. TQ Thach, Dr. GN Thomas and Prof. TH Lam of The University of Hong Kong as well as Prof. TW Wong of The Chinese University of Hong Kong.

- **Shanghai**

In Shanghai, a time-series study will be conducted to evaluate the association between mortality outcomes and major air pollutants, using four-year of daily data (2001-2004). The target population will include all residents living in the urban area of Shanghai covering nine districts and having a population of more than six millions. Daily mortality data will be extracted from the database of Shanghai Municipal Center of Disease Control and Prevention, and will be classified into deaths due to cardiovascular diseases, respiratory diseases according to International Classification of Diseases, Revision 10. Daily air pollution data during the study period, including PM_{10}, SO_2, NO_2 and O_3, will be monitored in six fixed-site stations by Shanghai Environmental Monitoring Center. The investigators from Shanghai team include: 1. Drs Haidong Kan (PI), Bingheng Chen, and Naiqing Zhao from Fudan University School of Public Health; 2. Drs Guixiang Song and Changyi Guo from Shanghai Municipal Center of Disease Control and Prevention; 3. Drs Guohai Chen and Zuci Shan from Shanghai Environmental Monitoring Center.

- **Wuhan**

This study will be conducted to determine whether daily variations in ambient PM_{10} concentrations in Wuhan during the four years from July 1, 2000 to June 30, 2004 are associated with daily variations in non-accidental mortality and with daily cause-specific mortality. Five fixed-site air-monitoring stations of the Wuhan Air Quality Automatic Monitoring System, operated by the Wuhan Center of Environmental Monitoring and certified by the U.S. Environmental Protection Agency, will provide daily mean concentrations of PM_{10}, SO_2, and NO_2. (O_3 will be provided by only two stations). Daily mortality data from approximately 4.3 million permanent residents in the nine urban core districts of Wuhan will be available during the study period. The investigators include Dr. Zhengmin Qian (PI), Pennsylvania State University (PSU); Prof. Qingci He (Co-PI), Wuhan Academy of Environmental Science (WAES); Dr. Hung-Mo Lin, PSU; Dr. Duanping Liao, PSU; Dr. Lingli Kong, WAES; Dr. Dunjing Zhou, Wuhan Centres for Disease Prevention and Control; and Dr. Beiwei Wang, Wuhan Center of Environmental Monitoring.

ii. HEI:

- The International Scientific Oversight Committee (ISOC) acting on behalf of HEI, will oversee the conduct of the coordinated analyses via a combination of regular progress reports, periodic site visits, conference calls, and participation in HEI Annual Conferences. The ISOC and HEI staff will be available to provide support and technical advice to the investigators as needed upon request. Once the analyses have been completed a final report will be published by HEI after review by the HEI Review Committee. The Review Committee will also prepare a Commentary on the report that will be published with it.

B. DESIGN OF DATA

i. Health outcomes

The focus of the coordinated analysis will be on: 1) estimating daily mortality relative rates for all natural causes, and cardiovascular and respiratory diseases; and 2) estimating daily mortality relative rates for the causes of death categories by age and sex, as specified below. The quality of the health data will be assessed and taken into account in both analysis and interpretation of results, to the extent possible.

Causes of death	Age group	Sex	ICD-9	ICD-10	Notes
All natural causes	all ages, 0-4, 5-44, 45-64, 65+, 45+ (optional)	both sexes; stratified by male and female	001-799	A00-R99	All natural causes include all non-traumatic, non-suicidal and non-poisoning causes.
Cardio-pulmonary	all ages	both sexes	390-459, 460-519	I00-I99, J00-J98	This includes both cardiovascular and respiratory diseases rubrics.
Cardiovascular	all ages	both sexes	390-459	I00-I99	This is the whole circulatory disease rubric. However, cardiovascular is a better term and one that is commonly used. This would include *cor pulmonale* including acute and chronic pulmonary heart diseases with ICD-9 = 415-416; ICD-10 = I26-I27.
Stroke	all ages	both sexes	430-438	I60-I69	(Optional) This includes the whole cerebrovascular diseases rubric. However calling it stroke may reduce confusion with cardiovascular. It will include a few uncommon cerebrovascular conditions not manifested as stroke.
Cardiac or heart diseases	all ages	both sexes	390-398, 410-429	I00-I09 I20-I52	(Optional)
Respiratory	all ages	both sexes	460-519	J00-J98	This is the whole respiratory disease rubric.
Lower respiratory infections	all ages	both sexes	466, 480-487	J10-J22	(Optional) This includes influenza, which at this level is usually pneumonic.

Chronic obstructive pulmonary diseases (COPD)	all ages	both sexes	490-496	J40-J47	(Optional) This is not really COPD in younger persons as it would also contain asthma (ICD-9 = 493; ICD-10 = J45-J46). This is acceptable because asthma is not a common cause of death, and because in the elderly there is little point in distinguishing between asthma and COPD.
Tuberculosis	all ages	both sexes	010-018	A15-A19	(Optional)
Control diseases: digestive and genitourinary	all ages	both sexes	520-629	K00-K93, N00-N99	(Optional) All these categories had been used as controls in an intervention study for Hong Kong with results published in Hedley et al. (Lancet 2002; 360: 1646-52).
all neoplasm excluding lung cancer	all ages	both sexes	140-161, 163-239	C00-C32, C37-D48	

We choose the above relatively wide range categories of cause of death for this coordinated time-series study for we expect that this approach may reduce misclassification of underlying cause of death among the four study cities.

It is recognized that ICD-9 and ICD-10 coded mortality datasets will be used to compile mortality time-series, with different degree of combination by study cities. The proposed study periods and dates of change from ICD-9 to ICD-10 in the four cities are as follows:

	Bangkok	**Hong Kong**	**Shanghai**	**PSU-Wuhan**
Study period	June 1st, 1997- May 31st, 2003	January 1st, 1996-December 31st, 2002	January 1st, 2001-December 31st, 2004	July 1st, 2000-June 30th, 2004
Date of change to ICD-10	1994	January 1st, 2001	January 1st, 2002	January 1st, 2003

To facilitate conversion and checking between ICD-9 and ICQ-10 codes, a supplementary information sheet for the two coding systems is provided in Annex A. Special attention from each city will be paid to recognize and identify a potential shift in mortality data around the change of ICD coding period. Utilization of ICD-9 or ICD-10 is often the decision from respective national center for disease control (CDC) or equivalent health surveillance agency. The investigators of these four studies have no influence on the decision. In other words, they were bounded by whatever is available from their respective CDCs. Since the time series data will be compiled according to the four very wide ranges of cause-specific mortality, potential misclassification of such widely-defined causes of death is less serious a problem than analyzing smaller categories of causes of death.

ii. Assessment of quality of health outcome data

Using mortality datasets that contain individual-level information, each city will conduct descriptive analyses to obtain the frequency distributions and/or univariate distributions for all categorical variables (e.g., sex) as well as continuous variables (e.g., age). Investigator in each city will carefully check these distributions for the miscoded, missing, and out of range data. Errors, questions, and/or concerns regarding specific data points will be discussed, validated, answered, and corrected in each city.
We notice that documentation of cross validation for causes of death (causes of death from death certificates vs. true causes of death from hospital chart review) may be available

locally among the four study cities. Each city should make effort to assemble the relevant literature and government publication documenting the validity and accuracy of classified causes of death.
In addition to examining univariate distributions for all categorical and continuous variables in each city, it will be important to examine the distributions of the causes of death as well.

iii. City-specific considerations (additional efforts each city needs to put and the difficulties each city would encounter in order to implement this protocol)

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- **Bangkok**

Bangkok team wish to capitalize on the natural economic occurrence that occurred in 1997 by examining whether the reductions in local traffic levels during the recession impacted mortality rates and resultant concentration-response functions.

- **Hong Kong**

Hong Kong team will not study the optional outcome, tuberculosis, as the numbers are small; but it will study mortality due to control diseases.

- **Shanghai**

(No specific considerations)

- **Wuhan**

PSU-Wuhan team will test interactions between PM_{10} exposure and low or high temperature on daily mortality. It may also perform district stratification analyses, depending on the results of correlations among the pollutants' measurements from the five monitoring stations, as well as the results of relevant sensitivity analyses.

iv. Air Pollution

The major analytic objective is to estimate the population daily average air pollution exposure in each city. Mortality relative rate ratios will be estimated for selected particulate and gaseous components of the air pollution mixture measured daily. The same averaging times will be applied to each pollutant. The quality of the air pollution data will be evaluated for each city and taken into account in both analysis and interpretation of results via review and analysis of the data, as well as documentation of past and current QC procedures, to the extent possible.

v. Monitoring period

- **Bangkok:** June 1st, 1997 – May 31st, 2003
- **Hong Kong:** January 1st, 1996 – December 31st, 2002
- **Shanghai:** January 1st, 2001 – December 31st, 2004
- **Wuhan:** July 1st, 2000 – June 30th, 2004

vi. Air quality indicators

After discussion at the PAPA Investigators' Workshop in Bangkok, the following air quality indicators are proposed:

Pollutant	Averaging time
Sulphur dioxide (SO_2)	24-hr average
Nitrogen dioxide (NO_2)	24-hr average
Particulate matters (aerodynamic diameter of 10 micrometres or smaller) (PM_{10})	24-hr average ($PM_{2.5}$ as optional indicator where available)
Ozone (O_3)	8-hr average (from 10:00 – 18:00)
Carbon monoxide (CO)	as optional indicator where available

vii. Site selection criteria

With respect to the site selection criteria of PAPA, it is recommended to use the criteria established below:

- Basically, the sites to be selected should be representative of the exposure of population and taken into account the time scale of their effects on health. The sites shall reflect the urban background level of air pollution, thereby excluding those in the direct vicinity of traffic or of industrial sources. The location shall also avoid buildings housing large emitters such as coal-, waste-, or oil-burning boilers, furnaces, and incinerators.
- The sites should not be influenced by local sources (highways, industries, open burning).
- The sites should be large enough to ensure the availability of space for monitoring, and should be located in flat space and elevated between one and 14 m above ground level. The elevated height shall be determined according to the relevant rules & regulations of each country. (Note: In the US, the monitoring site shall be elevated between 3 and 15 m above ground level according to "*40 CFR - CHAPTER I - PART 58 Probe and Monitoring Path Siting Criteria for Ambient Air Quality Monitoring*". However, European urban background sites are approximately 3m closer to the ground in general.)
- Curbside (or roadside) stations should not be included.
- The sites should be located 5 m upwind from building exhausts and at least 2 m from walls.
- A single monitor may be insufficient to assess the population exposure level in the study region. Therefore, it is recommended that a number of monitoring stations be used to reflect the exposure of the population at risk. These stations should comply with the site selection criteria described above. The correlations among the measurements from various stations will be examined.

viii. Measurement methods

The measurement methods used for air quality assessment in the four cities should comply with the relevant rules & regulations of each country. Methods of measurement for gaseous pollutants, for example, have been fairly standardized, in that UV fluorescence for SO_2 and chemilumisnescence for NO_2 are usually used. For PM_{10}, the measurement will be performed with TEOM or Beta absorption instruments in the four cities.

ix. QA/QC

Two primary documents, QAPP (Quality Assurance Program Plan) and SOP (Standard Operating Procedure), are needed for each city. Each city will obtain these documents and review them to answer data quality questions to be provided.
All four cities have quality control programme in order to conform to each country's requirements. In Wuhan and Shanghai, air quality data should generally be collected at the monitoring stations under National Quality Control.

x. Completeness criteria

For the calculation of 24-hour average concentration of NO_2, SO_2 and PM_{10}, it is required to have at least 75% of the one-hour values on that particular day. For the 8-hour average of O_3, at least six hourly values from 10:00 to 18:00 have to be available.
If a station has more than 25% of the values missing for the whole period of analysis, the entire station should be excluded from the study.

xi. Missing data

According to the completeness criteria, there may be missing values in the air pollutant series for a small **(NB the proportion may not be "small")** proportion of the study period. In the primary analysis in stage 1, only the actual collected data (based on each day having at least 75% of the hours collected and at least 75% of daily data are available for the whole study period for each station) will be used, and missing data will not be filled in. In the sensitivity analysis, the individual study centers will use a method of centering to adjust for the effect of difference in weighting between stations, as described below.

Box No.1: Method of Centering:

Non-missing daily means are first centered for each station i [i.e., individual daily concentrations (X_{ij}) are subtracted by an annual station mean (X_i) for each day j]. The centered data from all centers are then combined and added into the annual mean of all stations (X) to form $X'_{ij} = (X_{ij} - X_i + X)$. The daily (mean) concentrations of individual pollutant are computed for analysis by taking the mean of X'_{ij} over all stations (Wong *et al.* 2001).

Wong, C.M., Ma, S., Hedley, A.J., Lam, T.H. 2001. Effect of air pollution on daily mortality in Hong Kong. *Environmental Health Perspectives 109*: 335-340.

xii. PAPA/ISOC request for basic monitoring information

In order to facilitate harmonization and comparison of the information relevant to the exposure assessments in the 4 cities of PAPA, a questionnaire was prepared and attached below as Annex B in this protocol.

xiii. Other co-variates

The analytic objective is to identify and specify for purposes of analysis a common set of time-varying potential confounders to be controlled. These comprise meteorological, social, and medical factors.

- **Meteorological covariates**
  Temperature: daily average
  Humidity: daily average RH/Dew point

- **Calendar variables**
  Special events e.g. strikes
  Dummy variables for:
  (1) Official public holidays
  (2) Days of the week

- **Use of data on Influenza/other epidemics (optional)**
  The Hong Kong team will assess the effect of influenza in its city specific study. For all cities, influenza epidemics could be defined as weekly number of respiratory mortality above the 90th percentile in each year of the city, and be taken into account as one of the model improvement methods (Box No.2) in sensitivity analysis.

C. DESIGN OF ANALYSIS

A two-stage analysis of multi-city time-series data collected as part of the PAPA project is envisaged. The design of the second stage analysis will be constrained by the small number of studies that will be conducted (anywhere from 4 to 8). Nevertheless, summary estimates should be estimable at a minimum.

i. Single-city (1st stage) analysis

For the core model, all of the four study centers will use the same regression model. Specifically, the procedure will involve the following:

1. Generalized Additive Model (GAM) with penalized and natural spline smoothers in R.
2. Poisson function with mortality due to cardiovascular, respiratory and all natural causes as dependent variables.
3. Smoother for time using 4-6 dfs per year of data.
4. Smoothers for the mean daily temperature and mean daily humidity using 3 dfs (whole period of study) each at a zero day lag. (Individual study centers can employ sensitivity analysis to examine other specifications for weather terms.)
5. Day of week terms (i.e, dichotomous variables for each day of the week from Monday through Saturday).
6. Dichotomous variable relevant to individual city, if available: public holidays (Hong Kong) and extreme weather conditions (Wuhan).
7. Exposure at single-day lags of 0 to 4 days, a two-day average of lags 0 and 1 and a five-day average of lags 0 to 4 (inclusive).

The results will be reported to the Technical Support Group or to a website along with statistics indicating the degree of overdispersion and a graph of the autocorrelation function. The AIC will not be used as a model selection criterion for this core model. If there is overdispersion in the variance, this will then be adjusted in a second model. If first- or second-order autocorrelation of the residuals with $|rho|>0.1$ is present (independent of the associated p-values) based on the partial autocorrelation function (PACF), the study center will then alter (probably increase) the degrees of freedom in the smoother of time until $|rho|\leq 0.1$.

After this base case core model is developed, other specifications, using selected lags, will be used to examine the common mortality outcomes.
Ultimately, each study center will conduct sensitivity analysis on their own data sets (as detailed). For example, some centers will want to control for flu epidemics, examine different disease aggregations, weather variables, etc. However more harmonization of approaches to sensitivity analyses among centers will be suggested. Some analyses can and should be done by all.
For implementation of the core model development and data analysis, the following guidelines were established as shown in Box No.2 on the next page.

Box No.2 Data Analysis Guidelines (Notes of meeting on April 18, 2005, 6:00-7:30 pm at Baltimore)

1. Criteria for adequacy in core models: When the absolute magnitude of PACF plot is less than 0.1 for the first two lag days as specified in items no.1-7 of Section C (i) above, the core model is regarded as adequate. If these criteria are not met, it is advisable to take some steps to meet these criteria, as described in item No. 2 below.
2. Improvement of model adequacy by trying the following three methods in order and selecting 1-3 methods as appropriate.
    a. Localized smoothing:
        - Identify and define dummy variables (q) for periods with extra and/or systematic variation in the residual plot
        - Define interaction variables I = q x time
        - Add smoothing function of I with certain degrees of freedom
    b. Inclusion of epidemic variables as defined in item No.6 (b) below
    c. Introduction of auto-regression terms:

        Other than localized smoothing and inclusion of influenza epidemic indicator variables, the model can be improved by introduction of auto-regression terms for lag up to 7 days. This method is particularly useful when the PACFs are consistently positive or negative for the first several lag days. This method was added after discussion with members subsequent to the Baltimore meeting.
3. Missing data handling and centering: Clarify that missing data will not be filled in. But to eliminate discrepancies between stations daily data in each center will be centered (Box No.1) on each individual overall station mean before computation of city specific daily data. However since Shanghai does not have pollutant data for individual stations and cannot perform centering for the data, we may use simple averaging for the main analysis and use centering for the sensitivity analysis.
4. Multiple pollutant modeling: Decide to use same lag for pair of co-pollutants (PM_{10} with SO_2 and PM_{10} with NO_2) in the best model developed for all natural causes.
5. Dose-response curve: Smoothing function of each pollutant with 3-4 dfs using natural spline will be fitted for model of all natural causes of death. Y-axis should be residual after fitting of non-pollutant variables.
6. Sensitivity analysis: This should include changes in effect estimates (a) using definition of daily pollutant data with centering; (b) adjustment for epidemics defined by weekly respiratory mortality >90^{th} percentile each year; (c) varying the dfs of time smoother from 3 to 15.
7. Cross validation of results: Each team will validate the estimates derived from model of one other team.

ii. Multi-city (2nd-stage) analysis

In the 1st stage of the project, some common data analysis methods and guidelines have been established, in which a standardized analytical framework is applied to time–series data across 4 cities. In this way, this should have avoided some sources of biases which might have otherwise occurred and enable us to carry out a meta-analysis.

The main aim of meta-analysis is to enable the results of the studies to be visually inspected using Forest plots so that a judgment could be made about the overall direction of the evidence. We test for heterogeneity (variation between cities in individual studies) and calculate combined estimate for effect on mortality.

1. **Quality assurance:**
   Before performing meta-analysis for combined estimates of effects across cities, quality of the data collection methods and data quality have to be recorded and assessed first. The size of the data and other factors, which would affect the variation in the estimates, should also be recorded and assessed first. The factors can then be taken into account when calculating a combined estimate for an effect. First a standardized data format is designed (Annex C) so that the coordinator of the project could arrange validation the study results. Data sets documented in the standardized format are sent to other groups for re-running the models or re-analysis of the data.
   Each team should also record the main effect estimates in another standardized forms (Annex D and E) and send them to the coordinator for cross-checking with results derived from re-analysis.

2. **Further analysis:**
   Single lag effects: In order to make results comparable to estimates from Poisson regression, log-relative risks (regression estimates) will be converted into a standard metric: log-relative risk associated with a 10 □g/m^3 increase in the pollutant.

3. **Co-pollutant effects:**
   In the first stage, we performed two pollutant models in which PM_{10} or NO_2 were analyzed with other pollutants in the model as part of sensitivity analysis. The aim was to see how robust each of these pollutants was to the inclusion of other pollutants. The concept is that those pollutants that are most robust in two pollutant or multi-pollutant models have a more convincing case for being closer to the causal pathway. Caution must be exercised in the interpretation of such analyses however, because the estimates obtained tend to be less precise. This means that confidence intervals may be widen even when the point estimate is relatively unchanged.
   It is proposed to obtain combined estimates for the following
   - PM_{10} single estimates
   - PM_{10} controlling for NO_2
   - PM_{10} controlling for O_3
   - PM_{10} controlling for SO_2

4. **Meta-analysis and summary estimates:**
   Regression estimates and standard errors for studies will be used to obtain combined effect estimates based on fixed- and random-effects models (DerSimonian and Laird, 1986).

5. **Cross-validation of results and sensitivity analysis:**
The guidelines for performing the sensitivity analysis were developed during the regional meeting held in Hong Kong on November 30th and December 1st of 2005. The notes of the meeting are outlined in Box 3 below.

Box No.3 Notes from regional meeting held in Hong Kong on November 30, 2005 and December 1, 2005.

Cross-validation, sensitivity analysis and information for meta-analysis:

1. Cross-validate results by each other within Hong Kong-Wuhan, and Bangkok-Shanghai for
   a. All causes, 65+ with NO_2 and all lags,
   b. All natural causes, all ages with PM_{10} and all lags
2. Present dose-response curve of all pollutants for all causes with 4 df over time
3. Sensitivity analysis: repeat the analysis for all-cause and cardiovascular mortality (all lags) (with city-specific "best" core model) with
   a. PM_{10} & O_3: Top 5% percentile removed;
   b. PM_{10}: Measurements restricted to $\leq 180\ \mu g/m^3$ (2 separate analyses);
   c. PM_{10}: Monitors with the two highest NO/NO_X ($NO = NO_X - NO_2$) dropped, where NO/NO_X is a good marker for auto traffic (if data is not available, drop the two stations which are highly influenced by traffic or largely from industrial sources); and
   d. PM_{10}: Only the non-rainy period adopted (the non-rainy period varies according to cities)
4. Information required for meta-analysis:
   a. In order to perform the meta-analysis, the HK team needs the attached information (spreadsheets of Annex C, D, E and F) from all the cities.
   b. Ideally, the information should be based on city-level. If a city does not have the required information by city-level, district- or provincial-level would be acceptable.
   c. It is not necessary to have up-to-date information. If not all the above-mentioned information could be obtained, the cities should provide the information available.
   d. Unavailable information should be marked "NA" in the spreadsheets.

6. **Task and Budget Justification for coordinated studies:**
   a. Basic analysis - to be performed by each individual team (Budget $20,000x4)
      - Model for health outcomes specified in common protocol
      - Display and tabulate diagnostic results
      - Tabulate effect estimates
      - Submit the data sets and the effect estimates to the coordinator
      - Validate (repeat) the models for one other team
      - Participate in data analysis and interpretation of results
      - Contribute to report writing

   b. Meta analysis - to be undertaken by Hong Kong team ($10,000)
      - Receive the original and validated results from all other teams
      - Assess the validity of the models
      - Perform pooled or metal analysis for effect estimates of 4 cities
      - Plot and tabulate results
      - Write the methods and results sections for the meta analysis

   c. Report writing - to be undertaken by Hong Kong team ($5,000)
      - Write the introduction section with a literature review
      - Write the methods and results sections with input from b above
      - Address the issues of the coordinated studies
      - Finalize the report for the coordinated studies

   d. Communication - to be undertaken by Bangkok ($5,000)
      - Set time line
      - Facilitate tasks among teams and communication with HEI and APHENA

- Organize and prepare materials for meetings and workshops
- Communicate for the main tasks of the coordinated studies
- Consult (Dr Bart Ostro) for statistical methods in Tasks b and c
- Assist in producing the final report

D. PROJECT COORDINATION AND INTERACTION AMONG INVESTIGATORS

There are two main parallel courses in the implementation of the mortality time-series study for the 4 cities, that is, the individual city study and the coordinated study among the 4 cities.
A system of coordination and communication is needed to implement the study effectively and efficiently. In terms of interaction among the investigators, web-based communication (i.e. project message board with link to e-mail notification, and webpage for updating study activities) is developed. Summary of activities and problems encountered with remedial plan of each of the project components listed below may be posted on the message board. HEI is responsible for development and maintenance of the message board. For each of the components, one member from each team acts as the site facilitator who passes on relevant messages to other team members, and regularly posts updates from the team on the message board. One member from each team will be designated the first point of contact. The critical issues for the coordinated study focus on (1) the data management, (2) data analysis, report writing and (3) dissemination of results. A steering committee is to be coordinated by Hong Kong team to manage the coordinated study. The main functions include the following:

1. Guide the investigators during the study period when needed
2. Monitor the adherence of protocol, specifically, the aforementioned critical issues
3. Develop guideline for dissemination of results
4. Resolve any disagreement

The steering committee composes of two to three representatives including the P.I. from each of the four teams. The main communication mechanism is web-based, i.e. e-mail mainly and chat room. The steering committee, once formed, schedules a monthly forum (to be determined) to discuss specific issues. The regional meeting as proposed by HEI may also be used to resolve any challenges and update activities.
In addition, the coordination tasks may be divided into 2 main categories, i.e., coordination on technical issues and coordination on administrative issues. It is proposed that CM Wong, Bart Ostro, Hung-Mo Lin and Dr. Naiqing Zhao take the role of coordinators in the Technical Support Group for technical matters, and Aaron Cohen and Wei Huang assume the role of administrative coordinators.

----------End of Protocol----------

Appendix 3B: Comparison of the present study protocol with the PAPA protocol.

List	PAPA protocol	Present study
City	Bangkok, Hong Kong, Shanghai, Wuhan	Chiang Mai
Period	4-7 years	3 years
Exposure	Air pollutants (SO_2, NO_2, PM_{10}, O_3, CO)	Air pollutants (SO_2, NO_2, PM_{10}, O_3, CO) and Temperature
Outcome	Mortality due to cardiovascular, respiratory, and all natural causes	Morbidity due to respiratory, circulatory, diabetes, intestinal infectious and all causes
Design of analysis	Single-city (1st stage) and Multi-city (2nd stage)	Single-city
Procedure of the single-city analysis	1.GAM with penalized and natural spline smoothers in R. 2. Poisson function for mortality due to cardiovascular, respiratory, and all natural causes 3. Smoother for time using 4-6df per year of data 4. Smoothers for the mean daily temperature and humidity using 3 dfs (whole period of study) each at a zero day lag. (Individual study centers can employ sensitivity analysis to examine other specifications for weather terms.) 5. Day of week terms (i.e. dichotomous variables for each day of the week from Monday through Saturday). 6. Dichotomous variable relevant to individual city, if available: public holidays (Hong Kong) and extreme weather conditions (Wuhan). 7. Exposure at single-day lags of 0 to 4 days, a two-day average of lags 0 and 1 and a five-day average of lags 0 to 4 (inclusive).	1. GLM with natural spline smoother 2.Poisson function for morbidity due to respiratory, circulatory, diabetic, intestinal infectious and all causes 3. Monthly indicator variable will be used to control for seasonal patterns. Yearly indicator will be used to control for any time trend. 4. Natural cubic spline to control for daily mean temperature (when air pollution is the main exposure of interest), humidity, and rainfall – at longer day lags (to be decided later). Linear term above and below heat/cold temperature threshold will also be used. 5. Indicator variables for day of week and holidays will also be used to control for calendar effects. 6. Indicator variables for public holidays will be used. Influenza epidemics will be defined as the period comprising daily visits or admissions due to influenza above the 99th centile of the total respiratory visits or admissions. 7. Exposure at single-day lags of 0 to 4 days, a two-day average of lags 0 and 1 and a five-day average of lags 0 to 4 (inclusive) – for air pollution. 8. Linkage between OPD visits and subsequent hospital admissions will be established.
Note	Not using the AIC criteria function for model selection.	Not using the AIC criteria function for model selection.

***Source of the PAPA protocol:** Dr. Nuntavarn Vichit-Vadakarn and Dr. Nitaya Vajanapoom (team members of the project from Bankok, Thailand).

Appendix 3C: Grouping occupation by based on a 3-digit occupational code.

Note: Excluding children (0-14 year) and the elderly (≥65 year) for all groups.

Group 1Unemployed/Economically inactive people

Code	Occupation
000	No occupation
900	Student/housewives
901	Priest

Group 2Non-manual workers

Code	Occupation	Code	Occupation
101	Architects	127	Singers
102	Engineers	128	Musicians
103	Explorers	129	Social welfare workers
104	Mechanical engineers	130	Social scientists
105	Scientists	131	Statisticians
106	Doctors	132	Economists
107	Surgeons	133	Missionary
108	Dentists	134	Chaplains
109	Veterinarians	135	Accountants
110	University lecturers	136	Other related academic workers
111	School teachers	137	Legislators
112	Nurses	138	Fortune tellers
113	Pharmacists	201	Civil servants
114	Medical technicians	202	Military soldiers
115	Medical assistants	203	Navy soldiers
116	Judges	204	Air force soldiers
117	Public prosecutors	205	Policemen
118	Sculptors	206	Political civil servants
119	Artists	207	Other civil service officers
120	Technical artists	208	Pension civil servants
121	Cameramen	209	Temporary government employee
122	Authors/Writers	210	Permanent government employee
123	News-reporters	211	Senior village headmen
124	Journalists	212	Assistant senior village headmen
125	Actors	213	Village headmen
126	Models	214	Assistant village headmen
215	Sub-district family doctors	701	Brokers/Agents
301	Government enterprise administers	702	Salesmen
302	Government enterprise employee	703	Advertisers
303	Other government enterprise officers	704	Receptionists
401	Business owners	705	Waiters/Waitresses
402	Private sector workers	706	Hotel workers
405	Other related private workers	707	Entertainment service workers
406	Clerks	713	Baby sisters

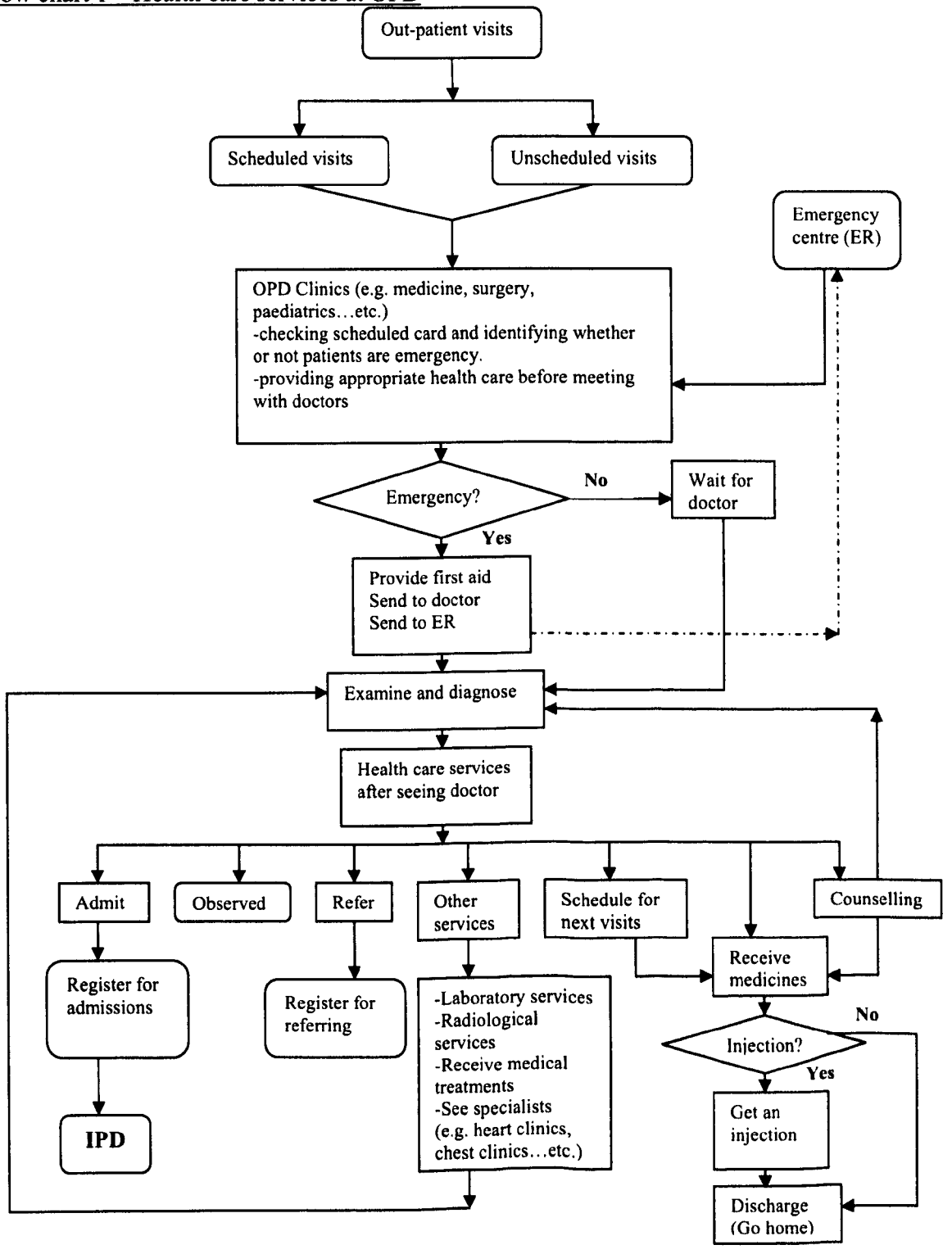
Group 3Manual workers

Code	Occupation	Code	Occupation
216	Janitors	718	Beauticians
403	Wage earners/employee	719	Other services workers
404	Labourers	720	Security officers/Guards
501	Farmers	801	Tailors/Dressmakers
502	Agriculturists	802	Leather craftsmen
503	Rice farming workers	803	Electrical equipment mechanics
504	Gardeners/Orchard workers	805	Car repairers
505	Farming workers	806	Electronic equipment mechanics
506	Husbandry workers	807	Car repainting mechanics
507	Fishery workers	808	Watch/Clock repairmen
508	Hunters	809	Gold craftsmen
601	Wholesales workers	810	Diamond/Jewellery craftsmen
602	Retail workers	811	Ironers/Blacksmiths
603	Peddlers/Street vendors	812	Metal related-material workers
604	Sales agents	813	Tinsmiths/Metal materials welders
605	Other related commercial workers	814	Structural metal materials moulders
606	Trades workers	815	Workers in quenching metal materials
708	Bus drivers	816	Carpenters
709	Wage drivers	817	Furniture makers
710	Cart drivers	818	Masons
711	Boat drivers	819	Painters
712	Chefs	820	Printmakers
714	Servants/Maids	821	Weavers
715	Cleaners	822	Photographers
716	Launderers	823	Photograph developers
717	Hairdressers/Barbers	824	Other handicraft workers

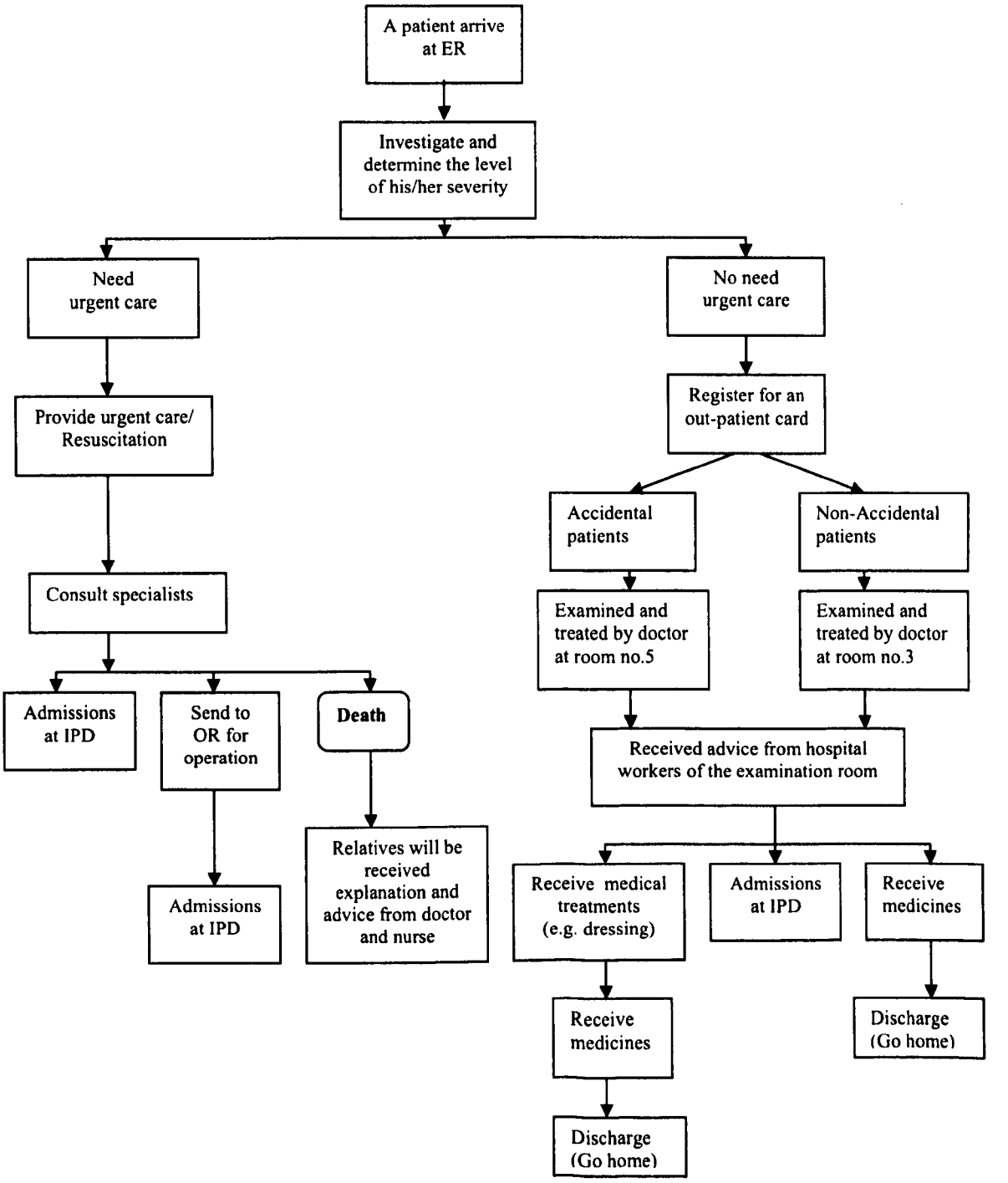
Appendices for chapter 4

Appendix 4A: Examples of health services at OPD and ER of hospitals in Thailand

Flow chart 1 Health care services at OPD



Flow chart 2 Health care services at emergency room (ER)



Appendix 4B: Summary of statistics of air pollution and meteorological data.

Note : Results from preliminary investigations before data collection.

1. Chiang Mai City Hall station (35T – urban area station, located in the outskirt area)

Daily mean	Two year period from October 2003- September 2005					
	Missing	N	Mean	SD	Min	Max
Pollution concentrations						
PM_{10} ($\mu g/m^3$)	12.8%	620	58.35	41.90	10.69	204.69
NO_2 (ppb)	8.9%	648	9.77	5.61	0.80	30.20
SO_2 (ppb)	12.3%	624	1.17	1.12	0.00	8.00
CO-1hr (ppm)	7.5%	658	0.48	0.30	0.00	1.79
CO-8hr (ppm)	8.6%	650	0.48	0.29	0.00	1.60
O_3 (ppb)	7.5%	658	21.49	9.66	2.00	52.29
Meteorological variables						
Temperature (◦C)	5.6%	689	26.0	2.8	18.3	32.6
Relative Humidity (%)	8.9%	665	70.1	18.0	33.1	100.0
Rainfall (mm/h)	4.1%	700	0.2	0.4	0.0	4.8

2. Yuparaj College station (36T – roadside station, located in the city central)

Daily mean	Two year period from October 2003- September 2005					
	Missing	N	Mean	SD	Min	Max
Pollution concentrations						
PM_{10} ($\mu g/m^3$)	25.4%	518	80.46	56.58	14.80	291.0
NO_2 (ppb)	25.4%	518	20.19	8.88	1.30	48.40
SO_2 (ppb)	26.9%	507	2.00	1.26	0.00	9.70
CO-1hr (ppm)	27.2%	505	0.81	0.47	0.10	2.79
CO-8hr (ppm)	18.2%	499	0.81	0.46	0.10	2.59
O_3 (ppb)	24.6%	523	19.6	8.05	0.69	51.70
Meteorological variables						
Temperature (◦C)	5.9%	688	26.5	2.7	19.7	33.0
Relative Humidity (%)	7.5%	676	70.4	15.0	31.1	99.1
Rainfall (mm/h)	4.5%	698	0.1	0.4	0.0	5.3

Appendices for Chapter 5

Appendix 5A: Distribution of daily out-patient visits by selected characteristics of the study population.

5A-1. Daily respiratory visits by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	38.28	20.58	0	14	22	36	51	65	149
15-64	1461	46.83	28.65	0	12	24	43	66	86	175
≥ 65	1461	9.67	6.92	0	2	4	9	14	19	39
Sex										
Male	1461	44.40	24.40	1	15	26	42	61	76.8	148
Female	1461	50.45	29.86	0	15	27	45	70	90	175
Occupation*										
Unemployed & economically inactive	1461	17.96	10.71	0	6	10	16	25	32	67
Non-manual workers	1461	23.06	15.23	0	4	10	21	33	43	87
Manual workers	1461	3.52	3.27	0	0	1	3	5	8	18
Total respiratory visits	1461	95.32	53.40	3	30.2	53	87	131	166	318

*Excluding children (0-14) and the elderly (≥65).

5A-2. Daily circulatory visits by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	0.92	1.41	0	0	0	0	1	3	9
15-64	1461	51.17	38.12	0	5	14	50	77	102	194
≥ 65	1461	31.25	23.49	0	3	8	33	45	62	126
Sex										
Male	1461	34.45	25.05	0	3	9	36	52	67	126
Female	1461	48.71	36.64	0	5	13	47	71	98	198
Occupation*										
Unemployed & economically inactive	1461	22.06	17.94	0	2	6	20	32	48	102
Non-manual workers	1461	21.24	15.45	0	2	6	21	32	42	71
Manual workers	1461	5.83	6.07	0	0	1	4	9	14	35
Total circulatory visits	1461	83.63	61.12	0	9	22	85	122	163	323

*Excluding children (0-14) and the elderly (≥65).

5A-3. Daily diabetic visits by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	0.31	0.77	0	0	0	0	0	1	8
15-64	1461	20.77	16.11	0	1	7	20	30	40	120
≥ 65	1461	9.61	8.09	0	0	3	9	14	20	41
Sex										
Male	1461	12.64	9.56	0	1	4	12	19	25	55
Female	1461	18.13	14.85	0	1	5	17	26	36	107
Occupation*										
Unemployed & economically inactive	1461	10.10	8.36	0	1	3	9	14	21	6
Non-manual workers	1461	8.45	7.26	0	0	2	7	13	18	48
Manual workers	1461	1.89	2.10	0	0	0	1	3	5	12
Total diabetic visits	1461	30.83	23.70	0	2	9	30	44	59	162

*Excluding children (0-14) and the elderly (≥65).

5A-4. Daily intestinal infectious visits by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	3.87	2.74	0	1	2	3	5	7	18
15-64	1461	4.48	3.26	0	1	2	4	6	9	17
≥ 65	1461	0.76	0.98	0	0	0	0	1	2	7
Sex										
Male	1461	4.26	2.97	0	1	2	4	6	8	24
Female	1461	4.86	3.39	0	1	2	4	7	9	23
Occupation*										
Unemployed & economically inactive	1461	1.94	1.72	0	0	1	2	2	4	11
Non-manual workers	1461	2.07	1.90	0	0	1	2	3	5	11
Manual workers	1461	0.31	0.61	0	0	0	0	0	1	4
Total intestinal infectious visits	1461	9.17	5.53	0	3	5	8	13	17	33

*Excluding children (0-14) and the elderly (≥65).

5A-5. Daily other visits by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	49.53	31.80	1	13	23	45	71	90	192
15-64	1461	286.86	184.75	11	68	125.5	245	435	547	861
≥ 65	1461	84.39	43.37	0	34	43	82	117	144	218
Sex										
Male	1461	181.58	104.49	9	58	91	163	264.5	319	599
Female	1461	237.73	150.65	7	60	105	211	358	454	636
Occupation*										
Unemployed & economically inactive	1461	114.29	78.90	6	30	50	93	160	241	389
Non-manual	1461	127.37	79.08	1	30	58.5	116	189	228	527
Manual	1461	28.53	28.25	0	3	7	19	40	76	132
Total other visits	1461	422.44	252.86	16	120	198	373	630	775.8	1163

*Excluding children (0-14) and the elderly (≥65).

Appendix 5B: Distribution of daily hospital admissions by selected characteristics of the study population.

5B-1. Daily respiratory admissions by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	1.9	1.6	0.0	0.0	1.0	2.0	3.0	4.0	13.0
15-64	1461	3.7	2.6	0.0	1.0	2.0	3.0	5.0	7.0	14.0
≥ 65	1461	2.2	1.7	0.0	0.0	1.0	2.0	3.0	4.0	11.0
Sex										
Male	1461	4.1	2.7	0.0	1.0	2.0	4.0	6.0	8.0	15.0
Female	1461	3.7	2.5	0.0	1.0	2.0	3.0	5.0	7.0	18.0
Total respiratory admissions	1461	7.8	4.3	0.0	3.0	5.0	7.0	10.0	14.0	29.0

5B-2. Daily circulatory admissions by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	0.2	0.5	0.0	0.0	0.0	0.0	0.0	1.0	4.0
15-64	1461	6.3	3.9	0.0	2.0	3.0	6.0	9.0	12.0	20.0
≥ 65	1461	4.5	2.8	0.0	1.0	2.0	4.0	6.0	8.0	15.0
Sex										
Male	1461	5.4	3.4	0.0	1.0	3.0	5.0	7.0	10.0	19.0
Female	1461	5.6	3.5	0.0	2.0	3.0	5.0	8.0	11.0	19.0
Total circulatory admissions	1461	11.1	8.9	0.0	4.0	6.0	10.0	15.0	19.0	32.0

5B-3. Daily diabetic admissions by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	2.0
15-64	1461	0.5	0.7	0.0	0.0	0.0	0.0	1.0	1.0	4.0
≥ 65	1461	0.3	0.5	0.0	0.0	0.0	0.0	1.0	1.0	3.0
Sex										
Male	1461	0.3	0.6	0.0	0.0	0.0	0.0	1.0	1.0	4.0
Female	1461	0.5	0.7	0.0	0.0	0.0	0.0	1.0	1.0	5.0
Total diabetic admissions	1461	0.8	1.0	0.0	0.0	0.0	1.0	1.0	2.0	6.0

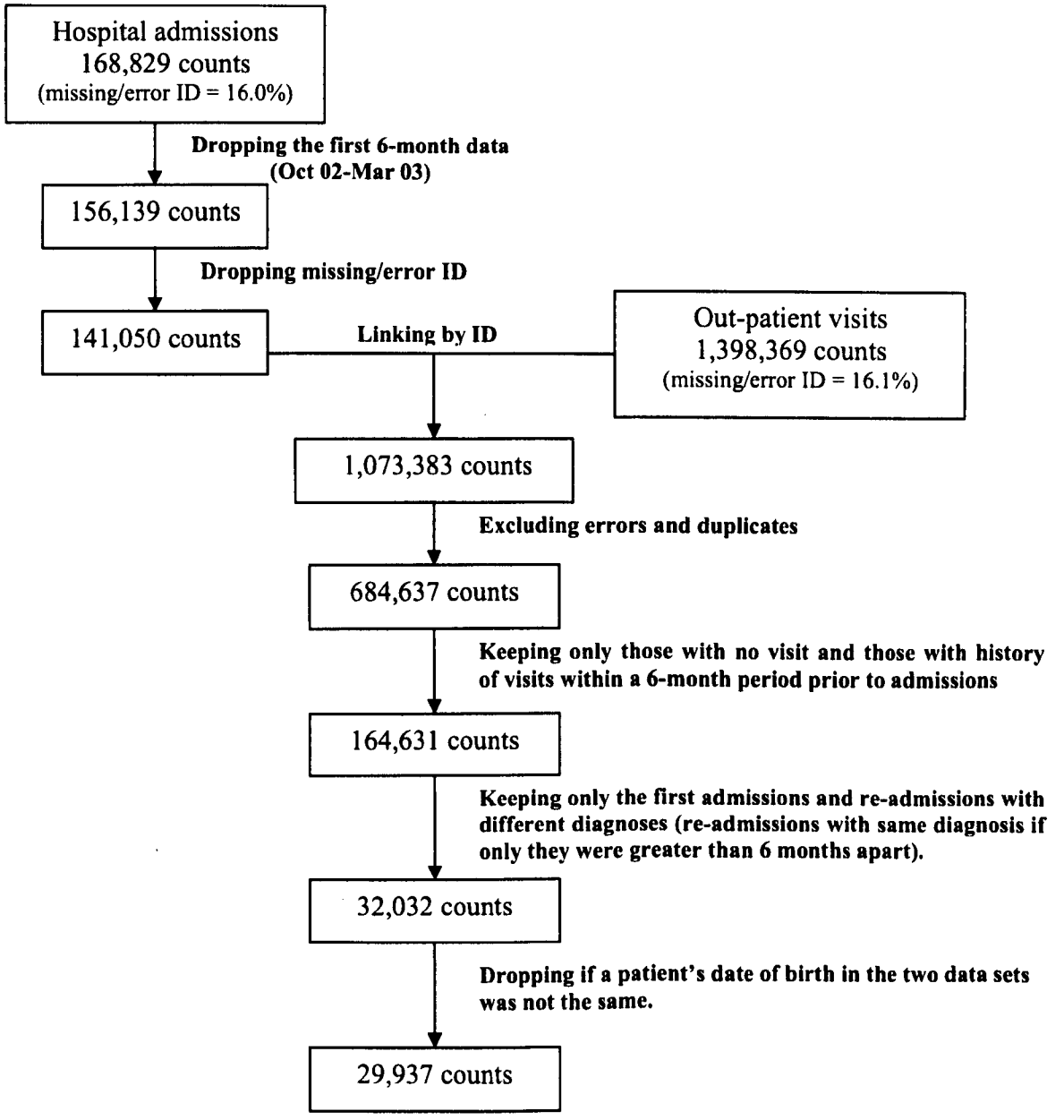
5B-4. Daily intestinal infectious admissions by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	0.9	1.1	0.0	0.0	0.0	1.0	1.0	2.0	7.0
15-64	1461	2.0	1.9	0.0	0.0	1.0	1.0	3.0	4.0	10.0
≥ 65	1461	0.4	0.6	0.0	0.0	0.0	0.0	1.0	1.0	4.0
Sex										
Male	1461	1.3	1.3	0.0	0.0	0.0	1.0	2.0	3.0	9.0
Female	1461	2.0	1.7	0.0	0.0	1.0	2.0	3.0	4.0	11.0
Total diabetic admissions	1461	3.3	2.5	0.0	1.0	1.0	3.0	5.0	7.0	13.0

5B-5. Daily other admissions by selected characteristics of study population from October 2002 to September 2006.

Group	Obs	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Age (year)										
0-14	1461	10.9	6.7	0.0	3.0	5.0	9.0	15.0	19.0	38.0
15-64	1461	53.7	26.8	8.0	19.0	30.0	46.0	74.0	90.0	138.0
≥ 65	1461	15.6	9.5	0.0	4.0	7.0	13.0	23.0	29.0	47.0
Sex										
Male	1461	38.1	18.9	3.0	15.0	22.0	35.0	53.0	65.0	93.0
Female	1461	42.0	22.5	3.0	15.0	22.0	39.0	60.0	74.0	122.0
Total other admissions	1461	80.4	40.1	13.0	32.0	45.0	75.0	115.0	137.0	203.0

Appendix 5C: Diagram of linking hospital admissions data with out-patient visits data by identification number (ID).



Appendix 5D: Daily hospital admissions in the linkage data by disease groups in relation to history of the visits prior to the admissions in Muang, Chiang Mai, from April 2003 to September 2006.

5D-1. All-cause admissions

History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	41.1	24.7	1	10	18	42	62	73	120
No visit	1276	2.7	2.3	0	0	1	2	4	6	12
1 visit	1276	10.7	7.1	0	2	4	11	16	20	36
2-5 visits	1276	18.2	12.2	0	3	7	17	28	35	59
> 5 visits	1276	9.6	6.4	0	1	4	9	14	19	30

5D-2. Respiratory admissions

History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	3.1	2.2	0	0	1	3	5	6	13
No visit	1276	0.2	0.5	0	0	0	0	0	1	4
1 visit	1276	0.7	0.9	0	0	0	1	1	2	6
2-5 visits	1276	1.2	1.2	0	0	0	1	2	3	6
> 5 visits	1276	0.9	1.1	0	0	0	1	1	2	5

5D-3. Circulatory admissions

History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	3.5	2.7	0	0	1	3	5	7	15
No visit	1276	0.3	0.5	0	0	0	0	0	1	4
1 visit	1276	1.0	1.2	0	0	0	1	1	3	7
2-5 visits	1276	1.5	1.6	0	0	0	1	2	4	9
> 5 visits	1276	0.8	0.9	0	0	0	0	1	2	6

5D-4. Diabetic admissions

History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	0.4	0.6	0	0	0	0	1	1	5
No visit	1276	0.0	0.1	0	0	0	0	0	0	1
1 visit	1276	0.1	0.2	0	0	0	0	0	0	2
2-5 visits	1276	0.1	0.4	0	0	0	0	0	1	3
> 5 visits	1276	0.2	0.4	0	0	0	0	0	1	2

5D-5. Intestinal infectious admissions

History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	1.2	1.2	0	0	0	1	2	3	6
No visit	1276	0.2	0.4	0	0	0	0	0	1	3
1 visit	1276	0.3	0.5	0	0	0	0	1	1	4
2-5 visits	1276	0.4	0.7	0	0	0	0	1	1	4
> 5 visits	1276	0.3	0.5	0	0	0	0	0	1	3

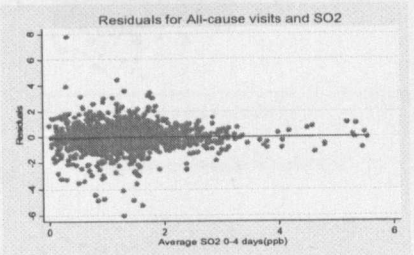
5D-6. Other admissions

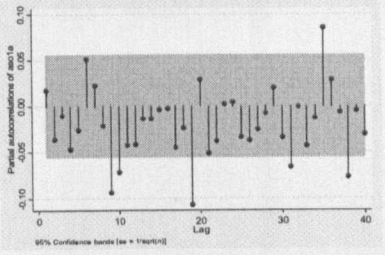
History of visits prior to admissions	n (day)	Mean	SD	Percentile						
				Min	10th	25th	50th	75th	90th	Max
Total	1276	32.9	21.6	0	6	13	33	52	62	108
No visit	1276	2.0	1.9	0	0	0	2	3	4	11
1 visit	1276	8.6	6.2	0	1	3	8	13	17	33
2-5 visits	1276	14.8	10.9	0	2	5	13	24	30	55
> 5 visits	1276	7.5	5.5	0	1	3	7	11	15	27

Appendices for chapter 6

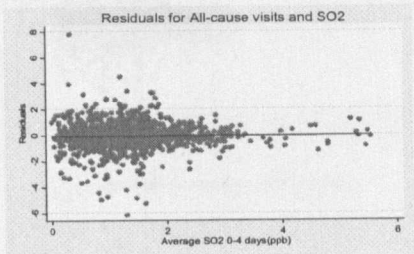
Appendix 6A: Sensitivity analyses for out-patient visits series.

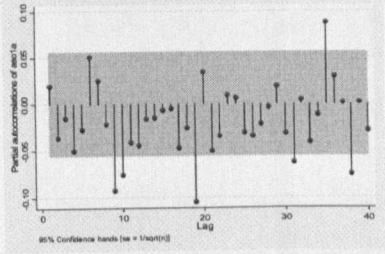
Figure 6A-1 Model diagnostics for all-cause visits & SO_2 in regard to degrees of freedom.



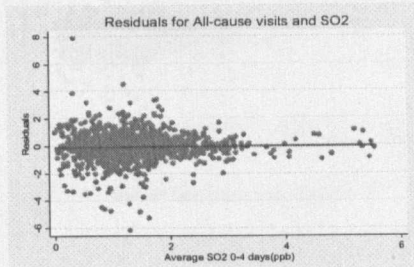


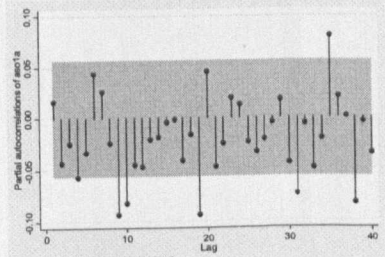
df = 1/year
(1/df) Deviance = 1.109032
(1/df) Pearson = 1.107341
AIC = 12.23004



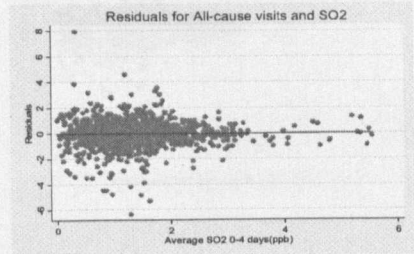


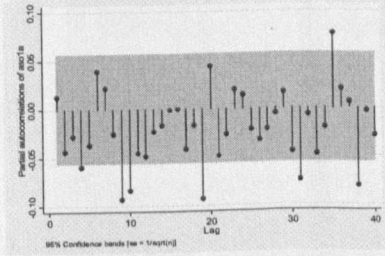
df = 2/year
(1/df) Deviance = 1.112764
(1/df) Pearson = 1.106861
AIC = 12.22838



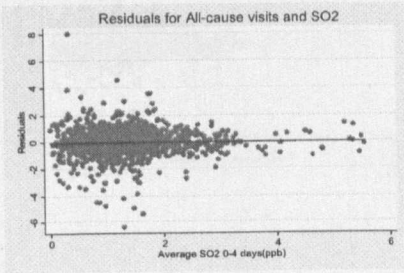


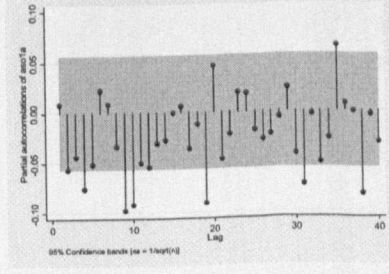
df = 3/year
(1/df)Deviance = 1.118798
(1/df) Pearson = 1.113537
AIC = 12.21857





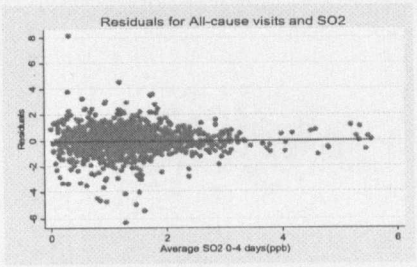
df = 4/year
(1/df) Deviance = 1.12323
(1/df) Pearson = 1.117231
AIC = 12.21477

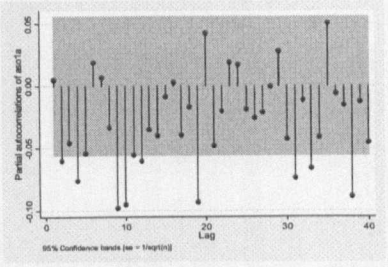




df = 5/year
(1/df) Deviance = 1.128016
(1/df) Pearson = 1.124632
AIC = 12.20257

Figure 6A-1 Model diagnostics for all-cause visits & SO_2 (continued).





df = 6/year
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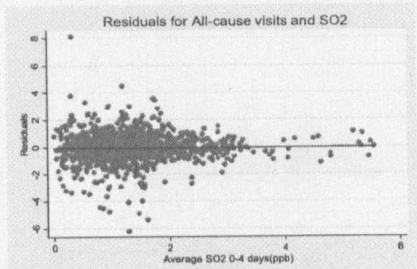
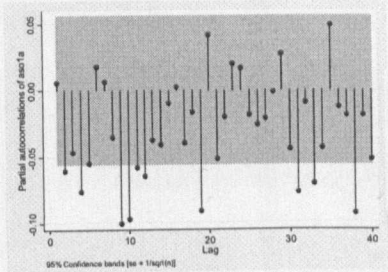
(1/df) Pearson = 1.131547
AIC = 12.20145





df = 7/year
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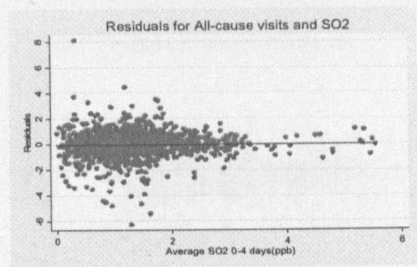
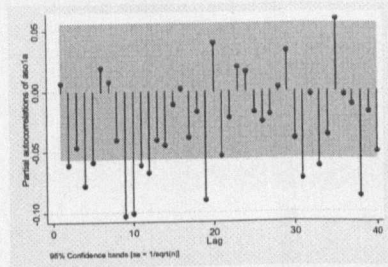
(1/df) Pearson = 1.138079
AIC = 12.20565





df = 8/year
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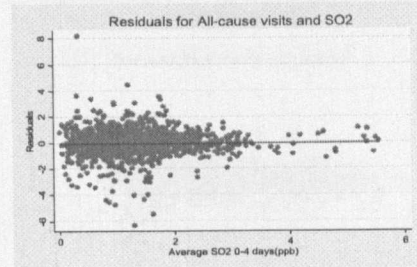
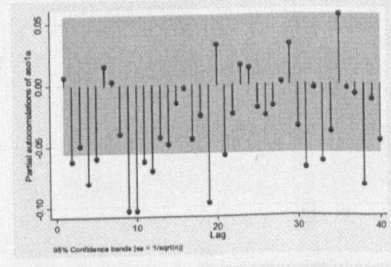
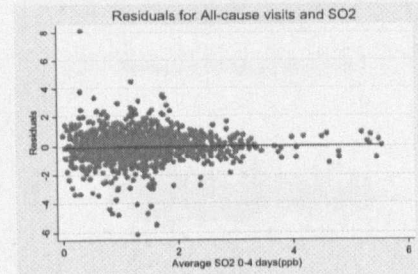
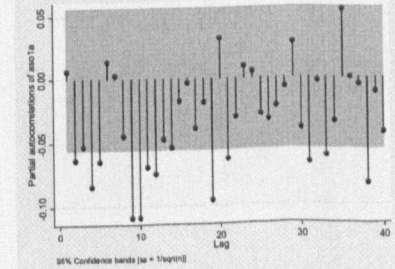
(1/df) Pearson = 1.142751
AIC = 12.20801





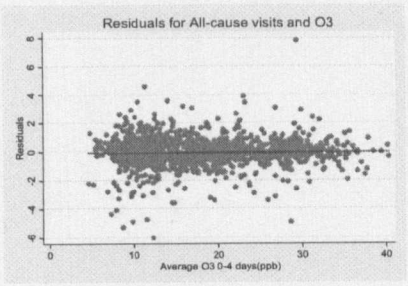
df = 9/year
(1/df) Deviance = 1.145984
(1/df) Pearson = 1.147605
AIC = 12.21014

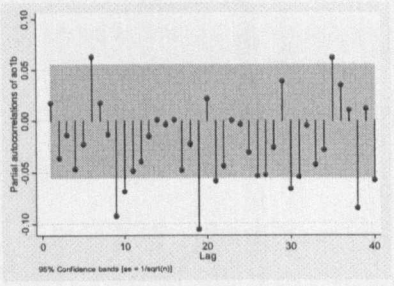




df = 10/year
(1/df) Deviance = 1.15171
(1/df) Pearson = 1.152316
AIC = 12.21215

Figure 6A-2 Model diagnostics for all-cause visits & O_3 in regard to degrees of freedom.





df = 1/year
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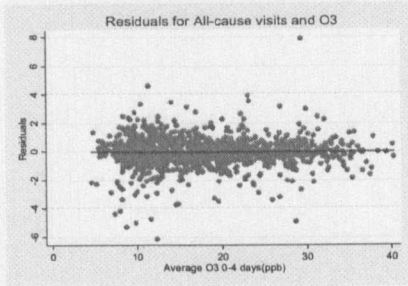
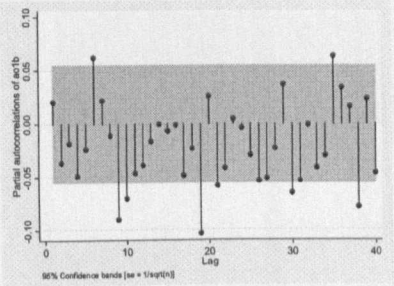
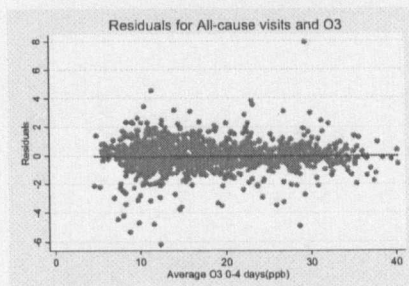
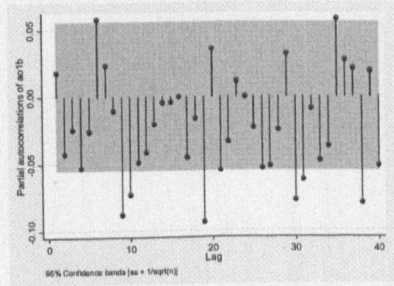
(1/df) Pearson = 1.105099
AIC = 12.23774



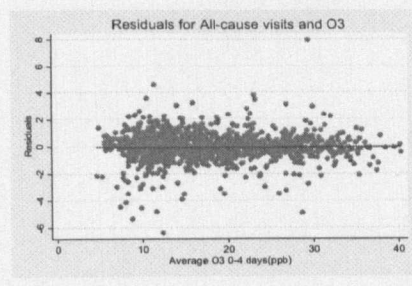


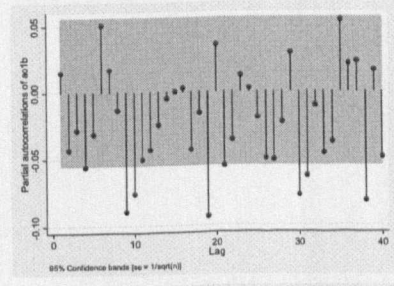
df = 2/year
(1/df) Deviance = 1.110388
(1/df) Pearson = 1.104541
AIC = 12.23578



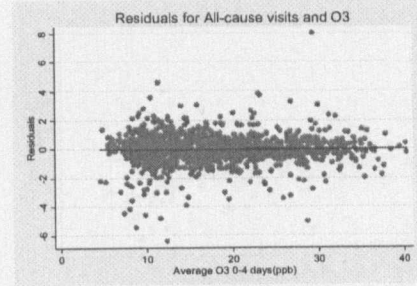


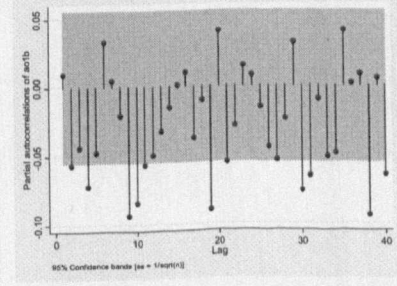
df = 3/year
(1/df) Deviance = 1.115808
(1/df) Pearson = 1.110853
AIC = 12.22638





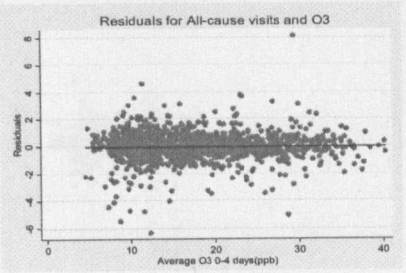
df = 4/year
(1/df) Deviance = 1.120004
(1/df) Pearson = 1.114407
AIC = 12.22143

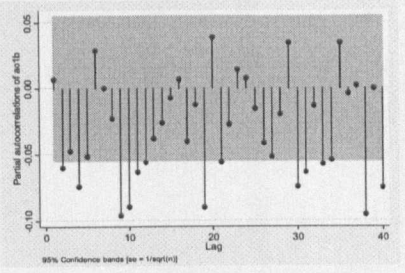




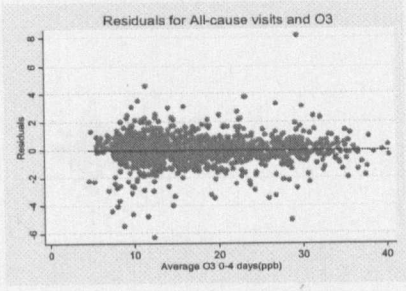
df = 5/year
(1/df) Deviance = 1.124705
(1/df) Pearson = 1.120881
AIC = 12.2093

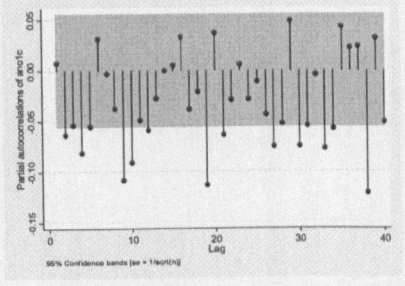
Figure 6A-2 Model diagnostics for all-cause visits & O_3 (continued).



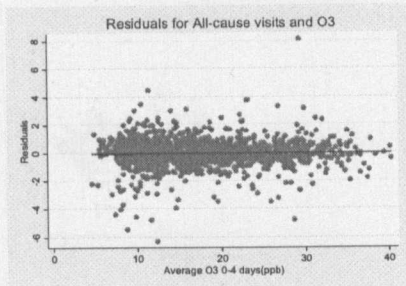


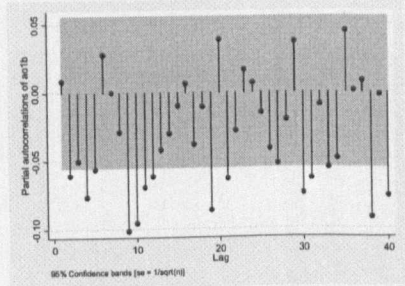
df = 6/year
(1/df) Deviance = 1.129293
(1/df) Pearson = 1.127214
AIC = 12.20964



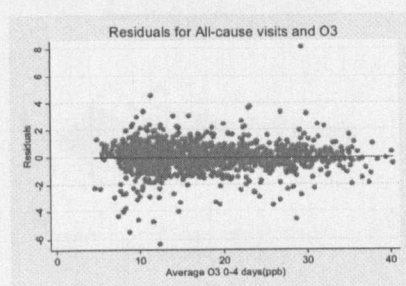


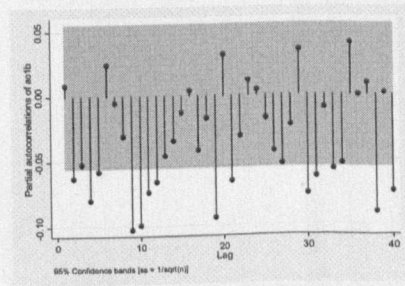
df = 7/year
(1/df) Deviance = 1.133648
(1/df) Pearson = 1.133435
AIC = 12.21388



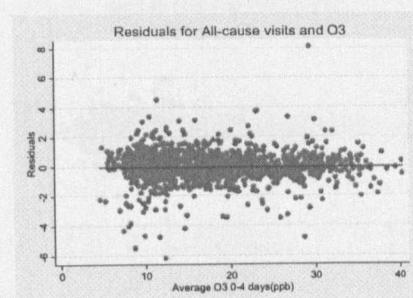


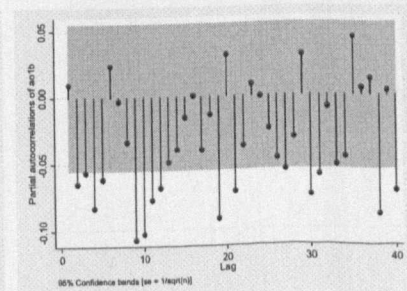
df = 8/year
(1/df) Deviance = 1.137591
(1/df) Pearson = 1.13784
AIC = 12.21683





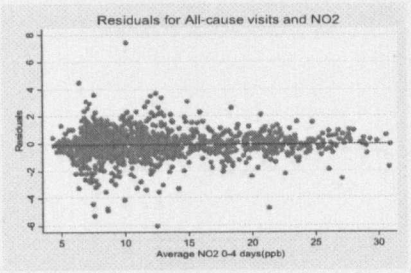
df = 9/year
(1/df) Deviance = 1.141532
(1/df) Pearson = 1.14217
AIC = 12.22014

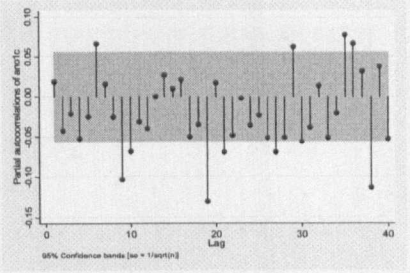




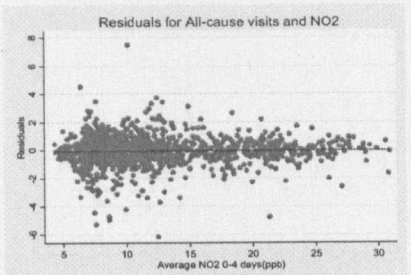
df = 10/year
(1/df) Deviance = 1.146901
(1/df) Pearson = 1.146633
AIC = 12.22212

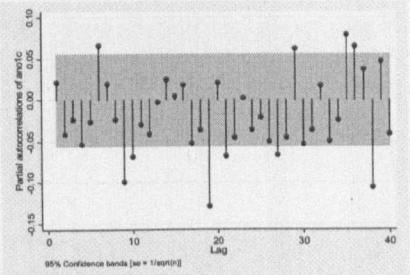
Figure 6A-3 Model diagnostics for all-cause visits & NO_2 in regard to degrees of freedom.



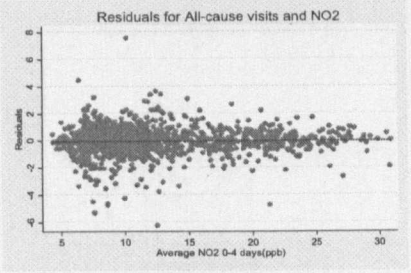


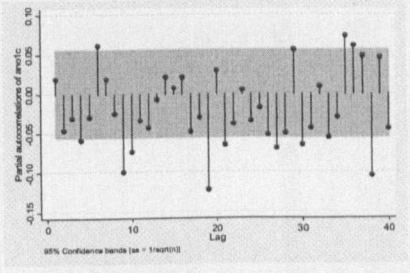
df = 1/year
(1/df) Deviance = 1.106713
(1/df) Pearson = 1.096692
AIC = 12.24105



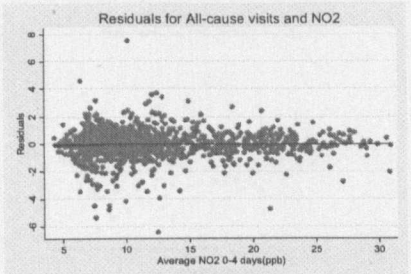


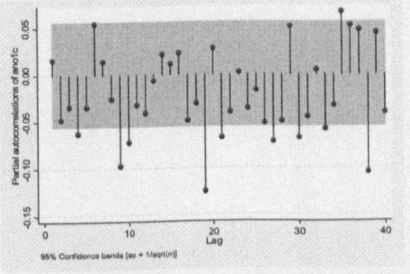
df = 2/year
(1/df) Deviance = 1.110327
(1/df) Pearson = 1.096548
AIC = 12.23996



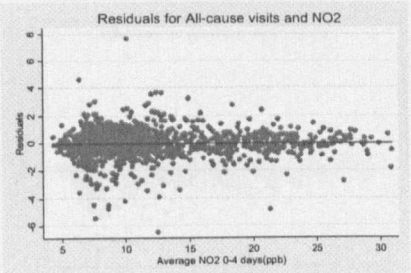


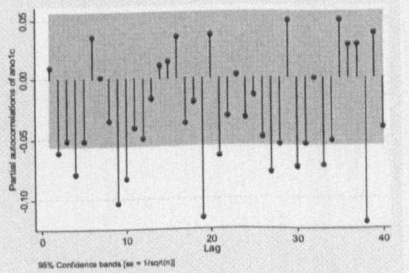
df = 3/year
(1/df) Deviance = 1.115914
(1/df) Pearson = 1.102819
AIC = 12.23052





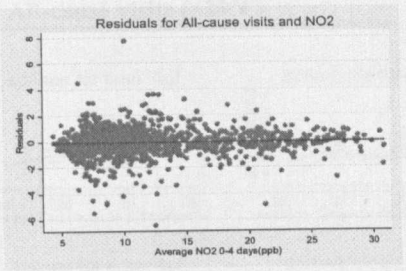
df = 4/year
(1/df) Deviance = 1.120098
(1/df) Pearson = 1.105043
AIC = 12.22433

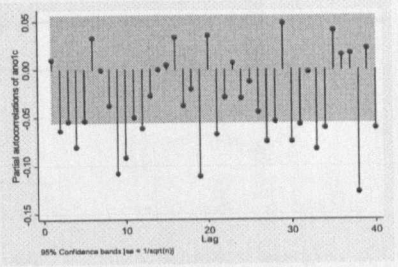




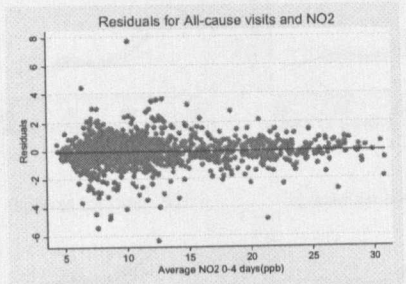
df = 5/year
(1/df) Deviance = 1.124902
(1/df) Pearson = 1.111857
AIC = 12.21161

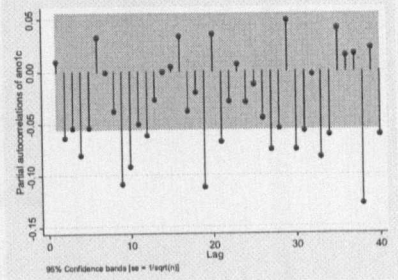
Figure 6A-3 Model diagnostics for all-cause visits & NO_2 (continued).



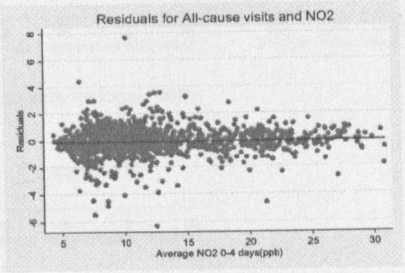


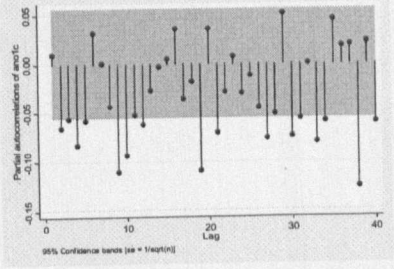
df = 6/year
(1/df) Deviance = 1.129532
(1/df) Pearson = 1.118425
AIC = 12.21316



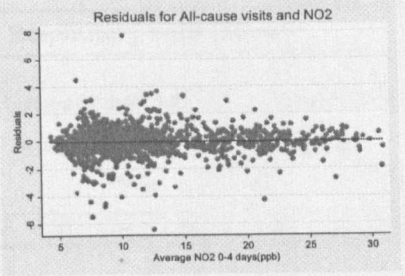


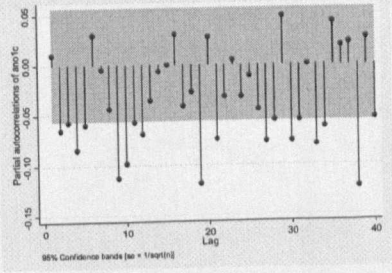
df = 7/year
(1/df) Deviance = 1.134119
(1/df) Pearson = 1.12453
AIC = 12.21754



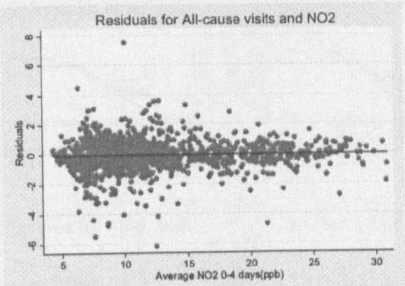


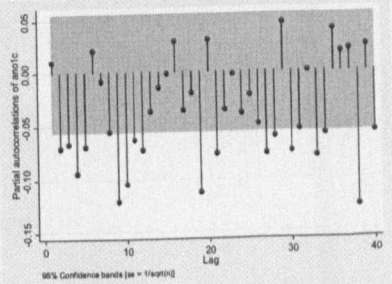
df = 8/year
(1/df) Deviance = 1.138145
(1/df) Pearson = 1.127409
AIC = 12.22012





df = 9/year
(1/df) Deviance = 1.142316
(1/df) Pearson = 1.133559
AIC = 12.22365

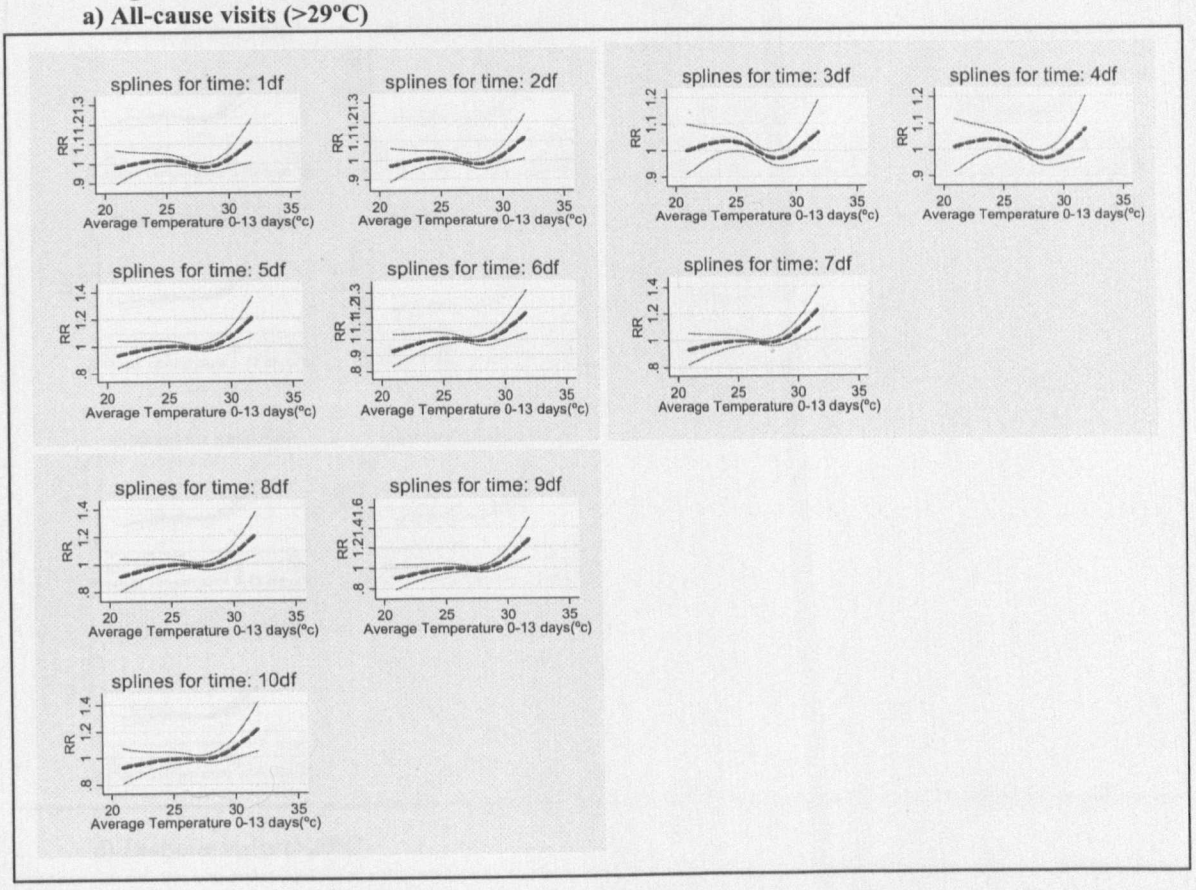




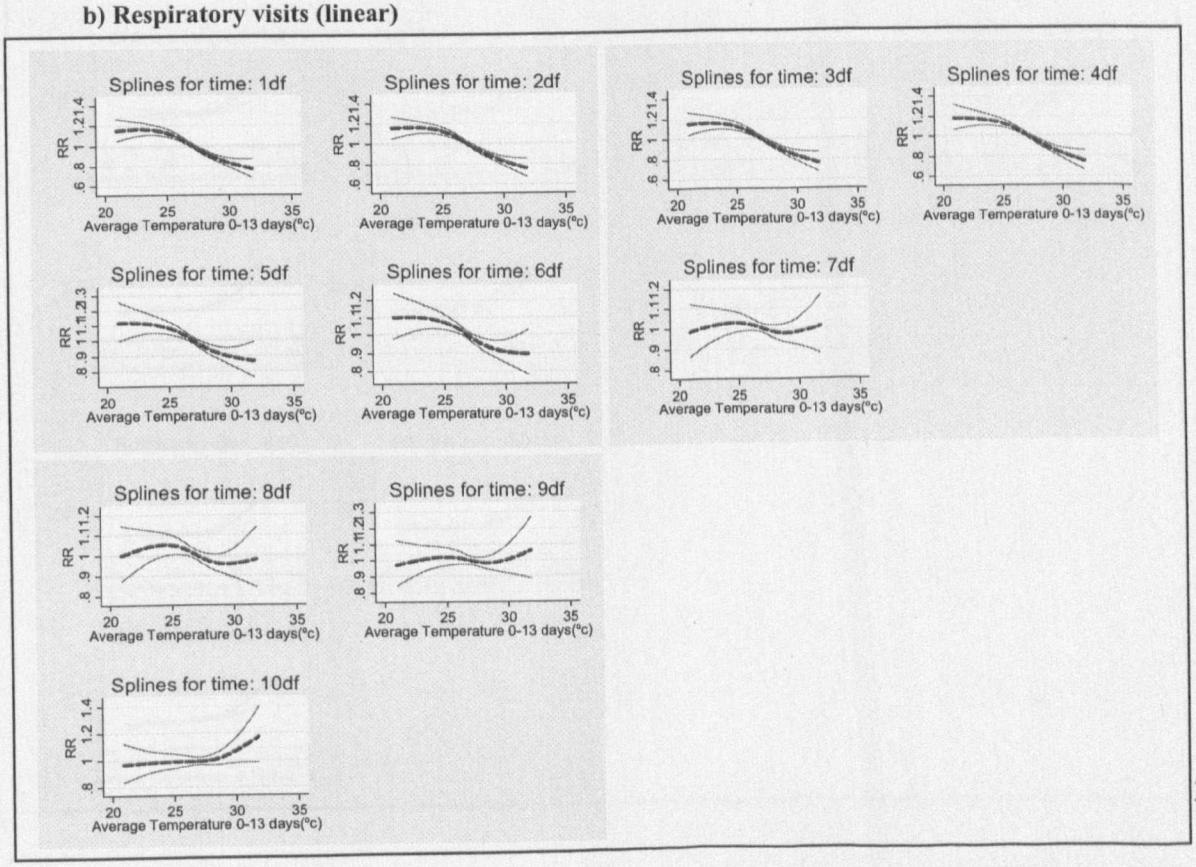
df = 10/year
(1/df) Deviance = 1.147922
(1/df) Pearson = 1.134113
AIC = 12.22299

Figure 6A-4 Plots of estimated RRs and CIs for temperature effects on daily out-patient visits when using different degrees of freedom.

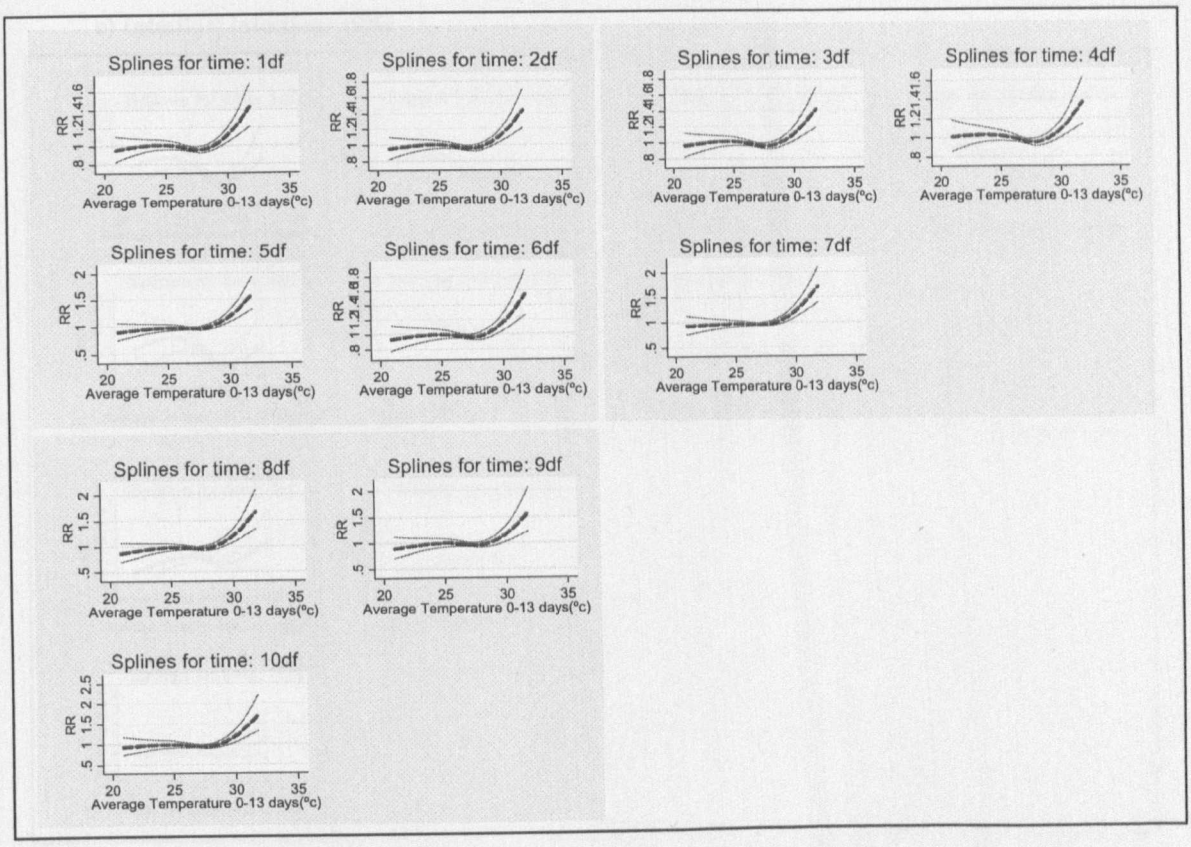
a) All-cause visits (>29°C)



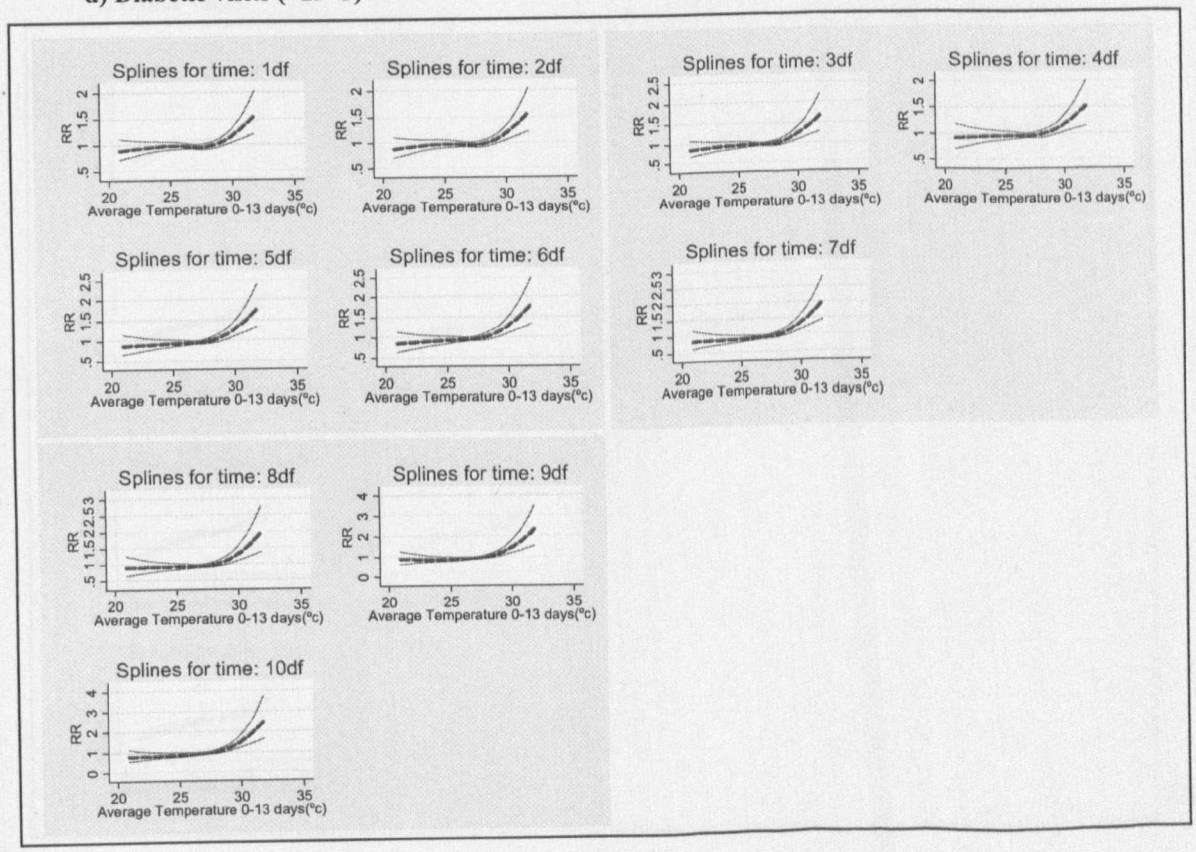
b) Respiratory visits (linear)



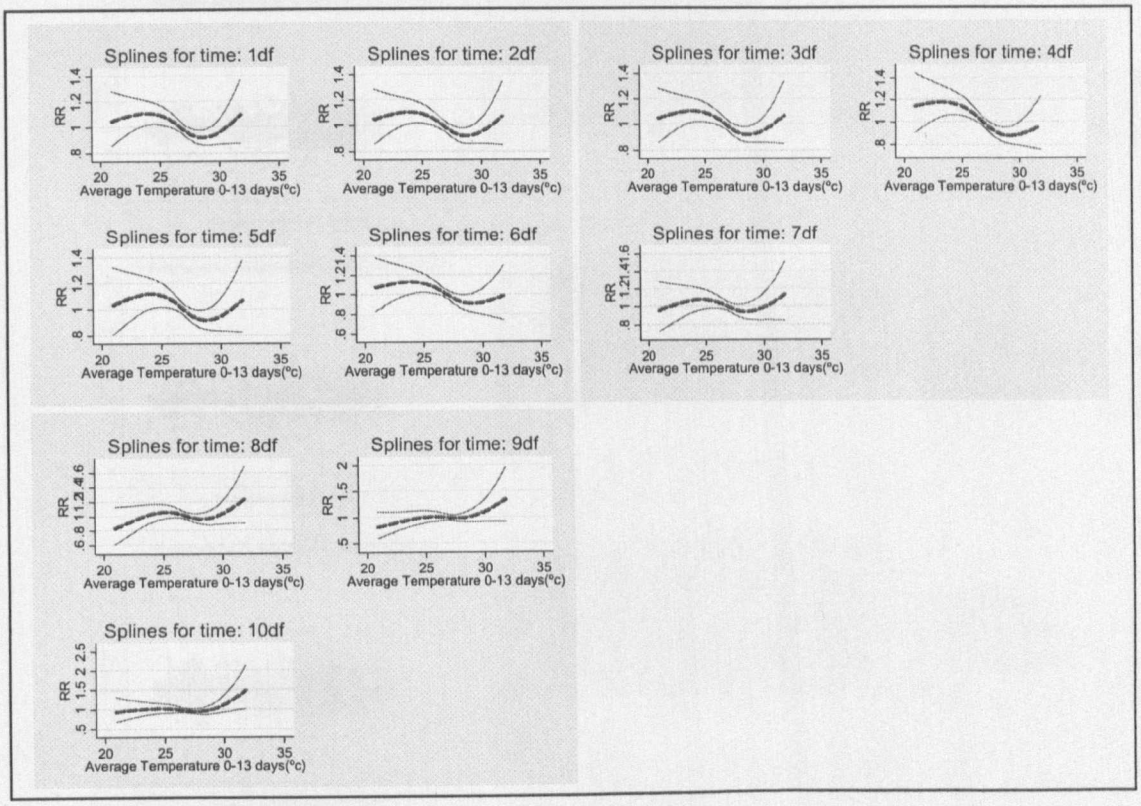
c) Circulatory visits (>29°C)



d) Diabetic visits (>29°C)



e) Intestinal infectious visits



f) Other visits

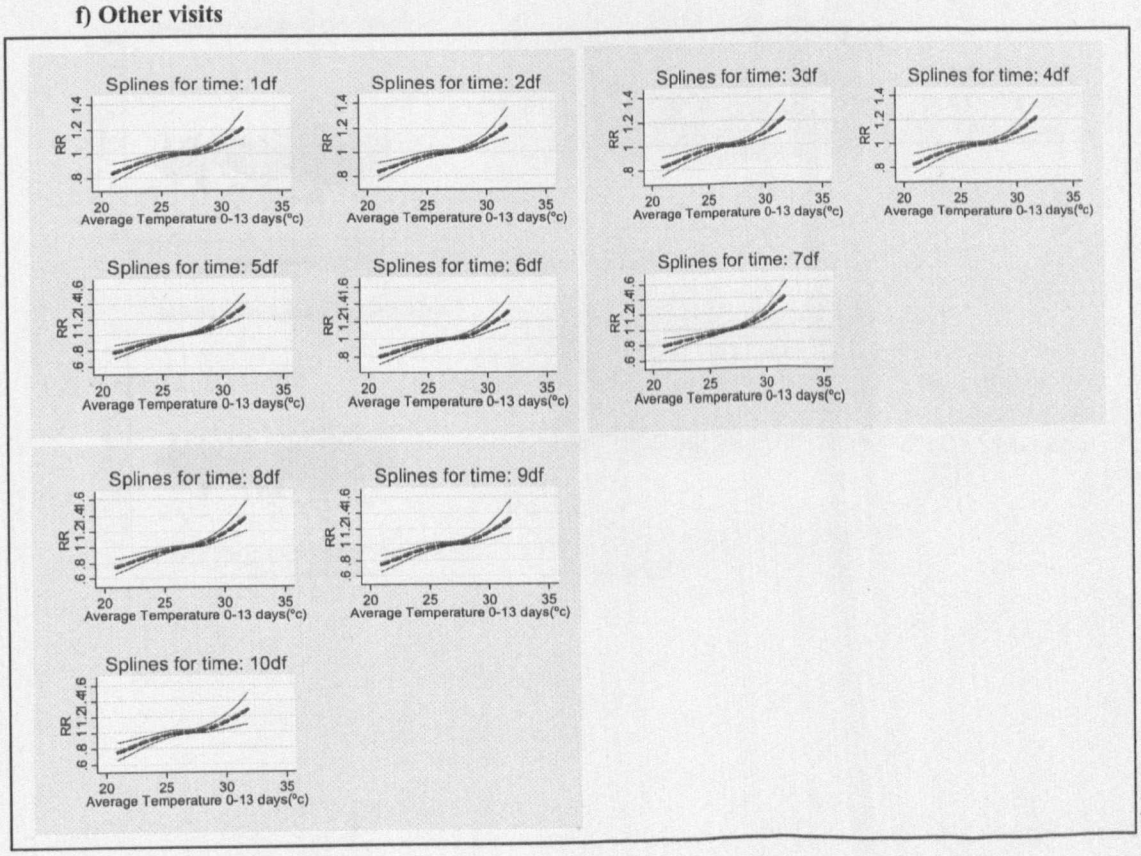
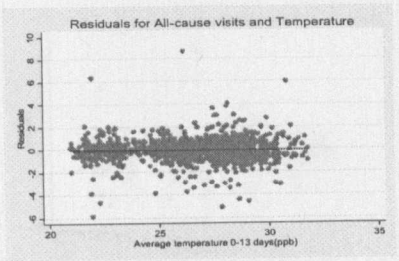
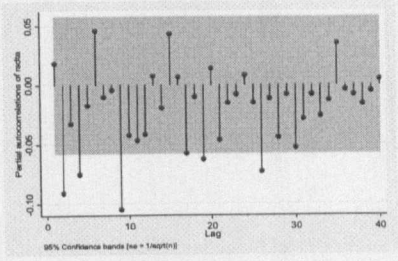
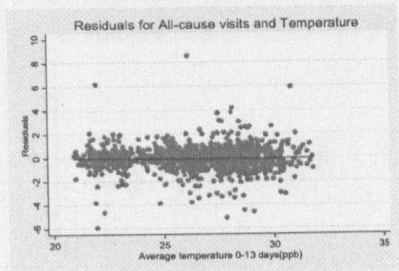


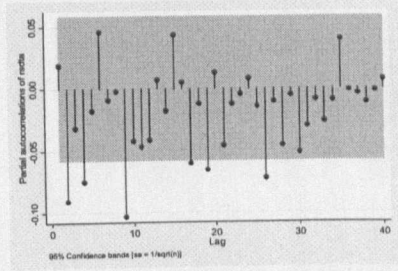
Figure 6A-5 Model diagnostics for all-cause visits & temperature in regard to degrees of freedom.



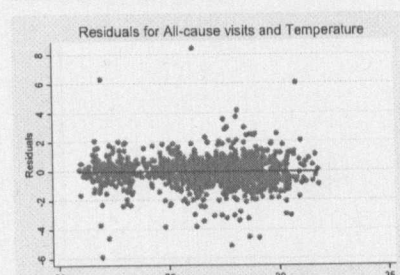


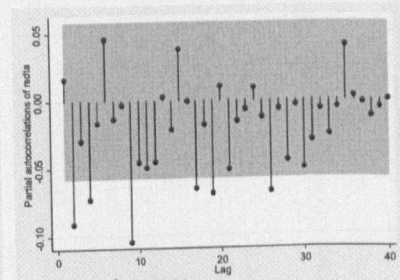
df = 1/year
(1/df) Deviance = 1.104724
(1/df) Pearson = 1.176327
AIC = 12.32891



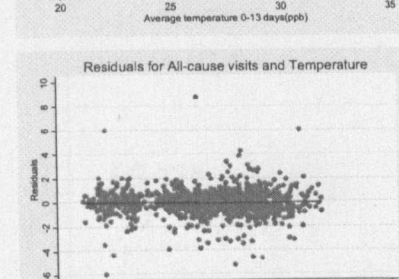


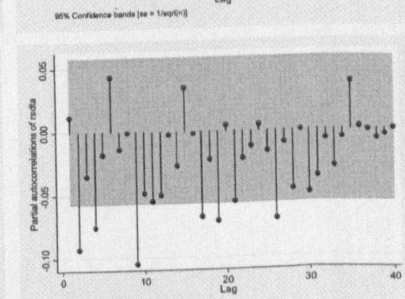
df = 2/year
(1/df) Deviance = 1.109073
(1/df) Pearson = 1.176796
AIC = 12.33075



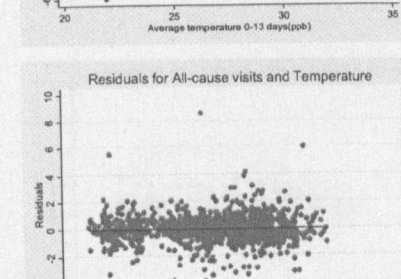


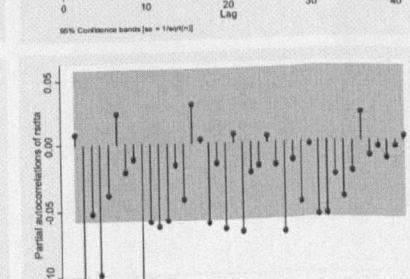
df = 3/year
(1/df) Deviance = 1.113809
(1/df) Pearson = 1.178985
AIC = 12.33165





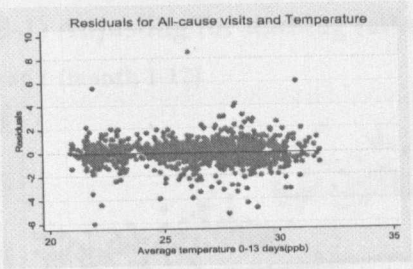
df = 4/year
(1/df) Deviance = 1.118059
(1/df) Pearson = 1.184367
AIC = 12.32335

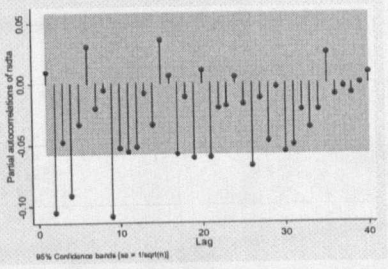




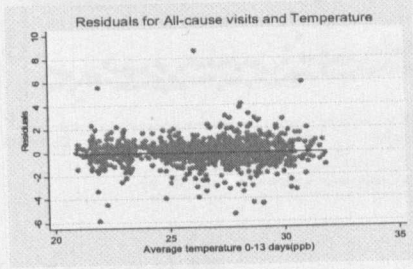
df = 5/year
(1/df) Deviance = 1.122867
(1/df) Pearson = 1.176973
AIC = 12.29553

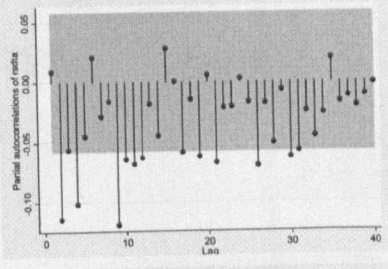
Figure 6A-5 Model diagnostics for all-cause visits & temperature (continued).



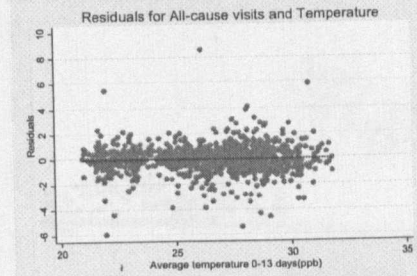


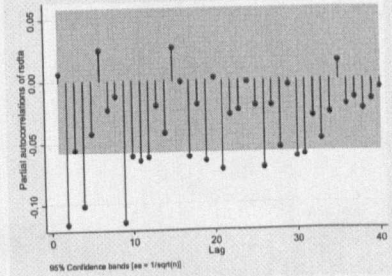
df = 6/year
(1/df) Deviance = 1.1266
(1/df) Pearson = 1.179871
AIC = 12.30661





df = 7/year
(1/df) Deviance = 1.131751
(1/df) Pearson = 1.189366
AIC = 12.3053





df = 8/year
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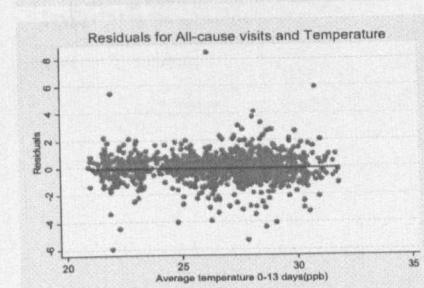
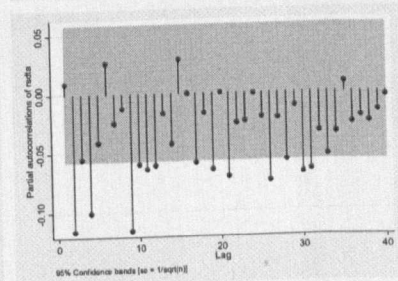
(1/df) Pearson = 1.190969
AIC = 12.3095





df = 9/year
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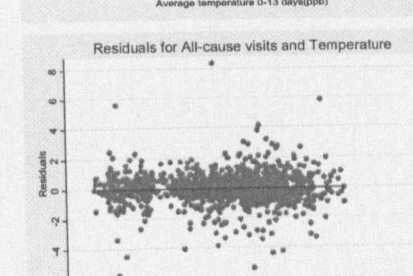
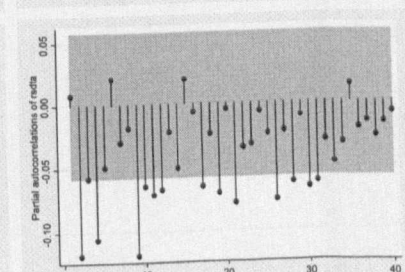
(1/df) Pearson = 1.193094
AIC = 12.31206



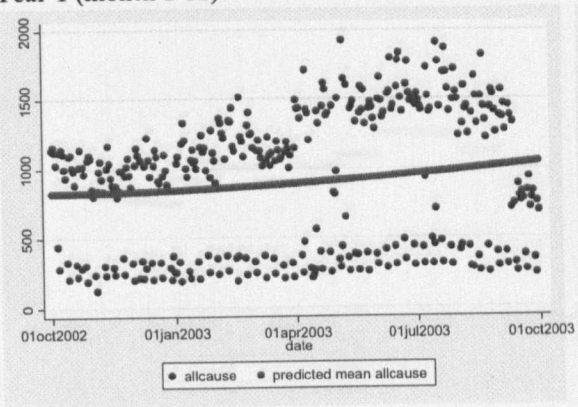


df = 10/year
(1/df) Deviance = 1.145913
(1/df) Pearson = 1.196943
AIC = 12.31647

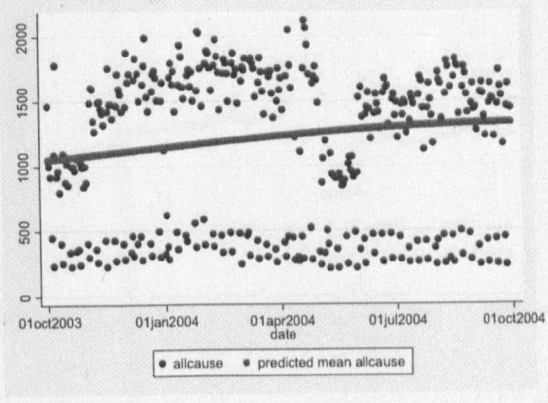
Appendix 6B Plots of the fitted values of all-cause visits over time.

6B-1) Adjusting for nothing (all-cause visits + splines of date).

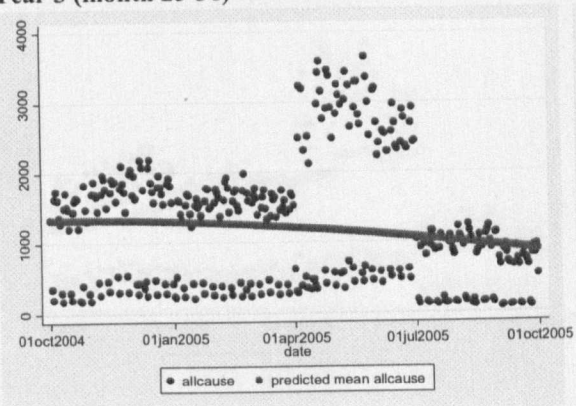
Year 1 (month 1-12)



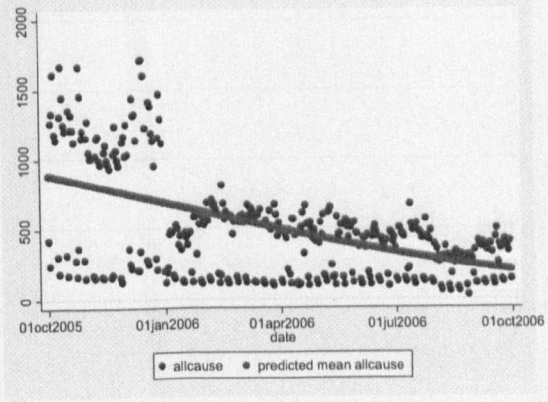
Year 2 (month 13-24)



Year 3 (month 25-36)

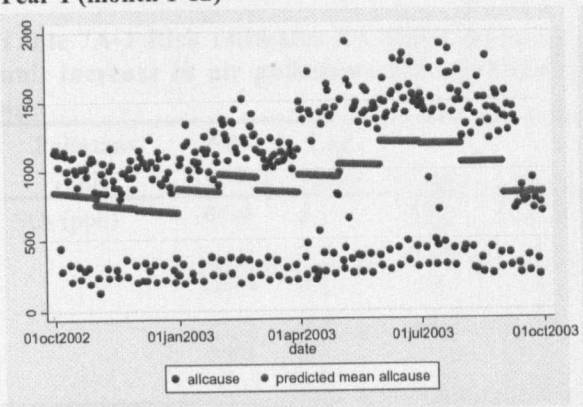


Year 4 (month 37-48)

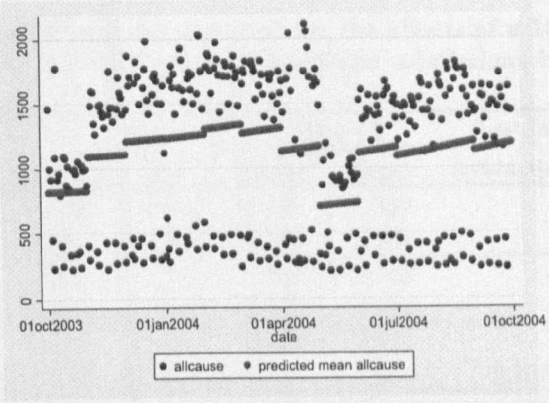


6B-2) Adjusting for month of the visits only (all-cause visits + splines of date + i.movisit).

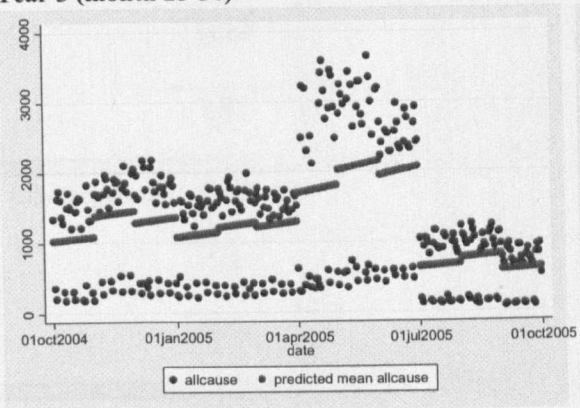
Year 1 (month 1-12)



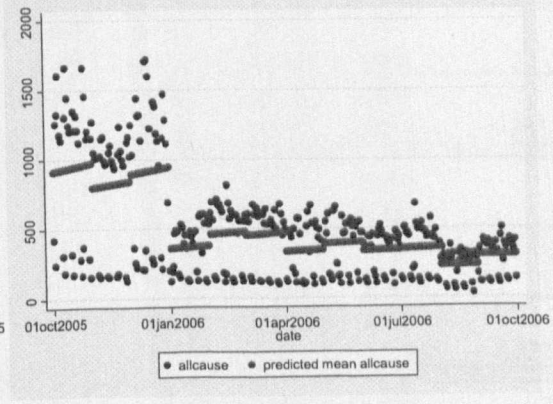
Year 2 (month 13-24)



Year 3 (month 25-36)



Year 4 (month 37-48)



Appendices for chapter 7

Appendix 7A: Air pollution and temperature effects on neoplasm admissions.

Table 7A-1 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase in air pollutants (one-unit increase for CO) on daily neoplasm admissions by age.

Pollutant (unit)	Age (year)	Lag (day)	Coef.	SE	p-value	RR	95% CI Lower	95% CI Upper	Test for interaction*
SO_2 (ppb)	0-14	0-1	0.012	0.033	0.722	1.126	0.585	2.169	
		0-4	0.030	0.046	0.514	1.349	0.550	3.309	
	15-64	0-1	0.010	0.011	0.387	1.100	0.887	1.364	
		0-4	0.027	0.015	0.068	1.312	0.981	1.756	
	≥ 65	0-1	-0.008	0.018	0.650	0.922	0.648	1.311	
		0-4	-0.023	0.025	0.353	0.794	0.489	1.291	0.208
NO_2(ppb)	0-14	0-1	0.006	0.009	0.536	1.059	0.884	1.268	
		0-4	-0.006	0.011	0.576	0.938	0.749	1.174	
	15-64	0-1	-0.003	0.003	0.388	0.973	0.914	1.035	
		0-4	-0.004	0.004	0.350	0.964	0.893	1.041	
	≥ 65	0-1	-0.008	0.005	0.104	0.921	0.835	1.017	
		0-4	-0.013	0.006	0.044	0.881	0.778	0.997	0.481
CO-8hr(ppm)	0-14	0-1	-0.241	0.154	0.118	0.786	0.581	1.063	
		0-4	-0.409	0.202	0.043	0.665	0.447	0.988	
	15-64	0-1	-0.081	0.052	0.117	0.922	0.833	1.021	
		0-4	-0.068	0.067	0.312	0.935	0.820	1.065	
	≥ 65	0-1	-0.171	0.084	0.041	0.843	0.715	0.993	
		0-4	-0.128	0.110	0.242	0.880	0.710	1.090	0.272
O_3(ppb)	0-14	0-1	0.015	0.007	0.048	1.158	1.001	1.338	
		0-4	0.009	0.009	0.327	1.092	0.916	1.303	
	15-64	0-1	0.005	0.002	0.031	1.055	1.005	1.107	
		0-4	0.004	0.003	0.221	1.038	0.978	1.102	
	≥ 65	0-1	0.009	0.004	0.018	1.097	1.016	1.185	
		0-4	0.007	0.005	0.178	1.068	0.970	1.176	0.789
PM_{10}($\mu g/m^3$)	0-14	0-1	-0.001	0.002	0.615	0.992	0.961	1.024	
		0-4	-0.002	0.002	0.227	0.976	0.938	1.015	
	15-64	0-1	-0.000	0.001	0.669	0.998	0.987	1.008	
		0-4	-0.000	0.001	0.696	0.997	0.985	1.010	
	≥ 65	0-1	-0.001	0.001	0.249	0.990	0.973	1.007	
		0-4	-0.002	0.001	0.050	0.979	0.958	1.000	0.259
$PM_{2.5}$($\mu g/m^3$)	0-14	0-1	0.000	0.003	0.897	1.004	0.943	1.069	
		0-4	-0.002	0.004	0.599	0.980	0.910	1.056	
	15-64	0-1	-0.002	0.001	0.118	0.983	0.962	1.004	
		0-4	-0.002	0.001	0.266	0.985	0.959	1.012	
	≥ 65	0-1	-0.002	0.002	0.285	0.981	0.947	1.016	
		0-4	-0.005	0.002	0.012	0.947	0.907	0.988	0.308

*p-value of the test for heterogeneity between groups in relation to a pollutant at lag 0-4 days.

Table 7A-2 Risk estimates for single pollutant, distributed lag models for the effects of a 10-unit increase in air pollutants (one-unit increase for CO) on daily neoplasm admissions by sex.

Pollutant (unit)	Sex	Lag (day)	Coef.	SE	p-value	RR	95% CI Lower	95% CI Upper	Test for interaction*
SO_2 (ppb)	Male	0-1	-0.013	0.014	0.347	0.874	0.660	1.158	
		0-4	-0.010	0.019	0.586	0.902	0.622	1.308	
	Female	0-1	0.022	0.012	0.059	1.244	0.992	1.560	
		0-4	0.035	0.016	0.025	1.424	1.045	1.942	0.064
NO_2(ppb)	Male	0-1	-0.004	0.004	0.299	0.959	0.886	1.038	
		0-4	-0.009	0.005	0.073	0.915	0.831	1.008	
	Female	0-1	-0.003	0.003	0.403	0.972	0.910	1.039	
		0-4	-0.004	0.004	0.328	0.960	0.884	1.042	0.458
CO-8hr(ppm)	Male	0-1	-0.154	0.066	0.020	0.857	0.753	0.976	
		0-4	-0.197	0.085	0.021	0.821	0.695	0.970	
	Female	0-1	-0.068	0.056	0.220	0.934	0.838	1.042	
		0-4	-0.022	0.072	0.762	0.978	0.850	1.126	0.116
O_3(ppb)	Male	0-1	0.008	0.003	0.008	1.086	1.022	1.154	
		0-4	0.004	0.004	0.335	1.037	0.963	1.118	
	Female	0-1	0.006	0.003	0.030	1.059	1.005	1.116	
		0-4	0.005	0.003	0.095	1.056	0.990	1.126	0.718
$PM_{10}(\mu g/m^3)$	Male	0-1	-0.001	0.001	0.281	0.993	0.979	1.006	
		0-4	-0.002	0.001	0.018	0.980	0.964	0.997	
	Female	0-1	-0.000	0.001	0.744	0.998	0.987	1.009	
		0-4	0.000	0.001	0.907	1.001	0.987	1.015	0.058
$PM_{2.5}(\mu g/m^3)$	Male	0-1	-0.001	0.001	0.629	0.993	0.967	1.021	
		0-4	-0.003	0.002	0.129	0.975	0.943	1.007	
	Female	0-1	-0.002	0.001	0.082	0.980	0.958	1.003	
		0-4	-0.002	0.001	0.156	0.980	0.954	1.008	0.815

*p-value of the test for heterogeneity between groups in relation to a pollutant at lag 0-4 days.

Appendices for chapter 8

Appendix 8A General relationship between daily hospital admissions and temperature in linkage data

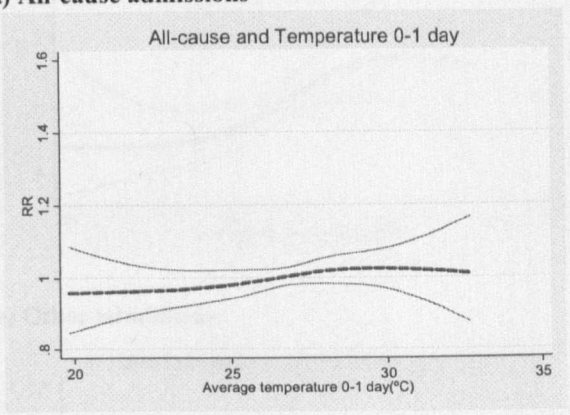
Figure 8A-1 Plots of the general relationships between daily hospital admissions and temperature at both short lag (0-1 day) and long lag (0-13 days) in the linkage data.

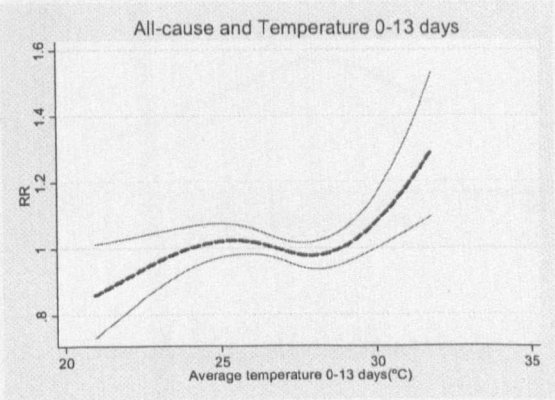
Note: -Relationship between temperature and daily hospital admissions, adjusting for dow, holidays, month of the study (7-40), Thai new year period, International new year period, influenza, humidity, rain, SO_2, and O_3.

-The x-axis represents temperature range (°C), and the y-axis represents the estimated relative risk (RR) of daily visits. The centre line in each graph is the estimated spline curve, and the upper and lower lines are the 95 percent confidence limits.

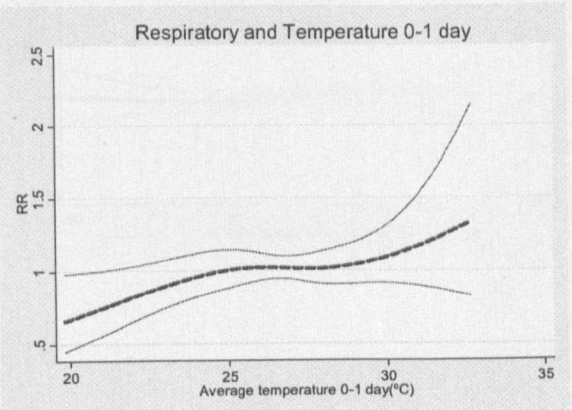
-The left graphs of each disease group show the relationship between hospital admissions and temperature at a short lag (0-1 day), whereas the right graphs of each disease group show the relationship between hospital admissions and temperature at a long lag (0-13 days).

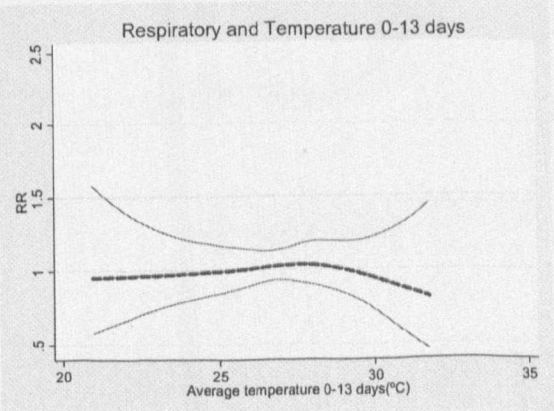
a) All-cause admissions



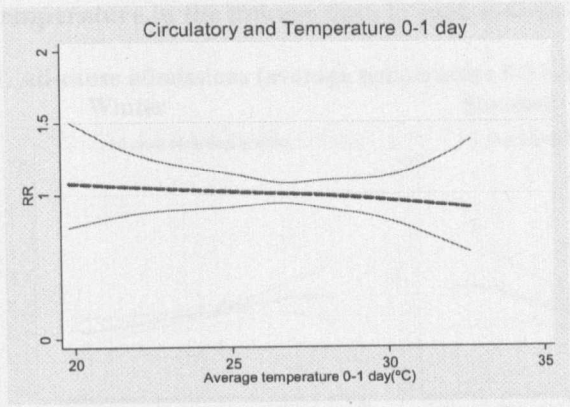


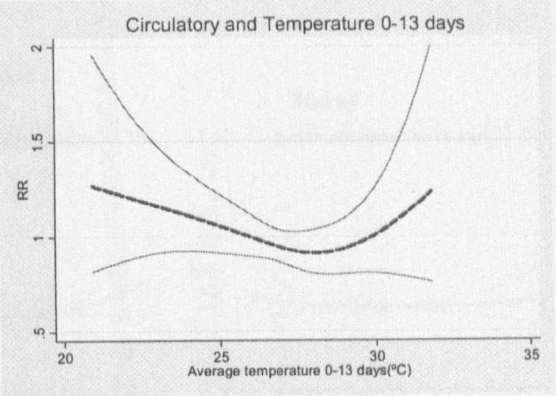
b) Respiratory admissions



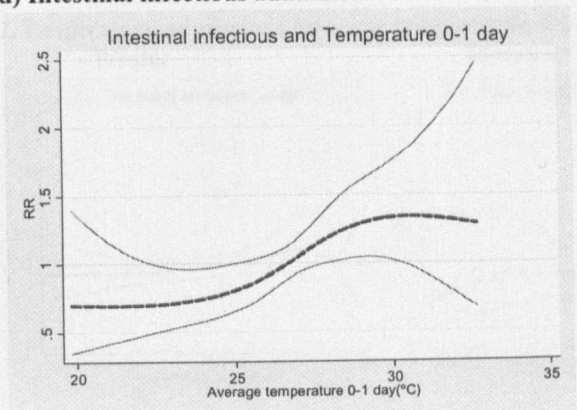


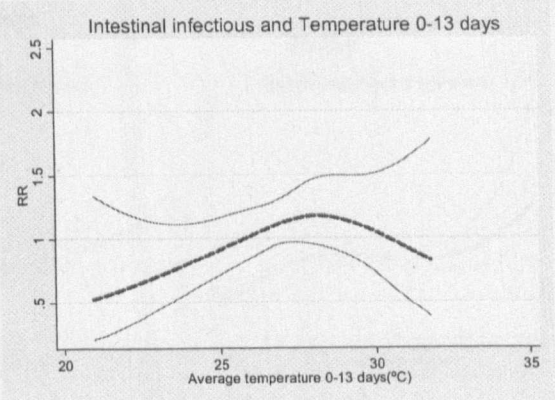
c) Circulatory admissions



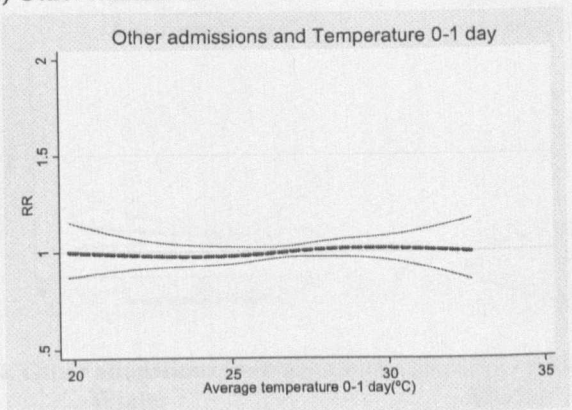


d) Intestinal infectious admissions





e) Other admissions



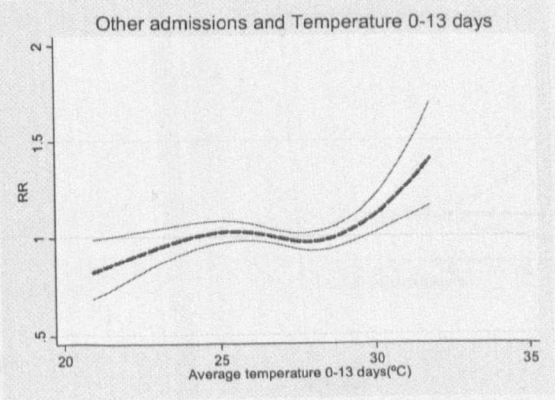
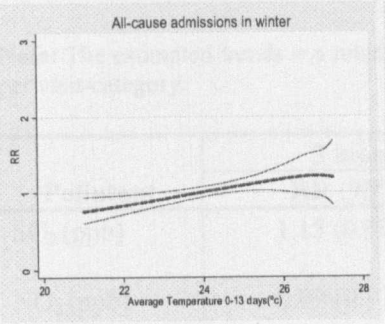


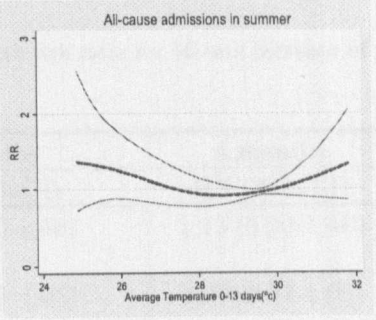
Figure 8A-2 Plots of the general relationships between daily hospital admissions and temperature in the linkage data in each season.

1. All-cause admissions (average temperature 0-13 days)

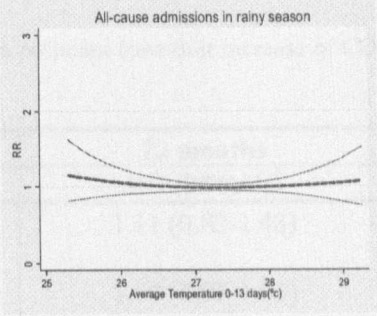
Winter



Summer

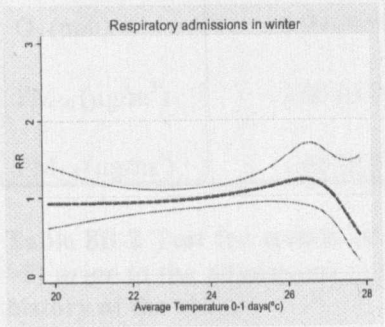


Rainy

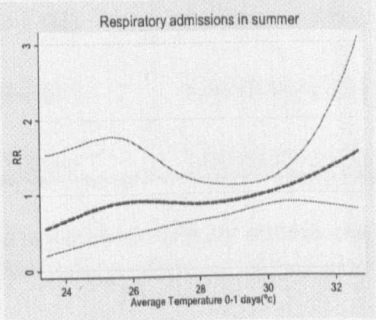


2. Respiratory admissions (average temperature 0-1 day)

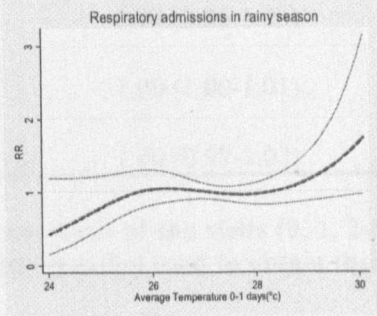
Winter



Summer

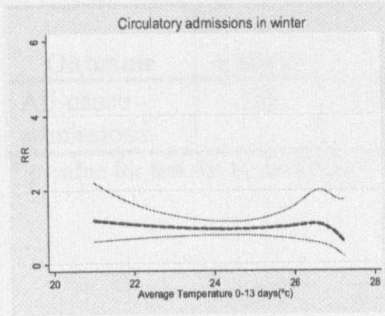


Rainy

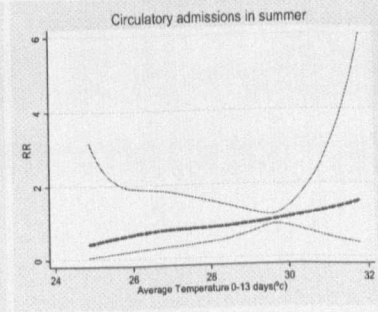


3. Circulatory admissions (average temperature 0-13 days)

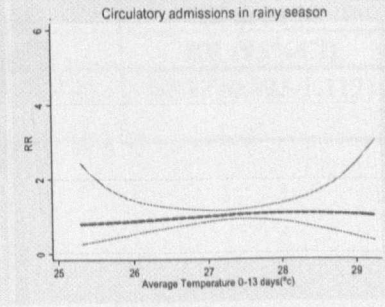
Winter



Summer

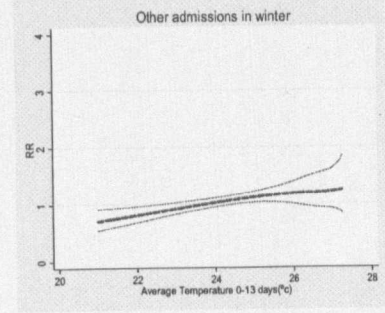


Rainy

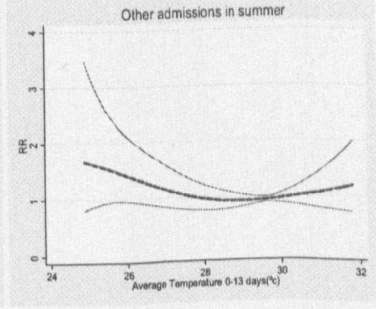


4. Other admissions (average temperature 0-13 days)

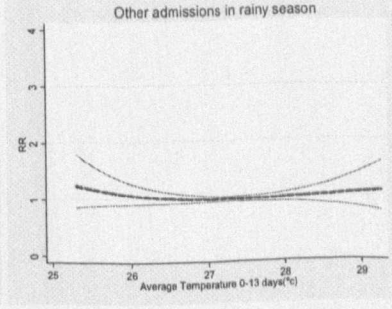
Winter



Summer



Rainy



Appendix 8B: Sensitivity analyses for the linkage series.

Table 8B-1 Test for trends of air pollution effects across the numbers of the visits prior to the admissions in the linkage data by linked period (months) used to obtain their history of the visits.

Note: The estimated trends = a relative risk ratio for 10-unit increase of a pollutant (one-unit increase of CO) per visit-category.

Pollutant	3 months	6 months	12 months
	RR (95%CI)	RR (95%CI)	RR (95%CI)
SO_2 (ppb)	1.15 (0.90-1.46)	1.13 (0.90-1.40)	1.11 (0.82-1.48)
NO_2 (ppb)	0.99 (0.93-1.06)	1.00 (0.95-1.05)	1.00 (0.95-1.05)
CO (ppm)	1.02 (0.91-1.14)	1.03 (0.95-1.12)	1.02 (0.93-1.13)
O_3 (ppb)	0.99 (0.94-1.04)	0.99 (0.95-1.03)	0.99 (0.96-1.03)
PM_{10} ($\mu g/m^3$)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (1.00-1.01)
$PM_{2.5}$ ($\mu g/m^3$)	1.00 (0.97-1.04)	1.00 (0.97-1.03)	1.00 (0.97-1.03)

Table 8B-2 Test for trends of temperature effects across the numbers of the visits (0, 1, 2-5, >5) prior to the admissions in the linkage data by linked period (months) used to obtain their history of the visits.

Note: The estimated trends = a relative risk ratio for 1°C increase in temperature (>29°C) per visit-category.

Outcome	n (day)	3 months	6 months	12 months
		RR (95%CI)	RR (95%CI)	RR (95%CI)
All-cause admissions	132	1.018 (0.885-1.160)	0.999 (0.899-1.111)	0.997 (0.893-1.112)

* p-value for test for heterogeneity of the trends between groups = 0.969.

Table 8B-3 Estimated trends of air pollution effects across the numbers of the visits prior to the admissions in the linkage data that used two different assumptions: matched cases only (data used in this study); and both unmatched & matched cases, in obtaining people with no history of the visits.

Note: The estimated trends = a relative risk ratio for 10-unit increase of a pollutant (one-unit increase of CO) per visit-category.

Pollutant	Matched cases only	Both unmatched and matched cases
	RR (95%CI)	RR (95%CI)
SO_2 (ppb)	1.13 (0.90-1.42)	1.10 (0.95-1.27)
NO_2 (ppb)	0.99 (0.95-1.04)	1.00 (0.96-1.03)
CO (ppm)	1.03 (0.92-1.14)	1.00 (0.94-1.07)
O_3 (ppb)	0.98 (0.95-1.02)	0.99 (0.96-1.02)
PM_{10} ($\mu g/m^3$)	1.00 (0.99-1.01)	1.00 (1.00-1.01)
$PM_{2.5}$ ($\mu g/m^3$)	1.00 (0.97-1.03)	1.00(0.98-1.02)

Table 8B-4 Estimated trends of temperature effects across the numbers of the visits (0, 1, 2-5, >5) prior to the admissions in the linkage data that used two different assumptions: matched cases only (used in this study); and both unmatched & matched cases, in obtaining people with no history of the visits.

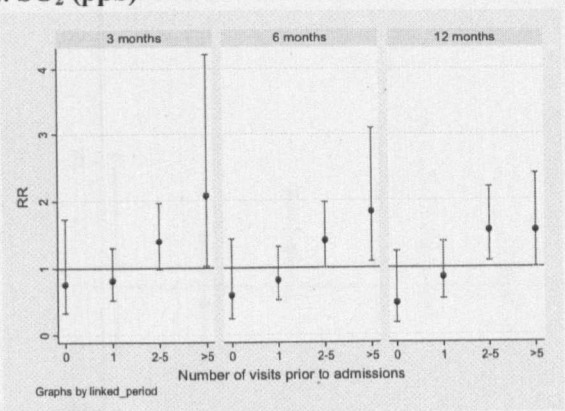
Note: The estimated trends = a relative risk ratio for 1°C increase in temperature (>29°C) per visit-category.

Outcome	n (day)	Matched cases only	Both unmatched & matched cases
		RR (95%CI)	RR (95%CI)
All-cause admissions	173	0.993 (0.911-1.082)	1.008 (0.947-1.073)

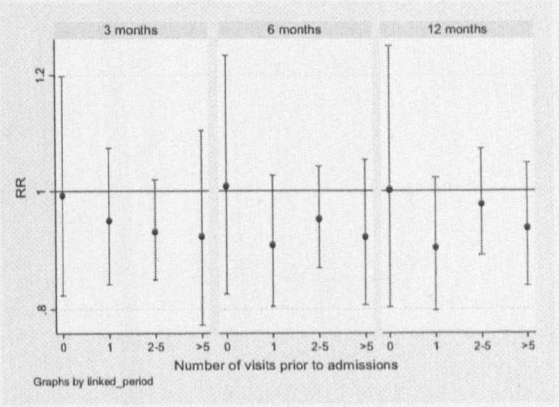
* p-value for test for heterogeneity of the trends between groups = 0.773.

Figure 8B-1 Risk estimates of air pollution effects (lag 0-4 days) on daily all-cause admissions for a 10-unit increase of a pollutant (one-unit increase of CO) across the number of the visits prior to their admissions in the linkage data by linked period (months) used to obtain their history of the visits.

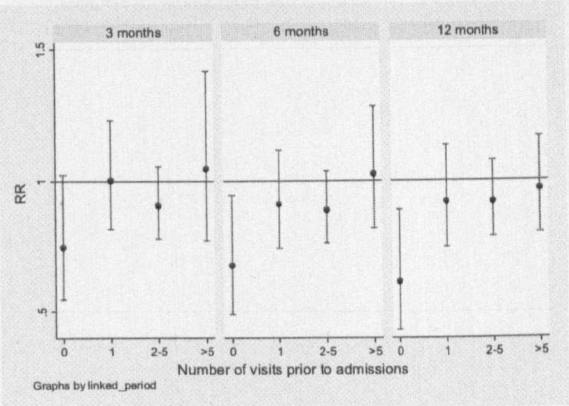
1. SO_2 (ppb)



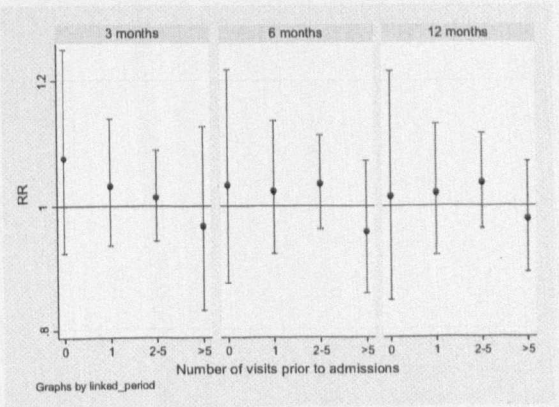
2. NO_2 (ppb)



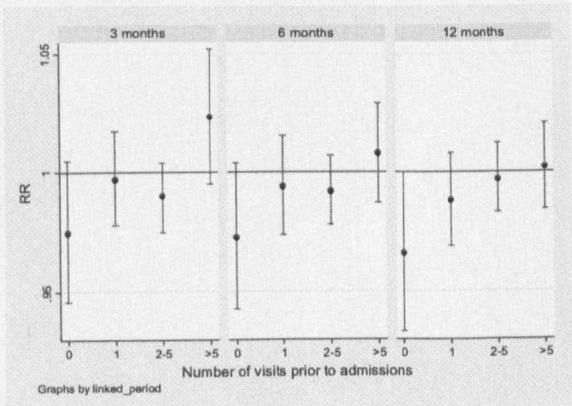
3. CO (ppm)



4. O_3 (ppb)



5. PM_{10} ($\mu g/m^3$)



6. $PM_{2.5}$ ($\mu g/m^3$)

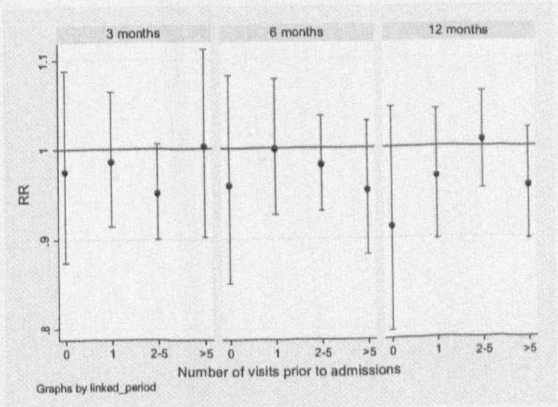


Figure 8B-2 Risk estimates of temperature effects on daily all-cause admissions for one degree Celsius increase in temperature (>29°C) across the history of the visits prior to the admissions by linked period (months) used to obtain the linkage data.

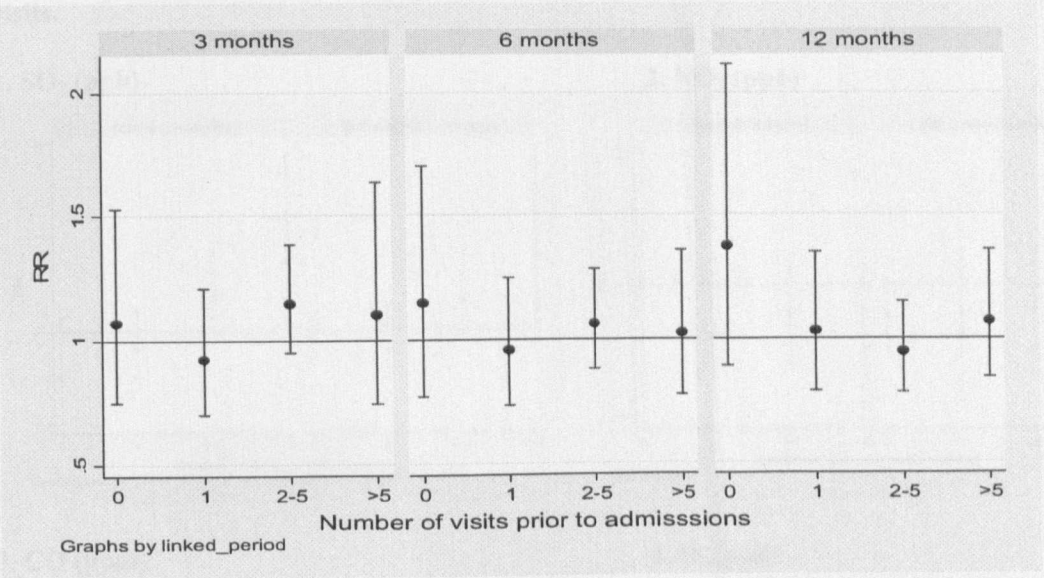
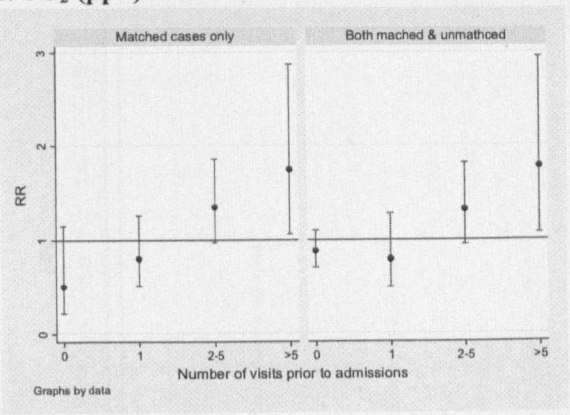
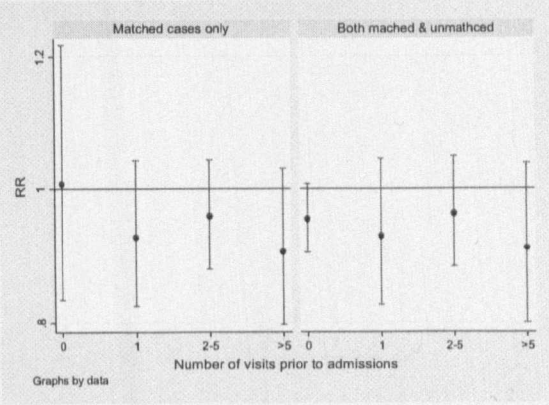


Figure 8B-3 Risk estimates of air pollution effects (lag 0-4 days) on daily all-cause admissions for a 10-unit increase of a pollutant (one-unit increase of CO) across the numbers of the visits prior to their admissions in the linkage data that used two different assumptions: matched cases only; and both unmatched & matched cases, in obtaining people with no history of the visits.

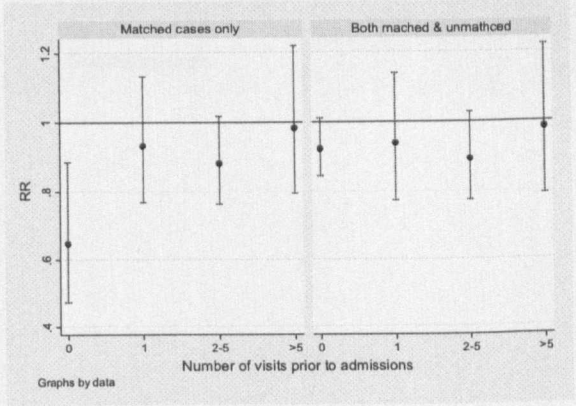
1. SO_2 (ppb)



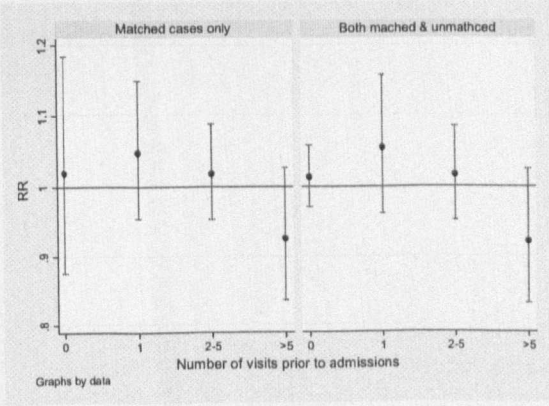
2. NO_2 (ppb)



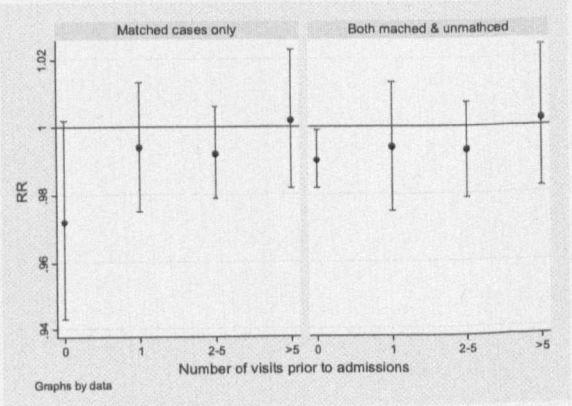
3. CO (ppm)



4. O_3 (ppb)



5. PM_{10} ($\mu g/m^3$)



6. $PM_{2.5}$ ($\mu g/m^3$)

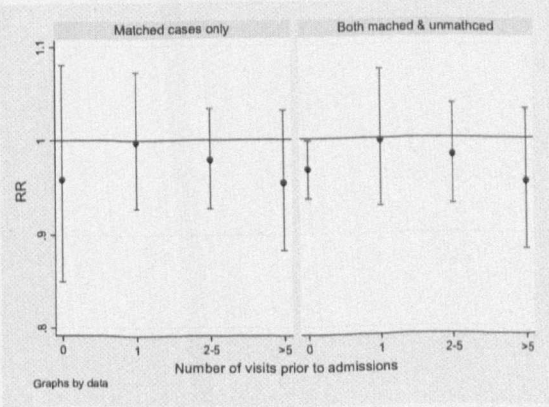
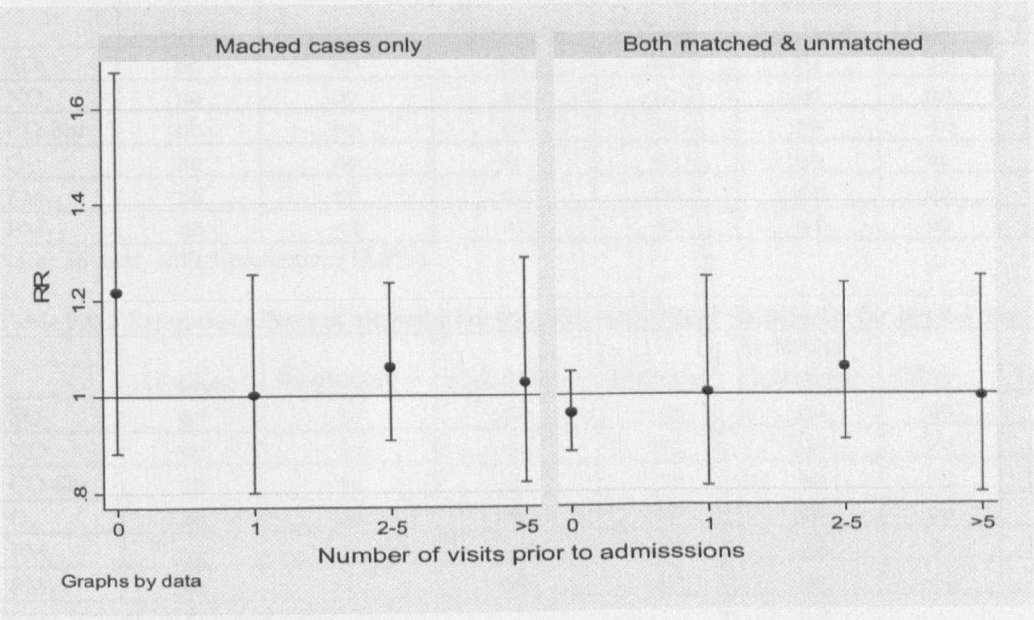


Figure 8B-4 Risk estimates of temperature effects on daily all-cause admissions for one degree Celsius increase in temperature (>29°C) across the numbers of the visits prior to their admissions in the linkage data that used two different assumptions: matched cases only (used in this study); and both unmatched & matched cases, in obtaining people with no history of the visits.



Appendices for chapter 9

Appendix 9A: Air pollution results with regard to multiple testing.

Table 9A-1 Estimated effects of air pollution from the out-patient visits series for lag 0-1 day.

	All-cause	Respiratory	Circulatory	Diabetic	Intestinal infectious	Other	Total
SO_2	no	no	no	no	no	no	no
NO_2	no	no	no	no	no	no	no
CO-8hr	no	no	no	no	no	-ve	1 -ve sig
O_3	no	no	no	no	no	no	
PM_{10}	no	no	no	no	-ve	no	1 -ve sig
$PM_{2.5}$	no	-ve	-ve	no	-ve	no	3 -ve sig

Note: 36 tests, with 5-protective (13.8%).

Table 9A-2 Estimated effects of air pollution from the out-patient visits series for lag 0-4 day.

	All-cause	Respiratory	Circulatory	Diabetic	Intestinal infectious	Other	Total
SO_2	no	no	no	no	no	no	no
NO_2	no	no	no	no	no	no	no
CO-8hr	no	no	no	no	no	-ve	1 -ve sig
O_3	no	no	no	no	no	no	no
PM_{10}	no	no	no	no	-ve	no	1 -ve sig
$PM_{2.5}$	no	-ve	no	no	no	-ve	2 -ve sig

Note: 36 tests, with 4-protective (11.1%).

Table 9A-3 Estimated effects of air pollution from the hospital admissions series for lag 0-1 day.

	All-cause	Respiratory	Circulatory	Diabetic	Intestinal infectious	Other	Total
SO_2	no	+ve	no	no	no	no	1 +ve sig
NO_2	-ve	no	no	no	no	-ve	2 -ve sig
CO-8hr	-ve	no	no	no	-ve	-ve	3 -ve sig
O_3	no	no	no	no	no	no	no
PM_{10}	-ve	no	no	-ve	-ve	-ve	4 -ve sig
$PM_{2.5}$	no	no	no	no	no	no	no

Note: 36 tests, with 1-adverse, and 9-protective (27.7%).

Table 9A-4 Estimated effects of air pollution from the hospital admissions series for lag 0-4 day.

	All-cause	Respiratory	Circulatory	Diabetic	Intestinal infectious	Other	Total
SO_2	no	no	no	no	no	no	no
NO_2	no	no	no	no	no	-ve	1 -ve sig
CO-8hr	no	no	no	no	no	no	no
O_3	no	no	no	no	no	no	no
PM_{10}	-ve	no	no	no	-ve	-ve	3 -ve sig
$PM_{2.5}$	-ve	no	no	no	no	no	1 -ve sig

Note: 36 tests, with 5-protective (13.8%).

Table 9A-5 Estimated effects of air pollution from the linkage series for lag 0-1 day, with no history.

	All-cause	Respiratory	Circulatory	Other	Total
SO_2	0	-ve	0	0	1 -ve sig
NO_2	0	0	0	0	0
CO-8hr	0	0	0	0	0
O_3	0	0	+ve	0	1 +ve sig
PM_{10}	0	-ve	0	0	1 -ve sig
$PM_{2.5}$	0	0	0	0	0

Note: 24 tests, with 1-adverse effect (8.3%), and 1-protective effects (8.3%).

Table 9A-6 Estimated effects of air pollution from the linkage series for lag 0-4 day, with no history.

	All-cause	Respiratory	Circulatory	Other	Total
SO_2	0	0	0	0	0
NO_2	0	+ve	0	0	1 +ve sig
CO-8hr	0	0	0	0	0
O_3	0	0	0	0	0
PM_{10}	0	0	0	0	0
$PM_{2.5}$	0	0	0	0	0

Note: 24 tests, with 1-adverse effect (4.16%).

Table 9A-7 Estimated effects of air pollution from the linkage series for lag 0-1 day, with history.

	All-cause	Respiratory	Circulatory	Other	Total
SO_2	0	0	0	0	0
NO_2	0	0	0	0	0
CO-8hr	-ve	0	0	0	1 -ve sig
O_3	0	0	0	0	0
PM_{10}	0	0	0	0	0
$PM_{2.5}$	0	0	0	0	0

Note: 24 tests, with 1-protective effects (4.16%).

Table 9A-8 Estimated effects of air pollution from the linkage series for lag 0-4 day, with history.

	All-cause	Respiratory	Circulatory	Other	Total
SO_2	0	0	0	0	0
NO_2	-ve	0	0	0	1 -ve sig
CO-8hr	0	0	0	0	0
O_3	0	0	0	0	0
PM_{10}	0	0	0	0	0
$PM_{2.5}$	0	0	0	0	0

Note: 24 tests, with 1-protective effects (4.16%).

Appendix 9B: Effect modification by previous admissions.

Table 9B-1 Summary of group numbers of admissions within 6-month period prior to those admissions.

Group of admissions	Count
0	80,449 (78.2%)
1	13,708 (13.33%)
2-5	7,591 (7.38%)
>5	1,125 (1.09%)
Total	102,873 (100%)

Table 9B-2 Distribution of previous hospital admission data by group numbers of history of admissions within 6-month period prior to those admissions.

Group	Obs	Mean	Std. Dev.	Min	10th	25th	50th	75th	90th	Max
0	1461	55.06	23.40	11	26	37	51	73	88	125
1	1461	9.38	6.12	0	2	4	8	14	18	34
2-5	1461	5.20	4.16	0	1	2	4	7	11	33
>5	1461	0.77	1.15	0	0	0	0	1	2	8
Total	1461	70.41	32.03	12	31	45	65	94	114	173

Table 9B-3 Risk estimates for single pollutant, distributed lag models (0-4 days) for the effects of a 10-unit increase of a pollutant (one-unit increase for CO) on daily all-cause admissions in relation to the history of hospital admissions within 6-month period prior to those admissions in Muang, Chiang Mai, from October 2002 to September 2006.

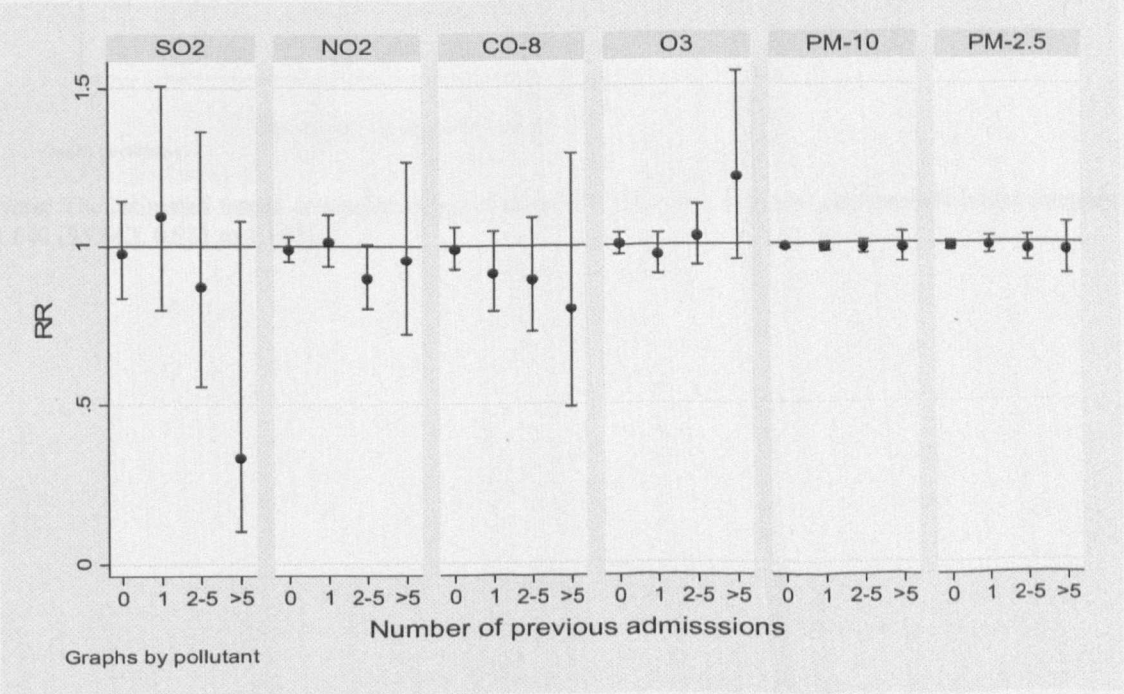
Pollutant (unit)	History of admissions	RR	95% CI Lower	95% CI Upper	p-value	Test for Interaction [a]
SO_2 (ppb)	No history	0.977	0.835	1.142	0.766	
	With history	0.973	0.749	1.265	0.840	0.979
NO_2(ppb)	No history	0.989	0.950	1.029	0.573	
	With history	0.969	0.906	1.037	0.361	0.610
CO-8hr(ppm)	No history	0.989	0.923	1.059	0.750	
	With history	0.896	0.798	1.006	0.063	0.151
O_3(ppb)	No history	1.005	0.972	1.038	0.787	
	With history	0.999	0.945	1.056	0.978	0.856
PM_{10}($\mu g/m^3$)	No history	0.992	0.985	0.999	0.022	
	With history	0.989	0.978	1.001	0.064	0.662
$PM_{2.5}$($\mu g/m^3$)	No history	0.990	0.976	1.004	0.176	
	With history	0.987	0.964	1.010	0.254	0.827

Table 9B-4 Estimated trends of air pollution effects across the group numbers of history of admissions (0, 1, 2-5, and >5 admissions) within 6-month period prior to those admissions in Muang, Chiang Mai, from October 2003 to September 2006.

Note: The estimated trends = a relative risk ratio for 10-unit increase of a pollutant (one-unit increase of CO) per admission-category.

		95% Confidence Interval		
Pollutant	**RR**	**Lower**	**Upper**	**p-value**
SO_2 (ppb)	0.914	0.694	1.203	0.295
NO_2 (ppb)	0.984	0.923	1.049	0.389
CO (ppm)	0.965	0.865	1.077	0.297
O_3 (ppb)	1.018	0.957	1.083	0.343
PM_{10} ($\mu g/m^3$)	0.999	0.988	1.010	0.650
$PM_{2.5}$ ($\mu g/m^3$)	0.999	0.979	1.020	0.870

Figure 9B-1 Risk estimates of air pollution effects on daily hospital admissions by history of admissions with 6-month period prior to those admissions per 10-unit increase of a pollutant (one unit increase for CO) for single pollutant, distributed lag models (0-4days).



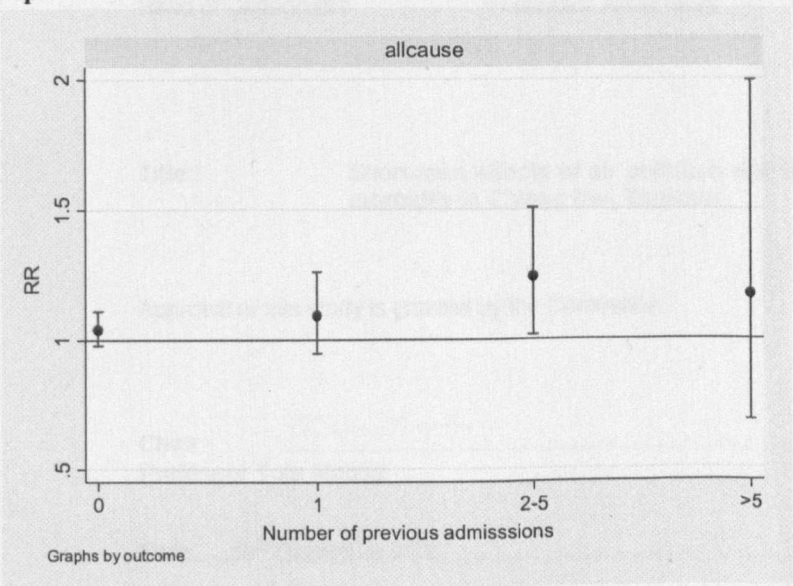
Note: There is no significant p-value obtained from test for heterogeneity between groups of previous admissions for each pollutant.

Table 9B-5 Relative risk estimates for distributed lag models (0-13 days) for temperature effects on daily hospital admissions among all people with respect to history of admissions within 6-month period prior to their admissions in Muang, Chiang Mai from October 2002 to September 2006.

Outcome	n (day)	Mean [a]	SD	RR	95%CI Lower	95%CI Upper	p-value	Test for interaction [b]
All-cause (29°C)								
No history	266	59.88	25.01	1.044	0.980	1.112	0.185	
With history	266	16.99	10.65	1.145	1.025	1.280	0.017	0.157

[a] Mean daily count of hospital admissions relative to temperature used for quantifying temperature effects.
[b] p-value for test for heterogeneity between groups.

Figure 9B-2 Relative risk estimates of temperature effects on daily hospital admissions for 1°C increase in temperature (>29°C) among all people with respect to history of admissions within 6-month period prior to their admissions in Muang, Chiang Mai, from October 2002 to September 2006.



Note: The estimated trends or a relative risk ratio for 1°C increase in temperature per admission-category = 1.040 (95%CI, 0.931 to 1.163).

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

ETHICS COMMITTEE

APPROVAL FORM
Application number: **5082**

Name of Principal Investigator	**Nareerut Pudpong**
Department	**Public Health and Policy**
Head of Department	**Professor Anne Mills**

Title: **Short-term effects of air pollution and temperature on daily morbidity in Chiang Mai, Thailand**

Approval of this study is granted by the Committee.

Chair T.W. Meade .....
Professor Tom Meade

Date .....19th December 2006.....

Approval is dependent on local ethical approval having been received.

Any subsequent changes to the consent form must be re-submitted to the Committee.

No. 067/2007

Certificate of Approval

Name of Ethics Committee : Research Ethics Committee 3 , Faculty of Medicine , Chiang Mai University
Address of Ethics Committee : 110 Intavaroros Rd., Amphoe Muang, Chiang Mai, Thailand 50200

Principal Investigator : Nareerat Pudpong
Public and Environmental Health Research Unit Department of Public Health & Policy London School of Hygiene & Tropical Medicine
Keppel Street,London WC1E 7HT

Protocol title: Short-term effects of air pollution and temperature on daily morbidity in Chiang Mai,Thailand

Documents filed	Document reference
Research protocol	- Version 1.0 – 27 February 2007
Informed consent document /Patient information sheet	
Curriculum vitae of Principal Investigator	
Advertisements (none)	
Other	

Opinion of the Ethics Committee/Institutional Review Board
____√____ Approval
_____ Conditional approval (specify in space below)

DECISION: By expedited review process

Date of Review : March 19 , 2007 Expiration Date: March 19 , 2010

This Ethics Committee is organized and operates according to principles of good clinical practice and relevant international ethical guidelines, applicable laws, and regulations.

Signed: ..... **Panja Kulapongs, M.D.**
(Chairperson, Faculty of Medicine)

Signed: ..... **Niwes Nantachit, M.D.**
(Dean, Faculty of Medicine)

GENERAL CONDITIONS OF APPROVAL:

Please refer to www.med.cmu.ac.th/research/ethics/tav_sop_announce.pdf, article 13. In particular, approval of this study must be renewed at least one month before the expiration date if work is to continue. Prior Research Ethics Committee approval is required before implementing any changes in the consent documents or protocol, unless those changes are required urgently for the safety of subjects.